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Perspective

# Lifestyle, daily habits, sleep hygiene, and diet: Proposal of a new approach for sleep bruxism management

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**This perspective presents a new comprehensive proposal for sleep bruxism management.**

## Sleep bruxism latest definition, epidemiology and etiology

In accordance with the latest consensus, sleep bruxism (SB) is defined as a masticatory muscle activity during sleep, characterized as rhythmic (phasic) or non-rhythmic (tonic), and is not considered a movement disorder or a sleep disorder in otherwise healthy individuals.[1] It is estimated to occur in up to 15% of the human adult population.[2] Despite many years of research, SB still constitutes a significant diagnostic and therapeutic challenge. There are various risk factors that can contribute to SB: exogenous risk factors, such as smoking, heavy alcohol intake, caffeine, medications, or illicit drugs; psychosocial factors, including perceived stress and anxiety; sleep disorders, involving sleep arousal; and comorbidities, such as obstructive sleep apnea (OSA) and gastro-esophageal reflux disease (GERD).[3] Recent research also indicates that SB may be related to the neurotransmission of the serotonin and/or dopamine pathway.[4,5] Severe SB seem to co-occur with lower serotonin blood levels, but is not correlated with the blood levels of the enzymes involved in the serotonin synthesis pathway.[5] There are also studies supporting the genetic background of SB. The latest studies suggest that the polymorphisms occurring within the genes encoding dopamine and serotonin receptors may be linked with predisposition to SB and SB pathogenesis, and may contribute to the association between SB and OSA in adults.[6] Similar associations with regard to the genes encoding dopamine receptors have been observed in children.[7] In children, the additional factors increasing SB are the consumption of sugar, screen-time and sleeping habits.[8,9]

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## Current management of sleep bruxism

So far, the most popular methods of SB management in cases with poor health outcomes have focused on minimizing the negative effects of SB. The methods include the use of intraoral appliances, physical therapy, biofeedback, and botulinum toxin injections.[1,3,10] Among the approaches aimed at eliminating the potential risk factors for SB, the most popular remain psychotherapy and therapies improving stress-coping strategies.[1,3] There are a few scientific reports suggesting that some drugs, e.g., opipramol, may be effective in reducing the number of SB episodes.[11] The therapy of the comorbidities for which SB occurred as a protective factor (OSA, GERD) is also pointed to be important.[1,3,10,12] In case of OSA, management methods include continuous positive airway pressure (CPAP) and the use of a mandibular advancement device (MAD).[12] With regard to the external factors influencing SB, prevention cannot be omitted.[1,3] Nevertheless, the available research is not conclusive, and does not provide clear evidence or a consensus on the most effective SB management methods.[10]

## New approach for sleep bruxism management

Taking into account the latest research indicating the genetic basis,[6,7] the possible involvement of neurotransmission[4,5] and the importance of sleep structure[9,13] with regard to the occurrence of SB, it would be worth considering the inclusion of new methods in SB management. These methods could combine issues regarding lifestyle, daily habits, sleep hygiene, and diet, and would be based more on the elimination of risk factors than on the prevention of the negative consequences of SB.

## Lifestyle, daily habits and sleep hygiene

As far as the lifestyle and daily habits are concerned, attention should be paid to 2 key elements of life that may have a significant impact on the occurrence of SB. These are psychological comfort (including stress and anxiety reduction) and sleep. A patient with SB should be aware of the harmful effects of chronic stress and poor-quality sleep. Some techniques should be used in everyday life to alleviate the symptoms of stress and improve stress-coping strategies. In recent years, much attention has been focused on everyday behaviors aimed at reducing stress. These include maintaining work–life balance, regular physical activity (especially outdoor, nature-related activities that are reported to reduce perceived stress) and breathing exercises. However, for patients who have problems with stress coping, mindfulness (including meditation) and cognitive behavioral therapy (CBT) may be recommended as well.[1–3,8–10]

Sleep hygiene is also of great importance, as it significantly affects the structure and quality of sleep. Patients with SB should avoid the consumption of alcohol and coffee, smoking, and quit sugar intake at bedtime. They should also remember to limit screen-time and exposure to blue light. Convenient sleeping conditions (silence, darkness, a proper room temperature), the appropriate number of sleep hours (depending on the individual) and sleep regularity also matter.[1–3,8–10]

Exposure to light greatly influences the human circadian cycle. In recent years, devices emitting blue light have emerged. Electronic devices are very popular and are used by people of all ages. Electronic devices emitting blue light cause the stimulation of the nervous system, which may lead to problems with sleep. There are scientific reports suggesting that two-hour exposure to blue light (460 nm) in the evening suppresses the secretion of melatonin.[14] What is more, one-hour exposure to bright light or blue light increases the levels of stress hormones in saliva, which means that the concentration of stress hormones can be altered by the type of light people are exposed to.[15] The daytime and bedtime use of electronic devices have been both reported to be related to sleep measures, with an increased risk of short sleep duration, long sleep onset latency and increased sleep deficiency.[16] The use of electronic devices among children is also a rising problem. The available studies indicate that screen-time can be related to an increased frequency of bruxism in children.[8] All the above-mentioned aspects suggest the need to limit the use of electronic devices emitting bright light or blue light, especially at bedtime, as part of the prevention of sleep disorders and SB.

There are also scientific reports suggesting that the dysfunction of the autonomic nervous system related to arousal during sleep is considered an underlying cause of the cardiovascular implications of SB. Sympathetic activity has been reported to increase heart rate variability, the inflammatory process, oxidative stress, endothelial remodeling, and hormonal disturbances, leading to hypertension and other cardiovascular complications. Hence, physical activity and other habits influencing the cardiovascular system could also be regarded as beneficial in patients with SB.[17]

## Diet

Diet may also play a potential role in SB management. Apart from the limitation of the intake of substances that seem to influence the severity of SB (caffeine, excess sugar,

narcotics, some medications), patients should also consider the consumption of substances that have a beneficial effect on the functioning of the nervous and muscular systems, stress reduction and sleep improvement. These include microelements, such as magnesium (Mg), calcium (Ca), potassium (K), zinc (Zn), and iron (Fe). Vitamins used in SB management include B vitamins, essential for the functioning of the nervous system, and vitamin D, influencing sleep and preventing sleep disturbances. Some authors also indicate the importance of omega-3 fatty acids, which support the overall health of the nervous system.[1,18,19] Moreover, in light of the latest research, it is worth noting that due to the reported role of neurotransmission, especially the neurotransmission related to the serotonin pathway, the diet of SB patients should be pro-serotonin, i.e., rich in tryptophan.[4,5] Such diet contains products rich in carbohydrates and protein, like fish, bananas, seeds, avocado, or eggs. There are also scientific reports that underscore the influence of dietary fiber consumption on SB. One of the studies showed that students with SB had a significantly lower dietary fiber intake than those without SB.[20]

## Highlights

Sleep bruxism still constitutes a major diagnostic and therapeutic challenge due to its complicated and not fully understood characteristics. This creates the need to constantly search for new therapeutic paths. Nowadays, apart from the standard methods previously used to manage bruxism, more attention should be paid to aspects related to lifestyle, daily habits, sleep hygiene, and diet (Fig. 1).

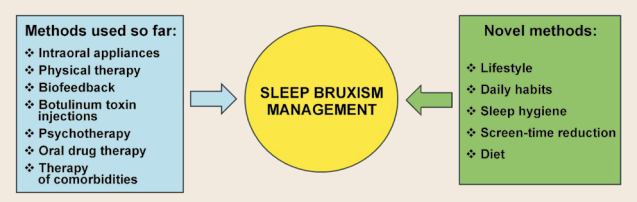


Fig. 1. Sleep bruxism (SB) management methods, including the methods used so far and novel approaches


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Perspective

# Insect flour and dental caries: Friends or foes?

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**This article explores the cariogenic potential of insect flours, highlighting their nutritional benefits and sustainability, while emphasizing the need for further research on their impact on oral health.**

Dental caries is a widespread non-communicable disease affecting individuals across all age groups globally. Recent advancements in the research on human oral microbiota have led to a paradigm shift from viewing dental caries as an infectious, communicable disease, primarily caused by *Streptococcus mutans*, to perceiving it as an 'ecological catastrophe'.[1] Oral microbiome, as part of human microbiota, can be interpreted in terms of ecological principles, system biology and a holistic approach.[2] From this perspective, the development of caries stems from a disruption in the balance of the resident oral microbiota, leading to a reduction in microbial diversity, favoring acidogenic species, adapted to low-pH environments. The main factors driving this dysbiosis include frequent sugar exposure, a reduced salivary flow and inadequate disruption of oral biofilm.[3,4] Consistently, diets rich in processed sugars and starches are linked to a higher incidence of caries. Starch, particularly from wheat-based grains, constitutes a significant portion of the human diet, accounting for 40–75% of total dietary intake in Western populations.[5] Processed starches, once gelatinized, are rapidly hydrolyzed by oral amylases into glucose, maltose, maltotriose, and low-molecular-weight dextrins. These starch-rich food particles, when trapped on the tooth surface, act as an ideal substrate for sugar retention and bacterial acid production, lowering the local pH and initiating the process of enamel demineralization.

Human exposure to foods prepared through the high-temperature cooking of refined sugar and starch suspensions leads to increased biofilm-induced acidogenicity. Among starches, flour starches exhibit the highest acidogenic potential, while processed starches result in prolonged pH drops below 5.5.[6] The combination of starch and sucrose is particularly harmful, causing the most significant enamel mineral loss. The Western diet, characterized by the frequent consumption of processed foods rich in sugar and starch, is associated with food addiction, overeating and obesity, and is a primary risk factor for the development of dental caries.

In recent years, Western dietary patterns have been shifting, with a growing preference for plant-based foods and reduced meat consumption.[7] This shift reflects the increasing consumer awareness of the environmental consequences of intensive farming, health concerns related to dietary risk factors and a broader openness to cultural influences from other regions. In light of these trends and taking into consideration the need for alternative protein sources, insects have emerged as a viable addition to the Western diet. In early 2023, the European Union (EU) approved the sale of crickets, locusts and darkling beetle larvae for human consumption, and insect flour can now be incorporated into various food products.[8] The edible insect market in Europe is expected to reach €2.7bn (£2.3bn) by 2030.[8] Globally, over 2 billion people already consume insects as part of their regular diet, as insect flour is rich in essential amino acids, calcium (Ca), iron (Fe), potassium (K), vitamins B2 and B12, and fatty acids.

## Considerations

This study sought to assess the cariogenic potential of insect flours in comparison with conventional flours. The rationale for this investigation arises from the increasing interest in insect-based diets, largely due to their environmental sustainability and purported nutritional benefits. Despite an extensive review of the literature, no studies that directly examine the impact of insect flours on dental caries were found. This lack of evidence emphasizes the novelty of the subject and highlights the necessity for focused research in this area.

The absence of studies on the cariogenic properties of insect flours raises several important considerations. Firstly, it suggests that the intersection between dental health and insect-based diets remains largely unexplored by the scientific community. Given the rising inclusion of insect products in the Western diet, driven by environmental and health concerns, this gap in research is particularly striking. With the EU's approval of insect flours for human consumption in early 2023 and the projected expansion of the edible insect market, this emerging area could have substantial implications for public oral health.[8]

The Food and Agriculture Organization of the United Nations (FAO/UN) predicts that the global population will exceed 9.1 billion by 2050, posing a significant challenge in meeting the corresponding food demand. Ensuring an adequate supply of high-quality protein will be essential for the physical and cognitive development of individuals. In this regard, entomophagy – the consumption of insects as a source of nutrients – presents itself as a sustainable and feasible alternative.[9] Edible insects, as a non-traditional food source, offer a promising solution to pressing issues, such as food security and environmental preservation. Insect farming presents numerous advantages, including minimal space and time requirements, the absence of reliance on cereal-based feeds, reduced $CO_2$ emission, and lower water and land usage.[10]

Despite these benefits, entomophagy is often met with aversion in many Western societies, where consuming insects is perceived as distasteful and associated with primitive behaviors. In contrast, in regions across Africa, Asia, Latin America, and among indigenous peoples in North America, insects have been regularly consumed as staple foods or delicacies, and they likely played an important nutritional role for early human ancestors. An estimated 1,900 species of insects have been utilized as food, with beetles (Coleoptera) accounting for 31% and caterpillars (Lepidoptera) for 18% of global insect consumption, while termites (Isoptera) represent only 3%.[11]

Insects are a valuable source of both micro- and macronutrients essential for human nutrition. The macronutrient content of insect flours varies significantly, with the protein levels ranging from 30% to 65%, lipids from 7% to 77%, and carbohydrates from 5% to 20%. Insect flours are particularly rich in protein, and provide essential amino acids, vitamins and minerals, though they generally contain lower carbohydrate levels than traditional grain flours.[12–14]

The reduced carbohydrate content of insect flours may potentially limit the substrates available for oral bacteria to generate acids, a key factor in the development of dental caries.[15] Additionally, the high protein and fat content in insect flours could contribute to creating a less cariogenic oral environment, although this assumption requires empirical validation. Furthermore, it is plausible that integrating insect flours into the diet may promote a more balanced oral microbiota, countering dysbiotic shifts commonly driven by frequent sugar intake, which contribute to dental caries.

The lack of research in this area emphasizes the need for targeted investigation. Key areas for future research include: in-vitro and in-vivo studies – laboratory and clinical studies to assess the influence of insect flours on the formation of dental plaque, acid production and enamel demineralization; comparative analyses – evaluating the cariogenic potential of insect flours relative to well-known grain flours like wheat and maize, which have established links to dental caries, as well as comparing them with other high-protein flours with similar macronutrient profiles; and long-term dietary studies – examining the long-term effects of incorporating insect flours into diets on oral health outcomes across diverse population groups.

Future investigations should adhere to robust methodologies, including well-designed randomized controlled trials (RCTs), appropriate sample sizes and standardized caries assessment measures. Employing validated tools for bias assessment and comprehensive data analysis will be essential to generate reliable, high-quality evidence.

The adoption of insect flours into Western diets reflects a broader shift toward more sustainable and health-conscious food choices. However, a thorough

Table 1. Key findings on the cariogenic potential, nutritional benefits, sustainability, and potential risks of insect flours

| Thematic area | Key message | Details |
|---|---|---|
| Cariogenic potential of insect flours | Insect flours may have a lower cariogenic potential as compared to conventional flours | Lower content of fermentable carbohydrates, reducing acid production by oral bacteria |
| Nutritional benefits | Rich in protein, essential amino acids, vitamins, and minerals | High protein content (30–65%), low carbohydrate content (5–20%) |
| Reduced caries risk | Lower content of fermentable carbohydrates | Less substrate for cariogenic bacteria, reducing acid production and enamel demineralization |
| Sustainability | Sustainable food sources with low environmental impact | Minimal land and water use, reduced $CO_2$ emission |
| Potential risks | Possible contaminants and allergens | Need for further research on contaminants, allergens and biological risks |

understanding of the health impact, including oral health, is vital. Public health policies and dietary guidelines will benefit from evidence-based insights about the implications of such emerging dietary trends.

It is important to note that the incorporation of insects into the human diet may pose several potential risks, which require further extensive research. These risks can be categorized into 3 key areas:

– contaminant risks: Insects may contain chemical contaminants, including mycotoxins, pesticides, heavy metals, organochlorine compounds, and dioxins, which can originate from their rearing substrates or environmental exposure.[16] Additionally, certain insect species from the Coleoptera, Lepidoptera and Orthoptera orders have been found to consume various types of plastic polymers, with infrared spectroscopy revealing degraded plastic fragments in insect frass.[17] While the impact of this on human health remains uncertain, there is insufficient evidence to dismiss it as insignificant;
– biological risks: Insects can harbor microorganisms, such as bacteria, viruses and parasites, which may pose a health risk to humans,[18] and could potentially serve as sources of future epidemics or pandemics;
– allergenic risks: Some insect components, such as chitin, can trigger allergic reactions, manifested through various symptoms, including eczema, rhinitis, conjunctivitis, bronchial asthma, urticaria, dizziness, and in severe cases, anaphylaxis.[19]

The European Food Safety Authority (EFSA) has indicated that the prevalence and concentration of contaminants in insects or insect-based foods depend on factors such as the method of production, the stage of harvest and the substrates used for rearing.

Furthermore, the recent introduction of insect flour-based products that contain concentrated amounts of insects presents a new safety concern. Unlike traditional insect consumption, which typically involves whole insects eaten fried or grilled, insect flours may allow higher intake of potential allergens and contaminants, potentially leading to unknown public health outcomes.

This article underscores the potential of insect flours as an alternative to traditional grain-based flours. Their reduced carbohydrate content, combined with nutritional benefits and environmental sustainability, positions them as a promising food source. However, further research is needed to address potential risks, including contaminants and allergens. Table 1 provides a concise summary of the key findings and their implications.

## Summary

This paper identifies a notable gap in research concerning the cariogenic potential of insect flours. The findings emphasize the novelty of this subject and the pressing need for focused investigation. Given the limited understanding of public health implications,[20] alongside the increasing consumption of insect-based products, it is crucial to explore their effects on both general and oral health. Future studies should address this gap with rigorous, high-quality research to inform dietary guidelines and public health policies.


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Original paper

# Oral health behaviors and tooth decay at the age of 12 and 15–18 years in Poland

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## Abstract

**Background.** Oral health behaviors are the primary determinants of dental health. They undergo modification and stabilization during adolescence, and can persist into adulthood.

**Objectives.** The aim of the study was to assess the oral health behaviors of individuals aged 12 and 15–18 years, and to examine the impact of these behaviors on the occurrence and severity of dental caries in different age groups.

**Material and methods.** A cross-sectional oral health national survey was conducted between 2016 and 2020, encompassing a total of 5,099 participants, including 2,496 individuals aged 12 and 2,603 participants aged 15–18 years. The presence of non-cavitated decay ($D_{1-2}$), cavitation ($D_{\geq 3}$), and missing (M) or filled (F) status at the tooth (T) or surface (S) levels was evaluated. The prevalence of caries ($D_{\geq 3}MFT > 0$), as well as the mean values of the $D_{1-2}$, $D_{\geq 3}MFT$ and $D_{\geq 3}MFS$ indexes were assessed. The questionnaire contained information on sociodemographic factors, oral health behaviors and the participants' diet.

**Results.** The prevalence of dental caries was 75% among 12-year-old and 90% among 15–18-year-old individuals. Indicators associated with a reduced likelihood and lower severity of dental caries in both groups included prophylactic dental visits (adjusted odds ratio (*AOR*) (12-year-olds): 0.83; *AOR* (15–18-year-olds): 0.64) and brushing teeth at least twice a day (*AOR* (12-year-olds): 0.72; *AOR* (15–18-year-olds): 0.59). Frequent consumption of sweet products and chips by 12-year-olds increased the likelihood of developing and exacerbating tooth decay. In the older group, the risk of developing caries was associated with the consumption of sweets and sugar-sweetened carbonated beverages.

**Conclusions.** Poor oral hygiene and inadequate diet are conducive to the development of caries, with the condition being exacerbated by these factors regardless of age. However, the influence of diet appears to be more pronounced in less mature dentition. The benefits of dental visits, oral hygiene practices and a preference for mineral water in quenching thirst have also been demonstrated. The health behaviors exhibited by older and younger adolescents are comparable, suggesting that these habits may persist into adulthood.

**Keywords:** diet, adolescence, dental caries, hygienic behavior

## Highlights

- Inadequate hygiene promotes the development of dental caries.
- The impact of diet on the development of caries is more pronounced in less mature dentition.
- Results highlight that health behaviors developed in adolescence may persist into adulthood.

# Introduction

Dental caries is a prevalent health problem that persists throughout an individual's life. The disease impairs a person's quality of life by causing pain, difficulty eating and speaking. The etiology of tooth decay is multifactorial, involving inadequate plaque control, dental defects, frequent consumption of dietary carbohydrates, characteristics of saliva, and/or hereditary genetic factors.[1–4] Tooth decay can also lead to pulpopathy, periodontal infections, tooth loss, and the need for endodontic treatment. The consequences of tooth decay include absenteeism from school or work, and high costs incurred for treatment.[5–8] In recent years, the incidence of tooth decay in Western countries has clearly decreased, although the condition still remains a significant health problem.[9,10] According to the World Health Organization (WHO),[11] the prevalence of dental caries among school-aged children is estimated to be as high as 60–90% in some countries (e.g., Lithuania, Portugal, Hongkong). A study of 9 European countries (e.g., the Czech Republic, France, the UK) revealed that caries affects approx. 52% of individuals between the ages of 11 and 13.[12]

The prevention of tooth decay can be achieved through the implementation of proper health behaviors. In childhood, the primary responsibility for the oral health of children lies with their parents, who must ensure their children receive the necessary care and instill the appropriate health behaviors. However, as an individual matures and becomes more independent, the responsibility for maintaining optimal health habits shifts increasingly to the child. At the same time, during adolescence, health behaviors undergo modification under the influence of various social and cultural factors. Adolescents frequently engage in behaviors that are detrimental to their health (e.g., consumption of alcohol and other stimulants, smoking). These behaviors not only contribute to the development of tooth decay, but also become permanent and persist into adulthood, exacerbating the health problem.[13–16]

Adolescence is defined as the developmental stage between childhood and adulthood. According to the WHO, an adolescent is an individual between the ages of 10 and 19.[17] This developmental stage is subdivided into 3 phases, namely early, middle and late adolescence. However, the authors point to shifts in individual age categories.[17] There is a discrepancy between the studies as to the exact time division of the mentioned periods of adolescence.[18] In our work, we distinguished between the early adolescence (11–14 years) and middle adolescence (15–18 years). The susceptibility of adolescents to factors modifying their health behaviors, their ability to accept standards, and short- and long-term health risk assessments vary during early and middle adolescence.[19] There are also differences in the susceptibility to caries in these phases, resulting from different degrees of maturity of tooth tissues. Typically, individuals aged 12–13 years possess full permanent dentition, with the exception of third molars. However, premolars and second molars are often characterized by immaturity, which can facilitate the onset of caries and the rapid spread of the disease process within tooth tissues. The risk of developing tooth decay is highest within the first 2–4 years following tooth eruption. This period is characterized by the exposure of the enamel to the oral cavity environment, which initiates changes known as post-eruptive maturation. Consequently, the susceptibility to cariogenic factors in tooth enamel is lower at the age of 15–18 compared to the enamel of an individual at the age of 12; however, this susceptibility remains higher than that observed in adults. Therefore, the age of patients is a particularly important factor when examining the incidence of caries.[20,21]

The high susceptibility of immature permanent teeth to caries and the rapid spread of the disease underscore the significant role of adolescent health behaviors. Therefore, the aim of the study was to assess the oral health behaviors of individuals aged 12 and 15–18 years, and to ascertain how these behaviors influence the prevalence and severity of tooth decay.

# Material and methods

The cross-sectional studies included adolescents aged 12 and 15–18 years from all Polish voivodships. The study groups were selected in a three-tier draw (district/community, city/village, and school levels). The inclusion of the educational institutions in the research was contingent upon their directors' consent. The inclusion criteria for the studies were as follows: patients aged 12 or 15–18 years; and the provision of signed informed consent to participate in the study. The signed consent forms for the sampled adolescents, along with informational letters detailing the study's scope, were distributed to the parents

by the teachers. To maintain anonymity, each participant was assigned a unique code number, which was included on the questionnaire and clinical trial card. The participants were not offered any additional incentives to participate in the study, apart from feedback on the health status of their dentition.

The data regarding the total number of adolescents was retrieved from the Central Statistical Office.[22,23] The size of the sample under study was calculated based on literature data concerning caries prevalence in this age group in Poland, i.e., about 85.4% were caries-affected. Assuming a 95% confidence interval (*CI*) and ±4% error tolerance, it was determined that approx. 600 subjects in each group represented a minimum sample size. The study sample was determined by selecting 3,000 12-year-olds and 3,000 adolescents aged 15–18 years. The total number of individuals enrolled in the study was 5,099, including 2,496 12-year-olds (50.4% from rural regions and 50.9% females) and 2,603 individuals aged 15–18 years (49.6% and 52.6%, respectively). The reasons for the exclusion of 901 subjects from the study were as follows: lack of signed informed consent (33.0%); absence from school on the day of the study (22.8%); or an incorrectly completed survey questionnaire (43.7%).

The study incorporated a questionnaire examination and a clinical assessment of the dentition. The survey contained closed-ended questions, with only 1 possible answer. The questionnaire inquired about various socioeconomic factors (place of residence, self-assessed financial situation and mother's education level), hygienic behavior (frequency of toothbrushing, conscious use of fluoride toothpaste, and the type and frequency of hygiene tools usage), diet (frequency of consumption of certain foods), and the use of dental care. The questionnaires were completed by students at school during classes. The questionnaire was developed in accordance with the WHO guidelines.[24] It has been used in numerous studies that have been conducted as part of the monitoring of the health of the Polish population.

When presenting research on the frequency of dental caries, it is worth mentioning the relationship between the incidence of dental caries and certain congenital defects, e.g., those related to the developmental defects in enamel[4] or malocclusion.[5] Malocclusion can impede patients' ability to maintain proper oral hygiene, which can lead to the development of dental caries. However, it should be acknowledged that the fundamental principle of epidemiological research is the randomness of the studied population. Accordingly, the study sample is presumed to be a representative of the general population, which necessitates the consideration of the possible occurrence of general health problems. The epidemiological studies presented have considered the factors recommended by the WHO.[24]

Clinical trials were conducted by dentists following training and calibration with a reference investigator (24 dentists participated in the research). The studies were conducted under artificial lighting, using a mirror and a WHO 621 probe, in accordance with the study rules and criteria for the classification of the WHO clinical conditions.[24] As part of the study, the condition of the dentition was assessed by examining each tooth surface in successive quadrants. Caries was evaluated using the ICDAS-II (International Caries Detection and Assessment System), where codes 1 and 2 were treated as non-cavitated decay ($D_{1-2}$) and code 3 was classified as a carious cavity ($D_{\geq 3}$).[25] The number of permanent teeth present in the oral cavity, the total number of teeth, and the surface of permanent teeth with $D_{1-2}$ and $D_{\geq 3}$, lost due to caries (M) or with fillings (F) at the tooth (T) or surface (S) levels, were determined. The mean values of the $D_{1-2}$, $D_{\geq 3}$MFT and $D_{\geq 3}$MFS indices were calculated. The number and percentage of patients with caries ($D_{\geq 3}$MFT > 0) were determined.

The level of fluoride in drinking water in Poland does not exceed 0.5 mg/L. In Poland, children and adolescents have access to free dental care, which encompasses treatment and prevention. The present survey was conducted as part of the project entitled "Monitoring of oral health condition in Polish population in 2016–2020", supported by the Ministry of Health of the Republic of Poland. The Bioethics Committee of the Warsaw Medical University provided its consent for the study (KB/190/2016 and KB135/2019).

## Statistical analysis

A comparison of the test results between the observation physicians and the reference physician was made using the Cohen's kappa coefficient. The studied variables were presented as percentage or mean and standard deviation (*M* ±*SD*). Comparisons of the means between the 2 groups were made using the *t*-test, while comparisons of percentages were conducted using the $\chi^2$ test. In order to determine the relationships between pairs of variables, Spearman's rank correlation analysis was performed. To assess the impact of different factors on the prevalence of caries in children, a bivariate logistic regression analysis was conducted, in which the impact of each individual factor was considered, as well as a multivariate logistic regression analysis, in which simultaneous impact of several factors was assessed.

The logistic regression analysis yielded odds ratios (*OR*s) for the relative risk of caries development, with *CI*s at the 95% level. An *AOR* was calculated, where socioeconomic factors were the constant confounding factors, and hygienic and/or dietary behaviors were the variables. The analyses were conducted using the IBM SPSS Statistics for Windows software, v. 22.0 (IBM Corp., Armonk, USA), Statistica 10 software (StatSoft, Inc., Tulsa, USA), and the R 3.2.0 software package (https://cran-archive.r-project.org/bin/windows/base/old/3.2.0).

**Table 1.** Frequency and intensity of dental caries in 2 groups of adolescents

| Variable | Age group | |
|---|---|---|
| | 12 years | 15–18 years |
| Number of subjects, *n* | 2,496 | 2,603 |
| Number of permanent teeth *M* ±*SD* | 25.74 ±3.08 | 27.75 ±0.76 |
| $D_{\geq 3}$MFT > 0 *n* (%) | 1,869 (75.0) | 2,346 (90.0) |
| $D_{\geq 3}$MFT *M* ±*SD* | 2.84 ±2.70 | 5.88 ±4.15 |
| $D_{1-2}$,$D_{\geq 3}$MFT *M* ±*SD* | 3.62 ±3.29 | 6.47 ±4.53 |
| $D_{1-2}$T *M* ±*SD* | 0.78 ±1.81 | 0.59 ±1.34 |
| $D_{\geq 3}$MFS *M* ±*SD* | 3.65 ±4.09 | 8.50 ±7.66 |

*M* – mean; *SD* – standard deviation; $D_{1-2}$ – non-cavitated decay; $D_{\geq 3}$ – cavitation; M – missing status; F – filled status; T – tooth level; S – surface level.

# Results

The Cohen's kappa coefficients between the reference investigator and the other researchers (dentists) ranged from 0.963 to 1.000. The prevalence of dental caries in the entire sample was 83% (4,215 participants). Within the 12-year-old group, 1,869 participants (75%) were diagnosed with caries, while in the 15–18-year-old group, caries was diagnosed in 2,346 participants (90%). The intensity of caries was more than 2 times lower in the younger age group than in the older age group (Table 1).

The socioeconomic characteristics and oral health behaviors of the subjects are presented in Table 2. Seven hundred sixty-four (30.6%) of the surveyed 12-year-olds were not aware of their mother's level of education, and 630 (25.2%) did not specify their family's financial situation. In the older group, this situation occurred in 337 (13.0%) and 485 (18.6%) respondents, respectively. As many as 858

**Table 2.** Socioeconomic factors and oral health and dietary behaviors in 2 groups of adolescents

| Parameter | | | Age group | | |
|---|---|---|---|---|---|
| | | | 12 years *n* (%) | 15–18 years *n* (%) | *p*-value |
| Socioeconomic factors | mother's education level | elementary | 586 (23.5) | 691 (26.5) | 0.536 |
| | | secondary | 468 (18.8) | 839 (32.2) | 0.092 |
| | | higher/incomplete higher | 678 (27.2) | 736 (28.3) | 0.762 |
| | self-assessed financial situation | below average | 32 (1.3) | 63 (2.4) | 0.372 |
| | | average | 1,032 (41.3) | 1,436 (55.2) | 0.199 |
| | | above average | 802 (32.1) | 619 (23.8) | 0.176 |
| Hygienic behavior | | brushing teeth at least twice a day | 1,555 (62.3) | 1,758 (67.5) | 0.453 |
| | | brushing teeth less than once a day, occasionally, or not at all | 246 (9.9) | 187 (7.2) | 0.166 |
| | | conscious use of fluoride toothpaste | 1,201 (48.1) | 1,126 (43.3) | 0.362 |
| | | using dental floss several times a week or every day | 993 (39.8) | 1,038 (39.9) | 0.528 |
| | | use of liquid mouthwash | 379 (15.2) | 1,293 (49.7) | 0.002* |
| Dental care | | have not visited the dentist so far or have not visited the dentist for a significant amount of time (the patient is unable to recall the last visit) | 350 (14.0) | 268 (10.3) | 0.888 |
| | | missed an appointment in the last 12 months | 292 (11.7) | 269 (10.3) | 0.911 |
| | | have not had an appointment in the last 2 years | 296 (11.9) | 101 (3.9) | 0.001* |
| | | reason for a dental visit was pain or other ailments | 241 (9.7) | 415 (15.9) | 0.039* |
| | | reason for a dental visit was check-up | 1,180 (47.3) | 1,084 (41.6) | 0.455 |
| | | postponing a dental visit | 456 (18.3) | 484 (18.6) | 0.810 |
| Dietary behavior (foods consumed at least once a day) | | fresh fruits and vegetables | 1,521 (60.9) | 1,313 (50.4) | 0.028* |
| | | biscuits/cakes/donuts/glazed rolls | 458 (18.3) | 335 (12.9) | 0.006* |
| | | jam/honey | 218 (8.7) | 160 (6.1) | 0.104 |
| | | chewing gum with sugar | 281 (11.3) | 525 (20.2) | 0.003* |
| | | sweets/candies | 573 (23.0) | 622 (23.9) | 0.591 |
| | | sugar-sweetened carbonated beverages (e.g., cola, lemonade) | 511 (20.5) | 515 (19.8) | 0.719 |
| | | tea with sugar | 1,227 (49.2) | 1,142 (43.9) | 0.778 |
| | | sweetened juices | 542 (21.7) | 509 (19.6) | 0.801 |
| | | chips | 194 (7.8) | 210 (8.1) | 0.848 |
| | | mineral water | 1,122 (69.7) | 2,036 (78.2) | 0.072 |

* statistically significant ($p < 0.05$, $\chi^2$ test).

(34.4%) respondents aged 12, and 1,283 (49.3%) respondents aged 15–18 were unaware whether the toothpaste they used contained fluoride. Among the 12-year-olds, 437 (17.5%) consciously used fluoride-free toothpaste, while this practice was adopted by 194 (7.4%) of the older adolescents. In the older group and among 1,610 participants aged 12 years, additional questions were posed regarding the frequency of still mineral water consumption.

Spearman's correlation analysis revealed a relationship between the occurrence and severity of caries, as well as socioeconomic factors and oral health behaviors (Table 3). However, there was no statistically significant relationship regarding the use of liquid mouthwash and the consumption of vegetables and fruits. The logistic regression analysis revealed that, irrespective of subjects' age and their hygienic and dietary behaviors, attendance

**Table 3.** Spearman's correlation coefficients demonstrating the relationship between the occurrence of caries and socioeconomic factors and oral health behaviors in 2 groups of adolescents

| Parameter | | Age [years] | $D_{\geq 3}MFT > 0$ | $D_{1-2}$ | $D_{\geq 3}MFT$ | $D_{\geq 3}MFS$ |
|---|---|---|---|---|---|---|
| Place of residence (village) | | 12 | 0.081 | 0.054 | 0.089 | 0.089 |
| | | 15–18 | 0.022* | 0.037* | 0.044* | 0.051 |
| Sex (female) | | 12 | 0.020* | 0.028* | 0.050* | 0.043* |
| | | 15–18 | 0.052 | 0.016* | 0.035* | 0.027* |
| Self-assessed financial situation | | 12 | –0.046* | –0.018* | –0.086* | –0.088* |
| | | 15–18 | –0.004* | –0.007* | –0.022* | –0.034* |
| Frequency of visits to the dentist | | 12 | 0.068 | 0.046* | 0.087 | 0.084 |
| | | 15–18 | 0.077 | 0.088 | 0.146 | 0.143 |
| Reason for a dental visit was pain or other ailments | | 12 | 0.044* | 0.047* | 0.064 | 0.075 |
| | | 15–18 | 0.043* | 0.012* | 0.078 | 0.115 |
| Reason for a dental visit was check-up | | 12 | –0.058* | –0.071* | –0.097* | –0.104* |
| | | 15–18 | –0.071* | –0.045* | –0.146* | –0.184* |
| Brushing teeth at least twice a day | | 12 | –0.079* | –0.049* | –0.082* | –0.081* |
| | | 15–18 | –0.070* | –0.055* | –0.097* | –0.108* |
| Conscious use of fluoride-free toothpaste | | 12 | 0.038* | 0.042* | 0.045* | 0.039* |
| | | 15–18 | 0.042* | 0.048* | 0.046* | 0.044* |
| Use of dental floss | | 12 | –0.022* | –0.017* | –0.028* | –0.042* |
| | | 15–18 | –0.017* | –0.029* | –0.029* | –0.048* |
| Dietary behavior (foods consumed at least once a day) | biscuits | 12 | 0.061 | 0.036* | 0.072 | 0.077 |
| | | 15–18 | 0.044* | 0.043* | 0.047* | 0.047* |
| | cakes/donuts/glazed rolls | 12 | 0.048* | 0.051 | 0.074 | 0.075 |
| | | 15–18 | 0.014* | 0.029* | 0.018* | 0.020* |
| | chewing gum with sugar | 12 | 0.106 | 0.048* | 0.113 | 0.120 |
| | | 15–18 | 0.018* | 0.019* | 0.033* | 0.031* |
| | sweets/candies | 12 | 0.026* | 0.035* | 0.041* | 0.042* |
| | | 15–18 | 0.069 | 0.052 | 0.061 | 0.062 |
| | sugar-sweetened carbonated beverages (e.g., cola, lemonade) | 12 | 0.084 | 0.086 | 0.099 | 0.104 |
| | | 15–18 | 0.029* | 0.022* | 0.064 | 0.084 |
| | tea with sugar | 12 | 0.080 | 0.040* | 0.090 | 0.090 |
| | | 15–18 | –0.009* | –0.006* | –0.005* | –0.001* |
| | sweetened juices | 12 | 0.072 | 0.059 | 0.075 | 0.069 |
| | | 15–18 | 0.026* | 0.031* | 0.028* | 0.038* |
| | chips | 12 | 0.074 | 0.064 | 0.093 | 0.096 |
| | | 15–18 | 0.035* | 0.021* | 0.058 | 0.064 |
| | sweetened coffee | 15–18 | 0.047* | 0.066 | 0.051 | 0.049* |
| | mineral water | 12 | –0.035* | 0.008* | –0.053 | –0.041* |
| | | 15–18 | –0.014* | –0.015* | –0.052 | –0.054 |

* statistically significant ($p < 0.05$, Spearman's correlation analysis).

at check-up visits was associated with a reduced likelihood of caries occurrence and severity (*AOR* for 12-year-olds: 0.83 (0.69–1.00), $p = 0.045$; *AOR* for 15–18-year-olds: 0.64 (0.49–0.83), $p < 0.001$) (Table 4,5).

In relation to oral hygiene practices, the occurrence of caries was found to be less probable and less severe among individuals who brushed their teeth twice daily. This effect was slightly attenuated by dietary habits (*AOR* for 12-year-olds: 0.72 (0.59–0.87), $p < 0.001$; *AOR* for 15–18-year-olds: 0.59 (0.43–0.80), $p < 0.001$). In none of the groups did the use of floss affect the likelihood of caries occurence. However, in both the younger and older groups, the $D_{\geq 3}MFS$ values were statistically significantly lower. Considering the dietary behavior, the results indicated that caries was more likely to occur among children aged 12 years who consumed sugar-sweetened beverages, tea with sugar, chips, sweetened juices, chewing gum with sugar, and biscuits at least once a day (Table 4). The younger group also showed a tendency toward higher $D_{\geq 3}MFT$ and $D_{\geq 3}MFS$ values. The introduction of hygienic behavior as a confounding factor into the statistical model did not alter, nor did it slightly reduce, the negative impact of erroneous dietary habits. In the group of 12-year-olds, there was no significant effect of mineral water consumption on the prevalence of caries.

The impact of dietary habits on the occurrence of dental caries in the older group was less pronounced (Table 5). The likelihood of tooth decay was increased only by the consumption of sweets (candies and carbonated drinks, such as cola or lemonade, and chewing gum with sugar). The importance of these factors remained unaltered by hygienic behavior; however, frequent consumption of cariogenic products did affect the severity of tooth decay. Furthermore, while the consumption of still mineral water did not influence the likelihood of developing dental caries, it was observed that individuals who preferred it to quench their thirst exhibited lower $D_{\geq 3}MFT$ and $D_{1-2}$ values compared to those who consumed water less than once a day.

**Table 4.** Results of the simple (odds ratio (*OR*)) and multiple (adjusted odds ratio (*AOR*)) logistic regression analyses for a group of 12-year-olds

| Parameter | | | $D_{1-2}$, $D_{\geq 3}MFT > 0$ *n* (%) | *OR* (95% *CI*) | *AOR* (95% *CI*) | $D_{1-2}$ | *p*-value | $D_{\geq 3}MFT$ *M* ±*SD* | *p*-value | $D_{\geq 3}MFS$ *M* ±*SD* | *p*-value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Reason for a dental visit was pain or other ailments | | yes | 234/313 (74.8) | 1.44 (1.02–1.96) $p = 0.039$* | 1.53 (1.11–1.87) $p = 0.019$* | 0.98 ±1.11 | 0.002* | 3.45 ±3.01 | 0.001* | 4.78 ±5.11 | 0.001* |
| | | no | 1,541/2,183 (70.6) | | | 0.73 ±10.94 | | 2.84 ±2.67 | | 3.62 ±3.91 | |
| Reason for a dental visit was check-up | | yes | 883/1,221 (72.3) | 0.77 (0.64–0.92) $p = 0.004$* | 0.83 (0.69–1.00) $p = 0.045$* | 0.66 ±1.11 | 0.016* | 2.52 ±2.40 | 0.001* | 3.11 ±3.36 | 0.001* |
| | | no | 986/1,275 (77.3) | | | 0.89 ±0.91 | | 3.15 ±2.94 | | 4.17 ±4.62 | |
| Hygienic behavior | brushing teeth at least twice a day | yes | 1,123/1,555 (72.2) | 0.68 (0.56–0.82) $p < 0.001$* | 0.72 (0.59–0.87) $p < 0.001$* | 0.68 ±1.00 | 0.001* | 2.69 ±2.67 | 0.001* | 3.46 ±4.05 | 0.001* |
| | | no | 746/941 (79.3) | | | 0.94 ±1.28 | | 3.10 ±2.75 | | 3.97 ±4.13 | |
| | use of dental floss | yes | 732/993 (73.7) | 0.90 (0.75–1.09) $p = 0.276$ | 0.92 (0.77–1.11) $p = 0.392$ | 0.74 ±1.24 | 0.102 | 2.76 ±2.65 | 0.190 | 3.38 ±3.66 | 0.007* |
| | | no | 1,137/1,503 (75.6) | | | 0.80 ±1.31 | | 2.90 ±2.74 | | 3.83 ±4.34 | |
| Dietary behavior (foods consumed at least once a day) | biscuits/cakes/ donuts/glazed rolls | yes | 257/321 (80.1) | 1.40 (1.05–1.87) $p = 0.022$* | 1.39 (1.04–1.86) $p = 0.028$* | 0.99 ±1.02 | 0.019* | 3.26 ±2.87 | 0.003* | 4.25 ±4.52 | 0.005* |
| | | no | 1,612/2,175 (74.1) | | | 0.71 ±1.18 | | 2.78 ±2.67 | | 3.56 ±4.01 | |
| | chewing gum with sugar | yes | 228/281 (81.1) | 1.50 (1.10–2.06) $p = 0.011$* | 1.49 (1.09–2.04) $p = 0.013$* | 1.11 ±1.43 | 0.001* | 3.26 ±2.61 | 0.006* | 4.38 ±4.36 | 0.001* |
| | | no | 1,641/2,215 (74.1) | | | 0.71 ±1.21 | | 2.79 ±2.71 | | 3.56 ±4.04 | |
| | sugar-sweetened carbonated beverages (e.g., cola, lemonade) | yes | 410/511 (80.2) | 1.46 (1.15–1.86) $p = 0.002$* | 1.39 (1.09–1.77) $p = 0.008$* | 0.98 ±1.17 | 0.032* | 3.20 ±2.71 | 0.001* | 4.21 ±4.47 | 0.001* |
| | | no | 1,459/1,985 (73.5) | | | 0.73 ±1.21 | | 2.75 ±2.69 | | 3.51 ±3.97 | |
| | tea with sugar | yes | 955/1,227 (77.8) | 1.36 (1.14–1.64) $p < 0.001$* | 1.36 (1.13–1.63) $p < 0.001$* | 0.83 ±1.21 | 0.188 | 3.01 ±2.68 | 0.003* | 3.85 ±4.07 | 0.015* |
| | | no | 914/1,269 (72.0) | | | 0.77 ±1.09 | | 2.68 ±2.71 | | 3.45 ±4.09 | |
| | sweetened juices | yes | 432/542 (79.7) | 1.41 (1.12–1.78) $p = 0.004$* | 1.37 (1.09–1.73) $p = 0.008$* | 0.93 ±1.20 | 0.001* | 3.11 ±2.77 | 0.008* | 4.01 ±4.36 | 0.019* |
| | | no | 1,437/1,954 (73.5) | | | 0.69 ±1.07 | | 2.77 ±2.68 | | 3.55 ±4.00 | |
| | chips | yes | 160/194 (82.5) | 1.63 (1.11–2.39) $p = 0.012$* | 1.52 (1.04–2.24) $p = 0.032$* | 1.11 ±0.89 | 0.001* | 2.98 ±2.35 | 0.463 | 3.85 ±3.74 | 0.476 |
| | | no | 1,709/2,302 (74.2) | | | 0.75 ±0.93 | | 2.83 ±2.73 | | 3.63 ±4.11 | |
| | mineral water | yes | 1,026/1,484 (69.1) | 0.76 (0.34–0.98) $p = 0.097$ | 0.74 (0.38–0.89) $p = 0.071$ | 1.02 ±0.92 | 0.190 | 2.33 ±2.23 | 0.545 | 2.99 ±2.11 | 0.221 |
| | | no | 86/126 (68.3) | | | 1.15 ±0.99 | | 2.41 ±2.11 | | 3.08 ±2.45 | |

*CI* – confidence interval; * statistically significant ($p < 0.05$, *t*-test).

**Table 5.** Results of the simple and multiple logistic regression analyses for a group of 15–18-year-olds

| Parameter | | | $D_{1–2}$, $D_{≥3}$MFT > 0 *n* (%) | *OR* (95% *CI*) | *AOR* (95% *CI*) | $D_{1–2}$ | *p*-value | $D_{≥3}$MFT *M* ±*SD* | *p*-value | $D_{≥3}$MFS *M* ±*SD* | *p*-value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Reason for a dental visit was pain or other ailments | | yes | 400/430 (93.0) | 1.56 (1.05–2.31) $p = 0.029$* | 1.52 (1.02–2.26) $p = 0.037$* | 0.66 ±1.32 | 0.038* | 6.68 ±4.41 | 0.001* | 10.71 ±8.97 | 0.001* |
| | | no | 1,946/2,173 (89.6) | | | 0.57 ±1.51 | | 5.73 ±4.08 | | 8.07 ±7.29 | |
| Reason for a dental visit was check-up | | yes | 992/1,131 (87.7) | 0.62 (0.48–0.81) $p < 0.001$* | 0.64 (0.49–0.83) $p < 0.001$* | 0.51 ±1.50 | 0.015* | 5.19 ±3.96 | 0.001* | 6.86 ±6.31 | 0.001* |
| | | no | 1,354/1,472 (92.0) | | | 0.65 ±1.45 | | 6.41 ±4.22 | | 9.76 ±8.34 | |
| Hygienic behavior | brushing teeth at least twice a day | yes | 1,559/1,758 (88.7) | 0.58 (0.43–0.78) $p < 0.001$* | 0.59 (0.43–0.80) $p < 0.001$* | 0.63 ±1.43 | 0.327 | 5.61 ±4.11 | 0.001* | 7.94 ±7.27 | 0.001* |
| | | no | 787/845 (93.1) | | | 0.59 ±1.51 | | 6.44 ±4.20 | | 9.68 ±8.30 | |
| | use of dental floss | yes | 929/1,038 (89.5) | 0.89 (0.69–1.16) $p = 0.382$ | 0.91 (0.70–1.18) $p = 0.473$ | 0.58 ±1.57 | 0.102 | 5.73 ±4.12 | 0.125 | 8.00 ±7.22 | 0.006* |
| | | no | 1,417/1,565 (90.5) | | | 0.61 ±1.61 | | 5.99 ±4.17 | | 8.84 ±7.92 | |
| Dietary behavior (foods consumed at least once a day) | biscuits/cakes/ donuts/glazed rolls | yes | 306/335 (91.3) | 1.18 (0.79–1.77) $p = 0.424$ | 1.17 (0.78–1.76) $p = 0.446$ | 0.76 ±1.32 | 0.002* | 6.38 ±4.47 | 0.019* | 9.61 ±8.98 | 0.005* |
| | | no | 2,040/2,268 (89.9) | | | 0.54 ±1.38 | | 5.81 ±4.10 | | 8.34 ±7.43 | |
| | chewing gum with sugar | yes | 577/622 (92.8) | 1.54 (1.10–2.15) $p = 0.012$* | 1.52 (1.09–2.13) $p = 0.014$* | 0.65 ±1.56 | 0.012* | 6.36 ±4.34 | 0.001* | 9.49 ±8.59 | 0.001* |
| | | no | 1,769/1,981 (89.3) | | | 0.56 ±1.55 | | 5.73 ±4.08 | | 8.20 ±7.32 | |
| | sugar-sweetened carbonated beverages (e.g., cola, lemonade) | yes | 478/515 (92.8) | 1.52 (1.06–2.19) $p = 0.023$* | 1.49 (1.04–2.15) $p = 0.031$* | 0.59 ±1.65 | 0.182 | 6.56 ±4.43 | 0.001* | 10.18 ±9.15 | 0.001* |
| | | no | 1,868/2,088 (89.5) | | | 0.56 ±1.71 | | 5.72 ±4.07 | | 8.09 ±7.19 | |
| | tea with sugar | yes | 382/421 (90.7) | 1.09 (0.76–1.56) $p = 0.647$ | 1.07 (0.74–1.53) $p = 0.727$ | 0.57 ±1.54 | 0.271 | 6.20 ±4.15 | 0.091 | 9.14 ±7.93 | 0.041* |
| | | no | 1,964/2,182 (90.0) | | | 0.52 ±1.61 | | 5.82 ±4.15 | | 8.38 ±7.60 | |
| | sweetened juices | yes | 194/210 (92.4) | 1.36 (0.80–2.30) $p = 0.255$ | 1.32 (0.78–2.24) $p = 0.305$ | 0.72 ±1.61 | 0.017* | 6.26 ±4.42 | 0.169 | 10.35 ±9.55 | 0.001* |
| | | no | 2,152/2,393 (89.9) | | | 0.58 ±1.58 | | 5.85 ±4.13 | | 8.34 ±7.45 | |
| | chips | yes | 1,832/2,036 (90.0) | 0.93 (0.67–1.27) $p = 0.635$ | 0.95 (0.69–1.30) $p = 0.740$ | 0.56 ±1.32 | 0.038* | 5.80 ±4.10 | 0.042* | 8.35 ±7.62 | 0.053 |
| | | no | 514/567 (90.7) | | | 0.68 ±1.32 | | 6.20 ±4.33 | | 9.05 ±7.77 | |

* statistically significant ($p < 0.05$, *t*-test).

## Discussion

The results of the present study demonstrated the prevalence of inappropriate oral health behaviors among adolescents, a finding that aligns with the reports from the literature.[26–33] These behaviors were accompanied by an increase in the incidence of caries and the values of $D_{≥3}$MFT, $D_{1–2}$ and $D_{≥3}$MFS with age. This finding is consistent with the notion that tooth decay is cumulative and chronic.[31,34] The incidence of caries in the older group was 15% higher, while the mean $D_{≥3}$MFT value doubled. This suggests that caries occurs at a younger age, and persistent causal factors contribute to the continuous progression of the disease process. At the same time, the average extent of cavities in both groups was comparable. In the older group, the carious cavity covered an average of 1.4 tooth surfaces, while in the younger group, it was 1.3. The lower prevalence of teeth with caries and the similar average number of tooth surfaces with carious cavities, as well as the higher number of teeth without cavities in younger adolescents compared to the average, may be the result of greater susceptibility of tooth tissues.

The statistical analysis confirmed that socioeconomic factors and oral health behaviors are statistically significantly correlated with caries parameters. It is worth emphasizing the relationship between the occurrence of tooth decay and rural residence in the younger group, and with the female sex among older adolescents. This finding is in contrast to the results of a study conducted on adolescents in Portugal, Romania and Sweden, where the severity of caries was found to be lower in girls and similar in urban and rural regions.[29] The differences between rural and urban regions are becoming indistinct in many countries, yet the correlation with sex is emphasized. Women are generally more prone to tooth decay.[35] The lower pH of saliva in women is attributed to physiological factors, such as the effect of sex hormones on the expression of salivary gland genes, and the smaller size of the salivary glands.[1,2,36] Despite the slightly superior oral health behaviors exhibited by girls, such as reduced consumption of sugar-sweetened beverages and more frequent toothbrushing, a predisposition to caries remains.[37] The correlation between caries and economic status is less pronounced, but this result is less reliable due to

incomplete data on the income of the surveyed adolescents' families. Similarly, the lack of knowledge among adolescents regarding the fluoride content of their toothpaste hindered the acquisition of a fully reliable result regarding the health benefits associated with its use. More than 30% of the respondents lacked awareness about the fluoride content in their toothpaste. However, it has been shown that the conscious use of fluoride-free toothpaste is associated with an increased prevalence of tooth decay.

Hygiene behaviors and diet are the main modifiable risk factors for oral disease, a notion that has been confirmed by numerous studies.[38,39] The frequency of toothbrushing reported by adolescents has been identified as a reliable predictor of tooth decay, with a predictive capability that surpasses that of clinical oral hygiene assessments.[40] The percentage of adolescents who brush their teeth at least twice a day is estimated to be between 53.4% and 90.6%,[27,32] which is in line with the results obtained in this study. The study reaffirmed the importance of brushing teeth at least twice a day, as it has been shown to reduce the likelihood of tooth decay by nearly twofold and, to a slightly lesser extent, its severity. This association remained statistically significant even when controlling for potential confounding factors, such as a static diet, in the model. A study of Finnish adolescents revealed a two-fold increase in decayed teeth (DT) values; however, this increase did not affect the occurrence of caries.[32] A limitation of our study was the lack of a question about the frequency of flossing, although even the confirmation of its use had a statistically significant impact on the condition of the teeth. In both groups, the $D_{1-2}$ and $D_{\geq 3}$MFT values were found to be statistically significant in individuals who reported flossing their teeth. Hygiene factors also include the practice of rinsing one's mouth with liquids. Studies have demonstrated that older age groups tend to rinse their mouths more frequently.[30]

The second causative factor of tooth decay is excessive sugar consumption. Alarmingly, a significant proportion of Polish adolescents consume foods and beverages with sugar at least once a day. Many authors have documented the high prevalence of processed food consumption, especially sweetened beverages.[28,29,31] In both age groups examined, frequent consumption of sweets and sugar-sweetened carbonated beverages emerged as a dietary factor increasing the risk and severity of caries. Studies of Romanian adolescents also confirmed the direct impact of excessive consumption of carbonated beverages on the DMFT (decayed, missing, and filled teeth) index.[31] Similarly, Methuen et al. established that frequent consumption of sugar-sweetened beverages and elevated carbohydrate intake increased the likelihood of DT > 0, and that heightened carbohydrate intake (E%) was associated with more DT in 15–17-year-old adolescents in Finland.[39] These results are consistent with our observations, as the average DT values in individuals who frequently consume starchy foods with sugar are higher relative to others.

Excessive sugar consumption, inconsistent dental care and postponing dental visits represent further issues. In Brazil and Portugal, 90.9% and 95.1% of adolescents, respectively, report having visited a dentist at least once.[41] As many as 7.5% of Brazilians aged 17–21 have never been to a dentist.[42] In our study group, more than 10% of the respondents had not been to the dentist so far, or had not visited the dentist for a significant amount of time and were unable to recall the last visit. Pain was reported as the cause of the last visit by 9.7% of 12-year-olds and 15.9% of 15–18-year-olds. In Romania, 40.6% of adolescents have missed regular annual dental check-ups and only sought treatment when they were in pain.[31]

The oral health behaviors of individuals in early and middle adolescence groups differ. Although older adolescents were less likely to consume sweetened starchy foods, they demonstrated a marked increase in the daily consumption of sugary gum. A significantly smaller percentage of people in this group consumed fruits and vegetables at least once a day. A favorable difference was an increase in the frequency of mouthwash use. Other hygiene behaviors remained comparable between the both groups. In a study by Jurišić et al., poorer oral hygiene attitudes were observed in the middle period of adolescence compared to the early adolescence.[43] The authors associated this with the lower influence of parents on the independence of young people. In our study, individuals aged 15–18 years were significantly more likely to cite toothache as the reason for visiting the dentist. Changes in dietary behavior, such as reduced consumption of sweetened starchy products and replacing them with chewing gum, as well as an increased consumption of mineral water, may be attributable to adolescents' incorrect perception regarding weight management. At the same time, the less frequent consumption of fruits and vegetables, and the less frequent use of dental services, may be related to a diminished parental influence on their offspring's behavior.

## Limitations

The present study was subject to certain limitations. Behavioral measures were analyzed based on survey responses, which are known to be subject to error resulting from repondents' desire to present themselves in a favorable light. Additionally, the survey question concerned the use of hygiene tools (dental floss, liquid mouthwash), but did not address the frequency of their use.

# Conclusions

The results of the present study confirmed the negative impact of hygiene negligence and poor diet on young permanent dentition, irrespective of age. However, the influence of diet appeared to be more pronounced in less

mature dentition. The findings underscore the significance of dental visits, oral hygiene practices, and a preference for mineral water in quenching thirst. The prevalence of inappropriate health behaviors among adolescents is comparable across age groups, indicating a potential for these behaviors to persist into adulthood. Therefore, it is essential to control these factors and implement educational programs that promote healthy lifestyles.

## Ethics approval and consent to participate

The study was approved by the Bioethics Committee of the Warsaw Medical University (KB/190/2016 and KB135/2019). All participants provided written informed consent.

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.

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Original paper

# Evaluating changes in dental status among Polish older adults over a decade: A comparative analysis of PolSenior (2009) and PolSenior2 (2019) surveys

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## Abstract

**Background.** The aging global population poses new challenges to healthcare systems, including dental healthcare. This study analyzes the evolution of dental status within the aging population of Poland over the last pre-pandemic decade.

**Objectives.** The goal of the study was to examine changes in dental health among Poland's aging population, with a specific focus on edentulism, partial tooth loss and functional dentition. Furthermore, the study aimed to evaluate the influence of sociodemographic factors on oral health, assess the effectiveness of public health initiatives, and identify persistent inequities in oral health.

**Material and methods.** The study utilized data from 2 representative population-based studies: the PolSenior (PS) (2008–2009); and the PolSenior2 (PS2) (2018–2019). The comparative analysis involved 4,773 (PS) and 4,627 (PS2) Polish adults aged more than 65 years. The participants were categorized based on the number of teeth present (0 – edentulism, 1–19 – partial tooth loss, ≥20 – functional dentition) and analyzed for various factors, including age, sex, education level, and place of residence.

**Results.** The dental status of Polish older adults has improved over the past decade, with the prevalence of edentulism decreasing from 45.8% to 36.1%, and the proportion of individuals with functional dentition increasing from 6.0% to 15.0%. The prevalence of edentulism dropped from 49.4% to 40.5% among women and from 40.3% to 29.3% among men, while functional dentition increased 2.5-fold in both sexes. The most significant improvements were observed among the youngest seniors, with a reduction in edentulism and an increase in functional dentition.

**Conclusions.** The findings of this study indicate a notable improvement in dental status of Polish older adults, as evidenced by a decline in the prevalence of edentulism and an increase in functional dentition. The research underscores the persistent disparities related to basic needs in relation to sociodemographic factors in dental treatment.

**Keywords:** geriatric dentistry, dental health, older adult population, edentulous mouth, demographic trends

## Highlights

- The prevalence of edentulism among Polish older adults decreased significantly from 45.8% in 2009 to 36.1% in 2019.
- Lower education levels, rural residency and female sex are associated with higher rates of edentulism.
- Continued investment in preventive programs, improved access to dental care in rural areas, and education on oral health are essential to reduce disparities among older adults in Poland.

# Introduction

The global demographic landscape is undergoing a significant transformation, characterized by an increasing proportion of older adults. This shift, evident not only in developed countries but also in emerging economies, carries profound implications for healthcare systems globally. The increase in lifespan is leading to demographic transformations that are likely to be among the most impactful social changes of our century. As reported by the United Nations (UN), the global population of individuals aged 65 and older was 727,000,000 in 2020, representing 9.3% of the world's population. This figure is projected to rise to 16% by the year 2050. A similar aging trend has been observed in the European Union (EU). From 1960, when only 9.6% of the EU population was over 65, the percentage rose to 20.3% by 2019 and is expected to reach 31.3% by the end of the century.[1,2] As reported by the Polish Central Statistical Office on December 31, 2022, 22.9% of the Polish population was of post-working age (over 60 years of age), compared to 16.8% in 2010.[3]

The older adult population is predisposed to various systemic ailments, including oral diseases that can substantially affect their quality of life. Common issues, such as difficulties with chewing, swallowing and speaking, exacerbate the challenges faced by this age group.[4,5] Notably, tooth loss in older adults is often linked to prevalent conditions like caries and periodontal disease.[6,7] Periodontitis has a significant influence on the quality of life of affected individuals, emphasizing the need for preventive dental care to improve overall well-being and reduce the burden of oral diseases.[8] Moreover, there is a widespread belief that oral health tends to decline with age. Additionally, research indicates that poor oral health may increase vulnerability to systemic diseases and exacerbate complications associated with coronavirus disease 2019 (COVID-19).[9,10]

Edentulism (toothlessness) is a common disability that has an influence on general health, including functional abilities as well as self-esteem and social interactions.[11] It is also associated with an increased risk of malnutrition, cardiovascular diseases, gastrointestinal disorders, and sleep apnea.[12–14] The global prevalence of edentulism in individuals aged 45 and above was 22% worldwide and 28% in Europe.[15] Therefore, identifying covariates of tooth loss is essential for the development of effective preventive strategies.

While preventive programs typically focus on children and adolescents, gerostomatology, the study of oral health in older adults, is still developing. However, its significance is expected to grow with the aging population and the increasing life expectancy. A range of classifications are utilized to systematize the clinical presentations of tooth loss, including topographic, quantitative and occlusal morphological categories, supporting both diagnostic and therapeutic analyses.[16] In broader health studies where dental aspects are not the primary focus, the World Health Organization (WHO) classifications based solely on the number of teeth present in the oral cavity are commonly used. These classifications provide a simplified assessment of the oral health status.

The PolSenior (PS) and PolSenior2 (PS2) studies aimed to assess the current health and socioeconomic status of the Polish elderly population, with a particular focus on the oldest cohorts.[17,18] The goal of this substudy was to conduct a comprehensive comparative analysis of dental health status of Polish seniors and to identify shifts in the oral health trends over the past decade.

# Material and methods

The PS project, a cross-sectional study conducted from 2008 to 2009, involved a representative group of 4,979 Polish adults aged 65 and above. Recognized as a pivotal project for monitoring the health of Polish seniors, it included the assessment of dental status, as well as prevalence and utilization of dentures.[18] A decade later, in 2018–2019, this survey was replicated under the PS2 study with 5,987 newly selected participants, including adults aged 60 and above. Both studies recruited participants from every administrative region in Poland, forming cohorts in 5-year age bands. These cohorts, which were comparable in size, maintained a balance between female and male participants.

The sampling method for both the PS and PS2 studies was based on a three-stage stratified and proportional random sampling design, ensuring representation from all regions of Poland. In the first stage, local administrative units (urban, rural and urban-rural municipalities) were selected arbitrarily. Next, within these units, specific

streets or villages were randomly drawn. Finally, individual participants were selected using the PESEL (Universal Electronic System for Registration of the Population) registry, a comprehensive database managed by the Ministry of the Interior and Administration of Poland, which ensures accurate representation of the population across different regions. In both studies, oversampling was applied to ensure a sufficient number of participants in older age groups, allowing for a detailed statistical analysis across all age cohorts.[17,18]

The present study undertakes an analysis of the corresponding groups from both studies, encompassing 4,773 individuals aged ≥65 from PS and 4,627 participants of a similar age from PS2.

The participants were categorized into 3 groups based on the number of teeth present: toothless individuals; those with partial tooth loss (1–19 teeth); and those with functional dentition (≥20 teeth). The analysis considered various factors, including age groups (65–74, 75–84 and ≥85 years), sex, place of residence, and education level: primary (primary or incomplete primary); vocational; secondary (high school or post-secondary school); and higher.

## Statistical analysis

The analysis involved a comparative evaluation of data from both surveys. Descriptive statistics were employed to summarize the findings. Comparative analyses, including the $\chi^2$ test for categorical variables, were conducted to discern significant differences in dental status between the 2 time points. Age standardization was applied to adjust for demographic changes over the decade.

The statistical analyses were performed with the use of R v. 3.6.3 (R Core Team; https://cran.mi2.ai) and SAS® 9.4 TS1M5 (SAS Institute, Inc., Cary, USA). The data was presented as percentages and 95% confidence intervals (95% *CI*s). Sampling weights were included in the statistical calculations to account for the complex survey design, using the R survey package. The post-stratification procedure was used to match the age–sex sample distribution to the population of Poland in 2019. The level of statistical significance was set at $p < 0.05$.

## Ethical considerations

Both the PS and PS2 surveys adhered to ethical guidelines throughout their execution. Moreover, written informed consent to participate in these studies was provided by the participants. The studies were conducted in accordance with the local legislation and institutional requirements and were approved by the Independent Bioethics Commission (NKBBN/257/2017).[17,18]

# Results

A comparative analysis of the PS (2009) and PS2 (2019) studies revealed a significant change in dental status of the Polish population aged ≥65 years (Fig. 1). The prevalence of edentulism decreased from 45.8% (*CI*: 42.3–49.3) to 36.1% (*CI*: 33.6–38.6), while the proportion of individuals with functional dentition increased from 6.0% (*CI*: 4.6–7.5) to 15.0% (*CI*: 12.8–17.2).

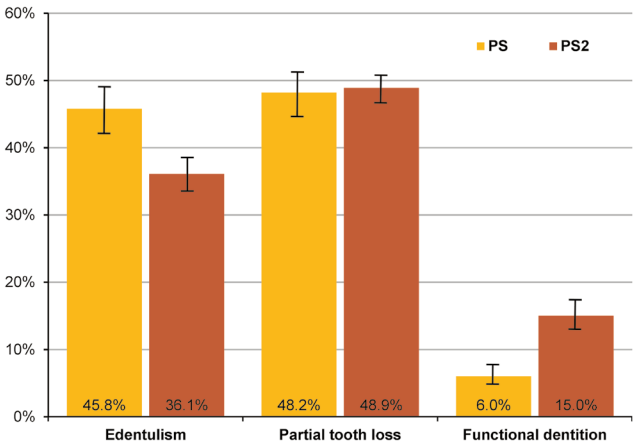


Fig. 1. Prevalence of edentulism, partial tooth loss and functional dentition in the PolSenior (PS) and PolSenior2 (PS2) population

## Demographic perspective

### Differences in sex

In women, the prevalence of edentulism decreased from 49.4% to 40.5%, with an increase in functional dentition from 4.9% to 12.5% between the PS and PS2 studies (Table 1). A more pronounced improvement has been observed in the male population, where edentulism rates decreased from 40.3% to 29.3%, and the proportion of individuals with functional dentition increased from 7.8% to 19.0%. In the group of respondents with partial tooth

Table 1. Prevalence of edentulism, partial tooth loss and functional dentition among the population of Polish older adults in the Polsenior (PS) ($n = 4,773$) and Polsenior 2 (PS2) ($n = 4,627$) studies

| Variable | | Edentulism | | Partial tooth loss | | Functional dentition | |
|---|---|---|---|---|---|---|---|
| | | PS | PS2 | PS | PS2 | PS | PS2 |
| Sex | female | 49.4 (45.5–53.4) | 40.5 (37.3–43.6) | 45.7 (41.8–49.6) | 47.1 (44.2–50.0) | 4.9 (3.1–6.7)* | 12.5 (9.9–15.0)* |
| | male | 40.3 (34.0–46.5)* | 29.3 (26.4–32.2)* | 52.0 (46.7–57.3) | 51.7 (48.5–54.9) | 7.8 (5.5–10.0)* | 19.0 (15.6–22.4)* |

* statistically significant difference between PS and PS2 ($p < 0.05$, $\chi^2$ test). Data presented as percentage (%) (95% confidence interval (*CI*)).

loss, no significant changes were observed among both women and men between the 2 studies. In the original PS study, the differences in the prevalence of edentulism and functional dentition between women and men were not statistically significant. However, a decade later, a marked improvement in dental health was observed among men compared to women, as evidenced by lower rates of edentulism and higher rates of functional dentition (Table 1).

## Age stratification trends

The prevalence of edentulism increased with age in both studies, reaching a peak of 67.3% in females and 54.7% in males in 2009, and 69.4% in females and 55.5% in males in 2019 among individuals over 85 years of age. The findings of both studies demonstrated an inverse relationship between functional dentition and age (Table 2 and Table 3).

In the 65–74 age group, the prevalence of edentulism exhibited a significant decline among women, from 40.8% in PS to 28.8% in PS2, and among men, from 36.8% to 21.1%, respectively. In parallel, an increase in functional dentition was observed, from 7.4% to 18.4% among women and from 9.3% to 24.4% among men.

In the 75–84 age cohort, a significant change was observed only in women with functional teeth: 2.2% in PS compared to 6.8% in PS2. No alterations in dental status were identified in the oldest analyzed group.

The difference in the prevalence of edentulism between men and women was not observed in the youngest analyzed cohort (65–74 years) in both studies. In PS, edentulism was more prevalent in women aged 75–84 years than in men, while 10 years later, the difference between sexes was statistically significant only in the oldest group (≥85 years).

**Table 2.** Prevalence of edentulism, partial tooth loss and functional dentition among the population of Polish elderly women in the Polsenior (PS) ($n$ = 2,314) and Polsenior 2 (PS2) ($n$ = 2,371) studies, categorized by age, education level and place of residence

| Variable | | Edentulism | | Partial tooth loss | | Functional dentition | |
|---|---|---|---|---|---|---|---|
| | | PS | PS2 | PS | PS2 | PS | PS2 |
| Age [years] | 65–74 | 40.8 (35.0–46.7)* | 28.8 (24.9–32.6)* | 51.8 (45.7–57.9) | 52.8 (48.2–57.4) | 7.4 (4.6–10.2)* | 18.4 (14.6–22.3)* |
| | 75–84 | 57.0 (51.3–62.7) | 47.8 (42.6–53.0) | 40.8 (35.2–46.3) | 45.4 (40.7–50.1) | 2.2 (0.9–3.6)* | 6.8 (4.6–9.0)* |
| | ≥85 | 67.3 (60.3–74.3) | 69.4 (64.4–74.3) | 31.9 (25.0–38.9) | 28.8 (23.8–33.7) | 0.8 (0.0–1.7) | 1.8 (0.9–2.8) |
| Education level | primary | 58.5 (52.9–64.1) | 56.9 (52.7–61.2) | 40.2 (34.5–45.9) | 40.8 (36.5–45.2) | 1.3 (0.5–2.0) | 2.2 (1.2–3.2) |
| | vocational | 40.4 (31.3–49.5) | 37.9 (31.1–44.6) | 52.9 (43.0–62.7) | 52.5 (45.0–60.1) | 6.7 (0.6–12.9) | 9.6 (5.6–13.6) |
| | secondary | 39.0 (32.4–45.6) | 31.2 (26.8–35.6) | 52.1 (43.5–60.6) | 52.0 (47.4–56.6) | 8.9 (4.1–13.7) | 16.8 (13.5–20.1) |
| | higher | 16.4 (9.0–23.9) | 18 (11.8–24.2) | 63.7 (54.3–73.0)* | 47.1 (40.4–53.8)* | 19.9 (11.5–28.2) | 34.9 (27.0–42.8) |
| Place of residence | rural area | 56.9 (49.7–64.1) | 50.7 (46.3–55.0) | 42.2 (35.0–49.5) | 44.0 (39.3–48.8) | 0.9 (0.2–1.5)* | 5.3 (2.9–7.7)* |
| | city (<50.000 residents) | 48.2 (42.0–54.5) | 38.3 (33.9–42.6) | 46.4 (40.3–52.6) | 49.9 (44.8–55.1) | 5.3 (2.6–8.1)* | 11.8 (8.5–15.1)* |
| | city (50.000–200.000 residents) | 51.3 (43.0–59.6) | 36.4 (28.2–44.5) | 43.2 (35.1–51.4) | 49.2 (41.1–57.3) | 5.5 (2.3–8.6)* | 14.4 (9.0–19.8)* |
| | city (>200.000 residents) | 34.5 (28.2–40.9) | 26.7 (21.2–32.3) | 53.6 (45.1–62.1) | 48.0 (41.1–54.8) | 11.9 (6.9–16.9)* | 25.3 (20.7–29.9)* |

* statistically significant difference between PS and PS2 ($p < 0.05$, $\chi^2$ test). Data presented as % (*CI*).

**Table 3.** Prevalence of edentulism, partial tooth loss and functional dentition among the population of Polish elderly men in the Polsenior (PS) ($n$ = 2,459) and Polsenior 2 (PS2) ($n$ = 2,256) studies, categorized by age, education level and place of residence

| Variable | | Edentulism | | Partial tooth loss | | Functional dentition | |
|---|---|---|---|---|---|---|---|
| | | PS | PS2 | PS | PS2 | PS | PS2 |
| Age [years] | 65–74 | 36.8 (27.8–45.8)* | 21.1 (17.1–25.2)* | 53.9 (46.6–61.3) | 54.5 (49.7–59.2) | 9.3 (6.1–12.4)* | 24.4 (19.6–29.2)* |
| | 75–84 | 44.2 (39.6–48.8) | 41.4 (37.3–45.5) | 50.0 (45.3–54.7) | 48.3 (44.3–52.2) | 5.7 (3.5–8.0) | 10.3 (6.9–13.8) |
| | ≥85 | 54.7 (47.1–62.4) | 55.5 (49.0–62.1) | 42.7 (34.9–50.5) | 41.1 (35.1–47.1) | 2.6 (1.1–4.1) | 3.4 (1.5–5.3) |
| Education level | primary | 45.3 (39.8–50.8) | 41.4 (35.6–47.1) | 50.4 (44.7–56.1) | 51.2 (46.0–56.5) | 4.3 (0.6–8.0) | 7.4 (4.0–10.7) |
| | vocational | 44.7 (28.6–60.9) | 27.6 (21.6–33.6) | 48.9 (34.1–63.7) | 54.0 (47.5–60.6) | 6.4 (2.2–10.6)* | 18.3 (12.3–24.4)* |
| | secondary | 37.4 (29.0–45.7) | 25.6 (21.3–29.8) | 55.2 (46.3–64.2) | 50.7 (45.0–56.4) | 7.4 (4.4–10.4)* | 23.7 (18.3–29.2)* |
| | higher | 18.6 (10.5–26.8) | 18.3 (12.4–24.1) | 59.5 (48.3–70.7) | 49.1 (39.5–58.7) | 21.9 (11.4–32.3) | 32.7 (22.9–42.4) |
| Place of residence | rural area | 42.5 (37.3–47.8)* | 30.3 (25.9–34.6)* | 53.7 (47.1–60.2) | 54.6 (49.6–59.6) | 3.8 (1.1–6.5)* | 15.1 (9.4–20.8)* |
| | city (<50.000 residents) | 38.8 (33.9–43.7) | 30.6 (25.3–35.8) | 54.3 (49.1–59.5) | 49.6 (43.7–55.6) | 6.9 (4.2–9.7)* | 19.8 (12.7–26.9)* |
| | city (50.000–200.000 residents) | 44.6 (38.3–50.9) | 32.2 (23.3–41.0) | 47.0 (39.7–54.4) | 45.5 (37.9–53.1) | 8.4 (2.9–13.8)* | 22.3 (15.4–29.3)* |
| | city (>200.000 residents) | 35.7 (14.9–56.4) | 23.0 (19.0–26.9) | 51.5 (35.5–67.4) | 54.1 (46.9–61.4) | 12.8 (7.1–18.6) | 22.9 (15.1–30.8) |

* statistically significant difference between PS and PS2 ($p < 0.05$, $\chi^2$ test). Data presented as % (*CI*).

### Educational impact

The findings of both studies indicated a significant relationship between the level of education and dental status, irrespective of sex (Table 2 and Table 3). The highest percentage of edentulous individuals was observed among those with primary education: 58.5% of women in PS and 56.9% of women in PS2; and 45.3% of men in PS and 41.4% of men in PS2. The results suggest that the prevalence of edentulism decreases with increasing educational levels, reaching the lowest values among individuals with higher education, both among women and men.

Consequently, an increasing percentage of people with functional dentition was observed as the level of education increased in both sexes. In 2019, only 2.2% of women and 7.4% of men with primary education had more than 20 teeth, compared with one-third of those with higher education. Statistically significant changes between the 2 studies were observed in functional dentition in men with vocational and secondary education (Table 3), and in women with partial tooth loss who had received higher education (Table 2).

### Place of residence

The findings of both studies indicated a tendency toward improved dental conditions with an increase in the size of the place of residence.

The prevalence of edentulism significantly decreased among male residents of rural areas over the course of a decade, from 42.5% to 30.3% (Table 3). A positive trend in reducing toothlessness was also demonstrated in all urban centers, but without any statistically significant differences.

Positive and statistically significant changes were observed among respondents with functional dentition, irrespective of their sex and place of residence. The prevalence of functional dentition increased most markedly, by almost fivefold, in rural areas: from 0.9% to 5.3% in women and from 3.8% to 15.1% in men (Table 2 and Table 3).

## Discussion

The present study provides a comprehensive analysis of changing dental health patterns among Polish seniors in the context of global demographic aging trends, which forecast a substantial increase in the older population by the year 2050. This transition presents unique healthcare challenges, including oral health. Notably, edentulism has been reported to affect over 60% of older adults in Brazil, while significantly lower rates have been observed in countries such as South Korea (11%) and Japan (13.8%).[19–21] These variations underscore the influence of geographic, economic and social factors on oral health outcomes on a global scale. For example, studies have shown that rural residents of China are more susceptible to edentulism, while urban residents of Ghana and South Africa face higher rates of this condition.[22]

This study is notable for its use of nationally representative data to evaluate long-term trends in dental health among older adults in Poland. The findings of this study revealed a substantial improvement in oral health over the course of a decade. Specifically, the edentulism rate decreased from 45.8% to 36.1%, and functional dentition increased 2.5-fold from 6.0% to 15.0%, mirroring advancements observed in Europe.[23,24] However, despite the overall positive trend, Poland's rates remain higher than the WHO benchmark of less than 15% of individuals aged 65–74 years who are edentulous, a target already reached by Germany (10.7%), France (9.1%) and Denmark (6.8%). Moreover, Sweden and Switzerland have been observed to report some of the lowest rates of edentulism in Europe.[25,26] This discrepancy highlights the need for the implementation of targeted public health strategies aimed at mitigating disparities rooted in socioeconomic and regional factors.

In accordance with international research, our study demonstrated that lower education levels are associated with higher rates of edentulism.[22] Socioeconomic factors and limited dental visits have been identified as significant predictors of oral health disparities in both international and regional studies.[27] Polish seniors with primary education exhibited higher edentulism rates, with only 2.2% of women and 7.4% of men in this group retaining functional dentition. Individuals with higher education levels exhibited a significantly higher tooth retention rate of approx. ⅓.[28] These disparities reflect patterns observed in both Europe and the United States, where lower educational attainment correlates with increased rates of tooth loss and fewer preventive dental behaviors.[14,29] This correlation between the level of education and oral health suggests that improving health literacy and access to preventive care could significantly enhance outcomes in Poland.

Geographic location plays a vital role in shaping dental health. As observed in other regions of the world, urban Polish residents generally exhibit better oral health, attributable to higher access to healthcare services and socioeconomic advantages.[30] Our study also identified encouraging improvements among rural residents, where the prevalence of functional dentition among rural women increased nearly fivefold, from 0.9% to 5.3%, and among men from 3.8% to 15.1% over the decade.[31,32] These positive shifts may be influenced by public health initiatives targeting rural areas and broader efforts within the EU to reduce health inequities. However, continued investment is needed to effectively address the urban-rural disparities.

Differences in dental health between sexes were also observed. A decline in the prevalence of edentulism was observed among both sexes; however, men demonstrated a more significant improvement in functional dentition, with a rise from 7.8% to 19.0%.[33] This pattern may reflect recent health initiatives, changing health behaviors, or

differential access to dental care. In contrast, women, who generally adopt a more proactive stance toward preventive health measures, encounter additional risks such as postmenopausal bone loss and a prolonged life expectancy. These factors contribute to elevated edentulism rates among older women.[34–37]

The findings of the present study indicate significant generational differences, particularly between the 65–74 and ≥85 cohorts. The youngest seniors, born between 1945 and 1954, have experienced marked improvements in functional dentition and a decline in edentulism. These changes likely reflect the post-World War II advancements in healthcare and socioeconomic conditions that benefited this cohort. Conversely, the oldest group, born during a period of economic hardship, exhibits persistently high levels of edentulism, emphasizing the long-term impact of early-life socioeconomic conditions on oral health.[28]

The stability of the group with partial tooth loss over the decade can be understood by recognizing it as a transitional group. The decline in the number of edentulous individuals and the increase in functional dentition were influenced by advancements in dental care, education and preventive measures. As dental health has improved, older adults have been able to maintain a significant number of teeth, which increased the proportion of individuals with functional dentition. This shift potentially reduced the size of the group with partial tooth loss. At the same time, the reduction in the prevalence of edentulism has led to a reduction in tooth loss. Individuals who would have been edentulous in the past are now more likely to retain their teeth, placing them in the partial tooth loss category. Consequently, the partial dentition group has remained stable, balancing the increase in functional dentition and the decrease in edentulism.

The results of the present study underscore the critical role of targeted public health initiatives in addressing oral health disparities across various demographic factors, including age, education, sex, and geographic location. Several countries have successfully implemented models for such initiatives. For instance, mobile dental clinics in underserved rural areas, widely used in countries such as the United States and Australia, could expand access to preventive and restorative care in Poland's rural regions.[38,39] Similarly, training general practitioners to conduct basic oral health screenings, a common practice in Scandinavian countries, could enhance early detection and improve outcomes for older adults.[40] Educational programs promoting oral hygiene and addressing factors like tobacco use, modeled after Japan and South Korea's public health campaigns, could also be beneficial.[41]

## Limitations

While the present study offers valuable insights into the dental health trends among Polish older adults over a decade, several limitations must be acknowledged. First, the response rates of 42% for PS and 56% for PS2 indicate potential sampling bias. Those who declined to participate may have had different oral health profiles compared to the participants, which could have affected the generalizability of the results. Furthermore, the cross-sectional design of the study provides a snapshot of health trends at 2 distinct points in time, which limits the ability to draw causal inferences regarding the factors driving changes in dental health between 2009 and 2019. Despite the efforts to standardize data collection methods across the 2 surveys, minor variations in data collection techniques or differences in participants' recollections over time may have introduced measurement bias. These potential differences could affect the comparability of the 2 cohorts. Finally, the findings of this study are largely applicable to Poland, and the generalizability of these results to other countries may be limited by differences in healthcare systems, economic conditions and demographic structures.[17,18]

# Conclusions

The comparative analysis of the PS (2009) and PS2 (2019) studies demonstrated a significant improvement in the dental health of Polish older adults over the span of a decade. These improvements are particularly evident in the youngest senior population (65–74 years), suggesting that advancements in dental care, increased health awareness and improved socioeconomic conditions have favorably impacted the oral health of older adults entering retirement age. Despite these encouraging developments, the study highlights persistent disparities related to sex, as well as sociodemographic factors, including education level and place of residence.

Continued efforts are necessary to maintain the positive trends observed and to ensure that all segments of the older adult population benefit equally from advancements in dental care. Collaboration among policymakers, healthcare providers and community organizations is crucial to prioritize oral health as a critical component of overall well-being in older adults. Future research should focus on longitudinal studies to monitor these trends and evaluate the effectiveness of implemented public health strategies. By doing so, Poland can work toward improving the quality of life for its aging population, contributing to better health outcomes and a more equitable society.

## Ethics approval and consent to participate

Not applicable.

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.

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Original paper

# Prevalence of systemic diseases in 82,363 patients at a dental school in San Luis Potosí, Mexico: A cross-sectional study

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## Abstract

**Background.** The prevalence of medically compromised patients seeking dental care varies across different countries. There have been no published reports about this clinical topic in Mexico.

**Objectives.** We aimed to determine the prevalence of systemic diseases in patients who attended the Diagnostic Clinic at the Faculty of Dentistry of the Autonomous University of San Luis Potosí in Mexico from 2011 to 2019.

**Material and methods.** The study was based on the analysis of electronic files from 82,363 medically compromised patients registered in the clinic during the aforementioned period. Each file was entered into an electronic medical record using the Microsoft Visual Basic.NET software and completed by an undergraduate student based on a personal interview. The collected information was then analyzed with the use of Stata 14 statistical package.

**Results.** The global prevalence of medically compromised patients among the patient population was 39.1%. Comorbidities were more prevalent in female patients (71.9%) compared to male patients (28.1%). The most prevalent diseases in adults were gastrointestinal diseases (16.5%), arterial hypertension (14.1%) and diabetes mellitus (8.6%).

**Conclusions.** In a third of the registered cases, an associated comorbidity was identified. It is therefore necessary for dental undergraduate students to receive comprehensive training during their academic formation to facilitate the timely and accurate diagnosis of systemic diseases, as part of the dental care protocol for adult patients.

**Keywords:** prevalence, dental care, systemic diseases, school setting

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## Highlights

- The detection of systemic diseases in dental patients is essential to ensure comprehensive and safe care.
- A third of registered dental patients report having at least one comorbidity, with a higher prevalence in women.
- The high incidence of gastrointestinal diseases in dental patients in Mexico enables clinicians to investigate dietary habits, make oral diagnoses and develop comprehensive treatment plans.

# Introduction

On a global scale, there has been an observed increase in the number of elderly individuals with compromised medical conditions, largely attributable to the improved socioeconomic status, enhanced access to healthcare facilities and advancements in medical technology. These factors have contributed to an increase in life expectancy.[1–3] The prevalence of systemic diseases among dental patients in different countries has been previously reported.[4,5] Diverse epidemiological studies have provided essential information, facilitating an extensive understanding of the medical profile of the patients seeking dental treatment. During the initial diagnostic process, it is crucial to detect the most common clinical systemic conditions to ensure that dental care protocols for medically compromised patients are safe and adequate.[2] Clinicians must be aware of the effects of medical conditions and their interactions as part of the dental treatment plan.[6,7] Moreover, it is important to acknowledge that a significant proportion of the global population, particularly in developing countries, does not receive routine medical checkups. This indicates that patients with asymptomatic diseases may remain unaware of their systemic health status.[8,9]

Given the potential for systemic diseases to manifest through oral symptoms, dental care professionals have the capacity to detect some signs suggestive of comorbidities through oral examination. For example, it has been demonstrated that periodontal disease has a substantial impact on an individual's general health and well-being.[10] The etiology of this multifactorial disease is believed to involve a host–microbial interaction in dysbiosis, leading to tissue degradation and an increase in gum permeability (leaky gum) associated with chronic periodontitis.[11] Its prevalence ranges from 20% to 50% worldwide, and one of its etiological processes is a persistent inflammatory response triggered by various mediators. Furthermore, a number of systemic disorders have been associated with the microbial spread that occurs during periodontal infections.[12,13] Recent studies have identified a correlation between infectious oral diseases, such as periodontal disease, and chronic degenerative conditions, cardiovascular diseases, and autoimmune diseases.[14] In a recent study, Lanau et al. reported that patients with moderate to severe periodontitis had a threefold increased risk of elevated blood pressure measurements.[13]

To the best of our knowledge, there is only 1 published broad epidemiological study on the subject.[4] Dhanuthai et al. reported the prevalence of compromised medical conditions in 58,317 patients seeking dental treatment at the Faculty of Dentistry in Chulalongkorn University, Bangkok, Thailand, from 2002 to 2004.[4] To date, no previous epidemiological reports have been conducted on the systemic medical conditions present in adult patients attending a university or private dental clinic in Mexico. Thus, the present study aimed to determine the prevalence of systemic diseases among 82,363 dental school patients residing in San Luis Potosí, Mexico, from 2011 to 2019.

# Material and methods

## Study design and ethical considerations

The present cross-sectional study was conducted based on the electronic medical histories of patients registered at the Diagnostic Clinic at the Faculty of Dentistry of the Autonomous University of San Luis Potosí, Mexico, from February 2011 to October 2019. The study adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines[15] and considered several methodological aspects of similar investigations on disease prevalence that have been recently published.[13,16] Only complete files were reviewed for demographic information and the occurrence of self-reported systemic diseases. The study included the electronic clinical histories of adult patients (aged ≥18 years) who provided their complete medical information in accordance with the Official Mexican Standard NOM-004-SSA3-2012. The data of the patients was recorded with the use of Microsoft Visual Basic.NET software, v. 16.0 (Microsoft Corporation, Redmond, USA). The present study involved minimal risk for the participants and was conducted in accordance with the Declaration of Helsinki principles. All personal information was handled anonymously and confidentially. The exported data did not include the patient's name and address or any other type of personal information. The study protocol was previously reviewed and approved by the Faculty of Dentistry's Ethics and Investigation Committee (CEI-FE-026-021).

San Luis Potosí is a city located in the central region of Mexico, with an estimated population of 2,000,000

people. The Faculty of Dentistry at the Autonomous University of San Luis Potosí primarily serves patients from low socioeconomic strata who do not have access to private dental care. During their initial visit, patients are registered in the diagnostic clinic for a complete oral and medical examination. Undergraduate fifth-year dental students receive adequate training in conducting comprehensive clinical histories obtained through direct interviews as part of their academic curriculum. During this process, students are taught to collect information about systemic diseases, which are classified into 12 categories: gastrointestinal diseases; arterial hypertension; diabetes mellitus; psychiatric disorders; renal diseases; thyroid disorders; neurological disorders; cardiovascular diseases; cancer; sexually transmitted diseases; tuberculosis; and typhoid fever. In instances where a positive answer is obtained, the students inquire further about the medical condition and its management to establish whether any modifications to the dental treatment plan are required. Afterward, the digital signature of the patient is obtained to confirm the accuracy of the provided data. Finally, when the clinical history is completed, the patient undergoes an examination by the responsible physician. The record is then electronically stored until its subsequent use.

In accordance with the recommendations of the World Health Organization (WHO),[17] the extracted data from the clinical histories was categorized into 7 age groups (18–29, 30–39, 40–49, 50–59, 60–69, 70–79, and ≥80 years) to describe the demographic characteristics and systemic disease prevalence per group. Furthermore, we registered supplementary data concerning the primary motivations for seeking dental care, encompassing education level, type of settlement, body mass index (BMI), tobacco and/or alcohol consumption, and illegal drug use.

## Statistical analysis

The data was described and summarized using the mean (*M*), standard deviation (*SD*), ranges, frequencies, percentages, and confidence intervals (*CI*s). For the purpose of inferential statistics, the study population was categorized according to the age group and compared by sex using the Mann–Whitney non-parametric test for continuous variables. The $\chi^2$ test was used to evaluate the differences among categorical variables determined by patients' age. The data was exported to Microsoft Excel® (Microsoft Corporation) and analyzed using Stata 14 software (StataCorp LLC, College Station, USA).

# Results

The study participants were adult patients who provided complete data on their general health, age and sex. Sixty-five individuals were excluded due to incomplete information, and 9,815 individuals were under 18 years old. The final sample size of the study was 82,363 individuals.

## Demographic characteristics

A statistically significant difference was observed in the sex distribution across the age groups, with a higher percentage of female participants ($p < 0.001$) (Fig. 1). The mean age of the study population was 40.01 years (*SD* = 16.7; range = 18–107 years), while 62.6% (95% *CI*: 62.2–62.9) of the patients were female. Furthermore, 36.7% of the individuals reported having a bachelor's degree. The predominant type of settlement was urban (Table 1). The main reasons for seeking dental care were routine dental checkups, acute oral pain, infection, and dental rehabilitation (Table 2).

## General health status

The prevalence of overweight patients among individuals aged 30–79 years was observed to range between 40.0% and 44.5%. In the group aged ≥80 years, the prevalence was 39.0%. The majority of the participants denied smoking cigarettes, consuming alcohol, or illicit drugs (Table 3).

Among the study population, 13.1% (95% *CI*: 12.9–13.5) of participants reported the presence of more than 1 systemic disease. The overall prevalence of medical conditions was 39.1% (95% *CI*: 38.8–39.5), with the highest prevalence recorded in the year 2018 (41.1%; 95% *CI*: 40.2–42.1) (Fig. 2). The conditions reported most frequently were gastrointestinal diseases (16.5%; 95% *CI*: 16.2–16.8; gastritis was reported in 56% and colitis in 34%), arterial hypertension (14.1%; 95% *CI*: 13.8–14.3) and diabetes mellitus (8.6%; 95% *CI*: 8.4–8.8). Furthermore, a statistically significant difference was observed in the prevalence of systemic diseases between men and women ($p < 0.001$) (Table 4). The gastrointestinal diseases were reported among all age groups, while the prevalence of hypertension, diabetes mellitus and psychiatric disorders increased with the patient's age (Fig. 3).

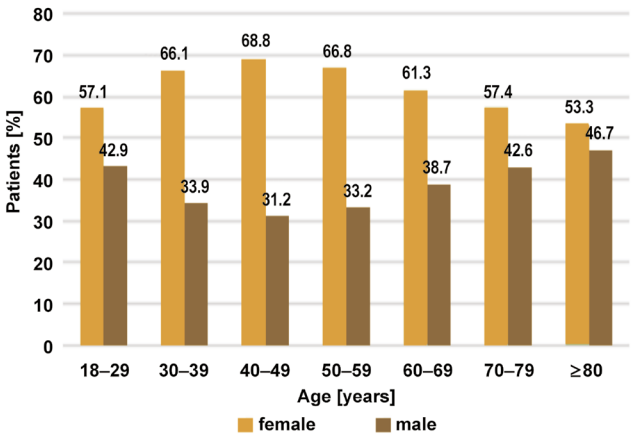



Fig. 1. Distribution of patients treated from 2011 to 2019 by age group and sex

**Table 1.** Descriptive characteristics of the study participants

| Variable | | Total | Age group [years] | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | 18–29 | 30–39 | 40–49 | 50–59 | 60–69 | 70–79 | ≥80 |
| Participants, *n* | | 82,363 | 28,839 | 13,896 | 15,461 | 12,220 | 7,394 | 3,520 | 1,033 |
| Age [years] *Me* | | 38 | 22 | 35 | 44 | 54 | 64 | 73 | 83 |
| Sex [%] | female | 62.6 | 57.1 | 66.1 | 68.8 | 66.8 | 61.3 | 57.4 | 53.3 |
| Education level *n* (%) | illiterate | 754 (0.9) | 25 (0.1) | 40 (0.3) | 82 (0.5) | 143 (1.1) | 187 (2.5) | 203 (5.8) | 74 (7.2) |
| | reads or writes | 78 (0.1) | 1 (0.0) | 1 (0.0) | 8 (0.1) | 10 (0.1) | 13 (0.2) | 34 (1.0) | 11 (1.1) |
| | elementary | 12,849 (15.6) | 723 (2.5) | 1,524 (11.0) | 2,392 (15.5) | 3,194 (26.1) | 2,924 (39.6) | 1,580 (44.9) | 512 (49.6) |
| | secondary (junior high school) | 18,440 (22.4) | 3,884 (13.5) | 4,596 (33.1) | 5,211 (33.7) | 2,922 (23.9) | 1,325 (17.9) | 415 (11.8) | 87 (8.4) |
| | high school | 17,131 (20.8) | 8,226 (28.5) | 3,118 (22.4) | 3,040 (19.7) | 1,749 (14.3) | 713 (9.6) | 239 (6.8) | 46 (4.4) |
| | bachelor's degree | 30,242 (36.7) | 15,558 (54.0) | 4,162 (30.0) | 4,325 (28.0) | 3,682 (30.0) | 1,728 (23.4) | 657 (18.7) | 130 (12.6) |
| | postgraduate | 1,221 (1.5) | 309 (1.1) | 353 (2.5) | 224 (1.4) | 220 (1.8) | 87 (1.2) | 21 (0.6) | 7 (0.7) |
| | unregistered | 1,648 (2.0) | 113 (0.4) | 102 (0.7) | 179 (1.2) | 300 (2.4) | 417 (5.6) | 371 (10.5) | 166 (16.1) |
| Human settlement *n* (%) | rural | 6,297 (7.6) | 1,552 (5.4) | 1,211 (8.7) | 1,268 (8.2) | 1,042 (8.5) | 733 (9.9) | 383 (10.9) | 108 (10.5) |
| | urban | 75,622 (91.8) | 27,149 (94.1) | 12,606 (90.7) | 14,110 (91.3) | 11,113 (90.9) | 6,606 (89.3) | 3,123 (88.7) | 915 (88.6) |
| | unregistered | 444 (0.5) | 138 (0.5) | 79 (0.6) | 83 (0.5) | 65 (0.5) | 55 (0.7) | 14 (0.4) | 10 (1.0) |

*Me* – median.

**Table 2.** Main reasons for dental consultations reported by the study participants (*N* = 82,363)

| Reason | Total | Age group [years] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 18–29 | 30–39 | 40–49 | 50–59 | 60–69 | 70–79 | ≥80 |
| Routine dental checkup | 26,373 (32.0) | 10,113 (35.1) | 4,265 (30.7) | 4,655 (30.1) | 3,758 (30.8) | 2,271 (30.7) | 1,026 (29.1) | 285 (27.6) |
| Prophylaxis/tooth whitening | 9,298 (11.3) | 6,239 (21.6) | 1,018 (7.3) | 1,058 (6.8) | 677 (5.5) | 220 (3.0) | 74 (2.1) | 12 (1.2) |
| Acute oral pain and/or infection | 24,293 (29.5) | 7,499 (26.0) | 5,203 (37.4) | 5,292 (34.2) | 3,628 (29.7) | 1,818 (24.6) | 693 (19.7) | 160 (15.5) |
| Dental rehabilitation | 22,145 (26.9) | 4,890 (17.0) | 3,379 (24.3) | 4,418 (28.6) | 4,115 (33.7) | 3,051 (41.3) | 1,717 (48.8) | 575 (55.7) |
| Others | 87 (0.1) | 47 (0.2) | 10 (0.1) | 9 (0.1) | 9 (0.1) | 11 (0.2) | 1 (0.03) | 0 (0.0) |
| Unregistered | 167 (0.2) | 51 (0.2) | 21 (0.2) | 29 (0.2) | 33 (0.3) | 23 (0.3) | 9 (0.3) | 1 (0.1) |

Data presented as frequency (percentage) (*n* (%)).

**Table 3.** Body mass index (BMI) and harmful habits of the participants (*N* = 82,363)

| Variable | | | Total | Age group [years] | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 18–29 | 30–39 | 40–49 | 50–59 | 60–69 | 70–79 | ≥80 |
| BMI | <18.50 | underweight | 2,254 (3.0) | 1,774 (6.0) | 162 (1.0) | 93 (1.0) | 80 (1.0) | 58 (0.8) | 43 (1.0) | 44 (4.0) |
| | 18.50–24.99 | normal weight | 30,375 (36.9) | 15,454 (54.0) | 4,584 (33.0) | 3,844 (24.9) | 2,983 (24.0) | 1,905 (26.0) | 1,160 (33.0) | 445 (43.0) |
| | 25.00–30.00 | overweight | 30,490 (37.0) | 7,849 (27.0) | 5,554 (40.0) | 6,669 (43.1) | 5,225 (43.0) | 3,290 (44.5) | 1,499 (42.6) | 404 (39.0) |
| | >30.00 | obese | 19,244 (23.4) | 3,762 (13.0) | 3,596 (26.0) | 4,855 (31.4) | 3,932 (32.0) | 2,141 (29.0) | 818 (23.2) | 140 (14.0) |
| Cigarette smoking | | yes | 13,682 (16.6) | 5,620 (19.5) | 2,392 (17.2) | 2,390 (15.5) | 1,922 (15.7) | 964 (13.0) | 339 (9.6) | 55 (5.3) |
| | | no | 68,681 (83.4) | 23,219 (80.5) | 11,504 (82.8) | 13,071 (84.5) | 10,298 (84.3) | 6,430 (87.0) | 3,181 (90.4) | 978 (94.7) |
| Alcohol consumption | | yes | 14,866 (18.0) | 7,462 (25.9) | 2,379 (17.1) | 2,125 (13.7) | 1,566 (12.8) | 885 (12.0) | 367 (10.4) | 82 (7.9) |
| | | no | 67,497 (82.0) | 21,377 (74.1) | 11,517 (82.9) | 13,336 (86.3) | 10,654 (87.2) | 6,509 (88.0) | 3,153 (89.6) | 951 (92.1) |
| Illegal drug use | | yes | 621 (0.8) | 404 (1.4) | 93 (0.7) | 62 (0.4) | 42 (0.3) | 15 (0.2) | 4 (0.1) | 1 (0.1) |
| | | no | 81,742 (99.2) | 28,435 (98.6) | 13,803 (99.3) | 15,399 (99.7) | 12,178 (99.7) | 7,379 (99.8) | 3,516 (99.9) | 1,032 (99.9) |

Data presented as frequency (percentage) (*n* (%)).

**Table 4.** Prevalence of diseases among the study participants

| Disease | Patients | | Gender | | | | |
|---|---|---|---|---|---|---|---|
| | [%] | 95% *CI* | female [%] | 95% *CI* | male [%] | 95% *CI* | *p*-value |
| Total | 39.10 | 38.79–39.46 | 43.90 | 43.46–44.32 | 31.20 | 30.63–31.67 | <0.001* |
| Gastrointestinal diseases | 16.50 | 16.25–16.76 | 19.80 | 19.46–20.15 | 10.98 | 10.63–11.33 | <0.001* |
| Arterial hypertension | 14.06 | 13.82–14.30 | 15.37 | 15.06–15.68 | 11.88 | 11.62–12.24 | <0.001* |
| Diabetes mellitus | 8.58 | 8.40–8.77 | 8.94 | 8.70–9.19 | 7.98 | 7.70–8.29 | <0.001* |
| Psychiatric disorders | 4.11 | 3.97–4.25 | 5.25 | 5.06–5.45 | 2.19 | 2.03–2.36 | <0.001* |
| Renal diseases | 3.08 | 2.97–3.21 | 3.07 | 2.93–3.22 | 3.11 | 2.91–3.31 | 0.764 |
| Thyroid disorders | 2.91 | 2.80–3.03 | 4.23 | 4.01–4.41 | 0.70 | 0.06–0.08 | <0.001* |
| Neurological disorders | 2.43 | 2.32–2.54 | 2.88 | 2.74–30.29 | 1.67 | 1.53–1.82 | <0.001* |
| Cardiovascular diseases | 2.27 | 2.20–2.40 | 2.19 | 2.06–2.32 | 2.41 | 2.24–2.59 | <0.005* |
| Cancer | 1.32 | 1.24–1.40 | 1.61 | 1.50–1.71 | 0.83 | 0.07–0.94 | <0.001* |
| Sexually transmitted diseases | 1.01 | 0.94–1.08 | 1.23 | 1.13–1.33 | 0.65 | 0.57–0.75 | <0.001* |
| Tuberculosis | 0.70 | 0.64–0.76 | 0.81 | 0.74–0.89 | 0.51 | 0.44–0.60 | <0.001* |
| Typhoid fever | 0.36 | 0.32–0.40 | 0.44 | 0.38–0.50 | 0.22 | 0.17–0.28 | <0.001* |

*CI* – confidence interval; * statistically significant ($p < 0.05$, Mann–Whitney non-parametric test).

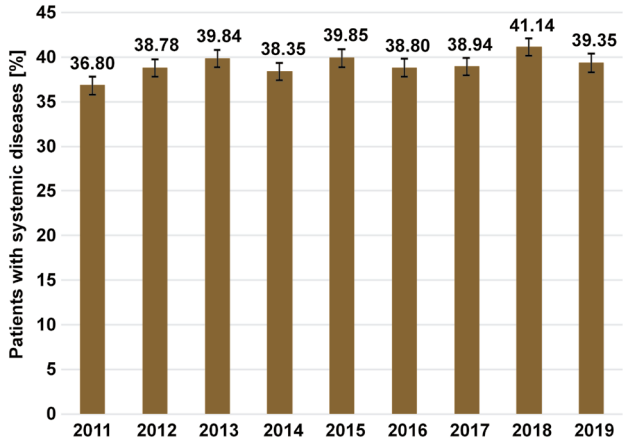
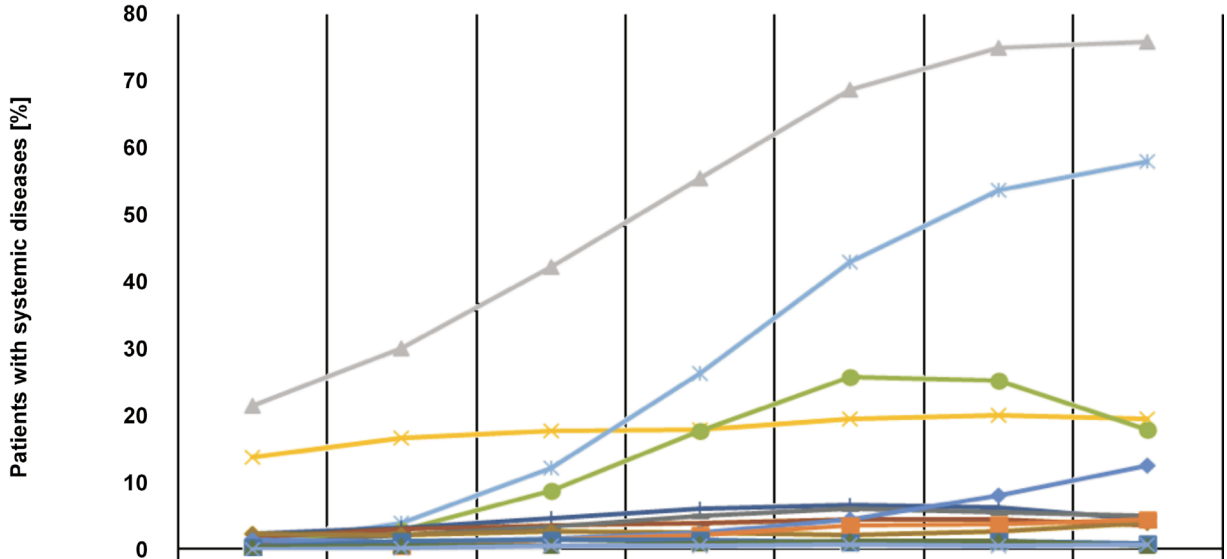



Fig. 2. Overall prevalence of systemic diseases self-reported by the patients from 2011 to 2019

## Discussion

Dentists must be prepared to treat patients with different medical conditions, as these become more and more prevalent among individuals seeking dental care. The ability to identify patients with systemic diseases and compromised conditions that can have an impact on, and be influenced by, oral health care is becoming an increasingly important task for dentists, dental students and other oral healthcare practitioners. Prior to commencing any dental procedures, it is imperative to conduct a comprehensive history and physical examination to identify patients with potentially compromised conditions that may not be evident. To ensure optimal and safe oral care, dental management must be adapted to account for these systemic diseases. Medically fragile individuals require special attention during the prescription process to avoid potential interactions with other medications they are concomitantly taking.[3]

To the best of our knowledge, the present work is the first cross-sectional epidemiological study conducted in Mexico to determine the prevalence of self-reported medical conditions in patients seeking dental treatment over a period of 9 years. Our study was conducted on 82,363 participants, which, to the best of our knowledge, constitutes the highest number of patients reported in a single study to date. The global prevalence of systemic diseases found in our study was 39.1%, which is very similar to that previously reported by Javali et al.[2] In a study conducted in Saudi Arabia in 2017, the authors reported a global prevalence of 40.1%.[2] However, our findings do not concur with those reported by Bhateja in 2012.[3] The author found a systemic disease prevalence of 1.02% in patients requesting dental treatment at the Hospital of Mathura City (India).[3] However, Bhateja's research was conducted for 2 years only, on a total study population of 36,729 patients, which is smaller than that of the present study. According to the findings of another study, the prevalence of systemic diseases in dental patients tends to vary depending on the site at which the patients receive dental care.[18] For example, some studies on the prevalence of systemic diseases in private dental offices have reported a prevalence of 27.6%, while in dentistry schools, the prevalence has been situated between 46.3% and 74.1%. The highest prevalence has been observed in dental clinics and hospital settings.[19–22] This variation can be attributed to the higher proportion of older adults receiving dental care in a hospital setting, accompanied by an evident increase in associated comorbidities.[18] The prevalence of systemic diseases in older adults aligns with our findings, wherein 75.9% of the adults aged ≥80 and attending clinics at our faculty presented any type of comorbidity. The prevalence of systemic diseases observed in older patients aligns with a report describing




| | 18–29 years | 30–39 years | 40–49 years | 50–59 years | 60–69 years | 70–79 years | ≥80 years |
|---|---|---|---|---|---|---|---|
| Total | 21.6 | 30.1 | 42.3 | 55.5 | 68.7 | 75.0 | 75.9 |
| Gastrointestinal diseases | 13.8 | 16.7 | 17.7 | 18.0 | 19.5 | 20.1 | 19.5 |
| Arterial hypertension | 0.8 | 4.1 | 12.2 | 26.3 | 43.0 | 53.8 | 58.0 |
| Diabetes mellitus | 0.5 | 3.0 | 8.8 | 17.7 | 25.9 | 25.3 | 18.0 |
| Psychiatric disorders | 2.4 | 3.2 | 4.7 | 6.1 | 6.6 | 6.4 | 4.5 |
| Renal diseases | 1.9 | 3.1 | 3.5 | 4.0 | 4.6 | 4.6 | 3.6 |
| Thyroid disorders | 0.8 | 2.2 | 3.5 | 5.1 | 6.1 | 5.7 | 5.1 |
| Neurological disorders | 2.3 | 2.1 | 2.7 | 2.6 | 2.3 | 2.7 | 4.0 |
| Cardiovascular diseases | 1.4 | 1.1 | 1.6 | 2.5 | 4.6 | 8.0 | 12.5 |
| Cancer | 0.2 | 0.6 | 1.4 | 2.3 | 3.6 | 3.8 | 4.6 |
| Sexually transmitted diseases | 0.4 | 1.3 | 1.4 | 1.4 | 1.2 | 1.4 | 0.9 |
| Tuberculosis | 0.4 | 0.6 | 0.7 | 1.0 | 1.3 | 1.2 | 0.6 |
| Typhoid fever | 0.1 | 0.2 | 0.5 | 0.7 | 0.7 | 0.6 | 0.8 |

Fig. 3. Prevalence of systemic diseases stratified by type and age group

that significant changes in health occur with aging, including geriatric syndromes, cardiovascular disease, osteoporosis, and dementia, the most common chronic degenerative diseases in the ≥80-year-old group.[19]

In the present study, the most prevalent systemic conditions were gastrointestinal diseases (16.5%), arterial hypertension (14.1%) and diabetes mellitus (8.6%). Previous studies have reported variable frequencies for systemic diseases in adult patients seeking dental care.[13,14] For instance, Parirokh et al. reported a higher prevalence of cardiovascular diseases, hypertension, allergies, and neurological disorders.[20] Similarly, Al-Bayaty et al. identified hypertension, diabetes mellitus and asthma as the most common conditions,[21] while Dhanuthai et al. reported allergies, hypertension and diabetes as the most prevalent.[4] Smeets et al. reported hypertension and cardiovascular diseases, neurological conditions, and endocrine conditions as the most common.[22] Other related systemic conditions mentioned in the literature include pulmonary infections, liver diseases, ankylosing spondylitis, rheumatoid arthritis, pre-eclampsia, and preterm low birth weight.[12,14] These differences are possibly due to each study population's characteristics, such as diet, education level and geographical region. Gastrointestinal diseases, predominantly gastritis or dyspepsia, emerged as the most prevalent comorbidities in our study population (16.5%), exhibiting variation according to age group. The prevalence of gastrointestinal diseases was particularly high among the 18–49 age group. Additionally, approx. 15–54% of the studied population exhibited dyspepsia symptoms, whereas the relative frequency of this condition in Mexico has been documented to be 8.5% among individuals aged 15.0–37.9 years. Dyspepsia predominates in the female population (65.5%).[23] The significant prevalence of this condition observed in our study can be attributed to the broad age range of the study population, which spanned from 18 to >80 years. In this regard, dyspepsia is the most commonly self-reported comorbidity among young adults, and its prevalence increases with age. Individuals over 70 years of age

exhibit the highest incidence of gastrointestinal diseases, including diabetes mellitus and arterial hypertension. The increased prevalence of gastrointestinal diseases in this age group may be attributable to the use of pharmacological treatments for other chronic medical conditions.[4] It should be noted that dyspepsia exhibits a higher frequency among young adults, which may be due to lifestyle risk factors, including a diet high in fat and refined sugars, as well as stress and addictive behaviors, such as alcoholism (25.8%) and tobacco use (19.4%). In the present study, the disorder was the most prevalent among individuals aged 18–29. This fact should also be noted in the context of the prescription of non-steroidal anti-inflammatory drugs (NSAIDs) in dental practice, with a 41% prevalence of NSAID prescriptions among dental treatments.[24] These medications have the potential to exert a direct impact on the digestive tract. The adverse effects of NSAIDs on the gastrointestinal mucosa are well-documented, and are due to the gastric irritation caused by the inhibition of prostaglandins.[25] Therefore, the use of COX-2 selective NSAIDs has been recommended as a substitute medication.[26] Although it is usually difficult to ascertain the exact type of a gastrointestinal condition, colitis was self-reported by 34% of the patients. Irritable bowel syndrome is the other common condition in Mexico, with a prevalence of 35.5%.[23] This disorder is most common in young people and women, which aligns with our data. While the etiology of this condition is multifactorial, the role played by bacterial overgrowth or dysbiosis is significant in the alteration of the gut–brain axis.[27] Dysbiosis causes the intestinal permeability, with the release of toxins and pro-inflammatory cytokines, generating a chronic inflammatory state.[27] Recent studies have established an association between the intestinal permeability and chronic degenerative conditions, such as diabetes mellitus, hypertension and autoimmune diseases.[27] Thus, it is of great importance that these disorders are early recognized and disclosed, given that they increase the risk of developing other comorbidities as patients age. Arterial hypertension was the second most prevalent comorbidity, predominantly observed among adults over 60 years of age. Additionally, type II diabetes mellitus was identified as the second most common condition, primarily affecting individuals in the 60–69 years age group. These findings are consistent with the Mexico National Survey of Health and Nutrition 2018 (ENSANUT).[28]

In the present study, the prevalence of comorbidities was higher in women than in men (43.9% vs. 31.2%), possibly due to the higher number of female patients seeking dental care at the faculty. This finding aligns with the data reported by ENSANUT in 2018, which indicated that women tend to use health services more frequently, both as outpatients (7.6%) and inpatients (5.8%).[28] In terms of the risk of developing systemic diseases by sex, the main influencing factors include the following: biological factors (genetic, physiological and hormonal); higher life expectancy in women; changes in the proportion of men participating in women's labor; differences in women's access to social protection; cultural norms and religious and familial beliefs that determine gender behavior and roles; gender differences in education level; and income differences.[29–33]

Among patients seeking dental care, 37.0% were overweight, a finding which concurs with the 39.1% prevalence reported by ENSANUT.[28] The prevalence of obesity in our sample was lower (23.4%) than that reported by ENSANUT, which was estimated at 36.1%. San Luis Potosí is a Mexican state with a 16.7% prevalence of obesity, while other states, such as Veracruz, Quintana Roo, Colima, Sonora, and Tabasco have a higher prevalence of obesity.[28] It is important to note that overweight or obese patients are at a greater risk of presenting comorbidities,[34] with a high percentage being unaware of their own health status. For this reason, a comprehensive clinical history and review of systems by the dentist are of great importance, along with laboratory tests, to ascertain the patient's overall health status.

To lessen their influence on the environment, dentists have recently adopted several eco-friendly practices. Green dentistry is a modern concept that uses technology and ecological practices to promote pollution control and environmental sustainability. The primary goals of green dentistry include the utilization of technology, the recycling of dental materials, and the reduction of energy, water and radiation usage. The oral care segment of the green dentistry personal care market, which has shown exponential growth over the past 25 years, is predominantly driven by this need. According to Mazur et al., the criteria for categorizing a product as "green dentistry" include the following: the use of substances of natural origin characterized by ecological and skin compatibility as well as good aquatic toxicity performance; the absence of genetically modified organisms in the finished product or its components; the use of natural fragrances (e.g., essential oils); the use of biodegradable detergents and surfactants; the absence of ionizing radiation; and the use of natural substances originating from controlled organic farming certified by a recognized institution.[35] Biomaterials have numerous applications in various dental specialties for the restoration of the masticatory system.[36] For example, natural polymer coatings are frequently employed in oral surgery, periodontics and other dental specialties (e.g., chitosan, a marine polymer with a linear aminopolysaccharide structure). Furthermore, they have been increasingly used as a matrix for drug delivery.[36]

In consideration of the study's limitations, it is important to acknowledge that in developing countries, a significant proportion of patients do not undergo routine medical checkups. Consequently, there is a possibility that asymptomatic patients with chronic comorbidities, such as diabetes mellitus, thyroid disorders and cardiovascular diseases, are unaware of their health status. On the other hand, the study's main strength lies in the meticulous

examination of 82,363 patient records, encompassing a 9-year period. This extensive data set provides a reliable foundation for analysis and reflects the health situation in the study population. The findings of this study may serve as a basis for the enhancement of undergraduate and postgraduate dentistry curricula, with the aim of effectively training students in the delivery of dental care and reducing the likelihood of adverse effects during dental treatment. Furthermore, the findings may contribute to the formulation of enhanced public health prevention policies.

Numerous epidemiological studies and systematic reviews have extensively defined and documented the relationship between dental health and general health. A multitude of systemic disorders have been associated with oral infections, including periodontal disease.[12] Affected patients often demonstrate worse oral hygiene, compromised dental and periodontal health, and increased bleeding, gingival inflammation and periodontal pocket depth. Additionally, the enhancement of oral hygiene and the initiation of non-surgical periodontal therapy have been demonstrated to attenuate the severity of systemic diseases.[12–14] Dental caries is recognized as a multifactorial disease, implying that a variety of factors, including an individual's systemic state, may contribute to its development. Therefore, the literature has consistently supported the multimodal therapy for dental caries. Determining an individual's caries risk is essential for effective management and prevention, as well as for offering feasible justifications and recommendations.[37] Thus, patients who are medically compromised require a more thorough evaluation, necessitating a deeper understanding of their medical condition. Consequently, it is necessary to expand the scope of medical education programs in dental institutions. Expanding courses in pharmacology, medical emergencies, and the care of medically impaired patients should be mandatory for dental schools. These topics should be also emphasized in continuing education programs. A comprehensive curriculum transformation is imperative in the field of dentistry, with a shift toward a more medically focused dental education. Dental educators should reevaluate their educational materials and methodologies concerning systemic diseases and pharmaceutical agents.

It is recommended that the present study be continued by extending, for periods of approx. 5 years, the analysis undertaken on the medical records of patients requesting dental care. This will allow for the identification of possible changes in the prevalence of systemic comorbidities. The rationale underlying this approach is that the collected data can be used to develop additional epidemiological reports and studies exclusively for older adults, focusing on the primary diseases affecting the oral cavity. The electronic record serves as a crucial repository for data, which is instrumental in enhancing the training and education of dental students, ultimately contributing to the improvement of the overall health of the general population.

# Conclusions

A third of the registered cases exhibited associated comorbidities. Therefore, it is necessary for dental undergraduate students to receive adequate training to facilitate a more precise and timely diagnosis of systemic diseases as part of the dental care protocol for adult patients.

## Ethics approval and consent to participate

The present study involved minimal risk for the participants and was conducted in accordance with the Declaration of Helsinki principles. All personal information was handled anonymously and confidentially. The study protocol was approved by the Faculty of Dentistry's Ethics and Investigation Committee, Autonomous University of San Luis Potosí, Mexico (CEI-FE-026-021).

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.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Original paper

# Effect of non-surgical periodontal therapy on the salivary levels of IL-18 and IL-35 in patients with periodontitis

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## Abstract

**Background.** Periodontal disease is the most prevalent chronic inflammatory condition that can cause the destruction of supporting periodontal tissues. It has been hypothesized that while the synthesis of pro-inflammatory cytokines causes tissue destruction and disease progression, anti-inflammatory cytokine production can result in protective immunity. The balance of inflammatory cytokines is central to the immunoregulation of the disease.

**Objectives.** The aim of the study was to assess and compare the salivary levels of interleukin (IL)-18 and IL-35 in subjects diagnosed with gingivitis, periodontitis, and healthy individuals. Additionally, the study sought to evaluate the difference in the concentration of IL-18 and IL-35 after non-surgical periodontal therapy (NSPT) in subjects diagnosed with periodontal disease.

**Material and methods.** A total of 69 individuals were divided into 3 groups: healthy (group 1; $n = 23$); gingivitis (group 2; $n = 23$); and stage II periodontitis (group 3A; $n = 23$). Saliva samples were obtained from each participant at baseline and, in the periodontitis group, at baseline and 12 weeks after NSPT (group 3B; $n = 23$). Probing pocket depth (PD), bleeding on probing (BoP), gingival index (GI), and clinical attachment level (CAL) were recorded and IL-18 and IL-35 levels were analyzed using an enzyme-linked immunosorbent assay (ELISA).

**Results.** The mean salivary level of IL-18 was significantly higher in the gingivitis group compared to the other groups ($p < 0.05$), whereas the mean IL-35 level was significantly higher in the healthy group compared to the other groups ($p < 0.05$). Twelve weeks after NSPT, the periodontitis group demonstrated a statistically significant difference in cytokine levels, characterized by a decline in the IL-18 concentration (229.63 ±49.35 pg/mL) and an increase in the concentration of IL-35 (29.47 ±17.88 pg/mL).

**Conclusions.** In the present study, a significant difference in the salivary levels of IL-18 and IL-35 before and after NSPT was observed. Therefore, these cytokines could serve as potential inflammatory biomarkers.

**Keywords:** cytokines, interleukin-35, periodontitis, interleukin-18, human enzyme-linked immunosorbent assay

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## Highlights

- Cytokine balance is a critical factor in the immunoregulation of periodontal disease.
- Anti-inflammatory cytokines contribute to a protective immune response and help prevent or limit the progression of periodontal disease.
- Results suggest that IL-18 and IL-35 could serve as potential inflammatory biomarkers.

# Introduction

Periodontal disease is the most prevalent inflammatory condition that can cause the destruction of supporting periodontal tissues.[1] Gingivitis can revert to its original state of health; however, a patient diagnosed with periodontitis remains with the condition even after successful treatment and requires supportive periodontal care.[2] Periodontitis is clinically diagnosed by measuring probing pocket depth (PD), clinical attachment level (CAL), bleeding on probing (BoP), and radiographic evaluation, often after the destruction of connective tissue and bone.[3] Biomarkers can quantify and analyze accurately the signs of normal biological or pathogenic processes or identify objectively physiological responses to a therapeutic intervention.[4] Circulating molecules are putative disease biomarkers that are present in whole saliva and gingival crevicular fluid (GCF) of patients diagnosed with periodontal disease at elevated concentrations.[5]

Every aspect of immunity and inflammation, including antigen presentation, bone marrow differentiation, cellular attraction and activation, transcription of adhesion molecules, and acute phase reactions, involves cytokines.[6] The synthesis of pro-inflammatory cytokines has been observed to be a primary driver of tissue destruction and disease progression. However, the production of anti-inflammatory cytokines can result in the establishment of protective immunity.[7,8] Some cytokines function primarily to induce inflammation and are referred to as pro-inflammatory cytokines. Conversely, anti-inflammatory cytokines play a role in the suppression of their action.[9] In the context of periodontal pathogenesis, the inflammatory activity is regulated due to the coexistence of pro- and anti-inflammatory cytokines, suggesting its destructive and protective immune mechanisms.[10]

Interleukin (IL)-18 is a pro-inflammatory cytokine that belongs to the IL-1 superfamily due to its expression in chronic inflammation and autoimmune diseases. It is recognized as the regulator of immune responses.[11,12] Interleukin-18 levels are elevated in GCF, saliva, serum, and gingival tissue samples from individuals with periodontal disease. The cytokine has been demonstrated to modulate inflammation by stimulating Th1 and Th2 cell responses.[13–15] Studies have reported increased concentrations of IL-18 in GCF of individuals with periodontitis compared to healthy individuals, and its decrease in concentration after initial periodontal therapy.[16] Thus, the expression of IL-18 in saliva can relatively signify its importance in the regulation of immune response in gingival inflammation.

Interleukin-35 is a novel anti-inflammatory signal molecule that mediates immunosuppression.[17] Some researchers have demonstrated the immunomodulatory response of IL-35 in various conditions.[18] Hence, an increase in the IL-35 levels plays a crucial role in the suppression of periodontal inflammation and is indicative of its potential as a biomarker in maintaining periodontal health.

A paucity of research has been conducted on the salivary levels of IL-18 and IL-35 in healthy patients, as well as in individuals with gingivitis and periodontitis.[16,18] A limited number of studies have investigated the difference in cytokine levels in periodontitis patients before and after non-surgical periodontal therapy (NSPT).[19] This study aims to assess and compare the salivary levels of IL-18 and IL-35 among individuals with gingivitis, periodontitis, and in healthy patients. Additionally, the study will evaluate the effect of NSPT on IL-18 and IL-35 levels in patients diagnosed with periodontitis.

# Material and methods

## Data collection

Each patient underwent a comprehensive oral examination. Socioeconomic demographic data, sex, age, and medical and dental history were recorded using structured proformas. The study participants were recruited from the Department of Periodontology at A B Shetty Memorial Institute of Dental Sciences, NITTE (Deemed to be University), Mangaluru, India. Prior to the initiation of the study, ethical approval was obtained from the Central Ethics Committee (NITTE) (Cert. No. ABSM/EC/114/2021). The study was registered with the Clinical Trials Registry – India (CTRI) under the identification No. CTRI/2021/12/038961. Written informed consent was obtained from all study participants. A total of 69 subjects were recruited for the study and subsequently categorized into 3 distinct groups: group 1 (healthy; $n$ = 23); group 2 (gingivitis; $n$ = 23); and group 3A (stage II periodontitis; $n$ = 23). Saliva

samples of 5 mL were collected from all study participants, and routine scaling procedures were performed on each subject. In group 3A, NSPT was performed, and the results were recalled after 12 weeks (group 3B (post-treatment)) to evaluate clinical parameters. Five milliliters of saliva sample were collected for the estimation of cytokine levels.

## Clinical parameters

The UNC 15 probe was used to assess various periodontal health parameters at all sites, namely PD, CAL, gingival index (GI) (Löe and Silness, 1963),[20] and BoP. The inclusion criteria for the study encompassed systemically healthy male and female patients aged 20–45 years with a minimum of 20 teeth present and who were non-smokers. The study excluded patients with less than 20 teeth, pregnant or lactating women, and menopausal women. The subjects who had undergone periodontal therapy within the preceding 6 months, patients with diabetes, hypertension, or other systemic diseases, and patients who were taking any medications were also excluded from the study.

## Criteria for diagnosis

The flowchart of the study is presented in Fig. 1. The participants were divided into 3 groups according to the American Academy of Periodontology (AAP) 2017 Classification of Periodontal and Peri-Implant Diseases and Conditions.[21] Subjects with GI ≤ 1, PD ≤ 3 mm and BoP ≤ 10% were categorized as periodontally healthy (group 1). Patients with GI > 1, PD ≥ 3 mm and BoP ≥ 10% were diagnosed with gingivitis (group 2). Individuals with GI > 1, CAL ≥ 3 mm and PD ≤ 5 mm were classified as having stage II periodontitis (group 3). Group 3 was further subdivided into group 3A (before NSPT) and group 3B (after NSPT), as subjects with stage II periodontitis underwent NSPT i.e., scaling and root planing (SRP) (Fig. 2), and were recalled after 12 weeks for the assessment of periodontal health parameters and saliva sample collection.

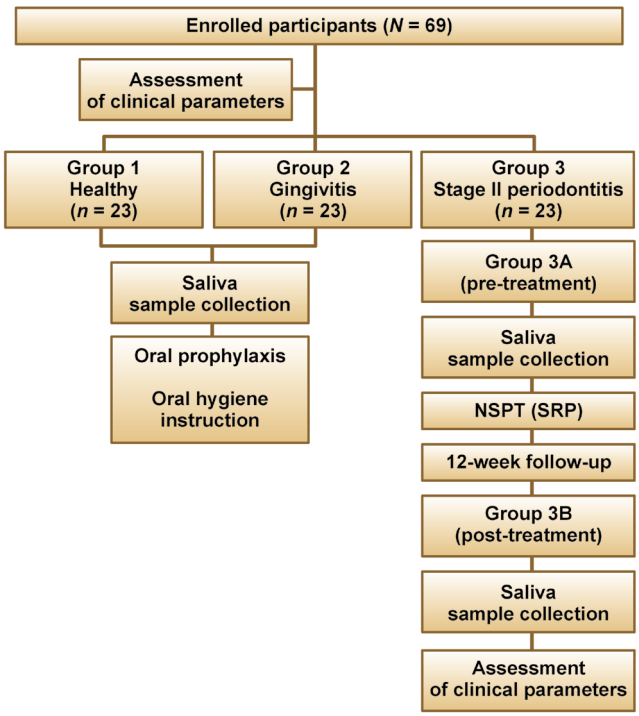


**Fig. 1.** Flowchart of the study
NSPT – non-surgical periodontal therapy; SRP – scaling and root planing.

## Saliva sample collection

The study participants were instructed to abstain from drinking and eating for 1 h prior to the collection of saliva samples. Participants were directed to sit comfortably in a quiet, enclosed space and thoroughly rinse their mouths with distilled water to ensure the removal of any food particles. They were then advised to adopt an upright posture with their heads in a lowered position, allowing the saliva to drip passively from the lower lip. Unstimulated whole saliva (5 mL) was collected into a graduated sterile container.

## Analysis of IL-18 and IL-35 levels

Salivary levels of IL-18 and IL-35 were analyzed using a commercially available human enzyme-linked immunosorbent assay (ELISA) (Krishgen Biosystems, Cerritos, USA) at Central Research Lab of K.S. Hegde Medical Academy (NITTE). The centrifugation process was executed at a speed of 3,000 rpm for 10 min to remove cells and debris. The supernatant obtained was then transferred into a microcentrifuge tube in 0.5-mL aliquots. The samples were stored at –80°C until further analysis. The salivary concentrations of IL-18 and IL-35 were measured in each subject using human ELISA kits (Krishgen Biosystems) specific for each analyte, according to the manufacturer's instructions.

**Fig. 2.** Scaling and root planing

## Sample size calculation

In this interventional study, the calculation of sample size for one-way analysis of variance (ANOVA) was performed using the following formula (Equation 1):

$$n = \frac{2(Z1-\alpha/2xk + Z1-\beta)^2 \times \sigma^2}{d^2} \quad (1)$$

where:
Z – confidence interval;
x – number of subjects;
k – number of groups;
σ – standard deviation (*SD*) = 0.925;
d – margin of error = 1; and
α, β – probabilities used to evaluate the results of the hypothesis.

The groups were compared at a 5% level of significance, with Z1–α/2xk = 2.39, and Z1–β = 1.28 (at 90% power).

The sample size required for the study was 23 subjects per group, resulting in a total of 69 subjects from groups 1, 2 and 3 being evaluated.

## Statistical analysis

The descriptive data was expressed as mean (*M*) ±*SD*. A *p*-value of <0.05 was considered statistically significant. The $\chi^2$ test was performed to analyze subjects based on age, sex, occupation, and address. To compare IL-35 and IL-18 concentrations across different groups, the Kruskal–Wallis ANOVA test was carried out. Additionally, the Mann–Whitney *U* test was conducted for intergroup analysis. The Wilcoxon signed-rank test was used to compare the cytokine concentrations in saliva among groups 3A and 3B (non-normal distribution). The data was analyzed using nMaster Software, v. 2 (https://nmaster.software.informer.com/2.0/).

# Results

There was no statistically significant association among the 3 groups based on age, sex, occupation, and type of settlement (Table 1). A comparison of IL-18 and IL-35 concentrations between healthy individuals, patients with gingivitis and stage II periodontitis (pre-treatment) exhibited the highest mean IL-18 levels in the gingivitis group (307.21 ±80.96 pg/mL) and the highest mean IL-35 levels in the healthy group (139.96 ±91.29 pg/mL) (Table 2). The mean differences (*MD*s) between groups 1 and 2 and between groups 1 and 3A were found to be –126.80 and –121.34, respectively. A statistically significant *MD* of 5.47 was reported between groups 2 and 3A (Table 3). A comparison of IL-18 and IL-35 levels between the pre- and post-treatment groups revealed a reduction in IL-18 levels, accompanied by an increase in mean IL-35 levels post-treatment. These values were statistically significant (Table 4). The observed and expected probing PD, GI, BoP, and CAL between the 3 groups were analyzed using the Kruskal–Wallis test (Table 5). Marked differences in clinical parameters were identified in GI, PD and BoP in group 1 when compared with groups 2 (–1.03; –0.58; –10.00), 3A (–1.10; –1.09; –9.69) and 3B (–0.02; –0.30; 1.69). The *MD*s observed between group 2 and group 3A as well as group 3B were statistically significant (GI: –0.08; PD: –0.51; BoP: 0.30 and GI: 1.01; PD: 0.28; BoP: 11.69, respectively) (Table 6).

**Table 1.** Distribution of subjects based on demographic data

| Variable | | Group | | | | Total | *p*-value ($\chi^2$ test) |
|---|---|---|---|---|---|---|---|
| | | healthy | gingivitis | stage II periodontitis (pre-treatment) | stage II periodontitis (post-treatment) | | |
| Sex | female | 16 (69.6) | 11 (47.8) | 9 (39.1) | 9 (39.1) | 45 (48.9) | 0.131 |
| | male | 7 (30.4) | 12 (52.2) | 14 (60.9) | 14 (60.9) | 47 (51.1) | |
| Age [years] | 20–30 | 21 (91.3) | 10 (43.5) | 4 (17.4) | 4 (17.4) | 39 (42.4) | 0.359 |
| | 31–40 | 2 (8.7) | 10 (43.5) | 10 (43.5) | 10 (43.5) | 32 (34.8) | |
| | ≥41 | 0 (0.0) | 3 (13.0) | 9 (39.1) | 9 (39.1) | 21 (22.8) | |
| Occupation | businessman | 0 (0.0) | 2 (8.7) | 7 (30.4) | 7 (30.4) | 16 (17.4) | 0.137 |
| | employed | 9 (39.1) | 8 (34.8) | 10 (43.5) | 10 (43.5) | 37 (40.2) | |
| | housewife | 3 (13.0) | 3 (13.0) | 4 (17.4) | 4 (17.4) | 14 (15.2) | |
| | IT | 0 (0.0) | 2 (8.7) | 0 (0.0) | 0 (0.0) | 2 (2.2) | |
| | student | 11 (47.8) | 7 (30.4) | 2 (8.7) | 2 (8.7) | 22 (23.9) | |
| | teacher | 0 (0.0) | 1 (4.3) | 0 (0.0) | 0 (0.0) | 1 (1.1) | |
| Settlement | rural | 5 (21.7) | 10 (43.5) | 16 (69.6) | 16 (69.6) | 47 (51.1) | 0.200 |
| | urban | 18 (78.3) | 13 (56.5) | 7 (30.4) | 7 (30.4) | 45 (48.9) | |

Data presented as frequency (percentage) (*n* (%)).

**Table 2.** Comparison of interleukin (IL)-18 and IL-35 levels between the study groups

| Group | IL-18 [pg/mL] *M* ±*SD* | *p*-value | IL-35 [pg/mL] *M* ±*SD* | *p*-value |
|---|---|---|---|---|
| Healthy (*n* = 23) | 180.40 ±53.85 | | 139.96 ±91.29 | |
| Gingivitis (*n* = 23) | 307.21 ±80.96 | 0.001* | 33.14 ±15.77 | 0.001* |
| Stage II periodontitis (pre-treatment) (*n* = 23) | 301.74 ±50.18 | | 23.93 ±18.26 | |

* statistically significant ($p < 0.05$, Kruskal–Wallis test); *M* – mean; *SD* – standard deviation.

**Table 3.** Results of the intergroup analysis for interleukin (IL)-18 and IL-35

| Group | | IL-18 *MD* | *p*-value | IL-35 *MD* | *p*-value |
|---|---|---|---|---|---|
| Healthy (*n* = 23) | gingivitis (*n* = 23) | −126.80 | 0.001* | 106.82 | 0.0001* |
| | stage II periodontitis (pre-treatment) (*n* = 23) | −121.34 | 0.001* | 116.04 | 0.0001* |
| Gingivitis (*n* = 23) | stage II periodontitis (pre-treatment) (*n* = 23) | 5.47 | 0.0001* | 9.22 | 0.002* |

* statistically significant ($p < 0.05$, Mann–Whitney *U* test); *MD* – mean difference.

**Table 4.** Comparison of interleukin (IL)-18 and IL-35 levels between the pre- and post-treatment groups

| Stage II periodontitis group | IL-18 [pg/mL] *M* ±*SD* | *p*-value | IL-35 [pg/mL] *M* ±*SD* | *p*-value |
|---|---|---|---|---|
| Pre-treatment (baseline) (*n* = 23) | 301.74 ±50.18 | 0.002* | 23.93 ±18.26 | 0.002* |
| Post-treatment (3 months) (*n* = 23) | 229.63 ±49.35 | | 29.47 ±17.88 | |

* statistically significant ($p < 0.05$, Wilcoxon signed-rank test).

**Table 5.** Comparison of clinical parameters between the study groups

| Group | PD [mm] *M* ±*SD* | *p*-value | GI *M* ±*SD* | *p*-value | BoP [mm] *M* ±*SD* | *p*-value | CAL [mm] *M* ±*SD* | *p*-value |
|---|---|---|---|---|---|---|---|---|
| Healthy (*n* = 23) | 1.74 ±0.25 | | 0.44 ±0.29 | | 4.78 ±2.37 | | – | |
| Gingivitis (*n* = 23) | 2.32 ±0.21 | | 1.46 ±0.17 | | 14.78 ±1.67 | | – | |
| Stage II periodontitis (pre-treatment) (*n* = 23) | 2.83 ±0.30 | 0.0001* | 1.54 ±0.17 | 0.0001* | 14.48 ±2.23 | 0.001* | 1.54 ±0.17 | 0.002* |
| Stage II periodontitis (post-treatment) (*n* = 23) | 2.05 ±0.25 | | 0.46 ±0.18 | | 3.09 ±1.04 | | 0.46 ±0.18 | |

* statistically significant ($p < 0.05$, Kruskal–Wallis test); PD – pocket depth; GI – gingival index; BoP – bleeding on probing; CAL – clinical attachment level.

**Table 6.** Results of the intergroup post hoc analysis for clinical parameters

| Group | | GI *MD* | *p*-value | PD *MD* | *p*-value | BoP *MD* | *p*-value |
|---|---|---|---|---|---|---|---|
| Healthy (*n* = 23) | gingivitis (*n* = 23) | −1.03 | 0.002* | −0.58 | 0.0001* | −10.00 | 0.0001* |
| | stage II periodontitis (pre-treatment) (*n* = 23) | −1.10 | 0.002* | −1.09 | 0.0001* | −9.69 | 0.0001* |
| | stage II periodontitis (post-treatment) (*n* = 23) | −0.02 | 0.001* | −0.30 | 0.001* | 1.69 | 0.020* |
| Gingivitis (*n* = 23) | stage II periodontitis (pre-treatment) (*n* = 23) | −0.08 | 0.001* | −0.51 | 0.001* | 0.30 | 0.0001* |
| | stage II periodontitis (post-treatment) (*n* = 23) | 1.01 | 0.001* | 0.28 | 0.001* | 11.69 | 0.001* |
| Stage II periodontitis (pre-treatment) (*n* = 23) | stage II periodontitis (post-treatment) (*n* = 23) | 1.08 | 0.0001* | 0.78 | 0.001* | 11.39 | 0.001* |

* statistically significant ($p < 0.05$, Mann–Whitney *U* test).

## Discussion

Periodontitis is a chronic, microbes-associated, host-mediated inflammatory condition that results in the loss of supporting periodontal tissues.[22] Although the microorganisms present in the dental plaque biofilm are the cause of gingivitis and periodontitis, the etiology and concurrent tissue loss are the result of a chronic, inflammatory host immune response.[23,24] Cytokines are the signaling molecules that play an important role in inflammation, functioning as either pro- or anti-inflammatory agents in the immune system.[25]

In the present study, a significant difference and change in the level of IL-18 was observed between the healthy patients and individuals with gingivitis and stage II periodontitis. The gingivitis groups exhibited the highest levels of IL-18. The observed variations in IL-18 levels between the study groups were found to be statistically significant. The mean difference in the concentration between the stage II periodontitis (post-treatment) and gingivitis groups was found to be lower, whereas the difference in the concentration between the healthy and gingivitis groups was comparatively higher. The variation in IL-18 levels can be attributed to the progression of the disease, with the similar values in the gingivitis and stage II periodontitis groups potentially indicative of a nearly clinically unnoticeable transition in the gingivitis group to periodontitis. Prior studies have reported elevated concentrations of pro-inflammatory cytokines in periodontitis; however, few studies have evaluated the alterations in the expression levels of certain pro-inflammatory cytokines during the progression of periodontal disease.[26,27] The results of the present study are consistent with those of the study by Figueredo et al., who analyzed IL-18 levels in pooled GCF obtained from individuals with gingivitis and sites with periodontitis and gingivitis in patients with chronic periodontitis.[16] According to the study, gingivitis sites in patients with periodontitis exhibited greater GCF IL-18 levels.[16] Similar results were reported in a study by Pradeep et al.,[11] which reported changes in the IL-18 levels during the progression of the disease, with only a limited number of samples from the gingivitis group exhibiting values that approximated those observed in the periodontitis group.[27]

Interleukin-35 is a novel member of the IL-12 family and an anti-inflammatory cytokine that possesses effective inhibitory properties by regulating Treg cells. It has been demonstrated that the strong inhibitory effect of T cell proliferation can be exerted by preventing mitosis without inducing apoptosis.[28] The present study reported that the difference in the salivary concentration of IL-35 between the groups is statistically significant. The healthy group exhibited a significantly higher concentration compared to the gingivitis and stage II periodontitis groups. These findings align with those reported by Köseoğlu et al., who sought to determine the expression of IL-35 in GCF, saliva and plasma of participants with gingivitis, chronic periodontitis, and healthy individuals.[29] In comparison with the gingivitis and chronic periodontitis groups, the healthy patients' saliva showed a significantly higher concentration of IL-35.[29]

It has been suggested that the cellular response of pro-inflammatory cytokines is subject to negative regulation by anti-inflammatory cytokines, thereby establishing a balance between inflammatory cytokines and serving as a pivotal factor in determining the immune pathology of periodontal disease.[30] In the present study, the levels of IL-18 and IL-35 were assessed at baseline and 12 weeks after NSPT in patients with stage II periodontitis. The mean IL-35 level was observed to be increased post-treatment compared to baseline, and this difference was statistically significant. A marked improvement was observed across all clinical parameters from baseline to 12 weeks following NSPT. The results demonstrated a decrease in the mean GI, BoP, PD, and an improvement in CAL 12 weeks after NSPT in patients with stage II periodontitis ($p < 0.05$). The obtained results are analogous to those of the study by Goswamy et al., who assessed and compared the levels of IL-35 in GCF of patients with moderate to severe periodontitis before and after NSPT.[31] The results showed that, from the 1$^{st}$ to the 3$^{rd}$ week of post-periodontal treatment, there was an increase in IL-35 concentration in GCF along with a notable improvement in clinical indicators.[31]

In the present study, a marked reduction in the level of IL-18 was observed from baseline to 12 weeks after NSPT. These findings are consistent with the results obtained by Oliveira de Campos et al., who evaluated the effect of NSPT on the concentration of IL-18.[32] The patients were categorized into 2 groups (gingivitis and periodontitis). Gingival crevicular fluid samples were obtained at baseline and 1 month after SRP. A significant difference in the plaque index (PI), GI, PD, CAL, and IL-18 was observed between baseline and 1 month post-NSPT.[32]

The primary goals of periodontal treatment are to eliminate inflammation, halt the progression of the disease, restore aesthetics, and establish an environment conducive to maintaining health.[33] The first method recommended for treating periodontal infections is SRP, which is widely acknowledged as the gold standard.[34] Scaling and root planing resulted in a significant enhancement in PD reduction, and an improvement in CAL and BoP values 4 weeks after its implementation compared to baseline. In addition, NSPT has significantly reduced the salivary concentration of IL-18, a key player in establishing a link between acquired and innate immune responses involving both amateur and expert immune cell lineages.[35] Coversely, an increase in IL-35 levels post-treatment was also observed. The results reported in the previous studies are similar to these obtained in the present study.[35]

Van der Weijden and Timmerman evaluated the effect of subgingival debridement on clinical parameters (BoP, PD and CAL) in chronic periodontitis patients.[36] Badersten et al. assessed the impact of NSPT on plaque scores, BoP, PD, and CAL at baseline and 5 months after NSPT, and observed marked improvement in clinical parameters.[37] The results of the current study align with those of the abovementioned studies, as it reported improvements in clinical parameters 12 weeks after NSPT, with a reduction in PD, GI, BoP, and an improvement in CAL. These findings support the effectiveness of NSPT in patients with stage II periodontitis.

The balance between cytokines determines the degree of the host response to antigenic stimulation during the course of chronic inflammatory processes. In this study, changes in the IL-18 and IL-35 levels after SRP, along with the enhancement in the clinical parameters, are indicative of a balance between pro- and anti-inflammatory cytokines. This balance plays a pivotal role in the immunoregulation of periodontal disease. Therefore, this study supports the notion of counter-regulation of cytokines as a strategy to avert subsequent tissue destruction. There was no statistically significant difference between the 3 groups regarding the demographic data. This finding aligns with the longitudinal research conducted by Faddy et al., who reported no effect of age on periodontitis except for the regression in the healing process.[38]

In general, NSPT is an effective treatment for the suppression of periodontal disease progression. The observed improvement in CAL, BoP, PD and GI, with a lower salivary IL-18 concentration and an increase in the concentration of IL-35 suggest that IL-18 may comprise the subclinical activation of periodontal inflammation, while IL-35 may have a suppressive effect on its activity. The findings of this study reported a significant difference in IL-18 and IL-35 levels among healthy individuals and those with gingivitis and stage II periodontitis. This observation suggests that both interleukins could serve as possible diagnostic biomarkers for periodontal disease due to their distinct levels after NSPT.

# Conclusions

The present study reported a decrease in the salivary levels of IL-18 and an increase in IL-35 levels between baseline and 12 weeks after NSPT in subjects with stage II periodontitis, suggesting that NSPT may be an effective mode of treatment in periodontitis. However, the study is not without its limitations, including a relatively small number of follow-up patients and a short follow-up period. Further investigations with prolonged follow-ups are warranted to provide a comprehensive understanding of the correlation between IL-18 and IL-35 and the impact of NSPT on periodontal health.

## Ethics approval and consent to participate

The study was approved by the Central Ethics Committee (NITTE) (Cert. No. ABSM/EC/114/2021). Written informed consent was obtained from all study participants.

## Trial registration

The study was registered with the Clinical Trials Registry – India (CTRI) under the identification No. CTRI/2021/12/038961.

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.

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Original paper

# Evaluation of the personality traits in subjects in need of orthodontic treatment using the Big Five model: A cross-sectional questionnaire-based study

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## Abstract

**Background.** Malocclusion can be regarded as a civilizational disease, and its psychological implications remain a subject of debate.

**Objectives.** The aim of the study was to examine different personality traits of the individuals with malocclusion using the Big Five personality trait model.

**Material and methods.** A cross-sectional questionnaire-based study was conducted on 260 individuals with malocclusion, aged 15–24 years. The subjects were examined for the dental health component (DHC) of the index of orthodontic treatment need (IOTN) and graded by an expert orthodontist. The questionnaire contained 44 questions designed to evaluate various personality traits, namely extroversion, agreeableness, conscientiousness, neuroticism, and openness. The subjects were instructed to complete the questionnaire within a designated time frame of 10 min. The collected data was organized and scored. The individuals were then sorted into different categories of personality traits. A descriptive statistical analysis was performed on the collected data, and an analysis of variance (ANOVA) was conducted to determine the difference between the IOTN grading and various personality traits.

**Results.** All the subjects demonstrated low levels of extroversion, agreeableness and conscientiousness. In comparison to individuals with IOTN grade 1, those with grades 2 and 3 exhibited significantly higher levels of neuroticism ($p < 0.005$). The scores for the openness personality trait were moderate for all IOTN grades. Individuals with a high and moderate need for orthodontic treatment demonstrated elevated levels of neuroticism.

**Conclusions.** A definite influence of malocclusion on the personality traits of an individual was observed. Subjects requiring more extensive orthodontic treatment exhibited a higher prevalence of neuroticism.

**Keywords:** IOTN, malocclusion, dental health component

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## Highlights

- The necessity for malocclusion treatment in individuals has been demonstrated to influence personality traits.
- Individuals with a low orthodontic treatment need tend to exhibit personality traits such as extroversion, agreeableness, conscientiousness, and openness.
- Results show that individuals with a moderate to significant need for treatment exhibit features of neuroticism.

# Introduction

Malocclusion is a condition characterized by the lack of proper alignment of the teeth. It has been demonstrated to result in reduced oral health-related quality of life (OHRQoL). Many researchers have described this phenomenon in the literature.[1–3] Malocclusions influence not only the OHRQoL, but also the psychological and mental well-being of a person. A direct correlation between malocclusion and low self-esteem has been demonstrated.[4,5] Individuals with malocclusion also experience negative body image and the related consequences.[6] Additionally, appearance can influence social acceptability and the development of positive interpersonal relationships.[7]

With the exception of an article by Lin et al., which reports that individuals with the neuroticism personality trait tend to exhibit low OHRQoL,[8] there is a paucity of research regarding the personality traits of individuals with malocclusions. There are numerous systems available for the classification of personality traits. However, the Big Five personality trait model has emerged as the most reliable, as it describes broad traits that serve as the foundational elements of personality.[9,10]

The Big Five personality traits encompass 5 facets: neuroticism; extraversion; openness to experience; agreeableness; and conscientiousness.[11,12] Neuroticism specifically refers to individuals' tendency to experience anxiety, hostility and impulsivity. Extraversion is defined by individuals' propensity to exhibit enthusiasm, optimism and a high degree of social interaction. Openness to experience indicates a proclivity for innovation and the pursuit of unconventional solutions. Conscientiousness is characterized by the tendency to exercise diligence and self-discipline. Agreeableness reflects an individual's level of trust, altruism and straightforwardness.

The classification or grading of malocclusions can be approached in a variety of ways. Although the most popular way of classifying malocclusions is the Angle's classification, it lacks specificity with regard to the severity of the condition, thereby hindering its application in scientific research. In this regard, the index of orthodontic treatment need (IOTN) is a promising alternative for evaluating the severity of malocclusions.[13] While the influence of malocclusion on personality traits is an interesting area of research, the existing literature on the subject is limited. Therefore, the present study was conducted with the aim of evaluating the influence of malocclusion on the personality traits of the individuals.

# Material and methods

## Subjects

A cross-sectional questionnaire-based study was conducted on a sample of 260 individuals with malocclusion, aged 15–24 years. Participants were randomly selected from individuals who visited the Department of Orthodontics and Dentofacial Orthopaedics, Mathrusri Ramabai Ambedkar Dental College and Hospital, Bengaluru, India, for the first time with a desire to treat their malocclusions. All the subjects were informed about the purpose of the study, and written informed consent was obtained for their willing participation. The study received ethical clearance from the Institutional Ethics Committee of Mathrusri Ramabai Ambedkar Dental College and Hospital (approval No. IEC/MRADC&H/EC-014/20223). The sample size was calculated at 90% confidence interval with a 5% margin of error at 50% response distribution using the sample size calculator (Raosoft®; http://www.raosoft.com/samplesize.html).

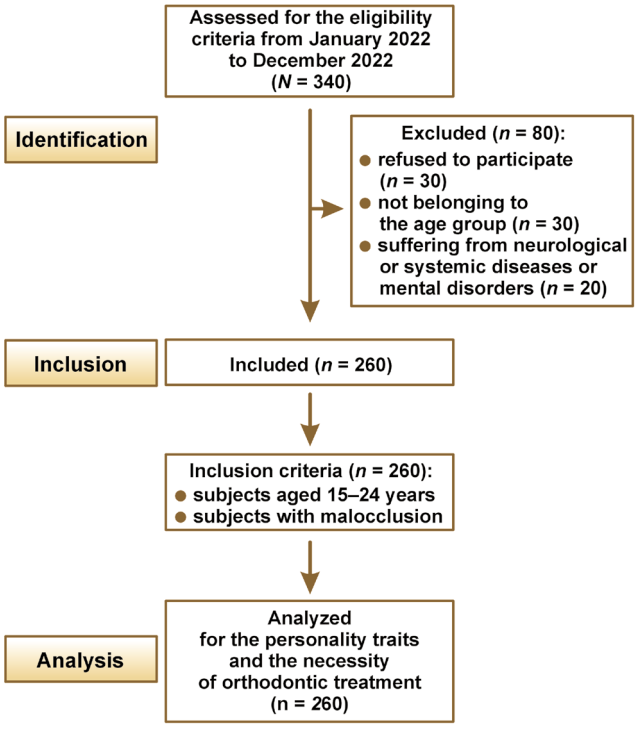


Fig. 1. STROBE (Strengthening the Reporting of OBservational studies in Epidemiology) flowchart of the study

## Method

Subjects aged 15–24 years with malocclusion were included in the study. Subjects who were syndromic, not belonging to the age group, unwilling to participate in the study, and those suffering from any neurological or systemic diseases or mental disorders were excluded from the study (Fig. 1).

The dental health component (DHC) of the IOTN[14] was used to classify the subjects into different malocclusion groups (Table 1), as follows:
– groups 1–2 (grade 1): little or no treatment need;
– group 3 (grade 2): moderate to borderline treatment need;
– groups 4–5 (grade 3): definitive need for treatment.

## Procedure

Following the provision of written consent, each individual was given a physical copy of a preformed questionnaire to complete. The study employed the Big Five personality trait model, which included a 44-item questionnaire (Table 2) to categorize individuals into different personality traits.[15] The participants were requested to complete the questionnaire within the designated time frame of 10 min. The questionnaire was bilingual (English and Hindi/Kannada) and included items requiring demographic details. The participants were instructed to respond to each question using the 5-point Likert scale, as follows:
– 1: strongly disagree;
– 2: disagree;
– 3: neutral;
– 4: agree;
– 5: strongly agree.

A single examiner (TS) assessed all subjects for the severity of malocclusion on the dental chair using the autoclaved instruments. The grading was noted in the questionnaire intended to be given to the subjects.

## Research tool

The Big Five personality trait model is among the most widely used structural personality models.[15] It uses a 44-item questionnaire as a tool to categorize personality traits, and according to the study by Satow,[16] the Big Five questionnaire is used more than 20,000 times every year as a clinical diagnostic aid and guide for career counseling and coaching. The reliability of the questionnaire was evaluated on 21,048 samples with a Cronbach's alpha ranging from 0.76 to 0.90, indicating high reliability of the tool.[16,17] The Big Five personality trait model proposes 5 broad personality traits based on the answers given to the pre-set questions (Table 2). These traits are openness to experience, extroversion, agreeableness, conscientiousness, and neuroticism (or its positive aspect, emotional stability). Each question is scored according to the Likert scale, and the following scoring criteria are used for different personality traits ("R" denotes reverse-scored items):
– extroversion: 1, 6R, 11, 16, 21R, 26, 31R, 36;
– agreeableness: 2R, 7, 12R, 17, 22, 27R, 32, 37R, 42;
– conscientiousness: 3, 8R, 13, 18R, 23R, 28, 33, 38, 43R;
– neuroticism: 4, 9R, 14, 19, 24R, 29, 34R, 39;
– openness: 5, 10, 15, 20, 25, 30, 35R, 40, 41R, 44.

**Table 1.** Dental health component (DHC) of the index of orthodontic treatment need (IOTN)

| IOTN score | | 5 | 4 | 3 | 2 | 1 |
|---|---|---|---|---|---|---|
| Need for treatment | | definitive | great | moderate | little | none |
| A | Overjet | >9 mm | 6–9 mm | 3.5–6 mm incompetent lip | 3.5–6 mm competent lip | – |
| B | Reverse overjet (with no masticatory or speech difficulties) | – | 3.5–5 mm | 1–3.5 mm | <1 mm | – |
| C | Crossbite | – | >2 mm | 1–2 mm | <1 mm | – |
| D | Tooth displacement | – | >4 mm | 2–4 mm | 1–2 mm | <1 mm |
| E | Open bite | – | >4 mm | 2–4 mm | 1–2 mm | |
| F | Overbite | – | increased, complete, with trauma | increased, complete, no trauma | <3.5 mm incomplete, no trauma | – |
| G | Pre- or postnormal occlusion | – | – | – | ½ unit discrepancy | – |
| H | Hypodontia | >1 tooth per quadrant | less severe | – | – | – |
| I | Impeded eruption | crowding, displacement, pathology | – | – | – | – |
| L | Posterior lingual crossbite | – | no functional occlusion | – | – | – |
| M | Reverse overjet (with reported masticatory or speech difficulties) | 3.5–5 mm | 1–3.5 mm | – | – | – |
| P | Cleft lip and palate | defects | – | – | – | – |
| S | Deciduous teeth | submerged | – | – | – | – |
| T | Partially erupted teeth | – | impacted | – | – | – |
| X | Supplemental teeth | – | present | – | – | – |

Table 2. Big Five personality trait questionnaire

| Item | Likert scale |
|---|---|
| 1. Is talkative | 1–5 |
| 2. Tends to find fault with others | |
| 3. Does a thorough job | |
| 4. Is depressed or blue | |
| 5. Is original and comes up with new ideas | |
| 6. Is reserved | |
| 7. Is helpful and unselfish with others | |
| 8. Is somewhat careless | |
| 9. Is relaxed and handles stress well | |
| 10. Is curious about many different things | |
| 11. Is full of energy | |
| 12. Starts quarrels with others | |
| 13. Is a reliable worker | |
| 14. Can be tense | |
| 15. Is ingenious and a deep thinker | |
| 16. Generates a lot of enthusiasm | |
| 17. Has a forgiving nature | |
| 18. Tends to be disorganized | |
| 19. Worries a lot | |
| 20. Has an active imagination | |
| 21. Tends to be quiet | |
| 22. Is generally trusting | |
| 23. Tends to be lazy | |
| 24. Is emotionally stable and not easily upset | |
| 25. Is inventive | |
| 26. Has an assertive personality | |
| 27. Can be cold and aloof | |
| 28. Perseveres until the task is finished | |
| 29. Can be moody | |
| 30. Values artistic and aesthetic experiences | |
| 31. Is sometimes shy and inhibited | |
| 32. Is considerate and kind to almost everyone | |
| 33. Does things efficiently | |
| 34. Remains calm in tense situations | |
| 35. Prefers work that is routine | |
| 36. Is outgoing and sociable | |
| 37. Is sometimes rude to others | |
| 38. Makes plans and follows through with them | |
| 39. Gets nervous easily | |
| 40. Likes to reflect and play with ideas | |
| 41. Has few artistic interests | |
| 42. Likes to cooperate with others | |
| 43. Is easily distracted | |
| 44. Is sophisticated in art, music or literature | |

To reverse score an item, responses recorded as 1 were assigned a value of 5, responses recorded as 2 were assigned a value of 4, responses recorded as 4 were assigned a value of 2, and responses recorded as 5 were assigned a value of 1. After reverse scoring, the total scores for E (extroversion), A (agreeableness), C (conscientiousness), N (neuroticism), and O (openness) were calculated.

## Statistical analysis

In order to evaluate the reliability of the IOTN grading, 10 patients were examined twice within a week, and their data was analyzed using Cohen's kappa, which indicated a high level of reliability (90%). The collected data was organized and tabulated in Microsoft Excel (Microsoft Corp., Redmond, USA) and subsequently subjected to a statistical analysis using the IBM SPSS Statistics for Windows software, v. 28.0 (IBM Corp., Armonk, USA). A one-way analysis of variance (ANOVA) was conducted to evaluate the relationship between different personality traits and the IOTN grading, followed by Tukey's post hoc test to determine the difference between each grade of malocclusion and the personality traits.

# Results

A total of 340 subjects were evaluated for the eligibility, out of which 80 subjects were excluded due to various reasons, resulting in a final sample size of 260 (Fig. 1). All subjects met the established inclusion criteria.

The distribution of the study population based on the IOTN DHC grading is outlined in Table 3. The mean age of the study participants was 17.8 ±1.1 years. Male and female subjects were evenly distributed. Of the 260 subjects, 27 were classified as having a grade 1 treatment need, 105 as having a grade 2 treatment need, and 128 as having a definitive need for orthodontic treatment (grade 3).

The descriptive statistics for the different grades of IOTN and personality traits are depicted in Table 4. The highest levels of extroversion, agreeableness and conscientiousness were observed in patients in the grade 1 IOTN DHC category, with mean values of 19.926, 20.259 and 23.444, respectively. However, neuroticism emerged as the prominent trait in grades 2 and 3, with mean values of 35.857 and 36.320, respectively. All malocclusion groups exhibited comparable levels of openness.

Table 3. Distribution of the study sample ($N = 260$)

| Subjects | Size | Grade 1 | Grade 2 | Grade 3 |
|---|---|---|---|---|
| Male | 130 | 15 | 51 | 64 |
| Female | 130 | 12 | 54 | 64 |
| Total | 260 | 27 | 105 | 128 |

grade 1 – little or no treatment need; grade 2 – moderate to borderline treatment need; grade 3 – definitive need for treatment. Data expressed as frequency ($n$).

**Table 4.** Descriptive statistics for the index of orthodontic treatment need (IOTN) grades and the personality trait scores

| Personality trait | Group | *n* | *M* | *SD* | *SE* |
|---|---|---|---|---|---|
| Extroversion | grade 1 | 27 | 19.926 | 5.061 | 0.974 |
| | grade 2 | 105 | 13.638 | 3.813 | 0.372 |
| | grade 3 | 128 | 10.703 | 3.973 | 0.351 |
| Agreeableness | grade 1 | 27 | 20.259 | 4.494 | 0.865 |
| | grade 2 | 105 | 17.914 | 3.417 | 0.334 |
| | grade 3 | 128 | 16.836 | 2.926 | 0.259 |
| Conscientiousness | grade 1 | 27 | 23.444 | 6.647 | 1.279 |
| | grade 2 | 105 | 17.105 | 5.713 | 0.558 |
| | grade 3 | 128 | 15.555 | 4.354 | 0.385 |
| Neuroticism | grade 1 | 27 | 27.333 | 7.380 | 1.420 |
| | grade 2 | 105 | 35.857 | 4.177 | 0.408 |
| | grade 3 | 128 | 36.320 | 4.158 | 0.368 |
| Openness | grade 1 | 27 | 29.444 | 8.750 | 1.684 |
| | grade 2 | 105 | 28.448 | 9.110 | 0.889 |
| | grade 3 | 128 | 29.914 | 7.702 | 0.681 |

*M* – mean; *SD* – standard deviation; *SE* – standard error.

Table 5 presents a comparison of individual personality traits with respect to different grades of malocclusion. A statistically significant difference was observed in the occurrence of each personality trait across different malocclusion groups ($p$ = 0.000), with the exception of the openness trait, which exhibited comparable levels across all malocclusion grades ($p$ = 0.414).

Tukey's post hoc test was used to determine the difference between each grade of malocclusion and the personality traits. The results of this analysis are presented in Table 6. A significant difference was identified between grades 1 and 2, grades 1 and 3, and grades 2 and 3 for extroversion and agreeableness. For the personality traits of conscientiousness and neuroticism, a significant difference was observed between grades 1 and 2 and between grades 1 and 3. However, there were no significant differences between grades 2 and 3 for these traits. Additionally, there was no significant difference between the grades of orthodontic treatment need for openness.

## Discussion

Malocclusion is a deviation from normal or ideal occlusion, which can cause a variety of issues, including functional and aesthetic concerns. With regard to appearance or aesthetics, it can be a potential cause of various psychological issues, including negative body image, low self-esteem, lack of confidence, depression, feeling like an outsider, or social withdrawal.[18–23] Although malocclusion is known to cause these problems, extensive studies related to the relationship between orthodontic treatment need and personality traits were never pursued. The current study tried to explore the different psychological and personality dimensions of the individuals with malocclusion.

It is a difficult task to attempt to fit individuals into a certain mold of personality. Each person exhibits different characteristics, and the individual's dominant personality is determined by their behavior during different situations. In this regard, the Big Five personality trait model is optimal, as it measures trait continuity in individuals and includes the bipolar trait dimension.[24] Therefore, we employed the Big Five model as a tool for studying personality traits of people in need of orthodontic treatment. The validity and reliability of the Big Five

**Table 5.** Analysis of variance (ANOVA) for the index of orthodontic treatment need (IOTN) grades and the personality trait scores

| Personality trait | Source | *df* | Sum of squares | Mean square | F-stat | *p*-value |
|---|---|---|---|---|---|---|
| Extroversion | between groups | 2 | 2,007.033 | 1,003.516 | 61.658 | 0.000* |
| | within groups | 257 | 4,182.824 | 16.276 | | |
| | total | 259 | 6,189.857 | – | – | – |
| Agreeableness | between groups | 2 | 275.857 | 137.929 | 12.539 | 0.000* |
| | within groups | 257 | 2,826.942 | 11.000 | | |
| | total | 259 | 3,102.800 | – | – | – |
| Conscientiousness | between groups | 2 | 1,389.849 | 694.925 | 25.697 | 0.000* |
| | within groups | 257 | 6,950.054 | 27.043 | | |
| | total | 259 | 8,339.903 | – | – | – |
| Neuroticism | between groups | 2 | 1,876.880 | 938.440 | 44.442 | 0.000* |
| | within groups | 257 | 5,426.777 | 21.116 | | |
| | total | 259 | 7,303.600 | 28.199 | – | – |
| Openness | between groups | 2 | 124.937 | 62.469 | 0.884 | 0.414 |
| | within groups | 257 | 18,156.740 | 70.649 | | |
| | total | 259 | 18,281.680 | – | – | – |

*df* – degrees of freedom; * statistically significant ($p < 0.05$).

**Table 6.** Tukey's post hoc test for the index of orthodontic treatment need (IOTN) grades and the personality trait scores

| Personality trait | Pair | Difference of means | *SE* | Q | Lower *CI* | Upper *CI* | Critical mean | *p*-value |
|---|---|---|---|---|---|---|---|---|
| Extroversion | grade 1–2 | 6.288 | 0.616 | 10.215 | 4.236 | 8.340 | 2.052 | 0.000* |
| | grade 1–3 | 9.223 | 0.604 | 15.266 | 7.209 | 11.237 | 2.014 | 0.000* |
| | grade 2–3 | 2.935 | 0.376 | 7.814 | 1.683 | 4.187 | 1.252 | 0.000* |
| Agreeableness | grade 1–2 | 2.345 | 0.506 | 4.634 | 0.658 | 4.032 | 1.687 | 0.003* |
| | grade 1–3 | 3.423 | 0.497 | 6.893 | 1.768 | 5.079 | 1.656 | 0.000* |
| | grade 2–3 | 1.078 | 0.309 | 3.492 | 0.049 | 2.108 | 1.029 | 0.038* |
| Conscientiousness | grade 1–2 | 6.340 | 0.794 | 7.990 | 3.694 | 8.985 | 2.645 | 0.000* |
| | grade 1–3 | 7.890 | 0.779 | 10.131 | 5.294 | 10.486 | 2.596 | 0.000* |
| | grade 2–3 | 1.550 | 0.484 | 3.202 | −0.064 | 3.164 | 1.614 | 0.063 |
| Neuroticism | grade 1–2 | 8.524 | 0.701 | 12.157 | 6.186 | 10.861 | 2.337 | 0.000* |
| | grade 1–3 | 8.987 | 0.688 | 13.060 | 6.693 | 11.281 | 2.294 | 0.000* |
| | grade 2–3 | 0.463 | 0.428 | 1.083 | −0.963 | 1.886 | 1.426 | 0.725 |
| Openness | grade 1–2 | 0.997 | 1.283 | 0.777 | −3.279 | 5.272 | 4.275 | 0.847 |
| | grade 1–3 | 0.470 | 1.259 | 0.373 | −3.727 | 4.666 | 4.196 | 0.962 |
| | grade 2–3 | 1.466 | 0.783 | 1.874 | −1.143 | 4.075 | 2.609 | 0.383 |

Q – studentized range statistic; *CI* – confidence interval; * statistically significant ($p < 0.05$).

model questionnaire have been demonstrated in children, adolescents and adults in earlier studies, making it a tool of choice for the current study.[25–27]

Although malocclusion can be classified in a variety of ways, the Angle's classification is the most common. However, it does not provide an exact idea of how severe the malocclusion is or what the need for treatment is. In light of these considerations, the DHC of the IOTN is a valuable tool for evaluating the necessity of treatment, depending on the severity of the malocclusion.[14] In the present study, the DHC of the IOTN was used to categorize the individuals into groups with little, moderate and definitive need for orthodontic intervention. The evaluation of the personality traits in relation to treatment need revealed that subjects with grades 2 and 3 exhibited higher levels of neuroticism compared to those with grade 1 (low treatment need). In a separate study, Rasooli and Lavasani correlated the body image concept with the 5-factor inventory.[28] Their findings revealed a significant positive relationship between neuroticism, agreeableness and openness, as well as a significant negative correlation between conscientiousness and extraversion.[28]

According to MacNeill et al., high levels of neuroticism are associated with a negative body image in females.[29] Malocclusion is related to the oral cavity, affecting an individual's facial and smile aesthetics, which can have a negative impact on their perception of body image. Another article on the correlation between large body type and the Big Five personality trait model demonstrated a significant negative relationship between conscientiousness and body image.[30]

For all the grades of orthodontic treatment need, extroversion received the lowest mean score, followed by agreeableness, conscientiousness and openness. Neuroticism, on the other hand, received the highest scores across all orthodontic treatment grades. The comparison between the different grades and the individual personality traits indicates that extroversion was more commonly observed in the grade 1 orthodontic treatment need group, which required little or no need for dental intervention.

The results of the current study demonstrate a significantly higher level of neuroticism in the grade 2 and 3 orthodontic treatment need groups as compared to the grade 1 group. Good dental appearance is a major factor determining the social and psychological well-being of individuals. Subjects with a healthy dentition usually exhibit better psychosocial adjustment and greater intellectual abilities.[31] As malocclusion affects dental appearance, it has a direct impact on the interpersonal social skills. Thus, individuals with malocclusions tend to exhibit lower levels of extroversion and elevated levels of neuroticism. Similarly, previous studies reported that malocclusion is one of the factors impacting the social success of individuals.[32,33] Subjects with neuroticism as their dominant personality trait experience emotional instability, irritability, anxiety, lack of self-confidence, depression, and self-consciousness.[34] This underscores the significance of orthodontic treatment for grade 2 and grade 3 individuals in order to improve their dental and facial aesthetics. Research has demonstrated that individuals with malocclusion experience an improvement in their OHRQoL following orthodontic treatment.[35,36]

Nevertheless, Spalj et al. discovered that personality traits do not mediate the self-perceived malocclusion rating,[37] which is in contrast to the findings of the present study. A recent study of a similar nature was conducted to assess how personality traits affect the relationship between malocclusion and the psychosocial impact of dental

aesthetics.[38] The authors observed that an increase in the severity of malocclusion was associated with higher scores for neuroticism.[38] These findings are similar to the results of the present study.

Given the absence of research comparing personality trait changes in malocclusion patients before and after orthodontic treatment, the present study assessed the impact of orthodontic therapy on the individuals' personality traits. Despite the formulation of the inclusion and exclusion criteria to eliminate the confounding factors, the influence of upbringing, socioeconomic conditions and environmental factors may have contributed to the inheritance of these traits in the study sample. Taking each factor into consideration is a tedious task that was beyond the scope of this study. However, it has been clearly established that individuals with poor OHRQoL exhibit higher levels of neuroticism and lower levels of conscientiousness,[39,40] while individuals who regularly visit the dentist show elevated levels of extraversion, conscientiousness and openness.[41]

Interestingly, the openness trait score remained consistent across all grades of orthodontic treatment need. It is safe to assume that the examined sample size was perceptive and open-minded, which enabled them to adapt to the changes.

A notable limitation of the study is the absence of a control group. Additionally, the study could be strengthened by comparing the personality traits of the malocclusion group with those of the normal occlusion group to validate the data. The study did not seek to evaluate the influence of the age group of individuals who required orthodontic treatment on the personality traits. A previous study that evaluated the influence of the years of experience in sports on the personality traits of an individual observed that the levels of extroversion increased in the individuals with more years of experience in the sports, and the levels of neuroticism decreased.[42] Thus, it might be hypothesized that an individual with malocclusion may adapt to its limitations and not be influenced by the condition negatively or, on the contrary, malocclusion may affect their personality in a negative way. Further in-depth research is necessary to ascertain whether the age of malocclusion patients has an impact on the development of personality traits.

# Conclusions

In comparison to the population with low orthodontic treatment need, the grade 2 and grade 3 orthodontic treatment need groups, i.e., those with a moderate to significant need for treatment, exhibited higher levels of neuroticism. Additionally, the grade 1 group exihibiting little or no treatment need displayed the attributes of extroversion, agreeableness, conscientiousness, and openess at a higher level.

## Ethics approval and consent to participate

All study participants were informed about the purpose of the study, and written informed consent was obtained for their willing participation. The study received ethical clearance from the Institutional Ethics Committee of Mathrusri Ramabai Ambedkar Dental College and Hospital (approval No. IEC/MRADC&H/EC-014/20223).

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.

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Original paper

# Influence of preoperative anatomy and functional status on outcomes after total temporomandibular joint replacement with patient-specific endoprostheses: A retrospective cohort study

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## Abstract

**Background.** Temporomandibular joint (TMJ) replacement may be indicated for various pathological conditions, and the type of condition can affect the surgical procedure and outcomes. The causes of limited range of motion after alloplastic TMJ replacement have not been extensively studied.

**Objectives.** The present study aimed to evaluate the impact of preoperative jaw anatomy and functional status on the immediate and long-term outcomes of total TMJ replacement using a two-component patient-specific TMJ endoprosthesis.

**Material and methods.** This retrospective study included 31 patients who underwent total TMJ replacement surgery between 2016 and 2020. The main outcome variable was the maximal incisal opening (MIO) after treatment. Secondary outcome variables included MIO improvement and the presence and type of postoperative complications. The primary predictive variable was the preoperative initial MIO. Secondary predictive variables included sex, age, indications for TMJ replacement, preoperative occlusion, condition of the glenoid fossa and/or condyle, shortening of the mandibular ramus, sagittal mandible position, lateral chin deviation, shape of the coronoid process, and type of surgery.

**Results.** The mean preoperative MIO was 13.0 ±8.0 mm, while the mean MIO 1 month after surgery was 20.6 ±5.5 mm, which was not statistically significant. However, at a later follow-up, functional parameters showed a significant improvement ($p = 0.003$), with a mean MIO of 32.5 ±5.0 mm 3 years after surgery. Statistical analysis indicated that the initial mouth opening is the strongest predictor of long-term functional recovery after TMJ replacement. Postoperative complications occurred in 4 cases (12.9%) following patient-specific endoprosthesis (PSE) placement.

**Conclusions.** The use of PSEs for TMJ replacement has enabled the restoration of anatomical relationships in complex clinical cases and an improvement in mouth opening. The preoperative MIO was the only factor that significantly influenced long-term functional outcomes.

**Keywords:** patient-specific implants, alloplastic temporomandibular joint replacements, maximal mouth opening, TMJ scarification

## Introduction

Alloplastic temporomandibular joint (TMJ) replacement is a widely accepted therapy for end-stage TMJ disease and a routine procedure for TMJ reconstruction after mandible resection in patients with malignant or benign tumors. Numerous publications have shown that TMJ replacement leads to significant improvements in quality of life, decreased pain scores, and increased mouth opening and food intake.[1–3]

Alloplastic TMJ prostheses, whether stock or patient-specific, typically consist of a polymeric fossa component and metallic condyle. These prostheses are fixed to adjacent bony structures using traditional preauricular and submandibular/periangular approaches.[4,5] However, a considerable variety of pathological conditions may indicate the need for TMJ replacement. Customized patient-specific endoprostheses (PSEs) have many advantages in complex cases where the anatomy is abnormal, or the patient has a history of multiple joint surgeries.

A patient-specific design promotes a good fit between the prosthetic components and bone surfaces, as well as adaptation to the patient's jaw anatomy, even in cases of severe deformity. This design type increases the precision of alloplastic TMJ placement, particularly when used in combination with cutting and positioning guides. Additionally, it simplifies the surgical procedure and reduces operation time. According to a study by Mercuri, PSEs provided significantly better outcomes than stock implants.[6] When using PSEs, the design of the artificial joint components can be adjusted to conform to the patient's preoperative anatomy.[6,7] However, in these cases, the ability to compensate for individual topographical changes and functional disorders caused by existing pathological processes may be overestimated and require further investigation.

The primary goal of total joint replacement is the restoration of appropriate anatomical relationships of the jaw and masticatory functions, including a normal physiological range of mouth opening and normal lateral and protrusive mandibular movement. Several authors have reported improved short- and long-term mouth opening following PSE placement.[7] However, data on improvements in protrusion and laterotrusion of the mandible remains controversial. It is evident that individuals who have undergone alloplastic reconstructions typically exhibit reduced jaw mobility, even in cases of the most successful procedures, when compared to those with normal jaw function.[8]

The existing literature lacks sufficient research on the causes of limited range of motion following alloplastic TMJ replacement. At the same time, there is an overestimation of the impact of patient-specific solutions on functional outcomes after TMJ replacement. Potential explanations of this finding include muscular detachment during surgery, irregularities in prosthesis design, and soft tissue changes such as scarring, muscular contraction, calcification, and ectopic bone formation.[9] It is also possible that the initial anatomy and functional status resulting from the etiology of TMJ pathology (ankylosis, tumors, condylar head fractures, severe arthritis, or secondary reconstructions) may significantly influence the immediate and long-term outcomes of TMJ replacement.[3] In addition, the literature suggests that additional factors associated with an increased surgical risk and procedural complexity include shortening of the ramus and attached musculature, malocclusion, marked asymmetry of the jaw, scarring from previous surgeries, and limited space for the PSE components.[10] However, the impact of these factors on long-term functional outcomes is not well defined. Novel data could provide clear indications for patient-specific TMJ replacement. Based on the aforementioned background, we hypothesized that the type of condition may influence the surgical procedure, the design of the alloplastic endoprosthesis, and the outcomes of the intervention.

The present study aimed to evaluate the impact of preoperative jaw anatomy and functional status on the immediate and long-term outcomes of total TMJ replacement using two-component PSEs.

## Material and methods

This retrospective cohort study analyzed data from patients who underwent total TMJ replacement surgery at the Department of Maxillofacial Surgery and Innovative Dentistry in Kyiv, Ukraine, and the Head and Neck Surgery Clinic for Children and Youth in Olsztyn, Poland, between 2016 and 2020. The inclusion criteria were as follows: individuals who underwent total joint replacement with an alloplastic two-component PSE for primary or secondary TMJ reconstruction and had complete documentation of their clinical case with a post-surgical follow-up of at least 3 years. Patients were excluded if they were under 16 years of age, had neurological or muscular diseases that affected mandibular movements and mouth opening, mental illness, active malignancy, or a history of radiation or chemotherapy, were non-adherent to medical recommendations, had no interaction with a physician during the postoperative period, or refused to participate in the study. The study was approved by the Ethics Committee of the Bogomolets National Medical University, Kyiv, Ukraine (approval No. 153; November 29, 2021).

Case histories of all patients were retrospectively reviewed, and the preoperative status, treatment outcomes and any complications were recorded. The main outcome variable was the maximal incisal opening (MIO) after treatment. Secondary outcome variables included MIO improvement (expressed as the difference between the postoperative and preoperative MIO) and the presence and type of postoperative complications.

The study's primary predictive variable was the preoperative initial MIO. Secondary predictive variables included the patient's sex, age, indications for TMJ replacement, preoperative occlusion, condition of the glenoid fossa and/or condyle, shortening of the mandibular ramus, sagittal mandible position, lateral chin deviation, shape of the coronoid process (normal, elongated or deformed), and type of surgery (primary or secondary, unilateral or bilateral TMJ replacement, and coronoid process preservation or resection).

The preoperative anatomy was evaluated and categorized by 2 experienced and independent observers based on presurgical multi-slice spiral computed tomography (CT) data. The length of the ramus was measured on separate 3D images of the mandible as the distance between the most superior point of the condyle and the most inferior point of the gonion. The shortening of the affected ramus in cases of unilateral TMJ pathology was determined by comparing its length with the unaffected side. In bilateral cases, the lengths were compared to the average statistical data found in the literature.[11,12] If the glenoid fossa and/or condyle were clearly visible with no pathological signs, they were considered to be preserved. Conversely, cases where the anatomy and interrelations of the bony structures were severely deformed were considered to be affected. The coronoid process was recorded as elongated or not according to previously described criteria.[13]

The surgical procedures were performed under general anesthesia following standard surgical protocols. Patient-specific endoprostheses from 3 different manufacturers (KLS Martin, Tuttlingen, Germany; ChM, Juchnowiec Kościelny, Poland; and Imatech Medical, Kyiv, Ukraine) were used. The PSEs were selected based on computer modeling and manufactured stereolithographic models and surgical guides. The fossa component was installed using a preauricular approach, while the condyle component was positioned using a periangular approach. Conventional physiotherapy and self-training were used in all cases to prevent postoperative decreases in mouth opening. After TMJ replacement, all patients were clinically evaluated at 1 week, 1 month, 6 months, 12 months, and 36 months, with a special focus on facial symmetry, occlusion, mouth opening, lateral and anterior movements, as well as complaints and the development of complications. All patients underwent a CT or orthopantomogram within 1 week of TMJ replacement and again 1 year after surgery to evaluate the position of the TMJ components and the condition of the adjacent anatomy.

To prevent bias, our study was conducted in accordance with rigorous inclusion criteria. Twenty-one patients were excluded from the study, including adolescents in various stages of mandible growth or those who had undergone previous mandibular distractions. These conditions can influence primary outcome variables compared to the rest of the evaluated patients.

The primary outcome variable used to determine statistical power was the MIO at 36 months. The level of significance was set at a $p$-value of <0.05. A power analysis indicated that 31 patients were required to achieve 81% power to detect a 50% difference from the initial mouth opening.

## Statistical analysis

The obtained data was initially described qualitatively, using absolute and percentage frequencies. For quantitative variables, mean and standard deviation ($M \pm SD$) were calculated for normally distributed data, and median ($Me$) and the interquartile range ($IQR$) were calculated for non-normally distributed data. Statistical analysis was performed using the Wilcoxon signed-rank test for non-parametric values and Student's $t$-test for parametric values. Fisher's test was used for the remaining values. Correlations between qualitative and quantitative variables were assessed using analysis of variance (ANOVA) and logistic regression models, built using the Akaike information criterion (AIC). Sample power and size calculations were performed using Pillai's trace test. The calculations were conducted using the R v. 4.2.2 software (https://cran.r-project.org/bin/windows/base/old/4.2.2/). A $p$-value <0.05 was considered statistically significant.

# Results

Fifty-two patients who underwent total TMJ replacement surgery were evaluated for compliance with the inclusion criteria. Seven adolescents under the age of 16 and 2 adults were excluded due to a lack of data, making it impossible to further evaluate correlations between the variables. Of the remaining 6 patients under the age of 16, 4 had previously undergone mandibular distraction. Six patients did not reach the follow-up period of 36 months due to complications or malignant recurrence. A total of 31 patients met the inclusion criteria and were enrolled in the study. Of these patients, 71% were female, and the mean age was 28.4 ±13.5 years. The indications for TMJ replacement are presented in Fig. 1.

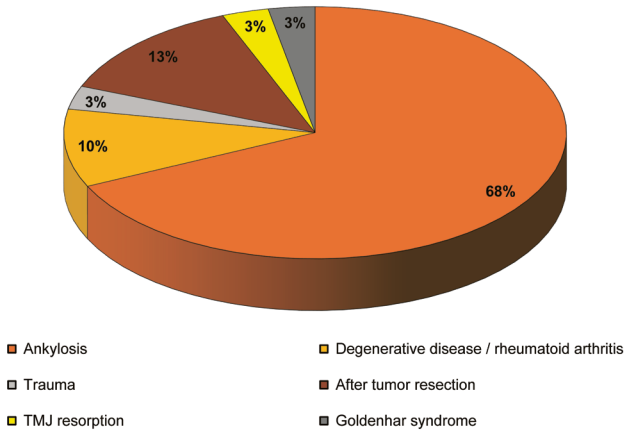


Fig. 1. Indications for temporomandibular joint (TMJ) replacement

Ankylosis was the most common TMJ pathology requiring alloplastic joint replacement, accounting for 68% of cases. Twenty-five patients (80.6%) had undergone surgery before the final alloplastic reconstruction. The mean number of surgical procedures per case was 1.68 ±0.64. In 15 patients, TMJ replacement was performed alongside orthognathic surgery or mandibular reconstructions following hemimandibulectomy (Table 1).

Initial preoperative mouth opening was measured and analyzed as a potential risk factor for inadequate rehabilitation. Seventeen patients (54.8%) had an MIO of less than 15 mm before surgery, while only 1 patient had an MIO greater than 30 mm. The median preoperative MIO was 13 ±8 mm (Table 2). An MIO of ≥40 mm was achieved during surgery in all cases. However, only 4 patients (12.9%) showed fairly good functional results (MIO > 40 mm) 1 month after surgery. At that time,

**Table 1.** Distribution of demographic and clinicopathological characteristics of the patients

| Patient No. | Sex | Age [years] | Diagnosis | Occlusion | Glenoid fossa | Coronoid process (shape) | Ramus size | Endoprosthesis | Timing of surgery | MIO before treatment [mm] | MIO 3 years after surgery [mm] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 17 | ankylosis | normal | affected | affected | shortened | unilateral | delayed | 14 | 28 |
| 2 | F | 60 | after tumor resection | malocclusion | intact | affected | normal | unilateral | immediate | 25 | 35 |
| 3 | F | 18 | ankylosis | normal | affected | affected | shortened | bilateral | delayed | 7 | 22 |
| 4 | F | 35 | ankylosis | malocclusion | affected | affected | shortened | bilateral | delayed | 1 | 25 |
| 5 | F | 25 | ankylosis | normal | affected | affected | shortened | unilateral | delayed | 8 | 26 |
| 6 | F | 41 | rheumatoid arthritis | normal | affected | intact | normal | unilateral | delayed | 4 | 21 |
| 7 | F | 18 | ankylosis | malocclusion | intact | affected | shortened | bilateral | delayed | 10 | 25 |
| 8 | M | 55 | ankylosis | normal | affected | intact | normal | bilateral | immediate | 1 | 35 |
| 9 | M | 27 | ankylosis | normal | affected | affected | shortened | unilateral | delayed | 13 | 25 |
| 10 | F | 31 | Goldenhar syndrome | malocclusion | affected | affected | shortened | unilateral | immediate | 20 | 35 |
| 11 | F | 64 | ankylosis | malocclusion | affected | affected | normal | bilateral | delayed | 7 | 29 |
| 12 | F | 40 | TMJ resorption | normal | intact | affected | normal | bilateral | immediate | 16 | 35 |
| 13 | F | 33 | degenerative disease | malocclusion | affected | affected | normal | unilateral | delayed | 5 | 32 |
| 14 | F | 50 | trauma | malocclusion | intact | affected | normal | unilateral | delayed | 6 | 25 |
| 15 | F | 37 | ankylosis | normal | intact | intact | normal | unilateral | delayed | 20 | 27 |
| 16 | F | 20 | ankylosis | malocclusion | affected | affected | shortened | unilateral | delayed | 1 | 24 |
| 17 | F | 26 | after tumor resection | malocclusion | intact | affected | normal | unilateral | delayed | 10 | 22 |
| 18 | F | 23 | after tumor resection | normal | intact | intact | normal | unilateral | delayed | 25 | 35 |
| 19 | M | 38 | after tumor resection | normal | intact | intact | normal | unilateral | immediate | 30 | 37 |
| 20 | F | 17 | ankylosis | malocclusion | affected | affected | shortened | unilateral | delayed | 20 | 40 |
| 21 | M | 21 | ankylosis | malocclusion | affected | affected | shortened | unilateral | delayed | 5 | 40 |
| 22 | F | 17 | ankylosis | malocclusion | affected | affected | shortened | unilateral | delayed | 20 | 30 |
| 23 | F | 17 | ankylosis | malocclusion | affected | intact | shortened | bilateral | delayed | 10 | 40 |
| 24 | F | 17 | ankylosis | malocclusion | intact | affected | normal | bilateral | immediate | 20 | 30 |
| 25 | F | 18 | TMJ resorption | malocclusion | affected | affected | shortened | unilateral | delayed | 20 | 40 |
| 26 | M | 20 | ankylosis | malocclusion | affected | affected | shortened | unilateral | delayed | 15 | 35 |
| 27 | M | 18 | ankylosis | malocclusion | affected | affected | shortened | unilateral | delayed | 20 | 40 |
| 28 | M | 23 | ankylosis | malocclusion | affected | affected | shortened | bilateral | delayed | 20 | 40 |
| 29 | M | 17 | ankylosis | malocclusion | affected | affected | shortened | bilateral | delayed | 0 | 30 |
| 30 | F | 19 | ankylosis | malocclusion | affected | affected | shortened | unilateral | delayed | 20 | 40 |
| 31 | M | 18 | ankylosis | malocclusion | affected | affected | shortened | unilateral | delayed | 10 | 30 |

M – male; F – female; MIO – maximal incisal opening.

the mean MIO was 20.6 ±5.5 mm, which was not significantly different from the preoperative values. However, at a later follow-up, significant improvements in functional parameters were observed ($p$ = 0.003), with a median MIO of 32.5 ±5 mm 3 years after surgery. Subsequent follow-up showed only moderate functional improvements, which were not statistically significant (Fig. 2). Further statistical analysis indicated that initial mouth opening was the most significant predictor of long-term functional recovery after TMJ replacement (Table 3).

**Table 2.** MIO values in different time periods

| MIO [mm] | *Me* | *IQR* |
|---|---|---|
| Before surgery | 13 | 6–20 |
| During surgery* | 41 | 37–45 |
| 1 month after surgery | 20.6 | 15–25 |
| 1 year after surgery* | 30.8 | 25–35 |
| 3 years after surgery* | 32.5 | 27–37 |

*Me* – median; *IQR* – interquartile range; * significant difference observed between preoperative results and group results ($p < 0.05$, analysis of variance (ANOVA)).

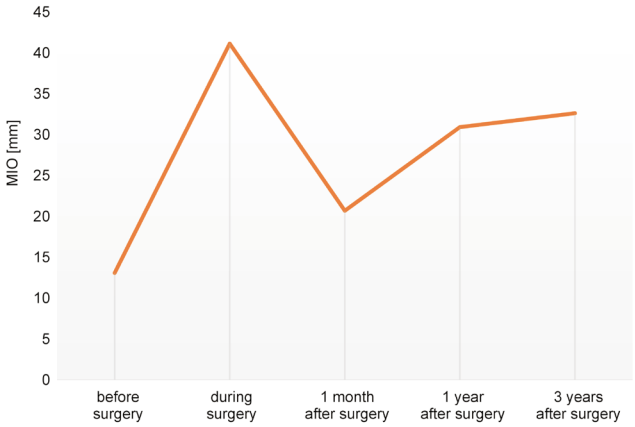


**Fig. 2.** Changes in maximal incisal opening (MIO) in patients who underwent TMJ replacement

Postoperative complications occurred in 4 cases (12.9%) following PSE replacement. These included 2 cases of artificial condylar head displacement (treated with closed reduction and prolonged immobilization) and 3 cases of auditory canal perforation (2 of which were successfully treated conservatively).

**Table 3.** Influence of various factors on long-term functional outcomes in patients after total TMJ replacement (after 3 years)

| Factors | | Patients with MIO > 30 mm ($n$ = 20) | Patients with MIO < 30 mm ($n$ = 11) | $p$-value |
|---|---|---|---|---|
| Age [years] | *M* | 28.7 | 28.4 | 0.45[W] |
| | *Me* | 23 | 33 | |
| | *SD* | 13.6 | 14.4 | |
| MIO before treatment [mm] | *M* | 15.45 | 8.55 | 0.023[t]* |
| | *SD* | 1.89 | 1.73 | |
| Sex *n* (%) | male | 8 (88.8) | 1 (11.2) | 0.106[F] |
| | female | 12 (54.5) | 10 (45.5) | |
| Occlusion *n* (%) | normal | 4 (40.0) | 6 (60.0) | 0.105[F] |
| | malocclusion | 16 (76.2) | 5 (23.8) | |
| Chin dislocation *n* (%) | yes | 13 (65.0) | 7 (35.0) | 1.000[F] |
| | no | 7 (63.6) | 4 (36.4) | |
| Ramus size *n* (%) | shortened | 12 (63.1) | 7 (36.9) | 1.000[F] |
| | normal | 8 (66.6) | 4 (33.4) | |
| Timing of surgery *n* (%) | immediate | 6 (100.0) | 0 (0.0) | 0.066[F] |
| | delayed | 14 (56.0) | 11 (44.0) | |
| Coronoid process (shape) *n* (%) | affected | 16 (64.0) | 9 (36.0) | 1.000[F] |
| | intact | 4 (66.6) | 2 (33.4) | |
| Glenoid fossa *n* (%) | affected | 15 (68.2) | 7 (31.8) | 0.683[F] |
| | intact | 5 (55.5) | 4 (44.5) | |
| Retrusion of the mandible (sagittal mandible position) *n* (%) | yes | 14 (66.6) | 7 (33.4) | 1.000[F] |
| | no | 6 (60.0) | 4 (40.0) | |
| Endoprosthesis *n* (%) | unilateral | 13 (61.9) | 8 (38.1) | 0.712[F] |
| | bilateral | 7 (70.0) | 3 (30.0) | |

*M* – mean; *SD* – standard deviation; TMJ – temporomandibular joint; * statistically significant ($p < 0.05$); [W] Wilcoxon signed-rank test; [t] Student's *t*-test; [F] Fisher's test.

## Discussion

Managing destructive and degenerative TMJ pathologies that require total joint replacement is a challenging task for maxillofacial surgeons.[6,14,15] The primary goal of total TMJ replacement is to achieve appropriate functional and aesthetic rehabilitation while minimizing the risk of complications.[16,17] However, replacement procedures can be challenging, both technically and surgically, due to the presence of complex conditions with underlying pathology, anatomical deformities, small joint size, and high expectations for functional and aesthetic outcomes.

Over the last decade, numerous publications have demonstrated the advantages of custom-made, patient-specific TMJ endoprostheses in comparison with standard prostheses.[18,19] According to the literature, PSEs provide better adaptation to the initial preoperative anatomy and have the potential to restore the height and shape of the ramus while correcting the position of the chin. They also facilitate reconstruction procedures for complex mandibular or zygomatic defects that require simultaneous TMJ replacement. Some authors have implanted PSEs of the TMJ simultaneously with orthognathic procedures to correct severe anatomical deformities and anomalies.[19–21]

The design of a modern PSE involves technical solutions to ensure that its predetermined positioning is correct. This can be achieved through the use of complex implant geometry, intraoperative navigation, or pre-drill guides. Incorrect positioning of the fossa component may cause inflammation of the auditory system or a dislocation of the condyle component, which in turn could lead to limited mouth opening and/or malocclusion.[9]

These advantages of PSEs provide significant anatomical benefits, including the correction of ramus height, occlusion, and facial proportions and symmetry. Numerous studies have suggested that patient-specific solutions are the optimal choice for TMJ reconstruction.[8,22,23] However, the extent to which functional outcomes improve with PSEs compared to stock TMJ replacement remains controversial. Kozakiewicz et al. and Zheng et al. achieved the average MIOs of 36.7 ±7.4 mm and 39.25 ±5.17 mm, respectively, after using PSEs to replace the TMJ.[18,24] Comparable results were reported by authors who found that the average MIO increased from 21.0 mm before surgery to 34.7 mm after 10 years of follow-up in patients who received stock TMJ Concepts replacements.[17] Other researchers have reported similar results with stock TMJ endoprostheses.[2,25,26] However, due to the limited number of patients in the series, heterogeneous study groups and different approaches to the evaluation of functional outcomes, it is challenging to make direct comparisons between the results achieved by different authors. Additionally, different underlying pathologies and respective indications for total joint replacement must be considered as a major source of heterogeneity in the results.

In our study, preoperative mouth opening was limited, with a median of only 13 ±8 mm. At one-year postoperative follow-up, it had improved by 2.37-fold. Although the intraoperative MIO was ≥40 mm in all cases, the functional outcome was partially lost at the end of the 1st month. There were no statistically significant differences between the mean preoperative MIO and MIO 1 month after surgery. Over the following months, the MIO increased significantly, reaching its maximum by the end of the 1st year. Subsequently, only minor improvements were observed in some patients, but these changes were not statistically significant. Aagaard and Thygesen reported comparable functional recovery timings following the implantation of stock TMJ endoprostheses.[27] In our study, we observed a more than 2.5-fold increase in MIO after long-term follow-up (3 years after surgery), which falls within the range reported in the literature. However, PSE implantation allowed for the procedure to be simplified and performed as a 'one-stage surgery' with highly acceptable anatomical outcomes in cases where orthognathic surgery or mandible reconstructions were indicated.

The main limitations of our study included the enrollment of a relatively small group of patients with heterogeneous pathologies, restricted inclusion criteria, and the use of implants from multiple PSE manufacturers. Despite these limitations, the study found no significant correlations between functional outcomes and initial anatomy (Table 4). In particular, the state of the glenoid fossa, occlusion, chin dislocation, ramus size, and coronoid process had no significant effect on the integral functional outcomes. Our study included patients with various pathologies and previous surgeries, and none of these factors had a significant influence on functional recovery. However, in contrast to Kozakiewicz et al., who found only weak correlations between the preoperative MIO and outcomes,[18] our study demonstrated a significant impact of the preoperative MIO on the postoperative MIO ($p < 0.05$). Even after eliminating

**Table 4.** Univariate logistic regression model predicting mouth opening after TMJ reconstruction

| Variable | *OR* | 95% *CI* | *p*-value |
|---|---|---|---|
| Age | 0.99 | 0.95–1.05 | 0.960 |
| Sex | 6.67 | 0.71–62.7 | 0.0972 |
| Malocclusion | 0.21 | 0.041–1.05 | 0.057 |
| Chin dislocation | 1.06 | 0.23–4.92 | 0.939 |
| Shortened ramus size | 0.86 | 0.19–3.92 | 0.842 |
| Timing of reconstruction | N/A | N/A | N/A |
| Coronoid process | 1.12 | 0.17–7.4 | 0.902 |
| Glenoid fossa | 0.58 | 0.12–2.97 | 0.507 |
| Retrusion of the mandible | 1.33 | 0.28–6.33 | 0.717 |
| TMJ replacement | 0.696 | 0.139–3.50 | 0.660 |
| MIO before treatment | 1.13 | 1.01–1.26 | 0.032* |

*OR* – odds ratio; *CI* – confidence interval; N/A – not applicable; * statistically significant ($p < 0.05$, multivariate logistic regression analysis).

bony defects and achieving appropriate mandibular length and position, reduced preoperative mouth opening was associated with worse functional recovery. This finding suggests that the condition of the soft tissues responsible for jaw function should also be considered, in addition to the clear importance of correct anatomical reconstruction. The main findings of our study are in agreement with the study by Mercuri, which highlighted the importance of the condition and functional training of masticatory muscles for functional recovery.[6]

In our study, we observed 3 cases of auditory canal perforation due to the surgical plan. The perforation resulted from sharp edges of the personalized fossa component being closely adjacent to the auditory canal. Two of these cases were managed conservatively (secondary healing using aseptic keratoplastic agent coverage and preventative antibiotics) without negative consequences for the TMJ endoprosthesis (i.e., no persistent infection). Additionally, we observed 2 cases of dislocation of the ramus and condyle components during the 1st week after surgery. Both cases were successfully treated with closed reduction and immobilization of the mandible for 2 weeks. The overall complication rate was 12.9% (4 cases), and it did not affect the final outcomes in the patient group. This rate is comparable to the results achieved by Rajkumar and Sidebottom in a larger group of patients.[17]

Personalized joint replacement enables the simultaneous reconstruction of the TMJ, mandible, temporal bone, and zygoma. This approach requires close interaction between the surgeon and the bioengineer during the modeling and design process, while also considering manufacturing and treatment strategies. However, our results suggest that despite the possibility of the precise determination of mandible length and position using different patient-specific solutions, TMJ-related soft tissue conditions are still being underestimated.[28,29]

# Conclusions

The use of PSEs for TMJ replacement has enabled the restoration of anatomical relationships in complex clinical cases and has improved mouth opening from 13 ±8 mm preoperatively to 32.5 ±5 mm after 3 years of follow-up. The intraoperative MIO was greater than the postoperative MIO in all cases. Maximal incisal opening at 1 month did not significantly differ from preoperative values. It significantly increased 1 year after surgery following physiotherapy and remained stable during 3 years of follow-up.

The preoperative MIO was the only factor that significantly influenced long-term functional outcomes. None of the other variables examined, including age, indications for TMJ replacement, preoperative occlusion, state of the coronoid process, glenoid fossa and/or condyle, shortening of the mandibular ramus, sagittal mandible position, jaw asymmetry, as well as the type of surgery (primary or secondary, unilateral or bilateral TMJ replacement, and coronoid process preservation or resection) had a significant impact on treatment outcomes.

## Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Bogomolets National Medical University, Kyiv, Ukraine (approval No. 153; November 29, 2021).

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.


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Original paper

# Retrospective analysis of the relationship between Schneiderian membrane thickness and periodontitis severity using cone beam computed tomography (CBCT)

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## Abstract

**Background.** Due to the close proximity of maxillary molars to the maxillary sinuses, the bacteria at the root tip region of the sinus can quickly access the maxillary sinus. This can result in maxillary sinus mucosal inflammation and thickening of the Schneiderian membrane.

**Objectives.** The aim of the study was to determine the thickness of the maxillary sinus membrane and to correlate this thickening with the severity of periodontitis using cone beam computed tomography (CBCT) analysis.

**Material and methods.** The CBCT data of 231 patients, with a mean age of 40.59 years, was assessed to evaluate the mucosal thickness (MT), the remaining height of the alveolar bone (RHAB), the type of periodontitis, the type of defect, and the extent of bone loss.

**Results.** When RHAB was ≤4 mm, mucosal thickening was evident in the majority of the images (128 (89.5%); $p = 0.000$). The multivariate logistic regression analysis demonstrated that the probability of MT increase is proportionate to the severity of periodontal disease (odds ratio (*OR*): 9.179, confidence interval (*CI*): 2.831–29.761; $p = 0.000$). First molars were most frequently associated with mucosal thickening (*OR*: 1.050, *CI*: 0.311–3.541; $p = 0.009$). Additionally, mucosal thickening was more evident on the sinus floor in cases where RHAB was less than 4 mm.

**Conclusions.** The increase in MT is associated with the severity and distribution of periodontal disease, particularly with horizontal defects.

**Keywords:** cone beam computed tomography, maxillary sinus, periodontitis, alveolar bone loss, Schneiderian membrane

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## Highlights

- The study revealed a correlation between the thickness of the maxillary sinus membrane and the severity of periodontitis.
- Mucosal thickening was more evident for RHAB ≤ 4 mm, indicating a link between alveolar bone loss and sinus membrane thickening.
- First molars were most frequently associated with membrane thickening, highlighting the importance of monitoring these areas in patients with periodontitis.

# Introduction

Periodontal disease is a chronic infectious condition that leads to the loss of supporting alveolar bone and mobility of the teeth. If left untreated, it eventually results in tooth exfoliation. Due to the intricate root architecture, which includes the contour of the root surface, and furcation, maxillary molars and premolars are more prone to periodontal infection.[1] Furthermore, the roots of maxillary posterior teeth are in the vicinity of the maxillary sinus floor, and infections in this region may affect the maxillary sinuses, leading to maxillary sinus mucosal thickening.

The etiology of maxillary sinusitis can be classified as either odontogenic or nasogenic, with the former accounting for 10–12% of all cases.[2] Odontogenic maxillary sinusitis is the result of the pathological interaction of periodontal structures with the maxillary sinus membrane. As maxillary molars are in close proximity to the maxillary sinuses, the bacteria at the root tip region of the sinus can rapidly become infected. Bacteria gain access to the maxillary sinus through the porous alveolar bone, causing an inflammatory reaction.

Various odontogenic conditions violate the physiological position of the sinus membrane, leading to its increased thickness. These conditions include periapical abscess, periodontal disease, dental trauma, implant placement, and tooth extraction. Periodontitis is an inflammatory condition that can contribute to odontogenic maxillary sinusitis, leading to Schneiderian membrane thickening.[3]

In dentistry, the maxillary sinus has been visualized via panoramic radiography, Water's view and intraoral radiography. However, the intricate design of the oral and maxillofacial area makes it challenging to visualize key anatomical traits due to superimposition.[4,5] The thickness of the maxillary sinus membrane is difficult to evaluate with the use of routine radiographic techniques. Since its introduction in dentistry and maxillofacial imaging, cone beam computed tomography (CBCT) analysis has enabled the diagnosis of sensitive structures in multiplanar reconstructions.[6] This technique also allows for an extremely high diagnostic level, such as perfect matching with photographic acquisitions of the patient's face, and thus enables surgical programming to achieve even more adequate aesthetics. The ability to perform precise cephalometric analyses for orthodontic and orthognathic surgery purposes represents a significant turning point in the orthodontic diagnosis.[7,8] Cone beam computed tomography can be used to visualize the paranasal sinuses, peri-apical and periodontal tissues due to its reduced radiation dosage and isotropic volume resolution. This imaging technique is the gold standard for sinus diagnosis, allowing for the examination of both hard tissue components in numerous sections of sinus in various planes.[9]

There are conflicting reports regarding the influence of periodontal disease on maxillary sinus thickness. Few studies have shown an association between increased mucosal thickness (MT) and periapical and periodontal infections.[1,2]

# Objectives

Although numerous studies have addressed the association between periodontal disease and MT, the literature lacks sufficient evidence to make any definitive statements. Therefore, further research is necessary to compare the severity of periodontal disease with MT. The present study aimed to assess the thickness of the Schneiderian membrane and correlate the results with the periodontal disease status using CBCT.

# Material and methods

## Study protocol and data collection

The Institutional Ethics Committee of Vishnu Dental College, Bhimavaram, India, approved the study protocol, which adhered to the 2013 Declaration of Helsinki. The CBCT data from periodontally healthy individuals and those with clinical signs of periodontitis was collected in the Department of Periodontics and Implantology of Vishnu Dental College between January 2020 and August 2021. The demographic and clinical data of the participants was obtained from the electronic medical record management system. The three-dimensional (3D) images in the maxillary premolar and molar regions were reconstructed using 3D visualization and evaluated with the SCANORA® Imaging System, v. 5.2 (SOREDEX, Tuusula, Finland).

## Sample size

A total sample size of 231 was calculated using G*Power software, v. 3.10 (https://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower). The calculations were based on MT in patients with periodontitis as the primary outcome, with an effect size of 0.04, a 95% confidence level, and a margin of error of 57%.

## Patient selection

The Cranex® 3D imagining system (SOREDEX) was used to obtain good quality images of the maxillary posterior sextants. The images were taken at 90 kVp and 8 mA with an exposure length of 10 s. The pictures had 0.13-mm voxels, a field of view of 6 cm × 4 cm, and a slice thickness of 0 mm.

Participants with signs or a history of sinusitis, common cold, rise in the body temperature, or symptoms of a viral or respiratory infection in the previous 3 months, as well as pregnant or lactating women, smokers, and individuals with a history of allergic rhinitis, bronchitis or chronic pulmonary diseases, and radiographic signs of sinusitis or sinus lesions were excluded from the study. Additionally, individuals with carious teeth, endodontically involved teeth, cracked teeth, existing dental restorations, premolars and molars requiring endodontic treatment, missing maxillary posterior teeth, the presence of any mucosal cysts or septa, and those who underwent periodontal therapy were excluded.

## CBCT image analysis

A total of 459 CBCT images were assessed, out of which 231 images met the selection criteria and were included in the study. The main reasons for exclusion were periapical lesions, the presence of dental caries, existing dental fillings or root canal treatment in posterior maxillary teeth, radiographic signs of sinusitis, or sinus lesions. The participants were categorized into 3 age groups based on the availability of CBCT images within the study period (i.e., from January 2020 to August 2021), as follows: 20–35 years; 36–50 years; and >50 years. All images of maxillary molars and premolars were examined in the coronal view to assess MT and the remaining height of the alveolar bone (RHAB) with the use of 3D imaging equipment. The type of defects and the extent of bone loss were examined in a panoramic view.

## Maximum MT measurement

The floor of the maxillary sinus was assessed for MT in the coronal view, allowing the complete length of the thickened mucosa to be examined. The thickness was measured from the sinus floor to the highest border of the mucosa in millimeters. The thickness of the sinus mucosa was described as normal if maximum MT was ≤2 mm, and as thickened if maximum MT was >2 mm.[10]

## Remaining height of the alveolar bone

The RHAB is defined as the shortest distance between the terminal alveolar bone of the tooth root and the crest of the maxillary sinus. Based on a study by Yoo et al., RHAB was divided into 3 categories: ≤4 mm; 5–9 mm; and ≥10 mm.[11] The measurement was obtained by scrolling over the scan of maxillary posterior teeth in the coronal and sagittal planes. An orientation line was created on the CBCT picture to represent RHAB.

## Estimation of the type of defects and the extent of bone loss

The defects were determined in the panoramic view by scrolling over the scans (Fig. 1), and subsequently categorized into horizontal and vertical based on the relation of the crest of the alveolar bone to the imaginary line joining the cementoenamel junction of the adjacent teeth. The extent of bone loss was graded as mild (<15%), moderate (15–33%) or severe (>33%), according to the 2017 Classification of Periodontal and Peri-Implant Diseases and Conditions by the American Academy of Periodontology (AAP).[12]

Fig. 1. Panoramic radiograph illustrating the extent of bone loss

## Evaluation of periodontitis

Patients exhibiting generalized chronic periodontitis with probing pocket depth (PPD) of 4 mm and clinical attachment level (CAL) of 1–2 mm were categorized as

healthy (mild periodontitis). Those with PPD of 6–7 mm and CAL of 3–4 mm were classified as moderate periodontitis group, and individuals with PPD ≥ 8 mm and CAL ≥ 5 mm were diagnosed with severe periodontitis. The study included first and second premolars as well as first and second molars from each quadrant of the mouth.

## Statistical analysis

The intragroup comparison was conducted using the $\chi^2$ test. The Pearson correlation coefficient was used to investigate the correlation between MT and the severity of bone loss. The evaluation of the effect of variables on MT was conducted using the multivariate linear regression analysis. The odds ratio (*OR*) with a 95% confidence interval (*CI*) was used to present the data. A *p*-value of less than 0.05 was considered statistically significant. The IBM SPSS Statistics for Windows software, v. 25.0 (IBM Corp., Armonk, USA), was used to analyze the data.

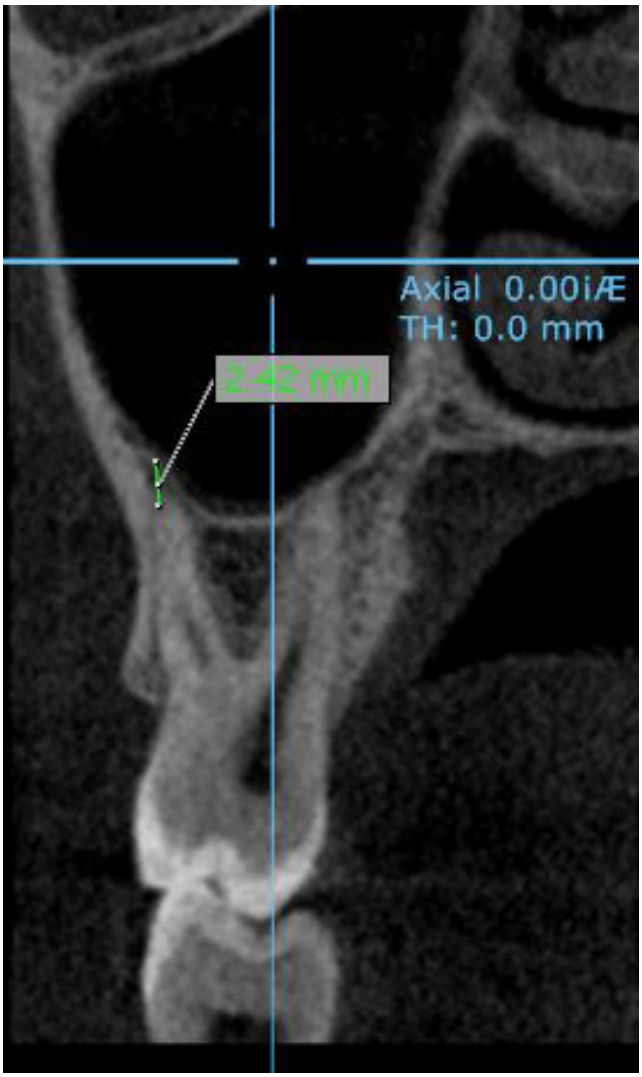


Fig. 2. Coronal view of the maxillary sinus with normal sinus mucosa
TH – thickness.

## Results

A total of 231 CBCT images of maxillary sinuses from both periodontally healthy and clinically diagnosed individuals with periodontal disease (121 males and 110 females, aged 20–63 years; mean age: 40.59 years) were evaluated. Patients above the age of 40 were found to have a higher prevalence of mucosal thickening. The CBCT images of normal and thickened mucosa in the maxillary sinuses are presented in Figures 2 and 3. Generalized mucosal thickening was observed in 179 sinuses (77.5%; $p = 0.000$). The average MT in sinuses with mucosal thickening was 4.24 mm (range: 2–14 mm). A higher frequency of mucosal thickening was observed in female patients compared to male patients (80.9% compared to 74.4%, respectively) (Table 1).

In cases where the alveolar bone height was less than or equal to 4 mm, mucosal thickening was observed in the majority of the images (128 (89.5%); $p = 0.000$). The maxillary sinus membrane was thickened in 68 CBCT images, characterized by significant alveolar bone loss (87.2%; $p = 0.020$). Mucosal thickening was considerable in horizontal defects in 121 images, i.e., 82.9% ($p = 0.001$).

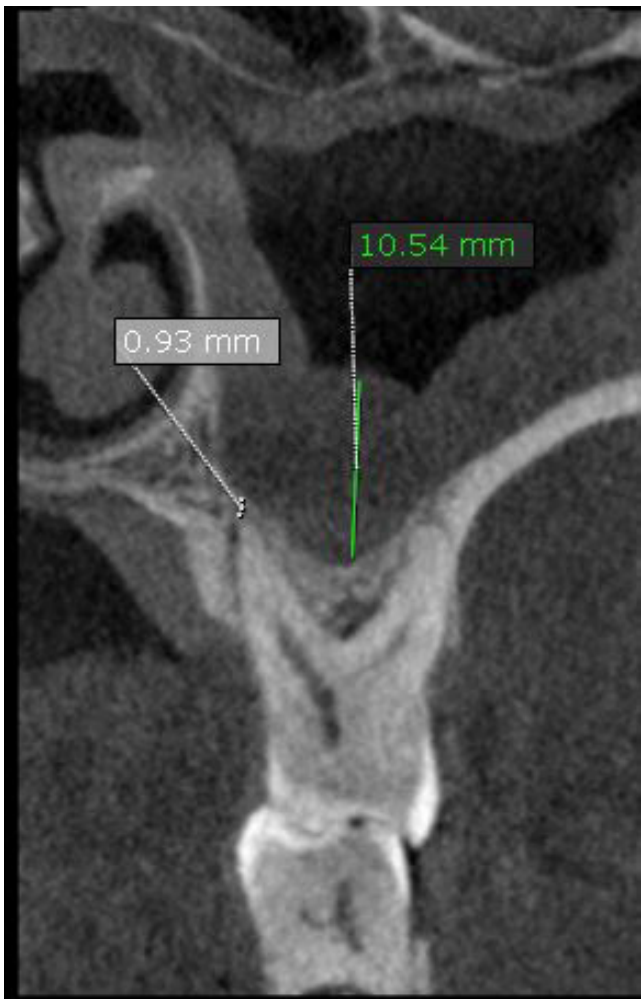


Fig. 3. Coronal view of the maxillary sinus with thickened sinus mucosa

**Table 1.** Association between demographic variables and mucosal thickening of the Schneiderian membrane

| Variable | | Mucosal thickening | | *OR* | *CI* |
|---|---|---|---|---|---|
| | | absent *n* (%) | present *n* (%) | | |
| Age [years] | 20–35 | 23 (25.6) | 67 (74.4) | 1.747 | 0.604–5.056 |
| | 36–50 | 11 (14.1) | 67 (85.9) | | |
| | >50 | 18 (28.6) | 45 (71.4) | 1.742 | 0.582–5.207 |
| Gender | male | 31 (25.6) | 90 (74.4) | 0.435 | 0.175–1.081 |
| | female | 21 (19.1) | 89 (80.9) | | |

*OR* – odds ratio; *CI* – confidence interval.

The thickening was most prevalent in second molars (83.3%), followed by first molars (82.6%), second premolars (75.8%) and first premolars (56.7%) ($p$ = 0.019) (Table 2). In patients with mucosal thickening, a mean bone loss of 4.765 ±2.100 mm was observed ($p$ = 0.034) (Table 3).

The multivariate linear logistic regression analysis revealed that the prevalence of mucosal thickening increased in response to the presence of periodontal disease (*OR:* 9.179, *CI*: 2.831–29.761; $p$ = 0.000). Mucosal thickening was more evident on the sinus floor in cases where RHAB was <4 mm (average RHAB: 2.746 ±1.659 mm) (*OR* = 1.292, *CI*: 0.00–0.041; $p$ = 0.000). First molars were most frequently associated with mucosal thickening (*OR* = 1.050, *CI*: 0.311–3.541; $p$ = 0.009) (Table 2). The mean RHAB of 2.746 ±1.659 mm was found to be statistically significant ($p$ = 0.023) in patients with MT ≥ 4.24 mm.

**Table 3.** Mean age, remaining height of the alveolar bone (RHAB) and bone loss of the study participants in relation to mucosal thickening of the Schneiderian membrane

| Variable | Mucosal thickening | *M* | *SD* | T value | *p*-value |
|---|---|---|---|---|---|
| Age [years] | present | 40.630 | 10.324 | 0.164 | 0.870 |
| | absent | 40.290 | 12.983 | | |
| RHAB [mm] | present | 2.746 | 1.659 | –2.296 | 0.023* |
| | absent | 3.480 | 1.636 | | |
| Bone loss [mm] | present | 4.765 | 2.100 | 2.134 | 0.034* |
| | absent | 3.903 | 2.039 | | |

* statistically significant ($p$ < 0.05, independent $t$-test); *M* – mean; *SD* – standard deviation.

## Discussion

The causes of mucosal thickening include periodontal disease, apical periodontitis, other odontogenic diseases, and tooth extraction.[13–16] The degree of thickening serves as a crucial factor in determining the likelihood of infection being caused by a tooth. A paucity of studies correlated the severity of periodontitis with maxillary sinus membrane thickening.[1,2,17] Furthermore, none of the early research included any clinical exams. The purpose of this study was to investigate the relationship between the thickness of the Schneiderian membrane and the periodontal condition of the corresponding maxillary posterior teeth, the severity of periodontal disease, the extent and type of bone loss, and RHAB.

**Table 2.** Association between periodontal parameters and mucosal thickening of the Schneiderian membrane

| Parameter | | Mucosal thickening | | *p*-value | *OR* | *CI* | *p*-value |
|---|---|---|---|---|---|---|---|
| | | absent *n* (%) | present *n* (%) | | | | |
| Alveolar bone loss | absent/minimal | 29 (32.6) | 60 (67.4) | 0.020* | – | – | 0.486 |
| | moderate | 13 (20.3) | 51 (79.7) | | 0.498 | 0.070–3.541 | |
| | severe | 10 (12.8) | 68 (87.2) | | 1.249 | 0.167–9.349 | |
| Defect | horizontal | 25 (17.1) | 121 (82.9) | 0.001* | – | – | 0.884 |
| | vertical | 27 (31.8) | 58 (68.2) | | 0.880 | 0.157–4.936 | |
| Minimum residual bone height [mm] | 0–4 | 15 (10.5) | 128 (89.5) | 0.000** | – | – | 0.000** |
| | 4–10 | 37 (49.3) | 38 (50.7) | | 0.104 | 0.041–0.261 | |
| | >10 | 0 (0.0) | 13 (100.0) | | 1.292 | 0.000–0.041 | |
| Group | healthy | 30 (52.6) | 27 (47.4) | 0.000** | – | – | 0.000** |
| | periodontitis | 22 (12.6) | 152 (87.4) | | 9.179 | 2.831-29.761 | |
| Teeth | first molars | 12 (17.4) | 57 (82.6) | 0.019* | – | – | 0.009* |
| | first premolars | 13 (43.3) | 17 (56.7) | | 0.180 | 0.050–0.651 | |
| | second molars | 11 (16.7) | 55 (83.3) | | 1.050 | 0.311–3.541 | |
| | second premolars | 16 (24.2) | 50 (75.8) | | 0.993 | 0.299–3.299 | |

* statistically significant ($p$ < 0.05); ** highly statistically significant ($p$ < 0.001, $\chi^2$ test).

Mucosal thickening was observed in 89.3%, 50.3% and 100% of participants with mild, moderate and severe bone loss, respectively. The results of this study are consistent with those of previous research.[1] The *OR* of severe alveolar bone loss was 1.249 (*CI*: 0.167–9.349; $p = 0.486$), suggesting that the risk of mucosal thickening increases with the severity of periodontal disease. The outcomes of the present study concur with those of a previous investigation by Phothikhun et al., who found a significant increase, i.e., threefold, in patients with severe alveolar bone loss compared to patients with mild bone loss.[18]

In the present study, mucosal thickening was more prevalent in females compared to males (80.9% vs. 74.4%, respectively). However, this difference was not statistically significant, presumably due to the inconsistency in patient selection. This finding is in contrast to the results of the study by Vallo et al., where thickening was more common in males, and was twice as prevalent in males than in females (18% vs. 8%, respectively).[19] The authors examined the occurrence of oral infections as a whole, rather than categorizing them.[19] Similar contradictory results in relation to age were reported in a study of a Chinese population, with a prevalence of 58.3% in males and 42.5% in females.[20]

The dimensions of the maxillary sinus vary depending on numerous factors, including the presence or absence of teeth, the duration of edentulousness, and periapical infection as the age of the individual increases.[21] In our sample size, with an average age of 40.59 years, mucosal thickening was found to be most prevalent in patients aged 36–50 years. The present findings are comparable with those reported by Ren et al., who described an increase in the prevalence of mucosal thickening in patients aged 26–40 years and a decline thereafter.[20] This observation could be attributed to the higher prevalence of aggressive forms of periodontitis in younger individuals, which could have led to increased thickening. However, these findings contradict those reported by Shanbhag et al., who observed a statistically significant increase in mucosal thickening in individuals older than 60.[16]

The mean MT was 4.24 mm, with a distribution of localized cases to molars in 55.1% and generalized cases in 87.0% of the patients. However, Zhang et al. reported an average MT of 4.2 ±2.1 mm with generalized mucosal thickening in all cases.[1] The potential reasons for this discrepancy could be the strict exclusion of any pathological cysts, tumors or overgrowths in our study.[1]

In the present study, mucosal thickening was more prevalent in horizontal defects (82.9%) than in vertical defects (68.2%). This finding contradicts the results reported by Ren et al., who observed a greater degree of mucosal thickening in association with vertical defects (90.2%).[20]

The dense cortical bone, which exhibits variability in thickness, usually separates the maxillary sinus membrane and maxillary posterior teeth. On occasion, this separation is confined to the mucoperiosteum. The infection from the teeth has various routes to enter the sinus cavity, including direct spread via the porous maxillary bone, as well as spread through the vascular and lymphatic channels. Therefore, it can be suggested that the proximity of a diseased tooth to the sinus lining is associated with an increased probability of infectivity transmission.[1,22]

One of the crucial criteria in the assessment of Schneiderian membrane thickening is the gap between the apical extent of the alveolar bone that supports the affected tooth and the crest of the sinus or lining, referred to as RHAB. According to Bornstein et al., the inflammatory reaction may cause thickening of the bone apical to periapical lesion as well as thickening of the mucous membrane of the maxillary sinus.[22] However, very little research has been conducted to establish a relationship between RHAB and MT.[1,23] The maximum thickness of the maxillary sinus mucosa was shown to be inversely linked with RHAB in the current investigation ($r = -0.660$, $p = 0.046$). The majority of sinus linings (89.5%) exhibited a substantial increase in MT when RHAB was less than 4 mm.

In the present study, MT was shown to be substantially associated with maxillary first and second molars, as well as second premolars, with a prevalence of 82.6%, 83.3% and 75.8%, respectively. This is in line with the study by Zhang et al. who examined the association between MT and maxillary first and second molars.[1]

In healthy individuals, MT of the sinus membrane averages 1 mm. However, thicker sinus membranes of up to 2 mm have been observed to be less susceptible to membrane perforation during sinus elevation procedures. Mucosal thickening of more than 2 mm, on the other hand, has been positively linked with sinus membrane perforation.[24,25] The current study demonstrated a correlation between MT and periodontitis, with respect to residual alveolar bone height and the extent of bone loss. Furthermore, mucosal thickening measurements exhibited statistically significant correlations with the extent of bone loss and RHAB.

## Limitations

Certain limitations must be considered when interpreting the results of the study. The assessment of changes in membrane thickness after periodontal treatment could reveal more about the association of the disease with sinus membrane thickening. A histological or microbiological examination of the thickened sinus membrane could have elucidated the association between periodontitis and Schneiderian membrane thickening.

# Conclusions

Mucosal thickening is associated with periodontitis and is proportional to the extent of bone loss. Horizontal defects show the highest incidence of mucosal thickening.

The extent of alveolar bone loss and RHAB adjacent to the infected molar are the 2 major factors related to alterations in MT. Patients with substantial furcation involvement should be questioned about sinus problems, especially if the sinus is adjacent to the teeth. While the prevalence of this type of condition is relatively low, proper evaluation and diagnosis could help avoid consequences. In patients considering implant placement, CBCT might be a useful tool for detecting periodontitis-related alterations in the sinus membrane.

## Ethics approval and consent to participate

The Institutional Ethics Committee of Vishnu Dental College, Bhimavaram, India, approved the study protocol, which adhered to the 2013 Declaration of Helsinki.

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.

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Original paper

# Comparison of the opinions and attitudes of medical doctors, dentists and mothers toward teething symptoms

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## Abstract

**Background.** The signs and symptoms associated with teething can be local or systemic. It remains unclear whether the disturbances are caused by the eruption of primary teeth or whether they simply coincide with tooth eruption. Parents and healthcare professionals can have different perceptions about teething symptoms, especially in different cultural or socio-economic contexts.

**Objectives.** The study aimed to compare the opinions and attitudes of medical doctors, dentists and mothers toward the symptoms of teething.

**Material and methods.** Data about the signs and symptoms was collected using a researcher-made questionnaire. The questionnaire was mailed in December 2019 to 800 randomly selected medical doctors and dentists working in the Central Aegean Region of Turkey. Mothers of children aged 0–3 years who were referred to the pediatric department were selected for the study. Data from 199 medical doctors (109 family physicians, 90 pediatricians), 293 dentists (169 general dentists, 124 pediatric dentists) and 352 mothers who completed the questionnaire was included in the study. The data was analyzed using the IBM SPSS Statistics for Windows program.

**Results.** Each participant identified at least one symptom related to teething. Statistically significant differences were found between the 3 groups in terms of symptoms except for stomach ache ($p < 0.05$). Gingival irritation was the most common symptom among dentists (95.6%) and mothers (70.7%), while irritability was the most common symptom among medical doctors (90.5%). Mothers believed to a greater extent than the other groups that fever, vomiting and cough were associated with teething ($p < 0.05$), whereas medical doctors tended to point to drooling, irritability, biting/chewing, diarrhea, and ear rubbing more often than the other groups ($p < 0.05$). In addition, sleep disturbance and loss of appetite were associated with teething less frequently by mothers as compared to the other groups ($p < 0.05$).

**Conclusions.** In the present study, medical doctors, dentists and mothers reported unproven and controversial associations between teething and certain local or systemic symptoms. Mothers especially were more likely to believe that systemic symptoms that can be confused with other serious diseases were associated with teething.

**Keywords:** signs and symptoms, teething, tooth eruption, primary tooth

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# Introduction

The eruption of primary teeth is a crucial moment in the life of infants, and it has remained a subject of great concern among those who directly deal with the health of these children, such as parents, dentists, pediatricians, and other healthcare professionals. Parents and healthcare professionals can have different perceptions about teething symptoms, especially in different cultural or socio-economic contexts.[1–3]

The relationship between the eruption of primary teeth and the general health of infants has been documented for over 5,000 years.[4] The signs and symptoms associated with teething may be local or systemic. Local symptoms include gingival irritation (red and sensitive gums, gingival edema, and rubbing), drooling, a drool-induced rash on the chin or face, a diaper rash, flushed cheeks, ear rubbing on the side of the erupting tooth, mouth ulcers, eruption cysts, biting objects, and finger sucking. Systemic symptoms include irritability, fever, restless sleep, the loss of appetite, crying, diarrhea, constipation, colic, vomiting, coughing due to hypersalivation, nasal discharge, strong urine odor, and stomach ache.[1,2,4–6] However, these symptoms vary from baby to baby. It remains unclear whether the eruption of primary teeth causes the disturbances or whether the symptoms coincide with tooth eruption. This is partly due to confusion between signs and symptoms. Symptoms are what the patient experiences, but children indicate that they are getting their first few teeth through signs and signals that only their caregivers can interpret.[7] According to healthcare professionals, local manifestations are more related to the process than systemic manifestations.[8,9] However, based on wrong information or beliefs, parents and healthcare professionals can mistakenly attribute the symptoms of minor or potentially fatal illnesses to teething.[10,11] These false/mistaken beliefs can contribute to the standard developmental needs of an infant going unaddressed. Also, they can lead to delays in the diagnosis of severe diseases.[1,12]

In previous studies, healthcare professionals investigated the symptoms by providing common descriptive results.[2,5,6,12–17] Only limited studies have evaluated opinions comparatively.[1,12,18,19] The present study aimed to compare the opinions and attitudes of medical doctors, dentists and mothers toward the symptoms of teething.

# Methods

This study was approved by the local Ethics Committee at Afyonkarahisar Health Sciences University, Turkey (No. 2011-KAEK-2/2019-206). The data regarding signs and symptoms was collected using a researcher-made questionnaire. The survey contained demographic factors and the signs/symptoms of teething (gingival irritation, drooling, irritability, sleep disturbance, biting/chewing, rash, loss of appetite, diarrhea, fever, ear rubbing, vomiting, cough, and stomach ache) that were frequently reported in previous studies.[1,2,4–6] The participating healthcare providers were asked: "What is the average percentage of patients who consult you for teething complaints monthly?". In December 2019, the questionnaire was mailed to 800 randomly selected medical doctors and dentists working in the Central Aegean Region of Turkey.

As mothers are generally thought to be more involved in childcare than fathers, they have been more frequently used as proxies. Our study included 400 mothers of children aged 0–3 years who were referred to the pediatric department of the university hospital in Afyonkarahisar, Turkey, for any reason from December 2019 to September 2020. The parents provided written informed consent for the various research procedures. The questionnaire included demographic factors, the educational level, and the signs/symptoms of teething (gingival irritation, drooling, irritability, sleep disturbance, biting/chewing, rash, loss of appetite, diarrhea, fever, ear rubbing, vomiting, cough, and stomach ache) that were frequently reported in previous studies.[1,2,4–6] Mothers were also asked: "Did you consult a healthcare center for your children's teething symptoms?".

The participants were divided into 3 groups for statistical analysis: medical doctors (family physicians and pediatricians); dentists (general and pediatric); and mothers. Data from the completed surveys of 199 medical doctors (109 family physicians, 90 pediatricians), 293 dentists (169 general dentists, 124 pediatric dentists) and 352 mothers were included in the study.

## Statistical analysis

The data was analyzed using the IBM SPSS Statistics for Windows program, v. 23.0 (IBM Corp., Armonk, USA). A descriptive analysis of the data is presented in the cross tables. Numbers and percentages of the demographic data were tabulated. Comparisons between the groups were performed using the $\chi^2$ and $Z$-ratio tests for categorical variables. Statistical significance was set at a $p$-value <0.05.

# Results

Out of the 844 participants, 41.7% ($n$ = 352), 34.7% ($n$ = 293) and 23.6% ($n$ = 199) were mothers, dentists and medical doctors, respectively. In the medical doctor group, 54.8% ($n$ = 109) were family physicians and 45.2% ($n$ = 90) were pediatricians. In the dentist group, 57.7% ($n$ = 169) were general dentists and 42.3% ($n$ = 124) were pediatric dentists. Figure 1 shows the group structure of the participants. The distribution of the participants by gender was as follows: 30% ($n$ = 253) were males and 70% ($n$ = 591) were females. While 42.3% ($n$ = 124) of dentists were males and 57.7% ($n$ = 169) were females, 64.8% ($n$ = 129) of medical doctors were males and 35.2% ($n$ = 70) were females. Table 1 shows the age distribution for all participants.

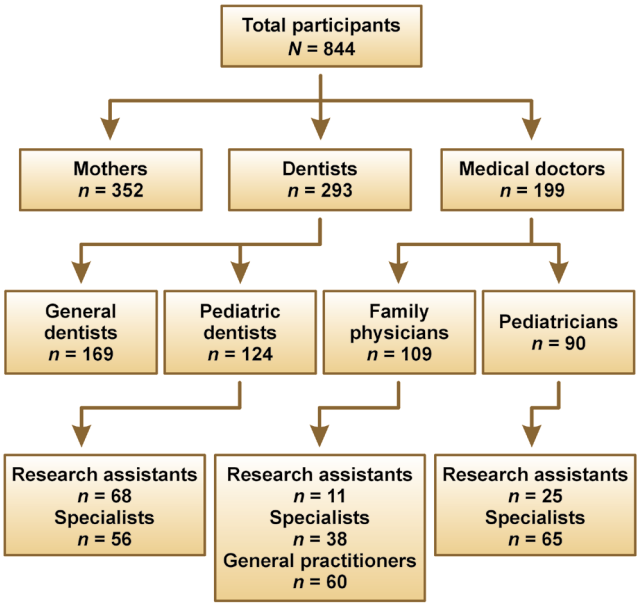


Fig. 1. Group structure of the participants

When the educational level of mothers was examined, 36.9% were found to be primary school graduates, 36.1% were high school graduates, 21.3% were university graduates, and 5.7% were Ph.D. holders. Our study found that 26.4% of the participating mothers worked outside home, while 73.6% were housewives.

Each participant in the study identified at least one symptom related to teething. Of the total number, 31.2% reported 1–4 symptoms, 40.5% reported 5–8 symptoms, and 28.3% reported 9 or more symptoms.

Statistically significant differences were found between the 3 groups in terms of symptoms except for stomach ache ($p < 0.05$). Gingival irritation (83.6%), irritability (75.0%) and drooling (70.4%) were the most common symptoms related to teething, while vomiting (8.8%), cough (6.5%), rash (6.0%), and stomach ache (2.5%) were the rarest symptoms attributable to teething.

There were significant differences in the percentage agreement between medical doctors and dentists regarding to gingival irritation ($p < 0.001$), irritability ($p < 0.05$), drooling ($p < 0.001$), biting/chewing ($p < 0.001$), diarrhea ($p < 0.001$), fever ($p = 0.028$), ear rubbing ($p < 0.001$), and rash ($p < 0.001$).

There were significant differences in the percentage agreement between medical doctors and mothers regarding gingival irritation ($p < 0.001$), irritability ($p < 0.001$), drooling ($p < 0.001$), sleep disturbance ($p < 0.001$), biting/chewing ($p < 0.001$), loss of appetite ($p < 0.001$), diarrhea ($p < 0.001$), fever ($p < 0.001$), ear rubbing ($p < 0.001$), vomiting ($p < 0.001$), cough ($p = 0.003$), and rash ($p < 0.05$).

Table 1. Age distribution of medical doctors, dentists and mothers

| Age [years] | Medical doctors *n* = 199 | Dentists *n* = 293 | Mothers *n* = 352 | Total *N* = 844 |
|---|---|---|---|---|
| <20 | 0 (0) | 0 (0) | 6 (1.7) | 6 (0.7) |
| 21–30 | 59 (29.6) | 170 (58.0) | 182 (51.7) | 411 (48.7) |
| 31–40 | 112 (56.3) | 107 (36.5) | 140 (39.8) | 359 (42.5) |
| >40 | 28 (14.1) | 16 (5.5) | 24 (6.8) | 68 (8.1) |

Data presented as number (percentage) (*n* (%)).

There were significant differences in the percentage agreement between dentists and mothers regarding gingival irritation ($p < 0.001$), irritability ($p < 0.001$), drooling ($p < 0.001$), sleep disturbance ($p < 0.05$), biting/chewing ($p < 0.001$), loss of appetite ($p < 0.001$), diarrhea ($p < 0.05$), fever ($p < 0.001$), and vomiting ($p < 0.05$).

According to groups, gingival irritation was the most common symptom listed by dentists (95.6%) and mothers (70.7%), while irritability was the most common symptom noted by medical doctors (90.5%). Mothers believed to a greater extent than the other groups that fever, vomiting and cough were associated with teething ($p < 0.05$), whereas medical doctors tended to point to drooling, irritability, biting/chewing, diarrhea, and ear rubbing more often than the other groups ($p < 0.05$). In addition, sleep disturbance and loss of appetite were associated with teething less frequently by mothers as compared to the other groups ($p < 0.05$). The distribution of symptoms according to groups is shown in Table 2.

Approximately 51.4% of mothers responded affirmatively to the question: "Did you consult a healthcare center for your children's teething symptoms?". Among these mothers, 87.3% stated that they took their child to medical doctors, while 12.7% of them visited dentists.

When medical doctors and dentists were asked: "What is the average percentage of patients who consult you for teething complaints monthly?", approx. 83.4% of medical doctors and 82.3% of dentists stated that "they are less than 10% of the patients I examine monthly". Only 16.6% of medical doctors and 17.7% of dentists stated that "they are more than 10% of the patients I examine monthly". The variation between medical doctors and dentists was not statistically significant ($p = 0.737$).

## Discussion

Teething has been a subject of studies and interest of healthcare professionals who deal with children. Previously, only a limited number of studies evaluated opinions comparatively.[1,12,18,19] However, the present study comparatively evaluates the opinions of the medical doctors (family physicians and pediatricians), dentists (general and pediatric) and mothers closely dealing with teething.

Gingival irritation (83.6%) was the symptom most associated with teething among all respondents, which is in accordance with previous clinical and survey studies.[5,7,14–17,20,21] Among the current study groups, gingival irritation was most commonly noted by dentists (95.6%), which is a finding similar to that reported by Aliabad et al.[19]

**Table 2.** Distribution of the answers of the participants about the signs/symptoms of teething

| Signs/symptoms of teething | Answers | Medical doctors *n* = 199 | Dentists *n* = 293 | Mothers *n* =352 | Total *N* = 844 | *p*-value |
|---|---|---|---|---|---|---|
| Gingival irritation | related | 177 (88.9)[a] | 280 (95.6)[b] | 249 (70.7)[c] | 706 (83.6) | <0.001* |
| | non-related | 22 (11.1)[a] | 13 (4.4)[b] | 103 (29.3)[c] | 138 (16.4) | |
| Irritability | related | 180 (90.5)[a] | 238 (81.2)[b] | 215 (61.1)[c] | 633 (75.0) | <0.001* |
| | non-related | 19 (9.5)[a] | 55 (18.8)[b] | 137 (38.9)[c] | 211 (25.0) | |
| Drooling | related | 179 (89.9)[a] | 221 (75.4)[b] | 194 (55.1)[c] | 594 (70.4) | <0.001* |
| | non-related | 20 (10.1)[a] | 72 (24.6)[b] | 158 (44.9)[c] | 250 (29.6) | |
| Sleep disturbance | related | 130 (65.3)[a] | 171 (58.4)[a] | 160 (45.5)[b] | 461 (54.6) | <0.001* |
| | non-related | 69 (34.7)[a] | 122 (41.6)[a] | 192 (54.5)[b] | 383 (45.4) | |
| Biting/chewing | related | 161 (80.9)[a] | 178 (60.8)[b] | 118 (33.5)[c] | 457 (54.1) | <0.001* |
| | non-related | 38 (19.1)[a] | 115 (39.2)[b] | 234 (66.5)[c] | 387 (45.9) | |
| Loss of appetite | related | 136 (68.3)[a] | 190 (64.8)[a] | 106 (30.1)[b] | 432 (51.2) | <0.001* |
| | non-related | 63 (31.7)[a] | 103 (35.2)[a] | 246 (69.9)[b] | 412 (48.8) | |
| Diarrhea | related | 104 (52.3)[a] | 60 (20.5)[b] | 115 (32.7)[c] | 279 (33.1) | <0.001* |
| | non-related | 95 (47.7)[a] | 233 (79.5)[b] | 237 (67.3)[c] | 565 (66.9) | |
| Fever | related | 13 (6.5)[a] | 37 (12.6)[b] | 217 (61.6)[c] | 267 (31.6) | <0.001* |
| | non-related | 186 (93.5)[a] | 256 (87.4)[b] | 135 (38.4)[c] | 577 (68.4) | |
| Ear rubbing | related | 63 (31.7)[a] | 39 (13.3)[b] | 33 (9.4)[b] | 135 (16.0) | <0.001* |
| | non-related | 136 (68.3)[a] | 254 (86.7)[b] | 319 (90.6)[b] | 709 (84.0) | |
| Vomiting | related | 7 (3.5)[a] | 21 (7.2)[a] | 46 (13.1)[b] | 74 (8.8) | <0.001* |
| | non-related | 192 (96.5)[a] | 272 (92.8)[a] | 306 (86.9)[b] | 770 (91.2) | |
| Cough | related | 5 (2.5)[a] | 18 (6.1)[ab] | 32 (9.1)[b] | 55 (6.5) | 0.010* |
| | non-related | 194 (97.5)[a] | 275 (93.9)[ab] | 320 (90.9)[b] | 789 (93.5) | |
| Rash | related | 3 (1.5)[a] | 26 (8.9)[b] | 22 (6.3)[b] | 51 (6.0) | 0.003* |
| | non-related | 196 (98.5)[a] | 267 (91.1)[b] | 330 (93.8)[b] | 793 (94.0) | |
| Stomach ache | related | 4 (2.0)[a] | 10 (3.4)[a] | 7 (2.0)[a] | 21 (2.5) | 0.453 |
| | non-related | 195 (98.0)[a] | 283 (96.6)[a] | 345 (98.0)[a] | 823 (97.5) | |

Data presented as *n* (%). Different letters in superscript show statistically significant differences between the groups at the level of $p < 0.05$; * statistically significant.

In most studies, irritability is listed as the most frequent symptom of teething.[1,6,15–17,20–22] In the current study, irritability (75.0%) was similarly associated with teething among most of the respondents. The rates were 90.5% for medical doctors, 81.2% for dentists and 61.1% for mothers. The current results are similar to those from a study showing that general practitioners reported irritability as a sign of teething more often than nurses and dentists.[19] This may be related to the fact that families more often visit medical doctors for teething complaints.

There is an increase in saliva production during the first 3–4 months of life as the salivary glands develop and during the teething period. Drooling (70.4%) was among the most often noted symptoms during the teething period among medical doctors (89.9%), dentists (75.4%) and mothers (55.1%), which is a finding similar to those of previous studies.[2,5,6,13–17,20,22]

Previous subjective parental information and most of prospective clinical studies pointed to sleep disturbance during the teething period.[3–6,13–17,23,24] In the present study, more than half of the participants (54.6%) attributed sleep disturbance to teething. In a study performed in Iowa, USA, a greater percentage of pediatric dentists and parents reported sleep disturbance than pediatricians.[18] However, the present study showed the following ranking for the observation of sleep disturbance: medical doctors (65.3%); dentists (58.4%); and mothers (45.4%). The differences between the studies may be due to the fact that our study groups were composed of pediatricians or pediatric dentists and non-specialists, like family physicians and general dentists. Also, sociocultural or educational differences as well as variations in the sample size between the study groups may have led to such discrepancies.

In the present study, 54.1% of the participants reported biting, chewing or sucking during the teething period, which is similar to previous clinical studies.[4,5,15,16] In a study conducted among pediatricians, general practitioners, dentists, and nurses, dentists had the highest level of agreement for biting (96%), followed by nurses (91%).[19] Biting or chewing were commonly stated symptoms during teething in parent surveys,[3,12,17,21,25] but in this study, medical doctors (80.9%) and dentists (60.8%) reported these symptoms more often than mothers (33.5%). It can be assumed that socioeconomic and cultural differences among mothers may have

contributed to the disparities in the findings of the abovementioned studies. Also, differences in the sample size of the study groups may have contributed to varied results.

In the present study, 51.2% of the respondents stated that the loss of appetite was associated with teething. Most parents and healthcare professionals in Turkey and other countries similarly attribute a decrease in appetite to teething. Additionally, the levels of interleukin-1 beta (IL-1β) have also been correlated with the loss of appetite.[3–6,13–16,21,25–27] According to the group data from the present study, medical doctors (68.3%) and dentists (64.8%) reported the loss of appetite more often than mothers (30.1%). This result may be related to the appetite level being a subjective finding among mothers.

In the current study, diarrhea was attributed to teething by 33.1% of all participants. In previous studies, mothers of varying cultures believed that their child's diarrhea at this age was due to teething.[1,5,7,17,21,23,25] Some researchers who followed children during the eruption period attributed diarrhea to teething, and the levels of IL-1β and interleukin-8 (IL-8), as well as to placing contaminated objects in the mouth, extra saliva and infectious agents.[1,2,6,20,23,27] In a study conducted among Florida pediatricians (USA), 34.9% of participants associated teething with diarrhea.[14] In a study on parents, pediatric dentists and pediatricians from Iowa, USA, the reported rates of diarrhea during teething were 56.7%, 52% and 9.1%, respectively.[18] In the present study, the rates were as follows: 52.3% for medical doctors; 20.5% for dentists; and 32.7% for mothers. The differences between the studies can be attributed to the sample size, differences in the definition of diarrhea, variations within the sample groups (including pediatricians, or pediatricians and general physicians), and cultural differences. Additionally, the lower rate noted among dentists can be attributed to the fact that diarrhea is not a typical subject evaluated in dental training or practice.

Fever is among the symptoms most frequently reported by mothers from different countries.[1–3,16,17,21,23,25] However, the results are controversial among healthcare professionals. Some authors reported fever during teething, and correlated it with early vital factors, or high levels of IL-1β and tumor necrosis factor (TNF) in the gingival crevicular fluid.[20,27,28] Alternately, some prospective studies reported a slight increase in body temperature only on the day of eruption (36.70 ±0.39°C); at other times, the temperature remained within normal limits and could not be defined as fever.[5,6,13] In the present study, 31.6% of the responders reported >38.5°C fever. Mothers (61.6%) reported fever more often than dentists (12.6%) and medical doctors (6.5%), which is similar to other studies.[1,18] The false beliefs associated with teething were found to be significantly associated with the educational level. Commonly, healthcare professionals and parents with a high level of education were found to have a better knowledge about teething.[29] Based on these results, it is not surprising that mothers having at least a university degree constituted only 27% of the group, which resulted in the group of mothers having more misconceptions.

In previous studies, mothers associated ear rubbing with teething.[17,29] However, a study by Tasanen showed no relationship between teething and ear rubbing.[16] In the present study, 16% of the respondents attributed ear rubbing to teething. Medical doctors (31.7%) noted ear rubbing more often than dentists (13.3%) and mothers (9.4%). These results may be related to the fact that patients generally consult a medical doctor for ear rubbing/earache, and when there are no symptoms of infection or other diseases, ear rubbing is attributed to teething.

Vomiting was associated with teething by only 8.8% of the respondents; mothers (13.1%) attributed it to teething more often than dentists (7.2%) and medical doctors (3.5%). Although vomiting was associated with teething in other studies conducted with the participation of parents,[2,23,26,29] in the majority of prospective studies, it was not associated with teething.[4,5,25,29]

In a study conducted in Egypt, Allam reported that 48% of mothers believed that cough could be due to teething.[23] On the other hand, in prospective studies, healthcare professionals did not attribute cough or bronchitis to teething.[5,16] In the present study, mothers (9.1%) associated cough with teething statistically more often than medical doctors (2.5%). Additionally, only 6.5% of the participants in total claimed cough to be a teething symptom. Although the rate was low, it should not be forgotten that attributing these symptoms to teething can lead to other severe illnesses, like bronchopneumonia, being overlooked. Therefore, mothers especially should be informed of this misconception.

Rash (6.0%) was one of the least often declared teething symptoms among the respondents, especially among medical doctors (1.5%). In parent surveys, cheek rashes or diaper rashes were attributed to teething.[6,17,23] Although some studies including physicians listed facial rashes,[15] most prospective studies reported that rash was not associated with teething.[4,5,25,29] It can be surmised that the circumoral area can be irritated by drooling. Otherwise, facial rashes along with other accompanying systemic manifestations should be associated with human herpesvirus 6 (HHV-6) or other infections common among children of that age.[4]

## Limitations

The limitation of this study is that the study group did not represent all demographics. A study with a larger population size that would include multiple geographical areas and different specialists is required for identifying relationships between the eruption of primary teeth and local or systemic manifestations.

# Conclusions

In the present study, medical doctors, dentists and mothers reported unproven and controversial associations between teething and local or systemic symptoms.

Mothers were more likely to confuse systemic symptoms that should be attributed to serious diseases with those of teething. Many of these signs can be part of the normal developmental process and can be attributed to teething, or may be due to a childhood disease. Neglecting important disease symptoms based on the belief that the symptoms are caused by teething as well as paying unnecessary attention to the complaints actually related to teething negatively affect a child's physical health and quality of life. Medical doctors and dentists should dispel longstanding cultural myths and false beliefs about teething, and share evidence that teething is not strongly associated with severe symptoms. Providing education about the teething period in infants during prenatal classes for mothers, in professional health programs and during the continuing vocational education for healthcare professionals should be considered.

## Ethics approval and consent to participate

This study was approved by the local Ethics Committee at Afyonkarahisar Health Sciences University, Turkey (No. 2011-KAEK-2/2019-206). Informed written consent was obtained from the paricipants.

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

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Original paper

# Potential protective role of parsley on induced tongue carcinogenesis in albino rats

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## Abstract

**Background.** Parsley has been traditionally used as a food additive and herbal medicament. The flavonoid apigenin and its glycosides constitute the most abundant phenolic compounds found in parsley. They exhibit numerous pharmacological effects, including antioxidant, anti-inflammatory, antitoxic, and anticancer properties.

**Objectives.** The aim of the study was to evaluate the potential chemopreventive effect of orally administered parsley extract on tongue cancer induced by 7,12-dimethylbenz[a]anthracene (DMBA) and formaldehyde in rats.

**Material and methods.** A total of 36 adult male albino rats were randomly allocated into 3 equal groups: the parsley group was administered 2 g/kg body weight parsley extract through oral gavage 3 times per week; the carcinogenesis group received a topical application of 0.5% DMBA in acetone and formaldehyde to the tongues; and the parsley-treated carcinogenesis group was administered parsley extract combined with a topical application of DMBA and formaldehyde. Additionally, a group of 5 rats served as a negative control group. After 8 weeks, the tongues of the rats were dissected and subjected to histopathological, immunohistochemical, histomorphometric, and quantitative real-time polymerase chain reaction (qRT-PCR) analyses.

**Results.** Histopathologically, the tongues from the carcinogenesis group revealed several signs of hyperplasia, dysplasia and the invasion of dysplastic cells into the underlying connective tissue. The tongues of the parsley-treated carcinogenesis group exhibited a reduction in dysplastic changes and almost regained their normal architecture, as observed in both the control and parsley groups. The immunohistochemical analysis of the area percentage of caspase-3 immunoexpression revealed a significant increase in the parsley-treated carcinogenesis group compared to the carcinogenesis group, which approached the results observed in both the control and parsley groups. The qRT-PCR results of tumor necrosis factor-alpha (*TNF-α*) expression displayed a significantly decreased expression in the parsley-treated carcinogenesis group as compared to the carcinogenesis group. These findings were comparable to those observed in the control and parsley groups.

**Conclusions.** In a rat model, oral administration of parsley extract has been shown to impede the initiation of several cellular carcinogenic changes in tongue tissues.

**Keywords:** apigenin, plant extracts, *Petroselinum*, anthracene, tongue neoplasms

## Highlights

- Oral administration of parsley extract hindered the progression of tongue cancer.
- Parsley's apiin triggered apoptosis and inhibited inflammation via the upregulation of caspase-3 and the downregulation of *TNF-α*.
- Parsley could be considered a good source of natural chemopreventive compounds.

# Introduction

Cancer is one of the leading causes of death worldwide. Among the most prevalent forms of the disease is oral squamous cell carcinoma (OSCC). Oral carcinoma includes cancer of the lip, floor of the mouth, buccal surface, hard palate, alveolar surfaces, salivary glands, and tongue.[1,2]

Tongue cancer accounts for approx. 40–60% of all deaths caused by oral cancer. Tongue squamous cell carcinoma (TSCC) is reported to be a life-threatening condition due to the complexity of the tongue, which is characterized by rich vascular and lymphatic networks. The musculature of the tongue fosters aggressive behavior, manifesting as local invasion and regional lymph node metastasis.[3,4]

The downregulation or high inactivation of caspase-3 expression is typically observed in cancer cells, making them resistant to local microenvironmental stresses as well as various treatments.[5] Caspase-3 and cleaved caspase-3 are considered biomarkers in the diagnosis of TSCC. The co-expression of cleaved caspase-3 and/or caspase-3 has shown tumor-suppressing properties in patients with TSCC.[6]

In carcinogenesis, tumor necrosis factor-alpha (TNF-α) is essential for the epithelial–mesenchymal transition of tumor cells, loss of intercellular adhesion, increased motility of tumor cells, and direct invasiveness or vascular metastasis. These effects are the result of changes in the tumor microenvironment that enhance tumor cell proliferation, migration, invasiveness, and metastasis.[7]

The primary goal of tongue cancer treatment is to eradicate the primary tumor lesion in the tongue by surgical excision or cryosurgery, control any other neck diseases (nodal metastasis) through chemotherapy or radiotherapy, and preserve tongue functions to the greatest extent possible.[8] Various treatment modalities are associated with serious side effects such as pain, necrosis and loss of function. Therefore, there is an urgent need for chemoprevention, defined as the administration of drugs or natural agents with the aim of preventing cancer.[9]

Cancer chemoprevention refers to the application of agents designed to hinder, delay, or even reverse carcinogenesis before the initiation, progression and invasion of cancerous tissue. This process usually involves a prolonged administration of natural or synthetic chemopreventive compounds.[9]

Parsley (*Petroselinum crispum*, family: Apiaceae) is a bright green, biennial plant that thrives in temperate climates. The leaves and stems, whether fresh or dried, as well as their seeds, have been introduced into the food industry, creams, soaps, and perfume manufacturing.[10] The flavonoid apigenin is the main polyphenolic compound of parsley, which has antioxidant, anti-inflammatory, antiproliferative, antiulcer, and immunosuppressive properties. It has been shown to inhibit the induction, proliferation and migration of various human cancer cell lines.[11] Thus, the present study aimed to investigate the potential protective effect of parsley in preventing or hindering the progression of carcinogenesis in induced tongue cancer in a rat model. The evaluation of this effect was conducted through histopathological analysis, immunohistochemical assessment of caspase-3, and by quantitative real-time polymerase chain reaction (qRT-PCR) analysis to determine *TNF-α* gene expression.

# Material and methods

## Ethics statement

The study was approved by the Institutional Animal Care and Use Committee (IACUC), Faculty of Science, Cairo University, Egypt (approval No. CU-III-F-15-19).

## Preparation of parsley extract

Fresh leaves of parsley (*P. crispum*) were air-dried at room temperature and ground into fine powder. The powdered leaves were then soaked in ethanol at room temperature (27°C) and extracted for 48 h with occasional shaking to obtain parsley extract. The extract was filtered and evaporated under reduced pressure (60°C) until it was completely dry. Subsequently, it was dissolved in distilled water prior to its administration to rats.[12]

## High-performance liquid chromatography analysis

The quantification of the active compound (apiin) was conducted by transferring a 7.5-mg sample of the alcoholic extract to a 10-mL measuring flask. The volume was then adjusted to the designated mark with methanol and sonicated for a few seconds. Subsequently, a sample

of this solution was filtered through a 0.45-μm membrane filter prior to the high-performance liquid chromatography (HPLC) analysis.[13]

## Sample size

The sample size was calculated using the G*power software, v. 3.0 (https://www.psychologie.hhu.de/arbeits-gruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower). The estimated sample size was 36, with 12 rats allocated to each experimental group. The primary outcome (hindering or preventing carcinogenic changes) was based on the study by Kasem et al.,[14] the results of which indicated that the administration of *Mentha piperita* extract, which has a similar antioxidant effect as parsley, resulted in a reduction of dysplastic carcinogenic changes induced by DMBA or formaldehyde by 61% and inhibited tumor incidence by 100%. A large effect size of approx. 0.6 was anticipated. The statistical power was set at 80% and the α error probability was set at 0.05.

## Animals

Thirty-six adult male albino Wistar rats (*Rattus norvegicus*), with an average age of 4–6 months and an average weight of 150–200 g, were used in this study. The subjects were randomly allocated into 3 equal groups. The animals were housed in specially designed stainless steel cages with a controlled environment (temperature: 25 ±2° and 12-hour dark/light cycles) under good ventilation. The rats were fed a standardized balanced laboratory diet of regular rat chow and distilled water ad libitum. The diet was formulated to meet the nutrient needs of rodents for the duration of the experiment. An additional 5 rats were used as a negative control group.

## Induction of tongue carcinogenesis

Formaldehyde and DMBA were used in carcinogenesis. These carcinogens were purchased from Sigma-Aldrich Chemical Pte. Ltd. (Cairo, Egypt). The dorsal and ventral surfaces of each rat's tongue were painted with 0.5% DMBA in acetone, 3 days per week, with the use of a size #3 camel hair brush. After 9 days, a 10% formaldehyde solution in water was applied in conjunction with DMBA for an additional 3 days per week over the course of 8 weeks.[14]

## Experimental design

The 36 rats were divided into the following groups:
– parsley group: 12 healthy rats supplied with a dose of 2 g/kg body weight of parsley extract via oral gavage 3 days per week for a period of 8 weeks[15];
– carcinogenesis group: 12 rats with induced tongue carcinogenesis. This group received no treatment;
– parsley-treated carcinogenesis group: 12 rats provided with parsley extract as in the parsley group, combined with DMBA and formaldehyde as in the carcinogenesis group.

## Postmortem specimen processing

Eight weeks after the beginning of the experiment, all rats were sacrificed via intraperitoneal injection of a mixture of ketamine (300–360 mg/kg) and xylazine (30–40 mg/kg), as outlined in the American Veterinary Medical Association (AVMA) guidelines.[16] Whole tongues were dissected from all subjects. Subsequently, the specimens were fixed in 10% neutral buffered formalin for 24 h, dehydrated in ascending grades of ethyl alcohol, cleared in xylene, and embedded in paraffin. Sections measuring 4–5 μm were obtained and subjected to the histopathological, immunohistochemical, histomorphometric, and qRT-PCR analyses.

### Histopathological examination

The hematoxylin and eosin (H&E) stains were used in accordance with the standard technique to assess the histopathological changes observed in the tongues of the subjects.[17]

### Immunohistochemical examination

Paraffin sections obtained from each group were mounted over positively charged slides. The caspase-3 antibody was used as the immunohistochemical marker. The immunostained sections were then examined with the use of a light microscope (Leica DMLB 2; Leica Microsystems GmbH, Wetzlar, Germany). The positive reaction manifested as brown membranous, cytoplasmic, and/or nuclear staining.[18]

### Histomorphometric analysis of caspase-3 immunoexpression

The immunohistochemically stained sections were evaluated using Leica QWin 500 image processing and analyzing software (Leica Microsystems GmbH). The image analyzer was calibrated automatically to convert the measurement units [px] produced by the program into micrometers [μm]. Immunostaining was measured as area and area percentage in a standard measuring frame in 5 fields for each specimen using ×400 magnification by light microscopy transferred to the screen. The areas exhibiting brown 3,3'-diaminobenzidine (DAB) immunostaining were selected for evaluation. These areas were masked by a red binary color to be measured by the computer system. The mean and standard deviation ($M \pm SD$) values were obtained for each group.

### qRT-PCR analysis for the evaluation of *TNF-α* gene expression

The tissue homogenate was processed for RNA extraction using the Promega spin or vacuum (SV) Total RNA Isolation System (Thermo Fisher Scientific, Waltham, USA), followed by reverse transcriptase for complementary DNA (cDNA) synthesis and qRT-PCR. The qRT-PCR amplification and analysis were performed using a StepOne™ System software v. 3.1 (Applied Biosystems, Foster City, USA).[19,20] Primer sequences of the studied genes are listed in Table 1.

Table 1. Primer sequences of the studied genes

| Gene | Primer sequence from 5′ to 3′ | GenBank accession number |
|---|---|---|
| *TNF-α* | forward: GCCTCTTCTCATTCCTGCTT<br>reverse: CACTTGGTGGTTTGCTACGA | AF_269160.1 |
| *β-actin* | forward: CTATGTTGCCCTAGACTTCG<br>reverse: AGGTCTTTACGGATGTCAAC | NM_031144.3 |

## Statistical analysis

The data obtained from the histomorphometric analysis as well as the qRT-PCR analysis was presented as *M* ±*SD*. The data was coded and evaluated using the IBM SPSS Statistics for Windows software, v. 21.0 (IBM Corp., Armonk, USA). The Kolmogorov–Smirnov test revealed a normal distribution of the data. Comparisons between the studied groups for normally distributed numeric variables were conducted using analysis of variance (ANOVA). A Tukey's post hoc test was employed for multiple pairwise comparisons. The value of $p < 0.05$ was considered statistically significant.

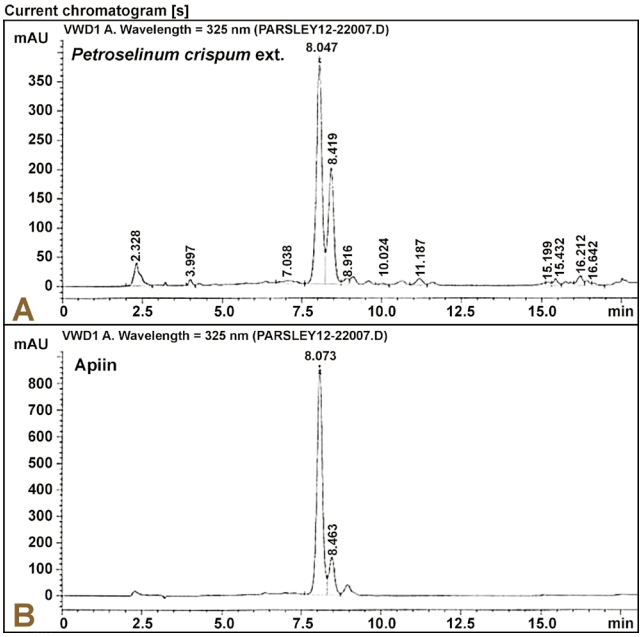


Fig. 1. High-performance liquid chromatography (HPLC) profile of ethanolic extract of *Petroselinum crispum* leaves (A) and standard apiin (B)

VWD – Variable Wavelength Detector.

# Results

## HPLC quantification of apiin

The quantity of apiin, a diglycoside of the flavone apigenin, was found to be 6.41 g% (w/w) in the alcoholic extract of parsley, as determined by the standard calibration curve of apiin, constructed based on the HPLC analysis (Fig. 1).

## Histopathological results

The histopathological examination of the tongues of the rats in the control group revealed normal tongue architecture, characterized by keratinized stratified squamous epithelium and filiform papillae covering the dorsal surface (Fig. 2A). The ventral surface displayed normal stratified squamous epithelium with a thin keratin layer

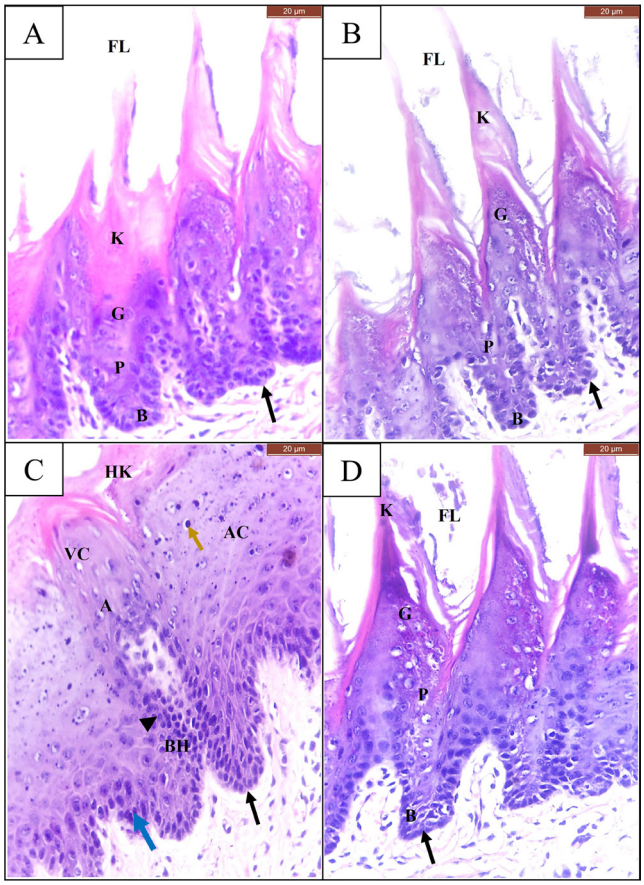


Fig. 2. Photomicrographs of the dorsal surface of rats' tongues from the control (A), parsley (B), carcinogenesis (C), and parsley-treated carcinogenesis (D) groups (hematoxylin and eosin (H&E), ×400 magnification)

The control, parsley and parsley-treated carcinogenesis groups exhibit normal mucosa covered by keratinized stratified squamous epithelium, filiform papillae (FL), intact basement membrane (black arrow), basal cell layer (B), prickle cell layer (P), granular cell layer (G), and keratin layer (K). The carcinogenesis group shows filiform papillae with intact basement membrane (black arrow), basal cell hyperplasia (BH), loss of basal cell polarity (blue arrow), acanthosis in the prickle cell layer (AC), vacuolated cells (VC), nuclear hyperchromatism (arrowhead), nuclear atypia (A), prominent nucleoli (orange arrow), and hyperparakeratinization (HK).

and short, saw-like rete pegs. The underlying connective tissue showed no evidence of infiltration of the inflammatory cells (Fig. 3A). The specimens in the parsley group did not exhibit marked histopathological differences in either the dorsal (Fig. 2B) or ventral (Fig. 3B) surfaces as compared to those of the control group.

The dorsal and ventral surfaces of the rats' tongues in the carcinogenesis group exhibited hyperplastic stratified squamous epithelium with hyperkeratinization, basal cell hyperplasia and dysplastic cellular changes. These changes included abnormal mitosis with atypical mitotic figures, alteration of the nuclear–cytoplasmic (N/C) ratio, nuclear hyperchromatism, nuclear atypia, and prominent nucleoli. Numerous vacuolated cells and individual cell keratinization (dyskeratosis) were easily identified across different epithelial layers. The connective tissue also exhibited areas of subepithelial inflammatory cell infiltration as well as dilated blood vessels (Fig. 2C,3C). The ventral surface demonstrated the rupture of the basement membrane, with the microinvasion of the dysplastic, hyperchromatic basal cells into the subepithelial connective tissue (Fig. 3C).

The histological examination of the parsley-treated carcinogenesis group revealed normal histology of both the dorsal and ventral surfaces of the rats' tongues, similar to those of the control group. However, 3 specimens were still showing signs of epithelial hyperplasia and hyperkeratinization (Fig. 2D,3D).

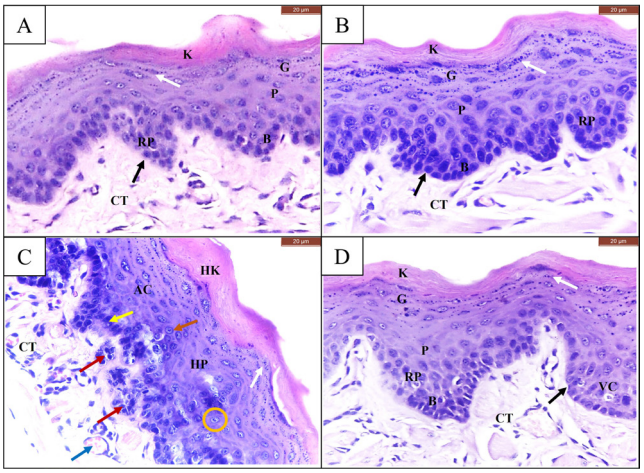


**Fig. 3.** Photomicrographs of the ventral surface of rats' tongues from the control (A), parsley (B), carcinogenesis (C), and parsley-treated carcinogenesis (D) groups (H&E, ×400 magnification)

The control, parsley and parsley-treated carcinogenesis groups exhibit normal mucosa covered by thin stratified squamous epithelium, normal basal cell layer (B), prickle cell layer (P), granular cell layer (G) with small keratohyalin granules (white arrow), thin parakeratin layer (K), vacuolated cells (VC), intact basement membrane (black arrow), and short saw-like rete pegs (RP) with underlying connective tissue (CT). The carcinogenesis group shows epithelial hyperplasia (HP) with hyperparakeratinization (HK), enlarged keratohyalin granules (white arrow) in the granular cell layer, acanthosis in the prickle cell layer (AC), abnormal mitotic figures (orange circle), alteration of the nuclear–cytoplasmic (N/C) ratio (yellow arrow), prominent nucleoli (orange arrow), and the dissolution of the basement membrane with the invasion of dysplastic epithelial cells (red arrows) into the underlying connective tissue (CT) with the blood vessel (blue arrow).

## Immunohistochemical results

The immunohistochemical examination of the tissue sections from rats' tongues in the control, parsley and parsley-treated carcinogenesis groups revealed moderate to strong membranous, cytoplasmic, and nuclear caspase-3 immunoreactivity in the entire epithelial thickness of both dorsal (Fig. 4A,4B,4D) and ventral surfaces (Fig. 5A,5B,5D). However, the carcinogenesis group revealed negative to weak cytoplasmic and nuclear caspase-3 immunoreactivity in the entire epithelial thickness of the dorsal surface (Fig. 4C). Additionally, the ventral surface showed a negative to weak cytoplasmic and nuclear caspase-3 immunoreactivity in the basal and granular cell layers. In contrast, the spinous cell layer exhibited moderate cytoplasmic and nuclear caspase-3 immunoreactivity (Fig. 5C).

## Histomorphometric results

The analysis of variance revealed a significant difference among all groups ($p$ = 0.000). The highest mean

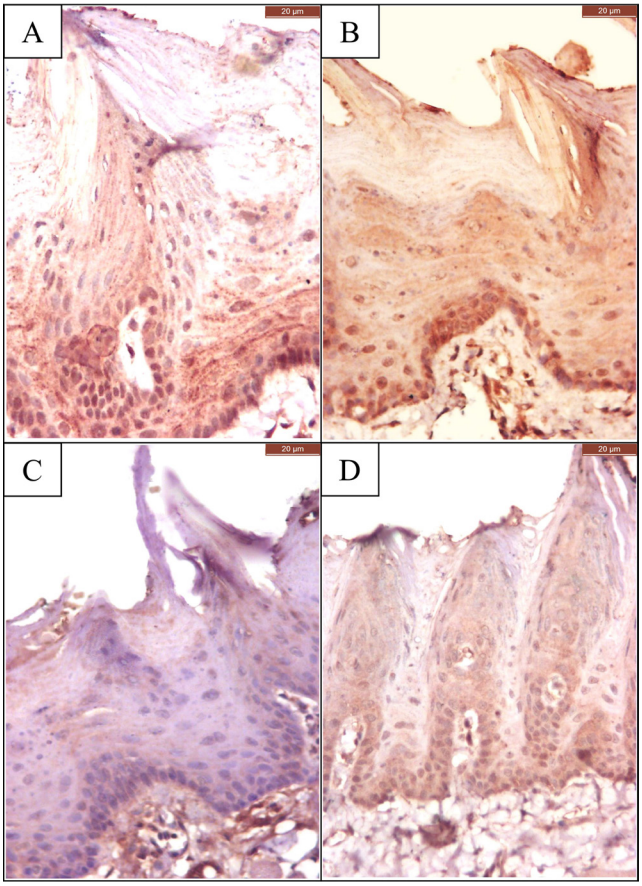


**Fig. 4.** Photomicrographs of the dorsal surface of rats' tongues from the control (A), parsley (B), carcinogenesis (C), and parsley-treated carcinogenesis (D) groups (3,3'-diaminobenzidine (DAB), ×400 magnification)

The control, parsley and parsley-treated carcinogenesis groups exhibit moderate to strong membranous, cytoplasmic and nuclear caspase-3 immunoreactivity in the entire epithelial thickness. The carcinogenesis group demonstrates negative to weak cytoplasmic and nuclear caspase-3 immunoreactivity in the entire epithelial thickness.

value of caspase-3 immunoexpression was recorded in the control group and the lowest value was observed in the carcinogenesis group. The Tukey's post hoc test for pairwise comparisons revealed a statistically significant decrease in the area percentage of caspase-3 immunoexpression in the carcinogenesis group in comparison to the control, parsley and parsley-treated carcinogenesis groups ($p$ = 0.000). Additionally, a statistically significant decrease in the area percentage of caspase-3 immunoexpression was observed in the parsley-treated carcinogenesis group compared to the control group ($p$ = 0.006). No statistically significant differences were identified in caspase-3 immunoexpression between the parsley and control groups ($p$ = 0.280), nor between the parsley and parsley-treated carcinogenesis groups ($p$ = 0.204) (Table 2).

## Results of the qRT-PCR analysis

The analysis of variance revealed a significant difference among all groups ($p$ = 0.000). The highest mean value of *TNF-α* gene expression was documented in the carcinogenesis group, while the lowest value was reported in the parsley group. The Tukey's post hoc test for pairwise comparisons revealed a statistically significant increase in *TNF-α* mRNA gene expression in the carcinogenesis and parsley-treated carcinogenesis groups compared to the control and parsley groups ($p$ = 0.000). In addition, a statistically significant decrease in *TNF-α* gene expression was observed in the parsley-treated carcinogenesis group compared to the carcinogenesis group ($p$ = 0.000). However, no statistically significant difference in *TNF-α* gene expression was observed between the parsley and control groups ($p$ = 0.999) (Table 2).

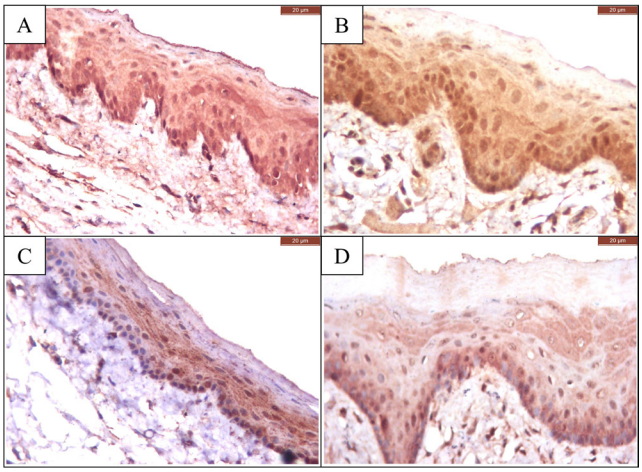


**Fig. 5.** Photomicrographs of the ventral surface of rats' tongues from the control (A), parsley (B), carcinogenesis (C), and parsley-treated carcinogenesis (D) groups (DAB, ×400 magnification)

The control, parsley and parsley-treated carcinogenesis groups show moderate to strong membranous, cytoplasmic, and nuclear caspase-3 immunoreactivity in the entire epithelial thickness. The carcinogenesis group displays negative to weak cytoplasmic and nuclear caspase-3 immunoreactivity in the basal and granular cell layers. Moderate cytoplasmic and nuclear caspase-3 immunoreactivity is visible in the spinous cell layer.

# Discussion

Cancer chemoprevention is defined as the use of pharmaceutical agents, including diet-derived nutritional compounds, to delay, disrupt, or reverse the process of tumorigenesis, especially at the promotion stage.[21]

Parsley, a natural herb, has been identified as a valuable candidate for anticancer treatment due to its anti-inflammatory, antioxidant, antiproliferative, antitumor, and apoptotic properties.[22]

The current study was based on the two-stage carcinogenesis model. The DMBA was applied topically as a chemical initiator mutagen, followed by formaldehyde, which was used as a chemical promotor of previously transformed cells. The continuous application of formaldehyde has been demonstrated to accelerate carcinogenesis.[14]

In this work, ethanol was used as a solvent for obtaining the alcoholic extract from parsley leaves. Using ethanol provides the highest extraction value of polyphenolic compounds, especially apigenin, due to their enhanced solubility in the substance compared to water.[23]

Regarding the histopathological findings of the present investigation, the tongue specimens of the control group exhibited normal tissue and cellular architecture of the keratinized stratified squamous epithelium with normal underlying connective tissue. These findings were also observed in the tongue specimens from the parsley group. The observations were corroborated by Silvan and Manoharan, who reported similar results upon administration of the flavonoid apigenin.[24]

On the other hand, tongue specimens from the carcinogenesis group showed variable degrees of epithelial

**Table 2.** Expression of caspase-3 area percentage and *TNF-α* mRNA in the studied groups

| Biomarker | Control group | Parsley group | Carcinogenesis group | Parsley-treated carcinogenesis group | *p*-value |
|---|---|---|---|---|---|
| Caspase-3 | 32.86 ±1.72$^{a}$ | 30.48 ±1.35$^{ab}$ | 18.72 ±2.70$^{c}$ | 27.85 ±2.02$^{b}$ | 0.000* |
| *TNF-α* | 1.02 ±0.01$^{a}$ | 1.01 ±0.01$^{a}$ | 4.97 ±0.25$^{c}$ | 2.06 ±0.02$^{b}$ | 0.000* |

* statistically significant ($p$ < 0.05, ANOVA). Data presented as mean ± standard deviation (*M ±SD*) of the area percentage of caspase-3 and mRNA gene expression of *TNF-α*. Mean values indicated by different superscript letters in the same row are statistically significant ($p$ < 0.05, Tukey's post hoc test for pairwise comparisons).

dysplastic changes as well as subepithelial inflammatory cell infiltration. These results align with the studies by Abd El Hameed et al.[25] and Said,[26] who used DMBA to induce carcinogenesis in albino rats' lips and hamsters' buccal pouches, respectively.

The observed changes in the histological architecture of the rats' tongue mucosa can be explained based on the study by El Yaagoubi et al., who characterized DMBA as an effective carcinogen that induced intracellular accumulation of reactive oxygen and nitrogen species (ROS, RNS).[27] This process resulted in DNA damage and mutations in several proto-oncogenes and tumor suppressor genes. Additionally, an elevated expression of proinflammatory mediators responsible for cell proliferation, maturation, angiogenesis, and metastasis was observed.[27]

In the present study, histopathological changes in the carcinogenesis group were observed in the ventral, rather than the dorsal, surfaces of the rats' tongues. Similar results were demonstrated by Vendruscolo et al.[28] and Thomson,[29] who reported that the ventral surface exhibited a thin covering epithelium with elevated proliferative cell activity in comparison to the thicker epithelium of the dorsal surface. The elevated proliferative cell activity prolongs the synthesis (S) phase DNA during the cell division cycle, resulting in chromosomal instability and many DNA damages. These chromosomal aberrations are considered endogenous predisposing factors for malignant transformation, especially under the influence of chemical carcinogens.

In our study, the parsley-treated carcinogenesis group showed a significant reduction in dysplastic changes. This anticancer effect may be attributed to the active compound apiin present in parsley extract, as quantified by the HPLC analysis. This finding aligns with the study by Zhou et al., who reported that the apigenin content of parsley can be considered a potent chemopreventive agent in human keratinocytes.[30]

In addition, El-fiky et al. examined rats' lung tissues and demonstrated that the concurrent oral administration of parsley and nicotine significantly ameliorated the histopathological dysplastic alterations induced by nicotine.[31]

Dysregulation of apoptosis is a critical process in carcinogenesis. Caspase-3, a crucial protein in apoptosis, is located at the end of caspase cascades. It is triggered by both extrinsic (death receptor) and intrinsic (mitochondrial) apoptotic pathways. Its dysregulation at various stages of OSCC leads to cancer cell proliferation and expansion.[5] Consequently, the present study investigated caspase-3 immunoexpression.

The immunoexpression of caspase-3 was significantly lower in the carcinogenesis group compared to the parsley-treated carcinogenesis group. This finding aligns with the observations reported by Jakubowska et al., who demonstrated that cancer cells exhibited a lower level of caspase-3 expression compared to normal cells.[32] This characteristic of cancer cells contributes to their enhanced resistance to various treatments and microenvironmental stresses.

Moreover, Silvan and Manoharan reported that oral administration of apigenin at a dose of 2.5 mg/kg body weight exerted a cancer chemopreventive effect through the upregulation of caspase-3 and caspase-9 expressions.[24] Additionally, Zhang et al. confirmed that flavonoids efficiently inhibited the proliferation of tumor cells through provoking apoptosis via the upregulation of caspase-3 expression.[33]

The inflammatory process plays an important role in tumor progression. Tumor necrosis factor-alpha is an inflammatory cytokine that promotes inflammation and cancer growth by regulating neoplastic cell proliferation without triggering cell differentiation or apoptosis. It also affects the epithelial–mesenchymal transition of cancer cells.[34] Therefore, it was crucial to assess mRNA gene expression of *TNF-α* in the present study.

The qRT-PCR assessment revealed that the expression levels of *TNF-α* mRNA gene were significantly higher in the carcinogenesis group compared to the parsley-treated carcinogenesis group. These results are consistent with the findings of Coelho et al., who established a significant increase in *TNF-α* value in rats' C6 glioma cell lines compared to the cells treated with 100 μmol/L flavonoid apigenin.[35] Furthermore, Ashry et al. concluded that parsley leaves extract significantly decreased the expression of *TNF-α* than that observed in the untreated nephrotoxicity group in rats.[36]

According to the outcomes of the current investigation, the pharmacological effects of parsley as a chemopreventive agent can be attributed to the active compound apiin. These outcomes could be mediated by caspase-3 activation and *TNF-α* downregulation. Our findings coincide with previous research that found apigenin treatment to target malignant cell mitochondria and decrease mitochondrial membrane potential and permeability transition pores, either via the upregulation of intracellular ROS production or directly binding to a specific pore molecule. This process results in the release of mitochondrial cytochrome c within the cell, the activation of caspase-3, and ultimately, the induction of apoptosis.[37]

Furthermore, the administration of apigenin inhibited the activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) by downregulating TNF-α production. This process is a key factor in cell survival and proliferation via the upregulation of pro-survival gene expression and inflammatory cytokine production. Consequently, these mechanisms result in a decreased inflammation and increased cancer cell apoptosis and autophagy.[38]

## Limitations

The present study was subject to certain limitations. With regard to in vivo cancer induction, it is recommended

that the experimental period be extended to more than 8 weeks in order to investigate cellular dysplasia and to attain an accurate histopathological diagnosis of squamous cell carcinoma. Moreover, further studies are recommended to investigate the bioactive chemopreventive compounds other than apiin, present in parsley extract, to better understand the molecular basis of its anticariogenic mechanisms.

# Conclusions

The current study found that oral administration of parsley ethanolic extract hinders the initiation and progression of several cellular carcinogenic changes in tongue tissues. These changes were detected histopathologically through increased cellular apoptosis, which was caused by the upregulation of caspase-3 immunoexpression and decreased inflammation, attributed to the downregulation of *TNF-α* gene expression.

## Ethics approval and consent to participate

The study was approved by the Institutional Animal Care and Use Committee (IACUC), Faculty of Science, Cairo University, Egypt (approval No. CU-III-F-15-19).

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.


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Original paper

# Micro-computed tomography evaluation of dentinal cracks after root canal preparation with different endodontic rotary files: An ex vivo study

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## Abstract

**Background.** The occurrence of dentinal cracks is rather frequent during root canal preparation and increases with some endodontic file systems. There have been few ex vivo studies on the incidence of the formation of microcracks after root canal preparation, using the micro-computed tomography (micro-CT) analysis.

**Objectives.** The aim of the present study was to compare the incidence of dentinal cracks after using the XP-endo® Shaper, TRUShape®, ProTaper Next™ (PTN), and ProTaper Universal™ (PTU) instruments in the preparation of mandibular premolar teeth with oval canals, using the micro-CT evaluation method.

**Material and methods.** Thirty-six extracted human mandibular premolars with single oval root canals were distributed randomly to 4 experimental groups ($n = 9$) for root canal preparation: group 1 – XP-endo Shaper; group 2 – TRUShape; group 3 – PTN; and group 4 – PTU. The teeth were scanned using micro-CT with high resolution, before and after mechanical root preparation. Then, the cross-sectional images of pre- and post-scanning were visualized simultaneously to detect new dentinal cracks. The number of dentinal cracks was determined as percentage for each group, and the results were statistically analyzed using the Wilcoxon signed rank test and the Kruskal–Wallis test.

**Results.** A total of 49,628 cross-sectional images were obtained from pre- and post-scanning with micro-CT. Dentinal cracks were observed in 11,223 (22.6%) of the images. No new dentinal cracks were formed after using XP-endo Shaper, TRUShape or PTN. New dentinal cracks were found in the PTU group, and the difference between the percentages of the pre- and post-preparation dentinal cracks was statistically significant (37.6% vs. 62.4%) ($p = 0.008$).

**Conclusions.** The use of the heat-treated nickel-titanium (NiTi) files (XP-endo Shaper, TRUShape, PTN) did not lead to the formation of new dentinal cracks. New dentinal cracks were formed while using the traditional NiTi file (PTU) only. Future studies are required to investigate the association between the formation of dentinal cracks and new endodontic file systems.

**Keywords:** root canal preparation, micro-computed tomography, dentinal microcracks, heat-treated nickel-titanium files, nickel-titanium file system

## Highlights

- Different types of files cause varying levels of dentinal cracks during preparation.
- Micro-CT effectively detects dentinal cracks before and after tooth preparation.
- Heat-treated NiTi files (XP-endo, TRUShape, ProTaper Next) prevent the formation of new dentinal cracks.
- Traditional NiTi files (ProTaper Universal) lead to the formation of new dentinal cracks.

# Introduction

Non-surgical root canal treatment (NSRCT) is a highly successful procedure, with significant chances to offer a favorable outcome.[1] Root canal preparation and chemical cleaning with the use of irrigants are the main steps in the endodontic treatment to control the success in NSRCT.[2] The main goal of root canal preparation is shaping the canal lumen, taking into consideration the original canal anatomy, to facilitate disinfection and decrease the count of microorganisms during endodontic therapy.[3] Byström and Sundqvist showed that instrumentation with saline irrigation reduced bacterial counts by 100–1,000 times.[4]

Nickel-titanium (NiTi) rotary instruments were introduced to the practice of endodontics by Walia et al. in 1988.[acc.5] In comparison with stainless-steel files, NiTi rotary instruments facilitate the mechanical preparation of root canals while respecting the canal anatomy.[6] The super-elasticity and shape memory of NiTi result from its transition from the austenite (A) to martensite (M) phases under mechanical stress and temperature changes.[7] Recent technological advancements in the mechanical properties of rotary NiTi instruments and their thermal treatment have introduced a new concept of a faster, easier and better shaping ability for root canals. Currently, new rotary instruments with asymmetrical movement inside the root canal are offered. These files have a three dimension (3D)-conforming design with an S-shape, e.g., TRUShape® (Dentsply Sirona, Tulsa, USA), others have off-centered geometry, like ProTaper Next™ (PTN) (Dentsply Maillefer, Ballaigues, Switzerland).[6,7]

The XP-endo Shaper file has been recently introduced as a single-file rotation tool with a unique design using Max-Wire (FKG Dentaire, La Chaux-de-Fonds, Switzerland). This 3D-conforming file demonstrates a higher flexibility and a greater fatigue resistance, with more dentin surface touched and less dentinal stress as compared to regular NiTi instruments.[8,9] As the manufacturer claims, the file has the ability to start shaping the canal at ISO diameter 15 until it achieves ISO diameter 30, and to increase the initial taper of 0.01 at the M phase through expanding inside the canal at body temperature up to 0.04 at the A phase, with the final preparation (30/.04). The XP-endo Shaper file is snake-shaped, with a triangular cross-section and the so called booster tip (BT) of unique geometry with 6 cutting edges, which makes canal shaping faster and easier.[10]

Some studies have found that patients with dental abnormalities are more predisposed to dental cracks in their incisor or molar teeth due to abnormal mineralization, often associated with syndromes or general disorders, such as oral-facial-digital syndrome (OFD)[11,12] or coronoid process hypertrophy (CPH).[13]

Initially, hand files were widely utilized for the root canal instrumentation of deciduous teeth and young permanent teeth.[14] Most hand files can cause microcracks in the root dentin, making it more susceptible to vertical root fractures, more often in deciduous teeth than permanent teeth, due to the intrinsic hardness of metal, which is exacerbated by the design of the instrument and the root canal morphology. When stainless-steel hand files are used in narrow curved canals, they tend to limit apical expansion, making obturation more difficult in child patients' deciduous teeth with open or closed apexes as compared to permanent teeth.[15,16] To overcome the challenges associated with using stainless-steel tools, NiTi instruments were developed for curved canals, with the intention not to induce aberrations.[14] A study by Barr et al. was the first investigation on the use of NiTi rotary files in the root canals of deciduous teeth.[17] A recently published study by Panda et al. compared the dentinal cracks which occurred in the extracted deciduous teeth after root canal preparation with hand and rotary files, and the self-adjusting file (SAF) technology.[18] The authors concluded that there were significant differences between the 3 instruments with regard to the formation of dentinal cracks.[18]

Cracked teeth can lead to complications, especially if left untreated. For example, in some advanced cases, infections may occur. The signs of infection involve increasing discomfort/pain,[19] hypersensitivity to heat/cold[20] and bad oral hygiene.[21] Some authors recommend a mouthwash for child patients with cracked teeth or oral thrush to enhance their oral hygiene.[22,23] Diagnosing cracked teeth has proven difficult for dentists, and is a cause of concern for both the dentist and the patient. Discomfort or pain might be improperly identified as the signs of other disorders, such as sinusitis, temporomandibular joint (TMJ) problems, headaches, ear pain, or unusual orofacial pain.[24–26]

During preparation with different NiTi files, dentinal cracks may appear as a result of stress on the dentin.[27]

These dentinal cracks can damage the root dentin and extend as vertical root fractures with unfavorable prognosis, possibly leading to tooth extraction.[28,29] Different methods can be used to evaluate dentinal cracks inside the teeth, including the sectioning methods[27,28,30–32] or the non-destructive method of micro-computed tomography (micro-CT).[33–36] The latter method offers better identification of cracks and prevents cracks that may be induced by applying the sectioning method.

In their study, Bayram et al. compared the incidence of cracks after the preparation of extracted mandibular molar teeth with the use of the XP-endo Shaper, SAF and ProTaper Gold™ files.[37] They found that none of the systems induced dentinal cracks.[37] Most of the studies compared the incidence of dentinal cracks in curved canals by micro-CT.[33,34] A recent review discussed the number of dentinal cracks when using different file systems and evaluation methods.[38] Three out of the 9 included micro-CT studies reported that new dentinal cracks were induced after root canal preparation with rotary file systems. This review confirmed that the number of dentinal cracks observed after root canal preparation varies, depending on the file system techniques and the assessment methodologies employed.[38]

No previous studies compared the incidence of dentinal cracks after using 3D-conforming files, such as XP-endo Shaper or TRUShape, in oval canals. Therefore, the aim of the present study was to compare the incidence of dentinal cracks after using the XP-endo Shaper, TRUShape, PTN, and ProTaper Universal™ (PTU) instruments in the preparation of oval canals, using micro-CT. The null hypothesis was that there would be no statistically significant differences between the experimental groups in terms of formation of dentinal cracks. The PTU file was considered as a reference for the regular design of NiTi files (the control group).

# Material and methods

## Sample selection

Freshly extracted, sound human permanent mandibular premolar teeth with single roots and oval canals, obtained from the Oral Surgery Clinic at the Faculty of Dentistry, King Abdulaziz University, Jeddah, Saudi Arabia, were selected for the experiment. The teeth were extracted for different reasons, not related to this study, and stored in a special solution (0.1% thymol solution) at 4°C for 1 week before the commencement of the experiment.

Initially, 50 mandibular premolars were collected. The teeth were examined under a stereomicroscope (EMZ-13TRD; Meiji Techno, Miyoshi, Japan) under ×12 magnification. The exclusion criteria comprised any teeth with the evidence of previous cracks or fracture along the root surface. The further evaluation of the teeth was performed using a digital radiograph from buccolingual and mesiodistal projections. The inclusion criteria were teeth with single oval root canals (<5°) with mature apices, and no evidence of internal resorption or calcification. The authors achieved a power of 0.92 with an alpha (α) level of 0.05 and a confidence level of 95%; a sample size of 36 was considered for the total sample.

## Production of a mounting device

A mounting device or tube was fabricated to facilitate the positioning of the teeth inside the micro-CT equipment. It was a custom-made plastic tube with impression material for each tooth of the sample. After rinsing each tooth with tap water and drying it with gauze, polyvinylsiloxane (PVS) putty (Zhermack, Badia Polesine, Italy) was mixed according the manufacturer's recommendation. Then, the putty was placed inside the plastic tube and the subsequent selected tooth was submerged in the putty before the impression material was set. The tooth was inserted up to the level of or below the cementoenamel junction (CEJ) approximately.

## Pre-root canal preparation scanning by micro-CT

Each tooth in the sample was pre-operatively scanned with the use of a micro-CT unit (SkyScan 1272; Bruker, Kontich, Belgium). The teeth were selected sequentially from the container box, dried gently with gauze and placed in their corresponding mounting tubes. The mounting tube was placed inside the Micro-CT unit. The scanning of the teeth was set at 100 kV and 100 μA with high resolution (15 μm). The rotational step was set at 0.6°, with a rotation of 360° around the vertical axis, 2,650-millisecond exposure time and the frame averaging of 3.

The SkyScan NRecon software, v. 1694 (Bruker), was used for the reconstruction of the images after tooth scanning with micro-CT. During image reconstruction, a 40% beam hardening correction, frame averaging and the reduction of ring artifacts were modified individually to the optimal value for each tooth in the sample. The field of interest was extended from CEJ up to the root apex for each tooth. Subsequently, a total of 600–800 axial cross-sectional images or slices were obtained for each tooth. After scanning, the teeth were placed back in the thymol solution at 4°C in a special box prior to mechanical instrumentation in the next step.[39]

## Access cavity and the working length

For each tooth in the sample, a conventional endodontic access cavity was done, with a cross-section of an oval shape from the occlusal view. The access cavity was done using a high-speed round carbide bur (557 bur; Brasseler, Savannah, USA) and a high-speed air-driven handpiece

(KaVo North America, Charlotte, USA) under water cooling. Then, a K file #10 (Dentsply Maillefer) was inserted until it exited the canal and became visible to confirm the patency of the canal. If the root canal was not patent, the tooth was excluded from the study.

The working length (WL) was determined for each tooth by subtracting 1 mm from the length of the K file #10 in the major apical foramen.[40] The rubber stopper was used for the file in a stable reference point (the cusp tip). After the file was removed from the canal, WL was recorded. In order to remove the tissue and debris from the pulp chamber and the canal space, each tooth was filled with 3 mL of 3% NaOCl solution activated through passive ultrasonic irrigation (PUI) for 5 min, using a 27-gauge side-vented needle (Vista Apex Dental Products, Racine, USA). Then, the solution was suctioned using a high-suction tube in the dental unit. After irrigation with NaOCl, the saline solution was used in the same amount of 3 mL and the canals were left moistened to prevent any desiccation. All teeth were returned to the container box until the next step of root canal preparation.

## Sample randomization

Thirty-six mandibular premolars were collected and randomly allocated to 4 experimental groups ($n$ = 9 each) as follows:

– group 1: XP-endo Shaper (a triangular cross-section, MaxWire) (FKG Dentaire, La Chaux-de-Fonds, Switzerland);
– group 2: TRUShape (a triangular cross-section, heat-treated wire) (Dentsply Sirona, Tulsa, USA);
– group 3: ProTaper Next – PTN (a rectangular cross-section, M-wire) (Dentsply Maillefer, Ballaigues, Switzerland); and
– group 4: ProTaper Universal – PTU (conventional NiTi wire) (Dentsply Maillefer).

In all 4 groups, tooth preparation was done using the Dentsply X-Smart Plus EndoMotor engine (Dentsply Maillefer).[10] In addition, the preparation time was calculated for each group. The whole experiment was done by one operator (M.M.A.), and for each tooth in the experiment, a separate rotary file was used.

## Root canal preparation and irrigation protocol

### Group 1: XP-endo Shaper system

The sample teeth in this group were sequentially selected from the container box and dried gently with gauze for root canal preparation. At first, a glide path for the canal was created using a K file #15 (Dentsply Maillefer), and then irrigation with 1 mL of 3% NaOCl solution was performed. The XP-endo Shaper file was used to its full WL with the final preparation (30/.04), with a speed of 800 rpm and a torque of 1 N·m, as recommended by the manufacturer. First, the file tip was inserted until resistance was felt, and then the file was adapted in the motor and started the preparation of the canal. For each canal, 5 long gentle strokes were progressed to WL, without forcing the file or using the pecking motion. Once WL was reached, another 15 strokes to WL were done with the file, as recommended by the manufacturer.[10]

### Group 2: TRUShape system

The sample teeth in this group were sequentially selected from the container box and dried gently with gauze for root canal preparation. At first, a glide path for the canal was created using a K file #15 (Dentsply Maillefer), and then irrigation with 1 mL of 3% NaOCl solution was performed. Then, the TRUShape file was used with a gentle in-and-out motion at a speed of 300 rpm and a torque of 3 N·m, as recommended by the manufacturer. The preparation of the canal was done by sequential enlargement toward WL, starting with size 20/.06, followed by sizes 25/.06 and 30/.06 in the full length of the canal (WL). The manner of canal preparation with the TRUShape file was the in-and-out passive motion with light apical pressure in an amplitude of 2–3 mm, without using the pecking motion while advancing toward WL.[41]

### Group 3: PTN system

The sample teeth in this group were sequentially selected from the container box and dried gently with gauze for root canal preparation. At first, a glide path for the canal was created using a K file #15 (Dentsply Maillefer), and then irrigation with 1 mL of 3% NaOCl solution was performed. Then, each root canal was prepared with PTN with a gentle in-and-out motion at a speed of 300 rpm and a torque of 2 N·m, as recommended by the manufacturer. The preparation of the canal was done by sequential enlargement toward WL, starting with the X1 (17/.04) file, followed by the X2 (25/.06) and X3 (30/.07) files up to WL. The manner of canal preparation with PTN was a gentle in-and-out brushing motion against the canal.[42]

### Group 4: PTU system

The sample teeth in this group were sequentially selected from the container box and dried gently with gauze for root canal preparation. At first, a glide path for the canal was created using a K file #15 (Dentsply Maillefer), and then irrigation with 1 mL of 3% NaOCl solution was performed. Subsequently, the enlargement of the coronal orifice and the preparation of ⅔ of WL was done using the SX instrument, followed by irrigation with 2 mL of 3% NaOCl solution. Thereafter, shaping files S1 (tip size 17) and S2 (tip size 20) were used for the preparation of WL. Full WL was prepared with finishing files F1 (20/.07),

F2 (25/.08) and F3 (30/.09). The preparation manner involved using the crown-down technique for the PTU instruments at a speed of 300 rpm and a torque of 2 N·m, as recommended by the manufacturer. Shaping files SX, S1 and S2 were used with a brushing motion, while the finishing files (F1–F3) were used with a gentle in-and-out motion until the instrument reached WL.[43]

In each of the tested groups, the irrigation of the canals during instrumentation was performed using 2 mL of NaOCl activated through PUI for 5 min, using a 27-gauge side-vented needle, followed by 2 mL of the saline solution to remove the debris left after preparation. Then, each tooth in all the 4 tested groups was dried using an absorbent paper point (Meta Biomed, Colmar, USA) before rescanning with the use of the micro-CT device in the next step.

## Post-root canal preparation scanning by micro-CT

Following mechanical preparation, all teeth from the 4 groups were placed in the corresponding mounting tubes for post-scanning with the micro-CT device. The scanning of the teeth was set at same parameters as before: 100 kV and 100 µA with high resolution (15 µm), the rotational step was set at 0.6°, with a rotation of 360° around the vertical axis, 2,650-millisecond exposure time and the frame averaging of 3.

The NRecon software was used for the reconstruction of the images after tooth scanning with micro-CT. During image reconstruction, a 40% beam hardening correction, frame averaging and the reduction of ring artifacts were modified individually to the optimal value for each tooth in the sample. The field of interest was extended from CEJ up to the root apex for each tooth. Subsequently, a total of 600–800 axial, cross-sectional images or slices were obtained for each tooth.

## Evaluation of dentinal microcracks

After the reconstruction of all cross-sectional images, they were transferred to the SkyScan DataViewer program, v. 1524 (Bruker), using 3D imaging. A total of 49,628 cross-sectional images were obtained from pre- and post-scanning, with the area of interest extending from CEJ up to the apical foramen. All the cross-sectional images of the teeth before and after mechanical root canal preparation were evaluated.

Both the pre- and post-root canal preparation images were opened simultaneously by the DataViewer program and evaluated for the presence of microcracks. First, the post-root canal preparation cross-sectional image was evaluated for the presence of cracks, and then the pre-root canal preparation image was checked for the presence or absence of the same cracks. Any cross-sectional images with at least one microcrack were identified and marked.

Any new crack, craze line or propagated crack extending from the internal or external surface of the canal was defined as 'defect or cracks', while 'no defect' meant the absence of any crack or craze line in the micro-CT image.[30] Each sample was then checked for the presence of dentinal cracks. Two examiners, blinded to the micro-CT analysis, separately reviewed the samples. The Pearson correlation coefficient (PCC) was employed to determine agreement between the 2 examiners for dentinal crack findings, and it amounted to 0.942. For the observation of dentinal cracks, there was a significant positive correlation between the 2 examiners.

## Assessment of the time required for root canal preparation

The operator performing the experiment used a digital timer to record the time required for root canal preparation. The beginning point was the first insertion of the file into the canal, and the end point was the completion of the final irrigation with distilled water. The time spent on changing the instruments was not taken into consideration.

## Statistical analysis

The PCC was used to determine the agreement between the 2 examiners for dentinal crack observation. The total number of cracks per tooth was reported as percentage, and recorded in the Microsoft Excel sheet (Microsoft Corporation, Redmond, USA). Each tooth in all the 4 tested groups, with the related pre-and post-scanning images, was divided to 3 levels with regard to the root part: coronal; middle; and apical. The data for each sample was analyzed using IBM SPSS Statistics for Windows, v. 20.0 (IBM Corp., Armonk, USA).

The Wilcoxon signed ranks test (a non-parametric test) was used to determine statistically significant differences between the pre- and post-preparation cross-sectional images within all rotary system groups. The Kruskal–Wallis test (a non-parametric test) was used to explore statistically significant differences between the pre- and post-preparation cross-sectional images across the 4 groups, and to explore significant differences between the pre- and post-preparation cross-sectional images among the 3 root levels (coronal, middle and apical). The level of significance was set at $p < 0.05$.

# Results

## Percentages of dentinal cracks

Among the 49,628 pre- and post-root canal preparation images obtained, dentinal cracks were found in 22.6% ($n$ = 11,223) of them. In the XP-endo Shaper group, 18.5% ($n$ = 2,076 out of 11,223) of the pre -and post-preparation

images showed dentinal cracks. In the TRUShape group, it was 24.7% ($n$ = 2,774 out of 11,223), in the PTN group – 26.8% ($n$ = 3,006 out of 11,223), and in the PTU group – 30.0% ($n$ = 3,364 out of 11,223).

Regarding the occurrence of new cracks, the dentinal cracks which were observed in the post-preparation cross-sectional images were already present in the corresponding pre-preparation images with the same directions and extension in 3 groups – XP-endo Shaper, TrueShape and PTN. Thus, no new dentinal cracks were formed after preparation with these 3 tested file systems (Fig. 1). On the other hand, postoperative dentinal cracks were observed in 2,100 out of 3,364 cross-sectional images (62.4%) as compared to the corresponding preoperative dentinal cracks in 1,264 out of 3,364 cross-sectional images (37.6%) in the PTU group. Thus, new dentinal cracks were formed after preparation with the PTU system only (Fig. 1).

## Statistical evaluation of dentinal cracks

The Wilcoxon signed ranks test showed a statistically significant difference only in the PTU group between the percentages of the pre-preparation dentinal cracks and post-preparation dentinal cracks (37.6% vs. 62.4%) ($p$ = 0.008), whereas the other 3 groups presented the same numbers and percentages of dentinal cracks pre- and post-preparation, with no new dentinal cracks formed: the XP-endo Shaper group ($n$ = 2,076) – 1,038 pre-preparation vs. 1,038 post-preparation ($p$ = 1.000); the TrueShape group ($n$ = 2,774) – 1,387 pre-preparation vs. 1,387 post-preparation ($p$ = 1.000); and the PTN group ($n$ = 3,006) – 1,503 pre-preparation vs. 1,503 post-preparation ($p$ = 1.000).

The Kruskal–Wallis test showed statistically significant differences between different groups (XP-endo Shaper, TrueShape, PTN, and PTU) in the mean rank of dentinal cracks pre-preparation ($p$ = 0.000) and post-preparation ($p$ = 0.000) (Table 1). However, no statistically significant differences were found in the mean rank of dentinal cracks, either pre-preparation ($p$ = 0.170) or post-preparation ($p$ = 0.325), across the 3 root levels (coronal, middle and apical) according to the Kruskal–Wallis test (Fig. 2).

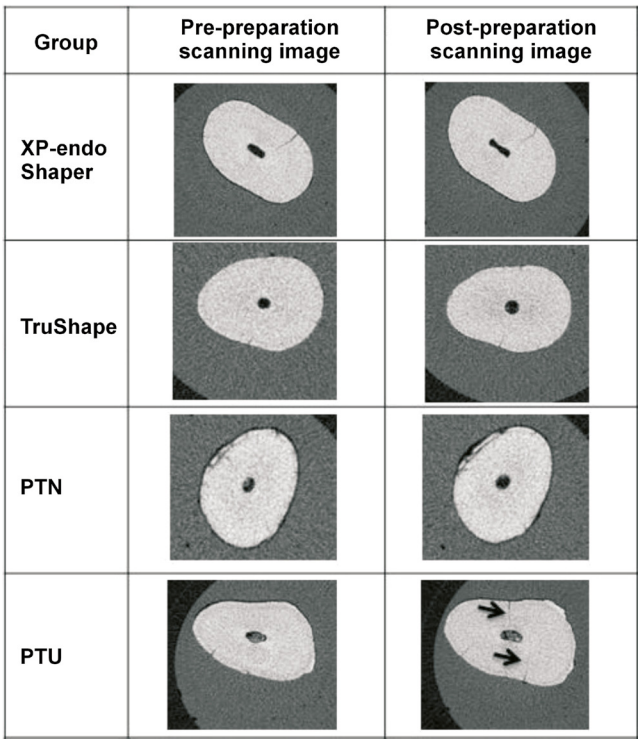


Fig. 1. Representative pre- and post-preparation scanning images for different groups tested

PTN – ProTaper Next; PTU – ProTaper Universal. Only in the PTU group, the post-preparation scanning image showed new dentinal cracks (black arrows).

## Preparation time for different groups

The mean preparation time for the XP-endo Shaper, TRUShape, PTN, and PTU groups was 69.33 s, 151.56 s, 150.44 s, and 155.67 s, respectively. The one-way analysis of variance (ANOVA) showed a statistically significant difference between the 4 tested groups ($p$ = 0.001), indicating that in the XP-endo Shaper group, root canal preparation required significantly less time as compared to the other 3 groups (Table 2, Fig. 3).

Table 1. Mean rank and $\chi^2$ values regarding pre- and post-root canal preparation dentinal cracks for different groups tested (non-parametric Kruskal–Wallis test)

| Groups | | Mean rank | $\chi^2$ | Degrees of freedom | $p$-value |
|---|---|---|---|---|---|
| Pre-preparation | XP-endo Shaper | 20.30 | 50.681 | 3 | 0.000* |
| | TRUShape | 75.37 | | | |
| | PTN | 69.74 | | | |
| | PTU | 52.59 | | | |
| Post-preparation | XP-endo Shaper | 15.93 | 83.941 | 3 | 0.000* |
| | TRUShape | 56.33 | | | |
| | PTN | 51.85 | | | |
| | PTU | 93.89 | | | |

* statistically significant.

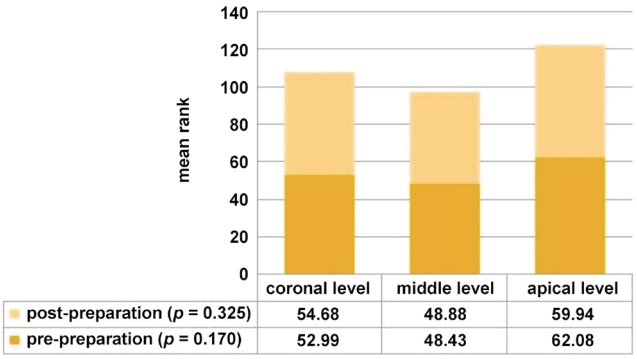


Fig. 2. Mean rank of dentinal cracks pre- and post-root canal preparation for 3 different root levels

**Table 2.** Mean preparation time for different groups tested (one-way ANOVA)

| Groups | Preparation time [s] | *p*-value |
|---|---|---|
| XP-Endo Shaper | 69.33 ±2.35 | |
| TruShape | 151.56 ±2.46 | |
| PTN | 150.44 ±1.88 | 0.001* |
| PTU | 155.67 ±1.73 | |
| Total | 131.75 ±36.66 | |

Data presented as mean ± standard deviation (*M* ±*SD*).
* statistically significant.

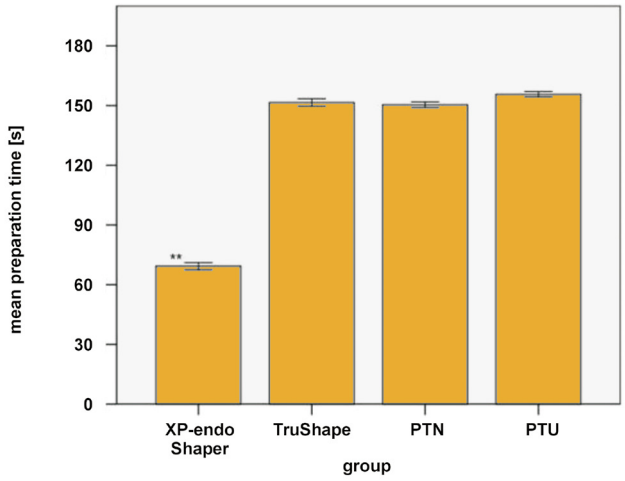


**Fig. 3.** Mean preparation time for different groups tested
** statistical significance ($p = 0.001$).

## Discussion

This study evaluated the incidence of dentinal cracks after the preparation of mandibular premolars with oval canals, using the recently introduced 3D files (XP-endo Shaper, TRUShape and PTN) in comparison with the PTU file, by means of micro-CT scanning. Thirty-six freshly extracted teeth were selected for the study and divided equally into the 4 groups (9 teeth per group). In order to standardize the incidence results for all groups and to eliminate other contributing factors, mechanical preparation was finished with size 30 in all experimental groups in the study.

In previous studies on dentinal cracks which used the destructive (sectioning) method, the incidence of cracks varied between 4% and 80%.[44,45] However, the examination of dentinal cracks with the use of the sectioning method has many limitations, such as the creation of cracks after sectioning, and studying few slices of the root rather than the evaluation of the entire root. Using the micro-CT method to examine dentinal cracks is preferrable.[46,47] Micro-CT provides hundreds of slices to be evaluated for each tooth, showing the details of cracks, their location and extension in the dentin. In endodontic research, the advantages of micro-CT are numerous – less sample preparation, less damage to the teeth, no need to cut the teeth, and reliable results as compared to the sectioning method.[46]

In the present study, 3D files (XP-endo Shaper, TRUShape and PTN) were selected for the preparation of mandibular premolars with oval canals due to their ability to reach all canal walls with 3D asymmetrical rotation. The PTU system represented conventional NiTi files with symmetrical rotation. No previous study compared these 3D files with regard to the incidence of dentinal cracks after the mechanical preparation of oval canals.

At the beginning of our study, before root canal preparation, the teeth were evaluated under a stereomicroscope and no visible cracks were found in the samples. However, the pre-instrumentation micro-CT scanning images showed dentinal cracks in all study groups. This is in agreement with De-Deus et al., who reported that microcracks were present in all canal walls before the preparation of the examined teeth.[47]

The null hypothesis of the present study stated that there would be no statistically significant differences between the experimental groups in terms of formation of dentinal cracks. In the XP-endo Shaper, TRUShape and PTN groups, no cracks were formed after root canal preparation. However, in the PTU group, dentinal cracks occurred after preparation, and thus, the null hypothesis of the study was rejected (Fig. 1).

In the PTU group, the percentage of dentinal cracks observed postoperatively was high (62.4%) as compared to the percentage of dentinal cracks in the corresponding pre-preparation images (37.6%). The formation of dentinal cracks after the preparation of root canals with PTU was not surprising, and this finding was in agreement with previous studies.[27,36,37,44]

In root sectioning studies, the percentages of dentinal cracks after using PTU ranged from 16% to 56%.[8,27,44] With regard to micro-CT studies, 3 of them evaluated the dentinal cracks formed after using PTU,[36,37,48] and reported the percentages of 21%[36,37] and 42%.[48] Our results regarding post-instrumentation dentinal cracks in the PTU group were higher (62.4%) as compared to previous micro-CT studies.[36,37,48]

There is a limited number of micro-CT studies in the literature addressing the formation of dentinal cracks after using the XP-endo Shaper files in root canal preparation. Bayram et al. concluded that the XP-endo Shaper file had no effect on the formation of dentinal cracks after the preparation of mandibular premolars.[37] In the present study, XP-endo Shaper did not induce cracks after the preparation of mandibular premolars with oval canals, which is in agreement with Bayram et al.'s findings.[37] It can be explained by the flexibility of XP-endo Shaper, stemming from the alloy used and the design of the file.

TRUShape is a heat-treated NiTi file with a characteristic S-shape design and a decreased taper.[49] Again, micro-CT studies addressing the formation of dentinal cracks after using the TRUShape files in root canal preparation are scarce.[50,51] In 2017, Bayram et al. compared TRUShape with the Vortex Blue® and HyFlex™ files in terms of dentinal

crack incidence after the preparation of mandibular incisors.[51] They concluded that none of the systems used induced new dentinal cracks after preparation.[51] Also, Zuolo et al. evaluated crack formation after using the TRUShape, SAF, BioRaCe™, and Reciproc® files, and concluded that none of the systems induced new dentinal cracks.[50] In our study, the TRUShape system did not induce cracks after the preparation of mandibular premolars, which is in agreement with previous studies.[50–52]

There are also few micro-CT studies in the literature regarding dentinal crack formation when using PTN.[47,53] De-Deus et al. compared PTN with the Twisted File (TF)™ Adaptive rotary systems with regard to the induction of dentinal cracks on mandibular molar teeth.[47] The authors concluded that the post-preparation cracks were already present in the pre-preparation scanning images, and none of the systems induced new dentinal cracks.[47] In our study, the PTN file did not induce cracks after the preparation of mandibular premolars, which confirms the results of some previous micro-CT studies,[47,53] and is in contrast with sectioning studies.[8,44] Although Choi et al. showed a variable range of vibrations inside the root canal, related to the use of PTN, no effects of these vibrations on crack formation was reported.[54]

In their recent research, Shantiaee et al. found that no new dentinal cracks were induced by rotary and reciprocal systems in curved canals during instrumentation, and they referred this outcome to the design of these instruments, which makes the files more flexible.[55] This finding in accordance with our results regarding the rotary files, with no dentinal cracks developed across the different section levels, as confirmed by micro-CT.

The variations in the preparation time between the 4 motorized techniques might be attributed to the mode in which each file was used to achieve WL. The tip of the XP-endo Shaper file has a unique shape that allows it to achieve WL quickly and with little pressure. The tip is subdivided into 2 parts. The apical portion of the tip features a non-cutting bullet form; it converts into 6 cutting blades that integrate into a thin shaft with a 0.01 taper. In comparison with the other 3 files evaluated, it appears that these attributes allow the XP-endo Shaper file to attain WL easily and rapidly with minimum resistance. The XP-endo Shaper file is not intended to shape the canal, but rather to clean it by accessing canal imperfections with each of the 15 lengthy pecking strokes suggested by the manufacturer.

There are some limitations to studies on dentinal cracks, such as the use of extracted teeth and the absence of the natural periodontal ligament (PDL) of the tooth during the experiment. In the present study, we used impression material to simulate PDL and allowing some freedom for the tooth movement. However, Soros et al. stated that impression material could collapse and get in direct contact with the teeth, which does not happen in bone environment.[56] During pre-preparation scanning with micro-CT, microcracks were found and the origin of these cracks could not be explained; they might have resulted from the extraction forces, the storage medium for the teeth or from the increased heat of scanning. Future studies on the issue of dentinal cracks after root canal preparation need to adopt an in vivo scenario, with the possibility to detect dentinal cracks clinically to avoid bias in the results. Some recent studies have tried to address cracks clinically, using strains gauges and infrared thermography.[57,58] In the present study, root canals were single oval canals, and future studies with curved or narrow canals may provide different results.

# Conclusions

Within the limitations of the present study, none of the tested instrumentation systems led to the formation of new dentinal cracks in mandibular premolars with single oval canals, except one group (PTU). The formation of new cracks resulted from the mechanized instrumentation in one of the 4 groups, which is the traditional super-elastic NiTi PTU, and not from the sectioning procedure itself. Future studies are required to investigate the association between the formation of dentinal cracks after root canal preparation and new endodontic file systems.

## Ethics approval and consent to participate

The study design was approved by the Research Ethics Committee at the Faculty of Dentistry, King Abdulaziz University, Jeddah, Saudi Arabia (approval No. 011-01-18).

## Data availability

The datasets supporting the findings of the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.

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Original paper

# Comparative evaluation of mechanical effects of two designs of immediately placed customized root-analogue zirconia implants in the maxillary and mandibular posterior regions: A finite element analysis

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D – writing the article; E – critical revision of the article; F – final approval of the article

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## Abstract

**Background.** Customized root-analogue implants (RAIs) with a press-fit design, inserted immediately after tooth extraction, have garnered attention from the researchers and dentists due to their ability to generate frictional force within the tooth extraction socket.

**Objectives.** The aim of this study was to evaluate the stress distribution and microdisplacement of 2 designs of customized root-analogue zirconia implants in the maxillary and mandibular posterior regions using finite element analysis (FEA).

**Material and methods.** Four computer-aided design (CAD) models of maxillary and mandibular bone with standard density were constructed based on standard tooth dimensions. The models featured 2 distinct designs, namely fin and bulb designs of RAIs, with 2 models designated for the maxillary first molar and 2 models for the mandibular first molar. All three-dimensional models were converted into finite element models using Altair® HyperMesh® software. Thereafter, loads of 300 N and 100 N were applied in the axial direction to analyze the stress distribution and microdisplacement on peri-implant bone areas using FEA.

**Results.** The customized root-analogue zirconia implant with the bulb design showed better stress distribution in the surrounding bone when compared to the RAI with the fin design. The micromotion values of the fin design were found to be lower than those of the bulb design, indicating that the former exhibits superior primary stability. The stress distribution of both designs demonstrated reduced stress values in the maxillary posterior region compared to the mandibular posterior region.

**Conclusions.** The customized root-analogue zirconia implant with added press-fit geometry, i.e, fin or bulb design, has a positive effect on stress distribution and provides enhanced primary stability.

**Keywords:** finite element analysis, zirconia, customized root-analogue implants, computer-aided design (CAD), targeted press-fit design

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## Highlights

- Customized root-analogue implants (RAIs) are designed to mimic the natural root of the tooth in both shape and function.
- The press-fit design of RAIs allows for a tight fit within the extraction socket, generating frictional force to stabilize the implant during the healing process.
- Customized root-analogue zirconia implants with the bulb design demonstrated superior mechanical performance.

# Introduction

From antiquity to the present day, the major affliction that troubles the individuals of all ages is tooth loss, as it affects the masticatory function and aesthetics. Among the various treatment options available, dental implants have gained popularity due to their ability to provide a natural appearance and comfortable fit, durability and reliability, a high success rate, and improvement in chewing and eating abilities, as well as preservation of facial and bone features.[1] However, the success of conventional dental implants is contingent upon numerous factors and can be compromised due to post-treatment complications such as crestal bone loss, implant screw loosening and peri-implantitis. The presence of these issues could be attributed to elevated levels of pro-inflammatory cells like interleukin (IL)-1β, IL-6 and matrix metalloproteinase-8 (MMP-8) in peri-implant support tissues compared to the periodontal support tissues.[2]

In 1950, Per-Ingvar Brånemark revolutionized the field of dental implantology by discovering, however inadvertently, that biocompatible materials like titanium-alloy implants inserted into the alveolar process can fuse with bone, a process he called osseointegration.[3] However, there are drawbacks associated with the utilization of titanium implants, including allergic reactions, galvanic current formation, cellular sensitization, and the visibility of black metallic components through the mucosa in cases of soft tissue recession.[3] To address these limitations, the ceramic implants were developed in the 1960s, with zirconia emerging as a promising alternative to conventional titanium-based implant systems for oral rehabilitation due to its superior biological, aesthetic, mechanical, and optical properties.[4]

The commercially available dental implants offer a limited range of parameters with regard to length, diameter and threads, and cannot fully meet the requirements for all oral conditions. A study performed by Ragucci et al. demonstrated successful osseointegration in immediately placed and loaded dental implants into the fresh extraction socket with high survival and success rates and minimal marginal bone loss.[5] However, a void still remained between the implant and the alveolar socket. While searching for a new solution, researchers posited that if the implant's design were to mirror that of the extracted root and conform to the socket geometry, no residual voids would remain, thus resulting in better healing and aesthetic outcomes. This concept led to the development of customized root-analogue implants (RAIs), which are designed to fit each patient's unique anatomy. These implants preserve the remaining hard tissues by maintaining the buccolingual and apico-coronal dimensions of the alveolar ridge immediately after extraction. The preservation of soft tissues is facilitated by the maintenance of the emergence profile and the remaining attached gingiva. In addition, RAIs majorly reduce the time required for implant placement and rehabilitation, offering a promising perspective for the field of implant dentistry.[5]

In recent years, customized RAI systems have been introduced and studied using computer-aided design/computer-aided manufacturing (CAD/CAM) technology. This development has led to the immediate replacement of teeth after extraction through the implementation of copy milling or a rapid prototyping technology, a process in which a computed tomography (CT) scan is processed and converted into an implant. These contemporary techniques have reduced the duration of surgery and simplified implant operations.[6] However, these methods have not been explored extensively and are not well established.

Finite element analysis (FEA) studies concerning commercial dental implants in bone are extant in literature. However, to the best of our knowledge, no FEA studies have been conducted to evaluate the biomechanical response of RAIs in the posterior region. Thus, this study aimed to evaluate the stress distribution in the peri-implant bone area with 2 different zirconia implant designs in the maxillary and mandibular posterior regions. Additionally, the primary stability of customized RAIs was evaluated immediately after placement.

# Material and methods

An in vitro study was performed to determine the stress distribution patterns in the maxillary and mandibular first molar regions with 2 different customized RAI designs, namely the fin design and the bulb design. Four models were prepared, and each model was subjected to loads of 300 N and 100 N in a vertical direction (90° angulations). Subsequently, three-dimensional FEA was employed for the assessment of the models.

## Instruments used for the study

The personal computer used for the design process featured a configuration comprising an Intel Core® i5-760 processor (2.80 GHz) with 8 GB of RAM memory and a 2 GB graphic card (NVIDIA, Santa Clara, USA). The software utilized for the study included SolidWorks (Dassault Systèmes SolidWorks Corporation, Waltham, USA), Inventor (Autodesk, San Francisco, USA), Altair® HyperMesh®, v. 13.0 (Altair Engineering, Troy, USA), and ANSYS, v. 12.1 (Ansys, Inc., Canonsburg, USA).

## Study design

### Geometry modeling

Three-dimensional CAD models of maxillary and mandibular bone with standard density were constructed by means of organic modeling using SolidWorks software. The construction of 4 CAD models with 2 RAI designs was based on standard tooth dimensions. Two models were constructed on the maxillary first molar and 2 on the mandibular first molar. The standard abutment shape of the RAIs was designed to mirror the morphology of the original tooth crown. The dimensions of the all-ceramic restoration were set to include a 1-mm width shoulder finish line and a smooth surface on the abutment. The shape of the root was modeled after the ideal natural tooth. The root was solid in structure, with the outer surface designed with fin and bulb designs, sparing 2 mm of cortical bone at the coronal region and 2 mm at the apical region to avoid trauma while placing implants. Subsequently, all CAD models were converted and saved in the standardized triangulation language (STL) file format. The design of the study is presented in Fig. 1.

### Dimensions of the CAD model

The external designs of maxillary and mandibular RAIs are presented in Fig. 2. They were constructed according to the ideal tooth dimensions provided by Wheelers et al.[7] The dimensions of the RAIs and their external designs[8] are outlined in Tables 1 and 2.

The bone model was based on the ideal adult maxillary and mandibular bone.[7]

### Conversion of the geometric model to the finite element model

The second step was the discretization of the geometric model into finite discrete elements. Discretization entails the division of the geometric model into several small elements and connecting them at the nodes. The process of connecting the elements and eliminating duplicate nodes is known as meshing. Using Altair® HyperMesh® software, the CAD model of the maxilla, mandible and 2 implants

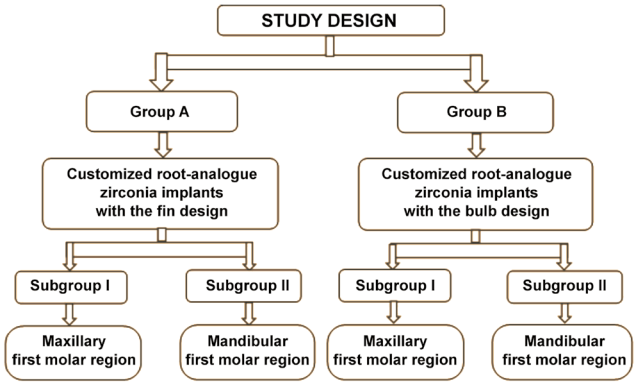


Fig. 1. Design of the study

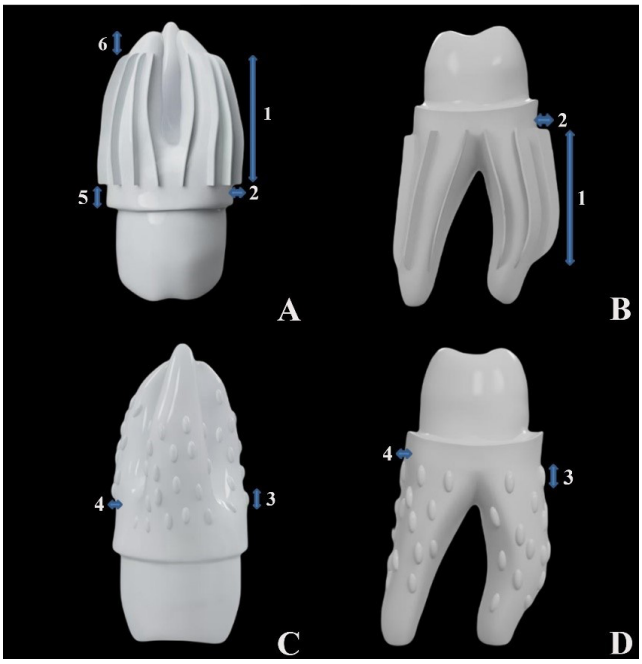


Fig. 2. Computer-aided manufacturing (CAD) models of customized root-analogue zirconia implants

A. Maxillary implant with the fin design; B. Mandibular implant with the fin design; C. Maxillary implant with the bulb design; D. Mandibular implant with the bulb design.
1 – fin's length = 10 mm; 2 – fin's protrusion = 0.80 mm; 3 – bulb's length = 1.20 mm; 4 – bulb's protrusion = 0.5 mm; 5,6 – space allocated for all implants in the coronal and apical regions = 2 mm.

Table 1. Dimensions of maxillary and mandibular root-analogue implants (RAIs)[7]

| Implant type | Length (crown + root) | Width (at tooth cervix) |
|---|---|---|
| Maxillary RAI | buccal – 18.5 mm<br>palatal – 19.5 mm | mesiodistal – 8.0 mm<br>buccolingual – 10.0 mm |
| Mandibular RAI | 20.5 mm | 9.0 mm |

Table 2. Dimensions of external designs of root-analogue implants (RAIs)[8]

| Design type | Protrusion | Length | Width |
|---|---|---|---|
| Fin design | 0.80 mm | 10.00 mm | 0.80 mm |
| Bulb design | 0.50 mm | 1.20 mm | 0.55 mm |

in the STL file format was meshed with quadratic tetrahedral solid elements. Refinements were made based on the convergence analysis to obtain 4 finite element models of implants and bone. Table 3 provides a summary of the number of elements and nodes for each model.

### Material properties

The different structures involved in the study were cortical bone, cancellous bone, teeth, and zirconia. Each material possesses distinct properties. Hence, the representation of material properties was necessary to ensure a comprehensive comparison of the stresses. To simulate a clinical scenario, 2 material properties were utilized, i.e., Young modulus (elastic modulus) and Poisson's ratio. It was assumed that all the materials were homogenous, linearly elastic and isotropic. Table 4 provides a summary of the physical and mechanical properties of the biomaterials used in the study.[9,10]

### Boundary conditions

When a model is constructed in a computer and force is applied, it will act freely and move in different directions, leading to rotation or translation, or both, without undergoing any strain or deformation. Hence, to study strain and deformation in bone after load application, some areas should be restricted in their degrees of freedom (movement of the node in each direction – x, y and z). These constraints are known as boundary conditions. In this study, the bottom and sides of the maxillary and mandibular bone were fixed during load applications.

### Bone–implant contact interface

To simulate immediate implant placement after tooth extraction (non-osseo-integrated contact), non-linear surface-to-surface frictional contact conditions were employed at the implant and bone interface to allow for sliding behaviors.

**Table 3.** Meshing details of bones with root-analogue implants (RAIs)

| Model | Elements, *n* | Nodes, *n* |
|---|---|---|
| Maxillary bone with RAI (bulb design) | 1,249,926 | 258,749 |
| Mandibular bone with RAI (bulb design) | 63,220 | 118,037 |
| Maxillary bone with RAI (fin design) | 886,390 | 196,051 |
| Mandibular bone with RAI (fin design) | 84,088 | 156,899 |

**Table 4.** Physical and mechanical properties of the biomaterials used in the study[9,10]

| Material | Young modulus [Mpa] | Poisson's ratio |
|---|---|---|
| Teeth | 19,600 | 0.3 |
| Cortical bone | 13,700 | 0.3 |
| Cancellous bone | 1,370 | 0.3 |
| Zirconia | 200,000 | 0.3 |

### Loading conditions

The models were loaded at the uppermost surface of the implant as a static load to simulate centric occlusion at an axial direction (90°), which were directed parallel to the long axis of the implant. Two loads were applied: one at 300 N to observe the maximum implant stress at the peri-implant bone; and at 100 N to observe the masticatory response during normal mastication.

### Linear static analysis

The assembled finite element models of implants with maxillary and mandibular bone were imported into ANSYS software for linear static analysis. This analysis was performed after the application of 2 different loads (300 N and 100 N) to determine maximum principal stress, equivalent von Mises stress on cortical bone, cancellous bone and zirconia implants, and total deformation.

### Post-processing

The results were expressed as equivalent von Mises stresses in megapascals [MPa] and displacement in millimeters [mm]. Pictorial and/or tabular representations of the stresses were prepared. The stress flow in each component was plotted using contour plots and color-coded.

## Statistical analysis

As the values obtained through FEA of both designs were discrete and remained constant even after multiple analyses, there was no need for statistical analysis. The values obtained were compared directly.

# Results

The obtained color plots were analyzed, and the maximum von Mises stress and strain values were noted and graphed for each condition. The unit of stress was defined as the unit of force [N] divided by a unit of area or length squared, commonly expressed as Pascal [Pa]. In the majority of studies, megapascals [MPa] are employed, as was also the case in our study.

Stress distribution in the FEA models was expressed in numerical values and by color coding. Maximum von Mises stress values were denoted by color red, and minimum values were expressed by color blue. The in-between values were represented by bluish green, greenish yellow and yellowish red in the ascending order of stress distribution.

A comparison of maxillary and mandibular fin and bulb designs at 100 N revealed that the bulb design exhibited lower stress values than the fin design, indicating that the stress distribution was more pronounced in the bulb design. Additionally, when the equivalent stress distribution

of cortical and cancellous bone was compared, the cortical peri-implant bone exhibited more stress concentration than the trabecular bone in both designs. These findings were replicated at 300 N. The von Mises stress values were measured and averaged at the implant and supporting tissues for both groups (Fig. 3,4).

While comparing maxillary and mandibular RAIs with the fin design under both loads, the overall von Mises stress of the zirconia implant in the maxillary fins was three to four times lower than in the mandibular fins. Similarly, the overall von Mises stress of the bone and zirconia implant in the maxillary bulbs was three to five times lower than that of the mandibular bulbs. This indicates that the stress distribution is more favorable in the maxillary molar region compared to the mandibular molar region.

To ensure primary stability of the implant, the micro-displacement between the bone and the implant interface was evaluated. The lowest levels of contact separation were measured in the fin design of both maxillary and mandibular RAIs under vertical forces of 100 N and 300 N. Figure 4E displays the micromotion values of maxillary and mandibular RAIs with the fin and bulb designs.

## Discussion

Dental implants are a widely used treatment option for replacing missing teeth. Pure titanium and its alloys are the most preferred materials for implantation. However, titanium has its limitations in cases where aesthetic demands are high after soft tissue recession, when the black metallic components become visible through the mucosa, and also in instances of allergic reactions to metallic restorations. Conventional implants have not undergone significant changes in form or material over the past 40 years.[11,12] Ceramic restorations are now preferred by many patients. In response to this growing demand, technological advancements in additive manufacturing and CAD/CAM technology have led to the development of enhanced ceramic-based structures for patient-specific implant-supported prostheses.[1,13]

Zirconia-based materials are one of the most commonly used ceramic materials. They have the potential to replace titanium implants due to their excellent biocompatibility, improved aesthetic results, high flexural strength, fracture toughness, high chemical resistance, and tooth-like color. The invention of additive manufacturing and CAD/CAM technology has enabled the production of these materials in the shape of tooth roots, facilitating immediate placement in the socket following extraction.[14]

Conventional zirconia implant designs offer a limited range of diameter and length options, which may not suit the needs of all patients. To overcome this challenge, customized RAIs have been introduced, reducing both hard and soft tissue trauma and enhancing initial stability.[15,16] Additionally, to address the challenges associated with sandblasting and etching of RAIs, as well as to enhance

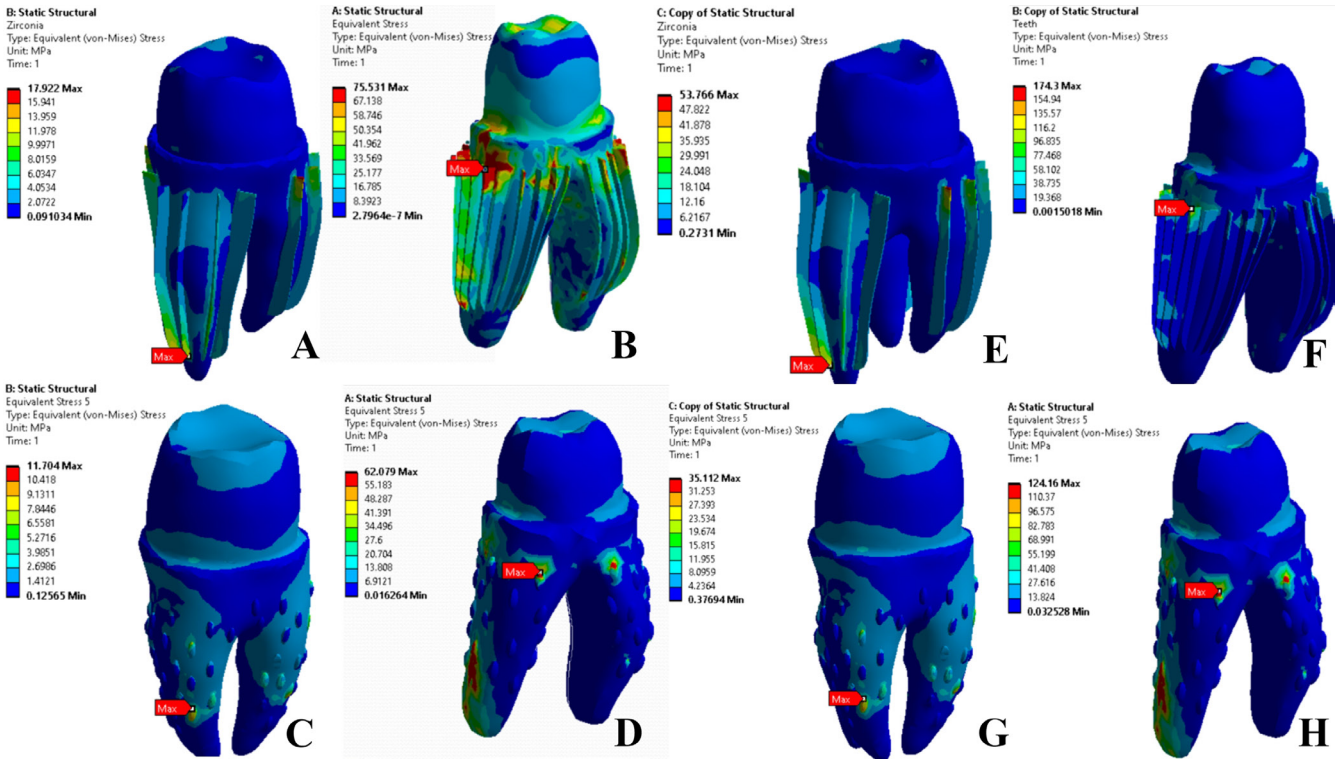


**Fig. 3.** Equivalent von Mises stress in root-analogue implants (RAIs) after the application of 100-N (A–D) and 300-N (E–H) loads

A,E. Maxillary implant with the fin design; B,F. Mandibular implant with the fin design; C,G. Maxillary implant with the bulb design; D,H. Mandibular implant with the bulb design.

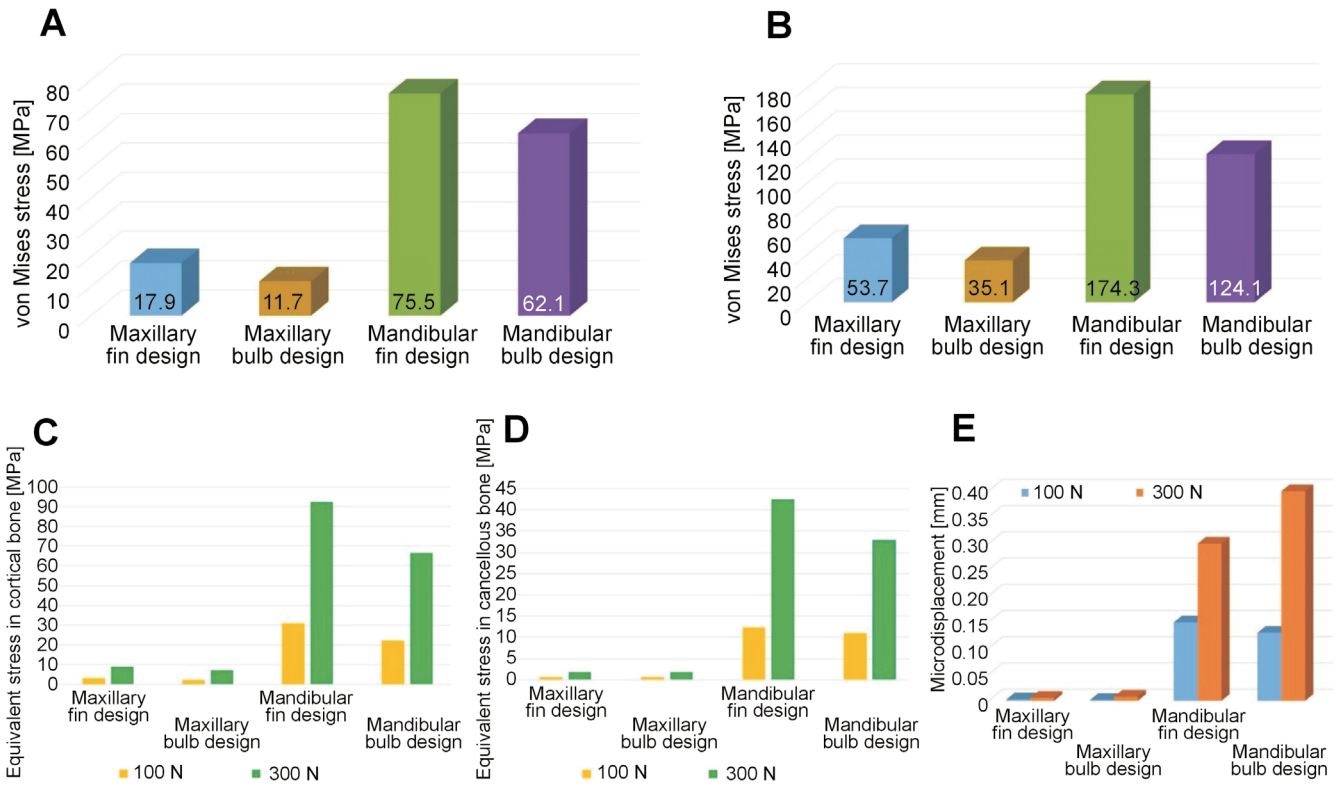


**Fig. 4.** Comparison of maxillary and mandibular fin and bulb designs

A. von Mises overall stress at 100 N; B. von Mises overall stress at 300 N; C. Equivalent stress in cortical bone at 100 N and 300 N; D. Equivalent stress in cancellous bone at 100 N and 300 N; E. Microdisplacement at 100 N and 300 N.

osseointegration, various micro- and macro-retentive modifications have been applied to the root surface of RAIs.[17–19] Other authors have analyzed more extensive root surface modifications and evaluated their biomechanical effects, such as stress distribution, and primary and secondary stability, using FEA as a tool prior to its application in a patient.[2,8,10,11,20]

Numerous studies have examined the biomechanical response of standard dental implants. However, literature on RAIs is limited, particularly with regard to the posterior region. Therefore, in this study, we planned to fabricate customized RAIs in the maxillary and mandibular posterior regions. Given the potential limitations of micro-retentions in ensuring implant mechanical stability, we incorporated 2 targeted press-fit macro-retentive features: fins and bulbs. These designs were selected based on the findings of Moin et al., who reported that incorporating targeted press-fit geometry, such as fins or bulbs, into the standard RAI design, enhances stress distribution, reduces the concentration of bone stress, and improves primary stability.[8] However, these modifications are novel and have not yet been tested in patients. The present study employed FEA as a tool to investigate bone stress and strain around implants and relative microdisplacement between bone–implant interfaces.

The finite element analysis revealed that the von Mises stress and microdisplacement values for both designs in the mandibular molar region exceeded those in the maxillary molar region. This discrepancy can be attributed to the fact that large and wide implants exhibit reduced compressive and tensile principal stresses compared to short and narrow implants. The larger implants exhibit increased bone-to-implant contact area to dissipate the masticatory forces, leading to functional load distribution. Additionally, implants with a wider diameter have superior circumferential bone contact, which reduces stress and the likelihood of implant fracture.[21] Maxillary molar teeth possess a larger cross section and buccolingual width compared to mandibular molar teeth, and maximum equivalent stresses occur in the mandibular molar region during mastication.[22] Furthermore, maxillary teeth have 3 roots, indicating that the area of bone–implant contact is more pronounced in maxillary implants compared to mandibular implants, which is more significant for stress distribution.[23,24]

A comparison of the fin and bulb designs demonstrated that the von Mises stress values for the implant, cortical bone and cancellous bone at both loads (300 N and 100 N) were lower for the bulb design than for the fin design in both the maxillary and mandibular molar regions. Previous studies have reported that the incorporation of targeted press-fit design characteristics into standard RAIs reduces the maximum von Mises stress in the peri-implant bone, leading to more positive load behavior.[8,20,25] However, the primary stability of the fin design was superior to that of the bulb design in both regions because the bulb design exhibited greater microdisplacement.

A comparison of the equivalent stress in cortical and cancellous bone revealed that the cortical bone exhibited greater stress concentration. Misch stated that the cortical bone had a significantly higher percentage of bone–implant contact than the trabecular bone.[26] Thus, inappropriate loading can lead to excessive stress accumulation and subsequent bone loss. To avoid this situation, the diameter of the implant was reduced near the cortical bone, thereby averting crestal bone loss and fracture. This phenomenon has been documented in the studies conducted by Lin et al.[11] and Memari et al.[24]

To the best of our knowledge, the present study is the first to compare the fin and bulb design modification of RAIs in maxillary and mandibular posterior regions using FEA. Previous studies have employed titanium to customize RAIs. However, numerous studies have shown that zirconia is a viable alternative to titanium, with greater soft tissue response, biocompatibility and aesthetics, as well as equivalent osseointegration.[9,27] Hence, zirconia was chosen as a RAI material. The majority of previous studies focused on the anterior and premolar regions.[8,20,25] Therefore, the present study was designed to test RAIs in the maxillary and mandibular posterior regions.

## Limitations

Despite the study's innovative nature, it had certain limitations. The loads used in the study were static and unidirectional, with amplitudes of 100 N and 300 N. However, it should be noted that changing loads are observed in patient clinical scenarios. The peri-implant bone was modeled as a homogeneous, isotropic, linearly elastic material. Furthermore, the biomechanical behavior of biological tissues is known to be diverse, anisotropic and non-linear. Given the complexity of non-linear contact analysis, the interaction between the bone and the implant was modeled as linear contact. It is also notable that the results of FEA in dentistry should be regarded as a complement to clinical investigations, with the objective of enhancing understanding of the impact of specific variables on the clinical performance of implants.

The present study investigated implant microdisplacement and the overall stress distribution at the bone–implant contact. Because bone possesses both ductile and brittle qualities, maximum (tensile stress) and minimum (compressive stress) principal stress, as well as maximum shear stress should be evaluated in future investigations. Additionally, studies that compare the von Mises stresses, principal stresses and displacement of root-analogue zirconia implants with root-analogue titanium implants are necessary. The clinical condition may not have been fully duplicated since FEA is a computational in vitro study. Furthermore, given the variability inherent in individual clinical situations, long-term in vivo investigations on root-analogue zirconia implants are required.

# Conclusions

In the context of the study's limitations, it can be concluded that the customized root-analogue zirconia implants with the bulb design exhibit superior stress distribution in the surrounding bone compared to the customized RAIs with the fin design. The micromotion values of the fin design were lower than those in the bulb design, indicating enhanced primary stability of the fin design. The stress distribution of both designs demonstrates lower stress values in the maxillary posterior region compared to the mandibular posterior region. However, long-term clinical trials are necessary to determine the optimal design and evaluate its long-term functionality and mechanical resistance.

## Ethics approval and consent to participate

Not applicable.

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.


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Original paper

# Fracture resistance in severely damaged primary maxillary central incisors restored with glass fiber and composite posts: An in vitro study

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D – writing the article; E – critical revision of the article; F – final approval of the article

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## Abstract

**Background.** A variety of non-metal prefabricated posts, including fiber posts, can be used as an alternative to metal posts due to their numerous feasible characteristics. Further research is necessary to assess physical and mechanical properties of restorations supported by intracanal posts in primary teeth.

**Objectives.** The aim of the study was to compare fracture resistance of maxillary central incisors that were extensively restored with glass fiber and composite posts.

**Material and methods.** A total of 40 primary maxillary central incisors were randomly divided into 4 equal groups. Group 1 received conventional intracanal composite posts, group 2 was treated with prefabricated intracanal glass fiber posts, group 3 received precured intracanal composite posts, and group 4 was treated with intracanal lucent glass fiber posts. Crowns were restored using composite resin, and the specimens were subsequently exposed to 5,000 thermal cycles and progressive load at a crosshead speed of 0.5 mm/min until fracture. The fracture resistance values were compared via one-way analysis of variance (ANOVA) followed by Tukey's test for pairwise comparisons ($\alpha = 0.05$).

**Results.** The highest fracture resistance was observed in the lucent post group (343.2 N), followed by the prefabricated glass fiber post (284.8 N), conventional composite post (270.3 N) and precured composite post (261.1 N) groups, respectively. A statistically significant difference in the mean fracture resistance was observed among the 4 groups ($p < 0.05$). Pairwise comparisons revealed that the mean fracture resistance of the lucent post group was significantly higher than that of the other groups ($p < 0.05$).

**Conclusions.** All of the intracanal posts provided apt fracture resistance and can be used to restore severely damaged primary maxillary central incisors. However, lucent posts demonstrated significantly higher levels of fracture resistance.

**Keywords:** deciduous teeth, flexural strength, composite resins, post and core technique

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## Highlights

- Lucent glass fiber posts demonstrated the highest fracture resistance, significantly outperforming other post types.
- Precured composite posts exhibited the lowest mean fracture resistance among all groups.
- Precured composite posts had the highest number of repairable fractures, followed by lucent and prefabricated glass fiber posts, and conventional composite posts.

# Introduction

Dental caries is the most prevalent chronic disease in children.[1] Early childhood caries (ECC) is a category of dental caries in young children representing a certain pattern of decays. Primary maxillary central and lateral incisors and primary first molars of both jaws are most commonly involved.[2] Primary maxillary incisors are often most severely involved with deep caries, extending to the dental pulp space. In severe cases, ECC can lead to complete loss of the coronal structure of the teeth.[3] Early childhood caries and early loss of primary teeth can result in abnormal tongue position, compromised masticatory force, impaired mastication, speech impairment, psychological issues arising from aesthetic problems, decreased facial vertical height, mouth breathing, etc. Moreover, literature states that children with ECC are more likely to develop growth retardation compared with non-ECC children.[4–6]

Extensive reconstruction of primary anterior teeth has been challenging due to the small anatomical size of the crown, the large pulp space and the relatively limited cooperation of younger patients. Insufficient sound remnant tooth structure and low fracture resistance frequently result in subsequent restorative failures.[7,8]

In the domain of dental restoration, particularly for anterior teeth, aesthetics can be equally important as the preservation of tooth structure or the restoration of the primary contour and function of the teeth. In this regard, composite resins are the optimal material of choice.

Due to structural differences between primary and permanent teeth, including their lower amount of accessible enamel for bonding purposes, the application of composite resins for the restoration of primary teeth can be quite demanding.[9] In severely carious incisors that have undergone pulpectomy, the fabrication of an intracanal post for further retention is required to ensure optimal clinical durability of the composite restoration.[10] Various types of intracanal posts are commercially available for pediatric patients, such as prefabricated posts,[11] γ, α[11] and Ω[12] forms of orthodontic wires, retentive cast posts,[13] short composite resin posts,[14] fiber posts,[11] and biological posts.[15]

Recently, a range of non-metal prefabricated posts have been introduced, including fiber posts, which exhibit excellent biocompatibility with different core materials, high fatigue, high corrosion resistance, and high tensile strength.[16] These posts have been proposed as an alternative to prefabricated metal posts.

Despite the existence of several clinical reports on restorations in primary teeth and their follow-up courses, comprehensive data regarding the physical and mechanical properties of restorations supported by intracanal posts, particularly fiber posts, is lacking. Moreover, the application of precured composite posts in primary teeth has not been assessed. In light of these observations, this study aimed to compare the fracture resistance of prefabricated glass fiber posts, precured composite posts, lucent glass fiber posts, and conventional composite posts for the restoration of severely damaged primary maxillary central incisors.

# Material and methods

This study was conducted on 40 extracted primary maxillary central incisors. The study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (IR.SBMU.DRC.REC.1398.222).

The sample size was calculated to be 40, assuming α of 0.05, β of 0.2 and study power of 80%.

The teeth were immersed in 0.5% chloramine T for 7 days, and then stored in distilled water at 4°C until use. Distilled water was periodically refreshed.

Primary maxillary central incisors with at least ⅔ of sound root structure were included in the study. The teeth were decoronated at 1 mm above the cementoenamel junction (CEJ) by a fissure diamond bur and a high-speed handpiece. Thereafter, the root canals were instrumented 1 mm shorter than their established working length by files that were 3 sizes larger than the initial file size. Patency and canal rinsing were carried out using saline. Upon drying with paper points, the canals were filled with calcium hydroxide paste along with iodoform (Forendo paste; Metapex, Colmar, USA), 1 mm shorter than their established working length. Then, the teeth were randomly divided into 4 equal groups by block randomization, and coded. The coronal 4 mm of the canal was emptied by a fissure diamond bur to create a post space. Subsequently, a light-cure cavity liner (Lime-Lite™; PULPDENT Corporation, Watertown, USA) was applied in 1-mm thickness and cured by a light-emitting diode (LED) curing unit for 40 s. Excess material was carefully

removed, preserving a 3-mm-long corono-apical space for the placement of the post. The remaining procedures were performed according to group indicators and the pertaining manufacturers' instructions.

## Conventional composite posts

In group 1, the teeth were rinsed and dried. After acid etching and rinsing for 15 s and 10 s, respectively, the teeth were gently dried to allow for the preservation of slight moisture in the dentin. Two layers of bonding agent (Single Bond; 3M ESPE, St. Paul, USA) were applied using a microbrush, gently air-thinned for 2–5 s, and light-cured for 10 s. Subsequently, composite resin (3M™ Filtek™ Z250 Universal Restorative; 3M ESPE) was applied incrementally into the canal, condensed and light-cured. A 4 mm-high tooth crown was formed by a plastic filling instrument. Each layer of composite resin for crown restoration had a thickness of 2 mm and was light-cured for 20 s.

## Prefabricated glass fiber posts

In group 2, cylindrical glass fiber posts (Reforpost; angelus®, Londrina, Brazil) with a diameter of 1.1 mm were cut into individual 5-mm segments using diamond burs and a high-speed handpiece, under copious water irrigation. Each post was aimed to be 3 mm inside the canal, with the remaining 2 mm available for utilization as a core. The posts were cleaned with alcohol and air-dried. The canal was prepared through rinsing and gentle drying so that the dentin remained slightly moist. Dual-cure cement (Embrace™ WetBond™ Resin Cement; PULPDENT Corporation) was applied, the posts were inserted in the canals, and excess cement was eliminated. The cement was subsequently light-cured for 40 s. After acid etching and rinsing for 15 s and 10 s, respectively, the teeth were gently dried to ensure that the remnant exposed dentin remained slightly moist. The application of the bonding agent and composite was performed as outlined for group 1 to achieve the final coronal restoration.

## Precured composite posts

In the third group, 5 fiber posts with a diameter of 1.1 mm were selected as the initial models for the duplication of their dimensional characteristics in precured composite posts. The fiber posts were affixed onto clear plastic acrylic resin, and a vacuum machine (MINISTAR S®; SCHEU-DENTAL GmbH, Iserlohn, Germany) formed the plastic acrylic resin around the fiber posts like a mold. Subsequently, the fiber posts were removed, and the composite was applied, condensed and cured for 40 s. Thereafter, the molds were discarded and the composite posts were cut into 5-mm-long sections using diamond burs and a high-speed handpiece, under copious water irrigation. The aim was to position each post 3 mm inside the canal, with the remaining 2 mm serving as a prosthetic core. The canal was prepared through rinsing and gentle drying so that the dentin remained slightly moist. Dual-cure cement (Embrace™ WetBond™ Resin Cement; PULPDENT Corporation) was applied in the canal, the post was inserted, and excess cement was eliminated. Then, the cement was light-cured for 40 s. After acid etching and rinsing for 15 s and 10 s, respectively, the teeth were gently dried to ensure that the remnant exposed dentin remained slightly moist. The application of the bonding agent and composite was performed as outlined for group 1 to achieve the final coronal restoration.

## Lucent glass fiber posts

In group 4, cylindrical lucent glass fiber posts (Reforpost; angelus®) with a diameter of 1.1 mm were cut into 5-mm segments with the use of diamond burs and a high-speed handpiece, under copious water irrigation. The posts were cleaned with alcohol and air-dried. The canals were then rinsed and dried, ensuring that the dentin remained slightly moist. Dual-cure cement (Embrace™ WetBond™ Resin Cement; PULPDENT Corporation) was applied to the canal, the post was inserted, and excess cement was eliminated. Subsequently, the cement was light-cured for 40 s. The application of the bonding agent and the composite was performed as outlined for group 1 to achieve the final coronal restoration.

The length and crown height of the posts were 3 mm and 4 mm, respectively, in all groups.[7,11] All restorations were finished with composite finishing burs and polished under copious water irrigation. Restored teeth were then mounted in acrylic resin molds, leveled at 1 mm below their CEJs, and subjected to 5,000 thermal cycles between 5°C and 55°C.

To assess the fracture resistance, the teeth were subjected to compressive load at a 148° angle[17] with a crosshead speed of 0.5 mm/min[16] in a universal testing machine (UTM) (ZwickRoell ProLine Z050; ZwickRoell, Ulm, Germany) (Fig. 1,2). The middle third of the palatal surface close to the incisal edge underwent loading until fracture. The load at fracture was recorded as fracture resistance in Newtons [N].

To determine the mode of failure, the fractured specimens were examined by an observer who was blinded to the group allocation of the specimens. The mode of failure was categorized as repairable (fractures above CEJ) or irrepairable (fractures below CEJ).

## Statistical analysis

The data was analyzed using the IBM SPSS Statistics for Windows software, v. 20.0 (IBM Corp., Armonk, USA). The Kolmogorov–Smirnov test was used to assess the normality of data, analysis of variance (ANOVA) was

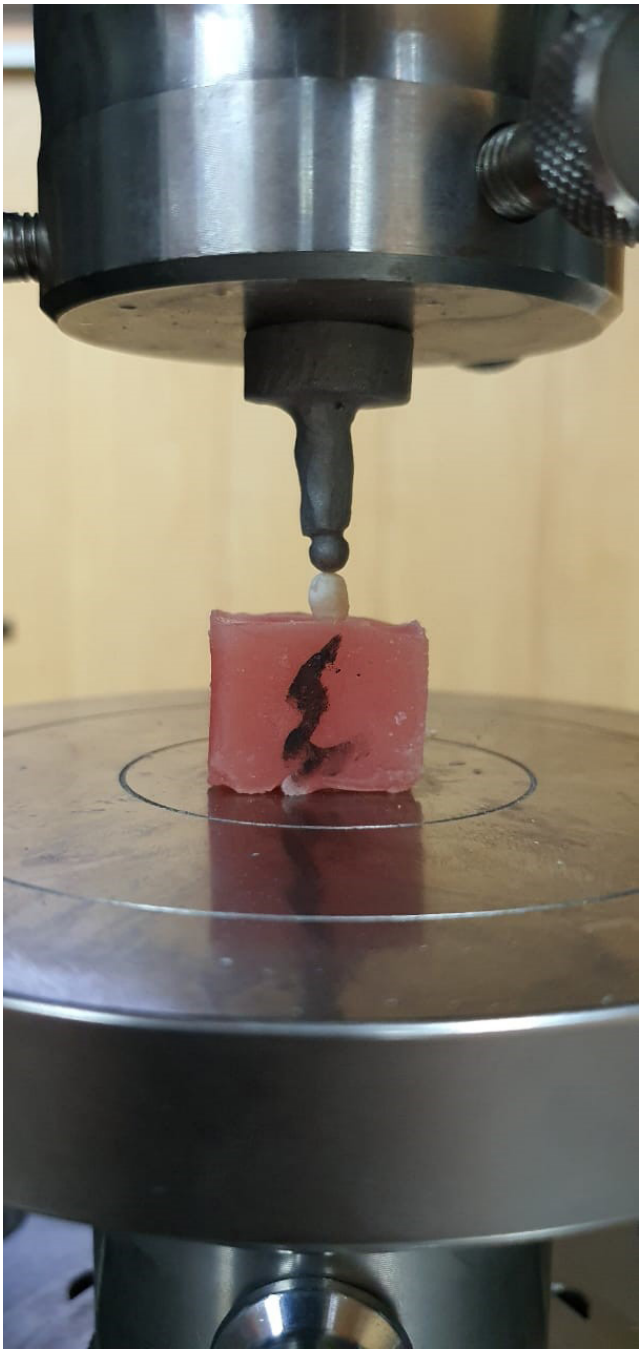

Fig. 1. Process of loading posts in the universal testing machine (UTM) (ZwickRoell ProLine Z050) at a crosshead speed of 0.5 mm/min


Fig. 2. Universal testing machine (UTM) (ZwickRoell ProLine Z050)

utilized for general comparisons, and Tukey's post hoc test was employed for pairwise comparisons. The value of $p < 0.05$ was considered statistically significant.

## Results

The lucent post group exhibited the highest mean fracture resistance, while the precured composite post group demonstrated the lowest fracture resistance. The Kolmogorov–Smirnov test confirmed the normality of data distribution ($p \geq 0.05$). The mean fracture resistance of the study groups is presented in Table 1. Analysis of variance revealed a significant difference in fracture resistance among all 4 groups ($p < 0.001$). Thus, pairwise comparisons were conducted using Tukey's test (Table 2). The lucent post group demonstrated a significantly higher fracture resistance compared to the other groups ($p < 0.05$). However, the differences among the other groups were non-significant.

An examination of the failure modes among the 4 groups revealed no statistically significant differences between them ($p = 0.116$). The frequency of repairable and irrepairable fractures across all groups is presented in Table 3.

**Table 1.** Fracture resistance of the study groups

| Group | Fracture resistance [N] | | |
|---|---|---|---|
| | *M* ±*SD* | 95% *CI* | |
| | | lower bound | upper bound |
| Conventional composite posts | 270.3 ±30.8 | 248.25 | 292.35 |
| Prefabricated glass fiber posts | 284.8 ±23.8 | 267.74 | 301.87 |
| Precured composite posts | 261.1 ±33.3 | 237.27 | 284.96 |
| Lucent glass fiber posts | 343.3 ±50.4 | 307.23 | 379.30 |

*M* – mean; *SD* – standard deviation; *CI* – confidence interval.

**Table 2.** Pairwise comparisons of the study groups regarding fracture resistance

| Group (I) | Group (J) | *p*-value |
|---|---|---|
| Conventional composite posts | prefabricated glass fiber posts | 0.803 |
| | precured composite posts | 0.940 |
| | lucent glass fiber posts | 0.000* |
| Prefabricated glass fiber posts | precured composite posts | 0.463 |
| | lucent glass fiber posts | 0.000* |
| Precured composite posts | lucent glass fiber posts | 0.000* |

* statistically significant ($p < 0.05$, Tukey's post hoc test).

**Table 3.** Frequency of repairable and irrepairable fractures in the study groups

| Failure mode | Lucent glass fiber posts | Precured composite posts | Prefabricated glass fiber posts | Conventional composite posts |
|---|---|---|---|---|
| Irrepairable | 3 (30) | 2 (20) | 3 (30) | 4 (40) |
| Repairable | 7 (70) | 8 (80) | 7 (70) | 6 (60) |

Data presented as frequency (percentage) (*n* (%)).

## Discussion

Obtaining a feasible fracture resistance with restorative materials is of crucial importance and can determine the durability of the restoration.[16] Fiber-reinforced composites consist of fibers embedded in a resin matrix. These composites have favorable mechanical properties, including optimal tensile and bond strength, translucency and facile manipulation.[18] In comparison to metal posts, fiber-reinforced composites demonstrate higher levels of flexibility, an elasticity efficiency comparable to dentin, and optimal aesthetics. Moreover, they enable the formation of an integrated root–post complex.[18] Fiber-reinforced composites are available in prefabricated and conventional forms. Precured composite posts had not been previously employed in pediatric dentistry.

The present study compared fracture resistance in prefabricated glass fiber posts, precured composite posts, lucent glass fiber posts, and conventional composite posts in restored severely damaged primary maxillary central incisors. The results indicated that the highest fracture resistance belonged to the lucent post group (343.27 ±50.37 N). This value was significantly different from the other groups ($p < 0.05$). Sharaf reported that glass fiber posts provided a significantly lower fracture resistance (230.6 N) compared to composite posts (277.9 N).[19] However, the difference between the mean fracture resistance of glass fiber and composite posts was statistically insignificant in the present study. Additionally, in the study conducted by Sharaf,[19] the mean fracture resistance of composite and glass fiber posts was found to be lower than in our study. This discrepancy may be attributed to differences in the type of employed posts, cements and composite resins. In addition, Seraj et al. reported the mean fracture resistance of composite posts to be 564.4 N, whereas, in the present study, the value of 270.3 N was obtained for conventional composite posts.[20] This discrepancy can be attributed to the 5,000 thermal cycles to which we subjected our specimens, which is in contrast with the study by Seraj et al.[20] Eshghi et al. reported no statistically significant differences in the retention of teeth clinically restored with fiber posts, composite posts, or metal posts, inspected after 12 months.[21] The authors demonstrated 90%, 98% and 100% success rates, respectively, which aligns with the studies by Judd et al.[22] and Sharaf,[19] who reported 100% success rates in teeth restored with composite posts and fiber posts.

The studies demonstrate that prefabricated posts with a smaller diameter can improve fracture resistance in teeth.[23] However, researchers often focus on the mesiodistal and labio-palatal widths of teeth at CEJ. They categorize specimens into different groups to mitigate potential confounding results.[23–26] Sharaf stated that the application of fiber posts in severely damaged primary anterior teeth can be a reliable method.[19] Only 2 out of 30 teeth were extracted over 1-year follow-up, due to mobility or failed pulp therapy. According to Sharaf, the application of fiber posts significantly increased the mean fracture resistance of teeth in vitro.[19] Similar to Seraj et al.[20] who stated that composite posts yield superior results over no post applications, the author observed that the application of composite posts significantly increased fracture resistance, as compared to teeth restored without intracanal posts.[10,19] In a similar study, Gujjar and Indushekar compared the retentive strength of composite posts, γ orthodontic wires and glass fiber posts in primary incisors.[27] Their findings indicated that glass fiber posts demonstrated a significantly higher tensile strength than composite posts. Notably, the composite post group displayed the lowest tensile strength among all groups. The enhanced strength of fiber posts can be attributed to the stronger post–cement bond and superior light transfer, which enhances cement polymerization at the apical region. Memarpour et al. evaluated the retentive strength of composite posts, glass fiber posts and polyethylene posts cemented with resin cement and

flowable composite.[28] They reported that composite posts with undercuts yielded the maximum mean retentive strength. However, the difference between composite posts and glass fiber or polyethylene fiber posts was not significant when cemented with flowable composite. The authors attributed the higher retentive strength of teeth restored using composite posts with undercuts to both their mechanical and micro-mechanical bonding to tooth structure. Nevertheless, this method is associated with an elevated risk of lateral root perforation. In addition, they correlated the higher retentive strength of posts cemented with flowable composite to the lower viscosity of flowable composite and, consequently, its better adaptation with prepared canal walls when compared to posts cemented with resin.[28]

In the present study, the mode of failure of teeth was indicated through the categorization of cracked teeth into 2 groups, namely repairable and irrepairable, using CEJ as the reference. However, Varvara et al. categorized modes of failure in permanent central incisors as repairable and irrepairable, with the alveolar bone margin as the reference.[26] Since crown lengthening operation is not routinely performed for pediatric patients, CEJ was used as a reference to differentiate the repairability of primary maxillary central incisors. The frequency of irrepairable fractures was 40% in conventional composite posts, 30% in glass fiber posts, 20% in precured composite posts, and 30% in lucent posts, with no statistically significant differences observed.

Pithan et al.[14] reported 80% of glass fiber posts and 47% of composite posts to cause an adhesive mode of failure, whereas Gujjar and Indushekar[27] provided values of 100% and 20%, respectively. This difference may be attributed to the occurrence of adhesive failure at the cement–root canal interface. In both studies, composite resin was used for the cementation of posts.[14,27] In our study, dual-cure resin cement was utilized for the cementation of glass fiber posts, due to its provision of high bond strength, facile manipulation and consequent accelerated procedure, longer working time, higher degree of conversion, and optimal mechanical properties.[29–31]

A study by Bitter and Kielbassa compared the efficacy of fiber posts and cast posts, revealing that the former resulted in more repairable fracture patterns.[32] In addition, Cai et al. observed that upon the application of fiber posts, the fracture site was limited to the coronal third of the root.[25]

In the present study, the minimum fracture resistance was 230 N. Mountain et al. reported that the maximum bite force at 3 points on first molars, second molars and central incisors ranged from 12.61 N to 353.6 N (with a mean value of 196.6 N) in children aged 3–6 years.[33] According to Owais et al., the maximum bite force was 126 N in the early primary stage and 240 N in the late primary stage.[34] Of note, bite force values are considerably higher in the oral cavity environment and under physiological conditions. Furthermore, the continuous application of stress can increase these values. In the current study, a mean fracture resistance of 237–370 N was observed, which remained within the clinically acceptable range for all groups. The thermocycling procedure was conducted to better simulate physiologic stresses.

A standardized canal diameter is necessary to obtain accurate results in terms of evaluating the impact of post adaptation with canal walls on fracture resistance. Post adaptation could be compared between composite and conventional posts, as well as prefabricated glass fiber posts. However, the lack of standardization of the canal diameters is a limitation of the current study. In addition, the in vitro design of our study constrains the generalization of the obtained data to the clinic.

Controlled clinical trials are warranted to obtain more clinically reliable results. Moreover, since bond failure has been suggested as a possible cause of fracture in glass fiber posts, the comparison of different adhesive systems for the cementation of fiber posts necessitates further studies.

# Conclusions

All of the intracanal posts studied demonstrated adequate fracture resistance and are suitable for the restoration of severely damaged primary maxillary central incisors. However, lucent glass fiber posts exhibited significantly higher fracture resistance.

## Ethics approval and consent to participate

The study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (IR.SBMU.DRC.REC.1398.222).

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.

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Original paper

# Effect of coating fillers with HEMA-phosphate copolymer on the mechanical properties of an experimental composite resin

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D – writing the article; E – critical revision of the article; F – final approval of the article

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## Abstract

**Background.** The water sorption and hydrolysis of silane over time can compromise the filler–resin matrix interface and cause the mechanical degradation of composite resins. The use of hydrophobic polymers for the surface treatment of fillers may improve the mechanical properties and durability of composites.

**Objectives.** The present study aimed to assess the effect of the surface treatment of fillers with hydroxyethyl methacrylate (HEMA)-phosphate copolymer on the mechanical properties of an experimental composite resin.

**Material and methods.** In this in vitro experimental study, HEMA-phosphate copolymer was synthesized and coupled with nano-silica powder. To assess the presence of the copolymer coating on the fillers, Fourier-transform infrared spectroscopy (FTIR) and thermogravimetric analysis (TGA) were performed. The fillers treated with different percentages of HEMA-phosphate copolymer were mixed with the resin matrix to fabricate experimental composites. The three-point flexural strength, microhardness and degree of conversion (DC) of 78 fabricated composite specimens were measured. Data was analyzed with the one-way analysis of variance (ANOVA) and Tukey's test.

**Results.** Fourier-transform infrared spectroscopy and TGA confirmed the attachment of the copolymer to the nano-silica filler for the synthesis of the composites. Group 1 (control) showed the maximum and group 6 showed the minimum hardness. Hardness decreased with an increase in the percentage of copolymer in the study groups. The maximum and minimum flexural strength and DC were noted in group 6 and the control group, respectively. Increasing the percentage of copolymer and its combination with silane non-linearly increased the flexural strength and DC of the experimental composites.

**Conclusions.** Increasing the percentage of HEMA-phosphate copolymer with/without silane for the coating of fillers improved the mechanical properties of the experimental composites, particularly their flexural strength and DC.

**Keywords:** copolymer, hydrolytic degradation, composite coupling agent, HEMA-phosphate

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## Highlights

- HEMA-phosphate copolymer significantly enhances composite material properties.
- Proven chemical bonding and improved material stability.
- Non-linear effect on hardness optimization for better performance.
- The synergistic combination of HEMA-phosphate copolymer and silane boosts composite performance.
- Increased durability potential for long-lasting, high-performance composites.

# Introduction

Despite the advances in the formulations of composite resins observed in the past decades, their performance is still inferior to that of dental amalgam.[1–3] One major cause of failure of composite restorations is the instability of the filler–resin matrix interface over long periods of time. So far, most investigations have focused on the type and composition of fillers, the size of filler particles, or the polymerization shrinkage of composites, and the coupling agents used for bonding fillers to the resin matrix have been less commonly addressed. Following the water sorption and hydrolysis of silane, the covalent bond between silane and silica shows ionic properties, and consequently, hydrolytic degradation occurs at the filler–matrix interface, which decreases the mechanical properties of the composite and can result in its eventual degradation.[4–7] The filler–polymer matrix interface greatly influences the properties of the composite. The surface treatment of fillers with polymers possessing certain characteristics may further stabilize the interface.[8–10]

The literature is controversial regarding the types of coupling agents and the surface treatment of filler particles.[4] Grafting the polymer on the filler surface and applying a tetraethyl orthosilicate coating are among the suggested kinds of surface treatment for fillers.[4,11] Mortazavi et al. used a polymethyl methacrylate graft for dental composite nanofillers, and reported the improvement of flexural strength and better distribution of fillers in the composite resin.[12] On the other hand, evidence shows that in the surface treatment of fillers, longer polymer chains cause higher hydrolytic stabilization of the interface.[13]

Hydroxyethyl methacrylate (HEMA)-phosphate monomer, with the formulation of 2-hydroxyethyl methacrylate phosphate or ethylene glycol methacrylate phosphate, has a functional phosphate group and a HEMA group in its composition. It has been previously used in the formulation of the 7th generation bonding agent (Adper™ Prompt™ L-Pop™), since it is completely disintegrated in aqueous media and creates acidic pH for the demineralization of the enamel and dentin.[14] Foscaldo et al. used HEMA-phosphate monomer as an alternative to phosphoric acid prior to the hybridization of the 5th generation adhesives.[15] They showed that this monomer created a significantly stronger dentin interface as compared to phosphoric acid. Also, they demonstrated that the use of HEMA-phosphate as a dentin conditioner significantly decreased nano-leakage.[15] The enhanced homogenous distribution of filler particles in the composite mass and the prevention of filler agglomeration are among other advantages of applying polymer chain coatings on the surface of fillers. Due to these advantages, HEMA-phosphate-methyl methacrylate copolymer has been recently used in composite orthopedic prostheses for adhesion to the bone surfaces.[16]

Considering all the above, the present study aimed to assess the effect of the surface treatment of fillers with HEMA-phosphate copolymer on the flexural strength, Vickers microhardness and degree of conversion (DC) of an experimental composite resin. The null hypothesis was that the surface treatment of the fillers of the experimental composites with HEMA-phosphate copolymer would have no significant effect on the flexural strength, Vickers microhardness and DC of the composites.

# Material and methods

In this in vitro experimental study, an experimental composite resin was first synthesized. Seventy-eight composite specimens were fabricated of the synthesized experimental composite and evaluated in 6 groups ($n$ = 13). The study protocol was approved by the ethics committee at Shahid Beheshti University of Medical Sciences, Tehran, Iran (IR.SBMU.DRC.REC.1397.006).

The sample size was calculated assuming $\alpha = 0.05$, $\beta = 0.2$ and a study power of 80%. In order to obtain the correct filler weight percentage for the optimal mechanical behavior of the experimental composite, a pilot study was performed at first.

## Synthesis of nano-silica composite fillers with hydroxyethyl methacrylate-hydroxyethyl methacrylate phosphate (HEMA-HEMAP) copolymer

To synthesize a specimen with 10% copolymer, 5 g of nano-silica powder (627346; Sigma Aldrich, St. Louis,

USA) was added to 50 mL of distilled water in a 100-cubic centimeter beaker; 0.25 g HEMA monomer (525464; Sigma Aldrich), 0.25 g hydroxyethyl methacrylate phosphate (HEMAP) monomer (463337; Sigma Aldrich), 0.06 g tert-butyl hydroperoxide (TBHP) (as a redox initiator), and 0.03 g sodium formaldehyde sulfoxylate (SFS) (to initiate the radical polymerization of acrylate monomers) were also added to the beaker. The contents of the beaker were stirred with a magnetic stirrer (MR Hei-Standard; Heidolph Persia Co. Ltd., Tehran, Iran) at 75°C for 1 h at 500 rpm. Next, the contents of the beaker were heated in an oven (Oven Wizards, Dublin, Ireland) at 100°C for 2 h for complete desiccation and the completion of monomer polymerization. The contents of the beaker were then milled in a dual mixer/mill (SPEX™ SamplePrep 8000D; SPEX SamplePrep, Metuchen, USA), and used as such in the formulation of the experimental composite resin (Fig. 1).

## Synthesis of specimens with 10% copolymer and A174 silane

The process of synthesis was the same as that explained earlier, except that in addition to HEMA and HEMAP monomers, 0.25 g A174 silane (1076730050; Merck, Darmstadt, Germany) was also added. In the process of the radical polymerization of monomers, A174 silane also participated in the structure of the copolymer (Fig. 2). During the sol–gel reaction, A174 silane bonds to the nano-silica structure with covalent bonds. In this process, the attachment of the copolymer to nano-silica becomes stronger as compared to the abovementioned synthesis without silane. The remaining steps were the same as those explained earlier. By doing so, specimens with 20% and 30% copolymer were synthesized. Specimens with 20% and 30% copolymer and 0.25 g silane were also fabricated in the same way as the 10% specimens. One group of specimens was fabricated containing only 0.25 g A174 silane acrylate monomer and 5 g nano-silica with the abovementioned synthesis protocol, to serve as the control.

Since this was an experimental study, considering the capacity of the equipment we had to synthesize and mix the experimental composites, we selected the optimal amount of filler powder and resin base that could be homogenously mixed and yield acceptable results in the pilot study. To fabricate specimens for each group of the experimental composites, the following protocol was applied: 0.66 g of modified filler powder containing nano-silica with 1.012 g resin (Table 1) were mixed manually using a mortar and a pestle for 5 min. The aforementioned values were selected by experimentation in a pilot study.[17]

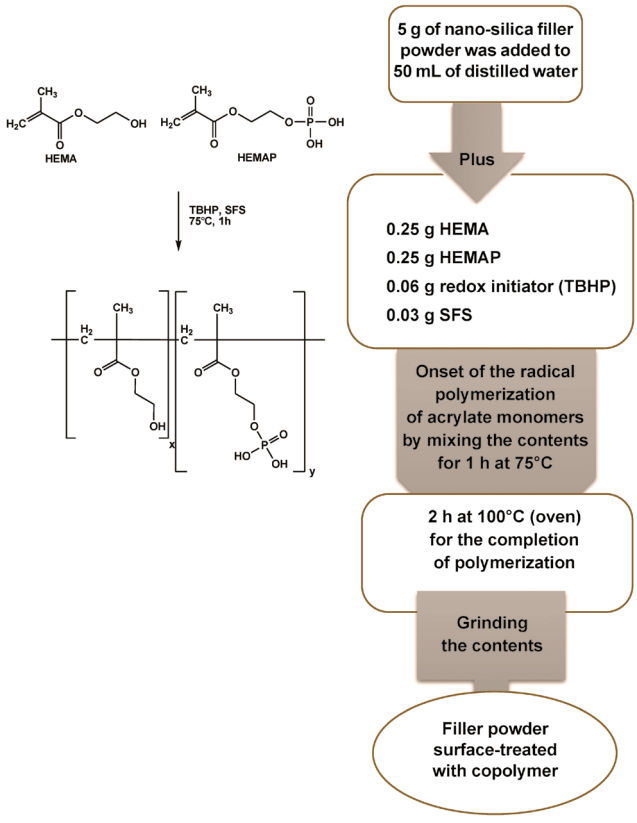


Fig. 1. Synthesis of hydroxyethyl methacrylate-hydroxyethyl methacrylate phosphate (HEMA-HEMAP) copolymer for the surface treatment of nano-silica fillers

TBHP – tert-butyl hydroperoxide; SFS – sodium formaldehyde sulfoxylate.

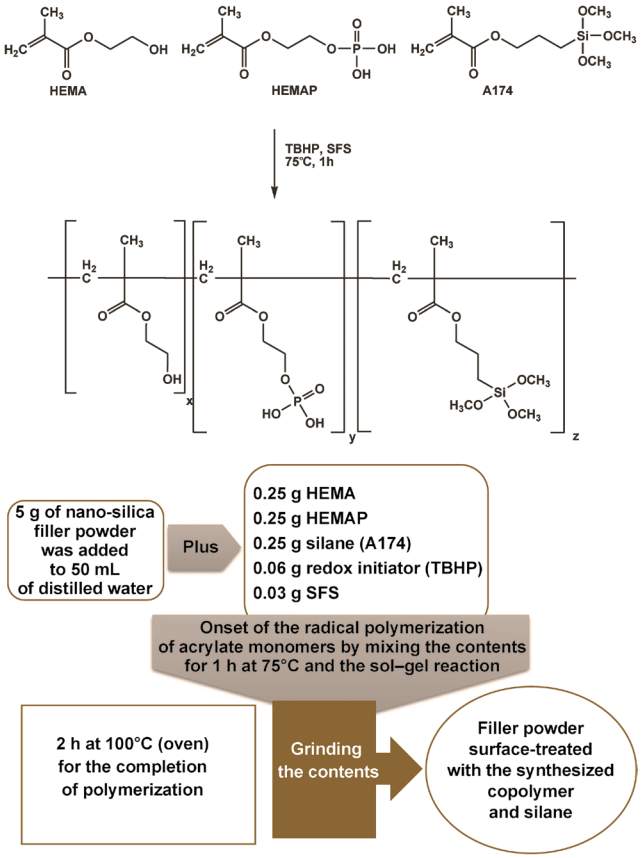


Fig. 2. Synthesis of hydroxyethyl methacrylate-hydroxyethyl methacrylate phosphate (HEMA-HEMAP) copolymer + A174 silane for the surface treatment of nano-silica fillers

Table 1. Ingredients of the resin matrix of the synthesized experimental composite resins

| Material | Weight percentage [%] | Manufacturer | CAS number |
|---|---|---|---|
| Bis-GMA | 48.0 | Sigma-Aldrich, St. Louis, USA | 1565-94-2 |
| UDMA | 25.0 | Sigma-Aldrich, St. Louis, USA | 72869-86-4 |
| TEGDMA | 17.0 | Sigma-Aldrich, St. Louis, USA | 109-16-0 |
| TMPTMA | 6.0 | Sigma-Aldrich, St. Louis, USA | 3290-92-4 |
| EDMAB | 2.0 | Sigma-Aldrich, St. Louis, USA | 10287-53-3 |
| CQ | 1.5 | Merck, Darmstadt, Germany | 10373-78-1 |
| TPO | 0.5 | Sigma-Aldrich, St. Louis, USA | 75980-60-8 |

CAS – Chemical Abstracts Service; Bis-GMA – bisphenol A-glycidyl methacrylate; UDMA – urethane dimethacrylate; TEGDMA – triethylene glycol dimethacrylate; TMPTMA – trimethylolpropane trimethacrylate; EDMAB – ethyl 4-dimethylaminobenzoate; CQ – camphorquinone; TPO – thermoplastic polyolefins.

For further mixing, the filler powder along with the resin were heated in a thermal box (Benchmark Scientific BSH200, Sigma Aldrich) at 56°C for 10 min to decrease the viscosity of the resin. The mixture was then transferred into a cartridge and mechanically mixed in an amalgamator (Owzan, Tehran, Iran) for 60 s at 5,000 rpm. The contents of the cartridge were manually mixed again in the dark for 5 min and placed in the amalgamator for another 60 s to obtain a homogenous mixture. Each composite was transferred into a syringe coated with aluminum foil and stored at 4°C.

The composite groups were as follows:

– group 1: Experimental composite containing the 5% silanized filler (control);
– group 2: Experimental composite containing the 10% filler coated with HEMA-phosphate copolymer;
– group 3: Experimental composite containing the 30% filler coated with HEMA-phosphate copolymer;
– group 4: Experimental composite containing the 10% filler coated with HEMA-phosphate copolymer plus the 5% silanized filler;
– group 5: Experimental composite containing the 30% filler coated with HEMA-phosphate copolymer plus the 5% silanized filler; and
– group 6: Experimental composite containing the 100% filler coated with HEMA-phosphate copolymer.

Pilot specimens were first fabricated and mechanical tests were performed on them. According to the results, groups containing 20% HEMA-HEMAP and 20% HEMA-HEMAP + silane were excluded, and replaced with the 100% HEMA-HEMAP group.

## Fourier-transform infrared spectroscopy (FTIR)

To confirm the successful coating of nano-silica fillers, 0.5 g of the fillers from each study group was mixed with potassium bromide in a ratio of 1:10, condensed in the form of a disk and subjected to Fourier-transform infrared spectroscopy (FTIR) under diffused reflection (spectrophotometer 1600 series; PerkinElmer Inc., Waltham, USA).

## Assessment of the degree of conversion (DC)

The DC of the control ($n$ = 3) and modified ($n$ = 3 from each experimental group) specimens was measured using attenuated total reflectance-Fourier transform infrared spectroscopy (ATR-FTIR) (Nicolet iS10; Thermo Fisher Scientific, Waltham, USA). For this purpose, the composite was first applied into standard molds with a diameter of 8 mm and a thickness of 2 mm, and condensed with glass slides at both sides. It was then cured with a curing unit (Dr's Light AT, Good Doctors Germany, Bonn, Germany) with a light intensity of 1,470 mW/cm$^2$ for 20 s from both sides. One specimen was fabricated from each composite type. The absorbance peaks were recorded using FTIR (Nicolet iS10; Thermo Fisher Scientific) over a wavelength range of 650–4,000 cm$^{-1}$ with a resolution of 4 cm$^{-1}$. The absorbance of the uncured specimens was also obtained under the same conditions. The DC value was calculated by estimating the changes in the peak height ratio of the absorbance intensities of the aliphatic C=C peak at 1,638 cm$^{-1}$ and that of the internal standard peak of aromatic C=C at 1,608 cm$^{-1}$, in relation to the uncured material. Thus, the DC of the specimen was calculated using the following formula (Equation 1)[17]:

$$DC = \left(1 - \frac{(1{,}638\ \text{cm}^{-1} \div 1{,}608\ \text{cm}^{-1})\ \text{after curing}}{(1{,}638\ \text{cm}^{-1} \div 1{,}608\ \text{cm}^{-1})\ \text{before curing}}\right) \times 100 \quad (1)$$

where:
DC – degree of conversion.

## Thermogravimetric analysis (TGA)

Thermogravimetric analysis (TGA) was also performed to assess the quality of the coating of nano-silica fillers with HEMA-phosphate copolymer. Prior to the synthesis of the composites, 10 mg of filler powder from each group was placed in a furnace (TGA-50; Shimadzu Corp., Kyoto, Japan) and heated up from room temperature (27°C) to 700°C at a speed of 10°C/min under nitrogen gas. A weight loss occurred due to the increase in temperature, and it was recorded as a function of temperature.

## Three-point flexural strength test

For this test, stainless-steel molds measuring 25 mm × 2 mm × 2 mm were used. The composite was applied into the molds ($n$ = 5), and each side was light-cured for 60 s with an intensity of 1,470 mW/cm$^2$. Each side was cured in three 20-second curing cycles using the overlapping technique. The specimens were then removed from the molds and stored in water at 37°C for 24 h. The three-point flexural strength test was performed according to the ISO 4049 standard,[18] using a universal testing machine (UTM) (Santam, Karaj, Iran). The distance between the 2 supports was 20 mm and load was applied at a crosshead speed of 0.75 mm/min. The maximum load was 50 N. The application of load was continued until the fracture of the specimen.[18]

## Vickers microhardness test

For this test, composite disks ($n$ = 5 from each group) were fabricated using stainless-steel molds with a diameter of 8 mm and a thickness of 2 mm. The specimens were fabricated as explained for the flexural strength test, and were then polished with 2,000-, 3,500- and 5,000-grit abrasive paper (Matador; Starcke, Melle, Germany). A Vickers hardness tester with a 136-degree pyramidal diamond indenter (ZwickRoell, Ulm, Germany) was used for this test. A load of 300 gf was applied for 10 s on the composite surface. Three indentations were created on the surface of each disk. The diameter of the created indentations was then measured under a microscope. The microhardness value was calculated accordingly.

## Statistical analysis

Data was analyzed using IBM SPSS Statistics for Windows, v. 24 (IMB Corp., Armonk, USA). The one-way analysis of variance (ANOVA) was applied to compare the groups, while pairwise comparisons were performed with Tukey's post-hoc test. The level of significance was set at 0.05.

# Results

## FTIR results

The FTIR analysis of nano-silica fillers showed stretching vibrations of the Si–O–Si functional group at 1,091 cm$^{-1}$. Stretching vibrations of the O–H group were also noted at 3,430 cm$^{-1}$. Stretching vibrations of the C=O carbonyl group at 1,750 cm$^{-1}$ confirmed the presence of the copolymer on the filler surface (Fig. 3). On the other hand, due to the presence of the hydroxyl group, the intensity of O–H vibrations slightly increased. While comparing the fillers containing HEMA-phosphate copolymer with the control group (5% silane), an increased intensity of peak at 1,240–1,310 cm$^{-1}$ was noted, which belonged to stretching vibrations of P=O. It indicated the presence of HEMA and the HEMA-phosphate groups in the composition of the composite, as well as the OH-groups of phosphate units.

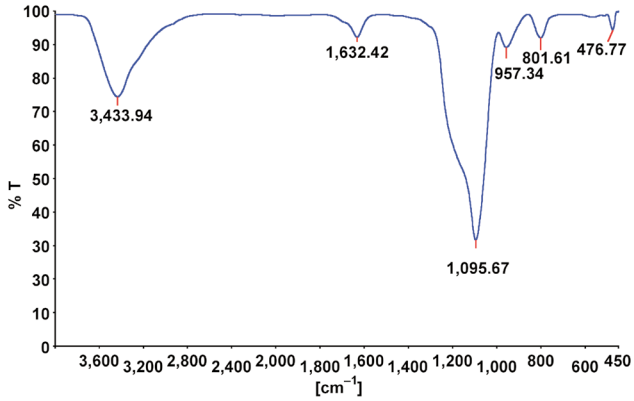


Fig. 3. Fourier-transform infrared spectroscopy (FTIR) spectrum for the control group (5% silane) fillers

The vibration peak of the C=C molecular bond in acrylate is located at 1,480–1,600 cm$^{-1}$. Following polymerization and the conversion of double bonds to single bonds, the intensity of this peak should decrease. This peak was not observed, which indicated the polymerization of the C=C bond with HEMA-phosphate.

In the control group (5% silane), a vibration peak at 1,750 cm$^{-1}$ confirmed the presence of the carbonyl group (Fig. 3). Since Si–O has a chemical structure similar to silica, its related vibration peak was noted beneath the vibration peak of silica. Similarly, for the group 5 fillers, the vibration peak of Si–O was observed beneath the peak of silica (Fig. 4).

## TGA results

Table 2 shows the percentages of weight loss for the specimens at each temperature range. As shown, a weight

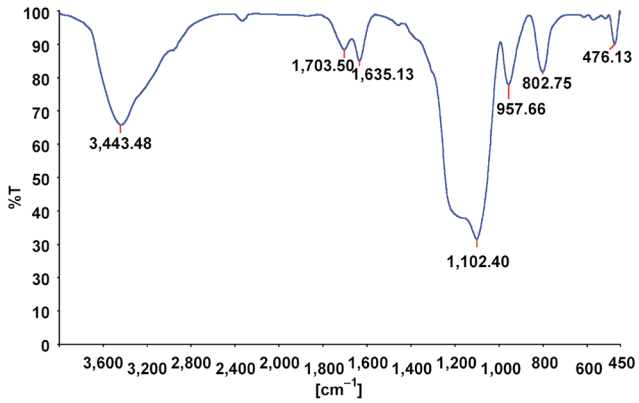


Fig. 4. Fourier-transform infrared spectroscopy (FTIR) spectrum for the group 6 fillers

**Table 2.** Percentages of weight loss [%] for the specimens at each temperature range

| Group | Temperature ranges | | | |
|---|---|---|---|---|
| | 25–175°C | 175–325°C | 325–475°C | 475–625°C |
| Nano-silica* | 9.20 | 0.90 | 1.54 | 0.79 |
| Group 1 | 7.17 | 1.30 | 2.65 | 2.27 |
| Group 2 | 9.26 | 1.55 | 3.72 | 2.76 |
| Group 3 | 8.95 | 1.70 | 6.61 | 2.74 |
| Group 4 | 7.48 | 1.12 | 4.65 | 2.99 |
| Group 5 | 10.00 | 0.34 | 5.22 | 2.49 |
| Group 6 | 6.98 | 5.20 | 13.96 | 1.79 |

Group 1 – 5% silane (control); group 2 – 10% hydroxyethyl methacrylate (HEMA)-phosphate; group 3 – 30% HEMA-phosphate; group 4 – 10% HEMA-phosphate + silane; group 5 – 30% HEMA-phosphate + silane; group 6 – 100% HEMA-phosphate.
* The weight loss of nano-silica powder alone is shown for the purpose of comparison with the weight loss of the experimental composite groups.

loss was noted at temperatures <200°C, which was attributed to the molecules physically bonded to the nano-filler surface. In other words, this weight loss was related to the loss of moisture from nano-silica powder and the water obtained from the completion of the sol–gel reaction. Another weight loss that occurred at temperatures 270–500°C indicated the presence of chemical bonds between the copolymer and nano-silica fillers (Fig. 5). Thus, the thermogram confirmed that the surface treatment of nano-silica fillers with HEMA-phosphate copolymer increased thermal stability.

## Vickers microhardness test results

Table 3 shows the Vickers microhardness values for the study groups. The microhardness data had normal distribution, as confirmed by the Kolmogorov–Smirnov and Shapiro–Wilk tests. Thus, ANOVA was applied for the comparison of the groups, and revealed significant differences in their microhardness ($p < 0.05$). Thus, Tukey's test was applied for pairwise comparisons, which revealed the maximum microhardness in the composite specimens from the control group (5% silane), while the minimum microhardness was noted in group 6. The differences between groups 1 (control), 2, 3, and 6 were all significant ($p < 0.05$). Also, significant differences were noted between groups 2 and 4 ($p = 0.310$), 3 and 4 ($p = 0.000$), 4 and 5 ($p < 0.05$), and 5 and 6 ($p = 0.000$).

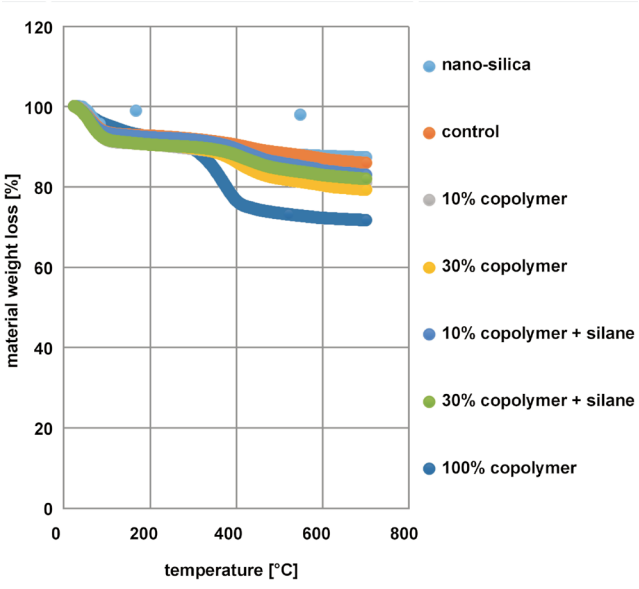


**Fig. 5.** Thermogravimetric analysis (TGA) diagram for the filler powder of the study groups

**Table 3.** Vickers microhardness values [HV] for the study groups ($n = 5$)

| Group | *M* ±*SD* | min | max |
|---|---|---|---|
| Group 1[a] | 35.60 ±2.90 | 30 | 42 |
| Group 2[a,b] | 31.67 ±1.88 | 29 | 34 |
| Group 3[a,c] | 31.13 ±1.88 | 30 | 33 |
| Group 4[b,c,d] | 34.67 ±2.90 | 30 | 40 |
| Group 5[d,e] | 33.53 ±4.07 | 25 | 41 |
| Group 6[a,e] | 30.07 ±2.02 | 25 | 33 |

Group 1 – 5% silane (control); group 2 – 10% hydroxyethyl methacrylate (HEMA)-phosphate; group 3 – 30% HEMA-phosphate; group 4 – 10% HEMA-phosphate + silane; group 5 – 30% HEMA-phosphate + silane; group 6 – 100% HEMA-phosphate.
*M* – mean; *SD* – standard deviation; min – minimum; max – maximum.
Groups with the same superscript letters showed a statistically significant difference according to Tukey's test ($p < 0.05$).

## Three-point flexural strength test results

Table 4 presents the flexural strength values for the study groups. The flexural strength data was not normally distributed. Thus, comparisons were made using the non-parametric Kruskal–Wallis test, which showed significant differences in flexural strength among the groups ($p < 0.05$). Pairwise comparisons revealed significant differences between groups 1 and 5 ($p = 0.010$), and 1 and 6 ($p = 0.000$). Also, groups 2, 3 and 6 differed significantly ($p < 0.05$), group 4 showed a significant difference with regard to group 1 ($p = 0.060$), and group 5 showed a significant difference with regard to group 2 ($p = 0.050$).

**Table 4.** Flexural strength values [MPa] for the study groups ($n = 5$)

| Group | *M* ±*SD* | min | max |
|---|---|---|---|
| Group 1[a,b,d] | 47.61 ±9.38 | 34.05 | 55.90 |
| Group 2[c,e] | 50.88 ±11.92 | 36.00 | 68.40 |
| Group 3[c] | 54.62 ±6.02 | 46.00 | 61.00 |
| Group 4[d] | 62.39 ±7.22 | 52.95 | 69.50 |
| Group 5[a,e] | 65.71 ±3.37 | 62.79 | 70.90 |
| Group 6[b,c] | 69.46 ±5.67 | 62.30 | 75.50 |

Group 1 – 5% silane (control); group 2 – 10% hydroxyethyl methacrylate (HEMA)-phosphate; group 3 – 30% HEMA-phosphate; group 4 – 10% HEMA-phosphate + silane; group 5 – 30% HEMA-phosphate + silane; group 6 – 100% HEMA-phosphate.
Groups with the same superscript letters showed a statistically significant difference according to the Kruskal–Wallis test ($p < 0.05$).

## Degrees of conversion

Table 5 presents the DC of the study groups. Since the DC data was not normally distributed, the Kruskal–Wallis test was applied for the comparison of the groups. It revealed significant differences ($p < 0.05$). Pairwise comparisons showed significant differences between group 1 and all other groups ($p < 0.05$), except for group 2 ($p = 0.340$). Group 2 differed significantly from groups 3, 5 and 6 ($p < 0.05$). Group 3 showed significant differences with regard to all other experimental groups ($p < 0.05$), except for group 5 ($p = 0.750$). Group 4 showed significant differences with regard to all other experimental groups ($p < 0.05$), except for group 2 ($p = 0.240$). Also, group 6 differed significantly from all other groups ($p < 0.05$).

# Discussion

This study assessed the effect of the surface treatment of fillers with HEMA-phosphate copolymer on the mechanical properties of an experimental composite. HEMA-phosphate monomer breaks down into HEMA and phosphoric acid in aqueous media.[14] It has been reported that the connection of the filler with the resin matrix through short polymer chains is difficult, and such a polymer layer would often create a less stable interface.[19] Thus, attention has been directed to the use of polymers with long hydrocarbon chains instead of silane to increase the stability and durability of the coupling layer. In the present study, HEMA-phosphate copolymer was synthesized to create a polymer with a long chain. Since this copolymer has never been used in the formulation of composite resins, we first conducted a pilot study and synthesized several composite specimens in each group to find the optimal method of synthesis, with a maximum filler percentage to achieve almost ideal mechanical properties. Accordingly, the group containing fillers modified with 20% copolymer was excluded from the final analysis, since the results in this case were very similar to those for groups 1 and 2.

**Table 5.** Degree of conversion (DC) values [%] for the study groups ($n = 3$)

| Group | *M* ±*SD* | min | max |
|---|---|---|---|
| Group 1[a] | 47.6 ±2.5 | 45.0 | 50.0 |
| Group 2[b] | 51.6 ±1.9 | 49.2 | 54.6 |
| Group 3[a,b,c] | 67.5 ±1.3 | 66.0 | 68.5 |
| Group 4[a,c,d] | 56.0 ±3.0 | 53.0 | 59.0 |
| Group 5[a,b,d,e] | 70.0 ±2.0 | 68.0 | 72.0 |
| Group 6[a,b,c,d,e] | 77.0 ±1.6 | 75.4 | 78.6 |

Group 1 – 5% silane (control); group 2 – 10% hydroxyethyl methacrylate (HEMA)-phosphate; group 3 – 30% HEMA-phosphate; group 4 – 10% HEMA-phosphate + silane; group 5 – 30% HEMA-phosphate + silane; group 6 – 100% HEMA-phosphate.
Groups with the same superscript letters showed a statistically significant difference according to the Kruskal–Wallis test ($p < 0.05$).

## FTIR analysis and TGA confirming the presence of copolymers in the composition of the synthesized composites

The chemical reactions of HEMA-phosphate copolymer with the surface of the filler were confirmed by FTIR and TGA. The vibration peak of the C=C molecular bond in acrylate is located at 1,480–1,600 $cm^{-1}$. Following polymerization and the conversion of double bonds to single bonds, the intensity of this peak should decrease. This peak was not observed, which indicated the polymerization of the C=C bond with HEMA-phosphate in our study. Also, the presence of a peak at 1,750 $cm^{-1}$, related to C=O, confirmed the presence of the copolymer on the filler surface.

Thermogravimetric analysis displays the weight loss of fillers as a function of a temperature increase.[20] The TGA of filler powder in all groups showed a reduction in the filler weight at temperatures <200°C due to the loss of water in the filler content and the unreacted coupling agent. Another drop in weight was noted at 270–500°C. The maximum percentage of reduction in the filler weight was noted in group 6 between 325°C and 475°C. The reduction in weight increased with an increase in the copolymer content, which indicated that HEMA-phosphate copolymer underwent thermal degradation at a higher temperature due to its chemical bond with nano-silica fillers.

## Flexural strength analysis of the synthesized composites

Groups 2, 3 and 6 (10%, 20% and 100% HEMA-phosphate copolymer, respectively) showed significant increases in the flexural strength and DC of the composites. Another study that used HEMA-phosphate copolymer reported that it increased the mechanical strength of zinc oxide and zinc polycarboxylate cements, and decreased their solubility.[21] It appears that if the percentage of unreacted monomers in the polymer matrix of the composite is lower, the polymer network on the filler surface can improve the mechanical properties of the composite resins, such as flexural strength. Also, it occurs that long polymer chains on the filler surface create ester repulsion and overcome the Van der Waals forces between particles, preventing the agglomeration of filler particles and leading to an increase in the composite strength.[22]

## DC analysis of the synthesized composites

A number of factors can affect the DC of composite resins, e.g., the cavity size, its location, the distance between the tip of the curing unit and the composite surface, the filler type, the type of curing unit, and light intensity.[23]

A review study demonstrated that the size, weight and volume of filler particles, and the filler/matrix ratio can significantly affect the DC and microhardness of composite resins.[24] In the present study, the composite specimens containing the maximum percentage of HEMA-phosphate copolymer showed the highest DC value. A lower filler/resin matrix ratio in this group, in comparison with other groups, appeared to be directly correlated with a higher DC value.[25]

The current study did not assess the rheological properties of the experimental composite resins; however, in the process of synthesis, it was noticed that filler groups with a higher percentage of copolymer (group 6) had lower viscosity and better handling, and were better mixed with the resin matrix. In other words, materials with lower viscosity have a lower filler content or contain more flowable resin monomers. A previous study demonstrated a greater movement of free radicals in the resin matrix of resin monomers with lower viscosity, which led to higher DC.[26] It has been reported that the modification of the filler surface by using oligomeric chains increases the DC of the composite as compared to composite resins with silane as the only coupling agent in their structure.[27] In the present study, increasing the percentage of copolymer increased the DC of the composite. The final polymerization of the composite involves 2 key processes: the polymerization of 60 wt% of the resin added to the filler; and an increased conversion of carbon–carbon double bonds into single bonds within the resin part of the pre-polymerized filler. Together these processes enhance the overall conversion of carbon bonds.

## Microhardness analysis of the synthesized composites

The Vickers microhardness test is commonly performed to assess the mechanical properties, DC and wear properties of composite resins.[17,28,29] In the present study, the control group (5% silane) showed the maximum microhardness, while group 6 showed the minimum microhardness. The calculation of the weight fraction of the filler in the synthesized composites revealed that increasing the resin matrix decreased microhardness. Pala et al. reported similar results.[30] On the other hand, they showed an inverse correlation between microhardness and flexural strength.[30] Chung and Greener found a significant correlation between the weight fraction and volume fraction of fillers and microhardness, which confirms our findings.[31] Nonetheless, Lee et al. found a positive correlation between microhardness and flexural strength, which is different from our results.[32] However, it should be noted that they assessed the mechanical properties of denture-base acrylic resins, while we evaluated composite resins. Marovic et al. demonstrated a correlation between DC and hardness.[33] They noted that increasing the pre-polymerized filler content in the composite decreased its microhardness. On the other hand, they showed that the microhardness of the composite was more influenced by the filler content rather than DC,[33] which is in line with the results obtained in our study.

Karabela and Sideridou reported that the structure of silane used for nano-silica silanization affected the adsorption and solubility of composite resins.[34] The silane molecule has two functional ends. One end bonds to the hydroxyl groups of silica particles and the other end can copolymerize with the polymer matrix. In the present study, in the process of synthesis of HEMA-phosphate copolymer, a 3D polymer structure was created on the silica matrix upon using the redox initiator. In this process, all insoluble 3D acrylate monomers were placed on silica particles. Phosphate groups in the structure of HEMA-phosphate are attached to the silica structure via strong ionic bonds. The presence of these bonds was confirmed by the TGA of the modified filler powders.

In groups 4 and 5 (the use of silane and HEMA-phosphate copolymer), silane monomer was incorporated in the structure of the copolymer during radical polymerization, while silane monomer forms covalent bonds with the nano-silica structure during the sol–gel reaction. Obviously, the attachment is stronger when silane along with HEMA-phosphate copolymer bond to nano-silica particles, as compared to the attachment of HEMA-phosphate copolymer without silane. Ye et al. used both silane and polyethylene glycol dimethacrylate oligomer for the surface treatment of colloidal silica fillers, and observed a uniform distribution of silica particles in the urethane dimethacrylate (UDMA) matrix, which enhanced the strength.[27] This result is in line with our findings in groups 4 and 5, where a combination of silane and HEMA-phosphate copolymer was used, with the difference being that the type of copolymer was different in the 2 studies.

Thus, a combination of HEMA-phosphate copolymer and silane as filler surface treatment may result in a more stable and reliable resin matrix–filler interface. However, long-term studies are required to assess the hydrolytic and mechanical stability of the interfaces containing HEMA-phosphate copolymer, with and without a silane base, to cast a final judgment in this respect. Also, the assessment of other mechanical properties of the synthesized composites, as well as the evaluation of the mode of failure (with the use of scanning electron microscopy (SEM)), are recommended.

# Conclusions

Increasing the percentage of HEMA-phosphate copolymer for the filler surface treatment of an experimentally synthesized composite, in both pure form and in combination with silane, improved its mechanical properties, particularly DC and flexural strength.

## Ethics approval and consent to participate

The study protocol was approved by the ethics committee at Shahid Beheshti University of Medical Sciences, Tehran, Iran (IR.SBMU.DRC.REC.1397.006).

## Data availability

The datasets supporting the findings of the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.

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Review

# Is prevalence of dental anomalies site-specific in cleft lip and palate patients? A systematic review and meta-analysis

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of the article

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## Abstract

The prevalence of cleft lip in conjunction with cleft palate is twice that of cleft lip or palate alone. Dental abnormalities are more frequent in patients with cleft lip and palate (CLP) than in non-cleft individuals. The present systematic review aimed to identify studies that examined the prevalence of dental anomalies in unilateral and bilateral clefts. Relevant articles that met the specified inclusion criteria were identified with the use of MEDLINE/PubMed®, Scopus and EBSCOhost databases. The systematic review protocol was formulated using the established PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist. The results of the meta-analysis demonstrated a statistically significant difference in the prevalence of supernumerary teeth (ST) in patients with left unilateral CLP ($p = 0.021$). The difference was statistically insignificant for ST between unilateral and bilateral CLP ($p = 0.542$). The present analysis demonstrated that the difference between unilateral and bilateral CLP, as well as between right and left unilateral CLP regarding tooth agenesis/missing teeth (A/MT) was statistically insignificant ($p = 0.301$ and $p = 0.130$, respectively). However, the black diamond presented in the forest plot indicates that the unilateral CLP and left unilateral CLP groups are in favor, respectively. Consequently, patients with left unilateral CLP exhibited a higher frequency of ST. The analysis suggests a potential association between the type of unilateral CLP and bilateral CLP concerning A/MT and ST in particular.

**Keywords:** supernumerary teeth, cleft lip, cleft palate, congenital abnormalities

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## Highlights

- Cleft lip and palate is a common congenital abnormality, occuring in approx. 1 in 700 live births.
- Local factors, such as the cleft itself and surgical procedures, may contribute to dental anomalies.
- Patients with left unilateral cleft lip and palate are more likely to have supernumerary teeth.
- Results suggest a weak association between cleft type and tooth agenesis/missing teeth and supernumerary teeth.

# Introduction

A common congenital abnormality that manifests in approx. 1 in 700 live births is cleft lip and palate (CLP).[1] The prevalence of cleft lip in conjunction with cleft palate is twice that of cleft lip or palate alone. These malformations involve the alteration of the middle third of the face, with varying degrees of severity. They may occur in isolation, particularly in non-syndromic patients, or they can be part of a group of abnormalities seen in syndromic cases.[2]

Developmental factors such as chromosomal abnormalities and gene mutations, as well as environmental factors, including maternal drug use, folic acid deficiency and radiation are concomitant to the etiology of cleft development.[3–6] However, the prevalence of CLP varies according to the type of population, race and geographical area.[7–9]

Dental abnormalities are more prevalent in patients with CLP than in non-cleft individuals, which may be a consequence of the cleft itself or any surgical intervention.[10] Additionally, the relationship between dental abnormalities and CLP is influenced by proximal anatomy, cleft formation time and dental development.[9,11] Dental anomalies in CLP patients are predominantly observed in the anterior maxilla, suggesting a potential correlation with surgical interventions performed in this region during tooth bud formation. It is believed that both the embryological cleft formation and surgical procedures may cause dental anomalies in the structure and position of the teeth.[12,13]

From an anatomical location and in terms of timing, the development of tooth germs and the formation of the oral clefts are associated embryologically with the construction of the teeth, lips and palate.[14,15] In comparison to the general population, individuals with oral clefts are more susceptible to dental variations.[8,16,17] The disruptions and alterations during the development of teeth at various stages, including morphodifferentiation and histodifferentiation, may result in the formation of supernumerary teeth (ST), which may emerge from the dental lamina as a discrete entity or from the dichotomy of a tooth bud.[18,19] The most common dental defect in the cleft region is agenesis of maxillary lateral incisors, which is presumably due to the local impact of the cleft.[14,20,21] The frequent absence of lateral incisors or their distal or mesial location concerning the cleft, as well as the presence of ST in the same region, may be attributed to the presence of CLP.[22] The second most frequent dental defect is the presence of ST.[22,23]

This systematic review aimed to identify studies that assess the prevalence of dental anomalies in unilateral and bilateral clefts. The review focuses on the prevalence of the most common anomalies, such as tooth agenesis/missing teeth (A/MT) and ST, in patients with unilateral and bilateral CLP, as well as between right and left unilateral CLP. This investigation also examines the existence of any quantitative differences among these groups.

# Material and methods

The protocol of this systematic review was formulated using the established PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist.[24] The review question was designed utilizing the PICO framework, as follows:

– Population: non-syndromic unilateral and bilateral CLP patients with A/MT or ST;
– Intervention: presence of A/MT or ST;
– Comparison: dental anomalies between unilateral and bilateral CLP patients and between right and left unilateral CLP patients;
– Outcome: prevalence of dental anomalies between unilateral and bilateral CLP patients and between right and left unilateral CLP patients.

The formulated research question sought to ascertain whether dental anomalies are more prevalent in patients with bilateral CLP or unilateral CLP. The review protocol was registered in PROSPERO (registration No. CRD42022346399).

## Eligibility criteria

Strict inclusion criteria were established to identify relevant articles from the database. The identification and filtration of articles was performed by 2 examiners (JW and SS). The full texts of relevant articles were obtained and independently screened by both reviewers. Only studies that considered and segregated data for unilateral as well as bilateral CLP were taken into consideration. This was done to compare the prevalence of anomalies strictly

between unilateral and bilateral CLP. The inclusion criteria encompassed studies that described different types of clefts, with cross-sectional or prevalence-based study design, and non-syndromic unilateral and bilateral CLP study sample with A/MT or ST. The anomaly data was to be given individually for right and left unilateral CLP patients. Additionally, data for unilateral and bilateral CLP patients must have been presented in the form of total anomalies for specific cleft categories (discrete data). The selection of articles was constrained to those written in English, and the scope included any dentition (permanent/primary). The focus was exclusively on dental anomalies, and the specific types of anomalies must have been clearly specified. The exclusion criteria encompassed studies that did not describe the type of cleft, those that involved syndromic unilateral and bilateral CLP patients, and studies that did not categorize data and present it as cleft and non-cleft groups. Additionally, data that was not provided individually for right and left unilateral CLP patients, or for unilateral and bilateral CLP patients, was excluded. Studies that considered more than 1 anomaly in an individual but included them as a single entity, studies in which the number of events (anomalies) exceeded the total population, as well as case reports, letters, short communications, case series, and views, were excluded. Articles in any language other than English were not considered for inclusion.

## Outcome assessed

The prevalence of dental anomalies was assessed between unilateral and bilateral CLP patients and between right and left unilateral CLP subjects.

## Information sources and search

A comprehensive search was conducted using MEDLINE/PubMed®, Scopus and EBSCOhost databases to identify relevant articles that met the specified inclusion criteria. Additionally, a manual search was carried out to identify relevant articles from the gray literature. The search was implemented by 2 examiners (JW and SS) in October 2022. The medical subject headings (MeSH) were paired with "AND" and "OR" to establish a search strategy. The search strategies and the databases are delineated in Table 1. Titles and abstracts were initially screened against the inclusion and exclusion criteria, and the full texts were independently obtained and evaluated during a second screening by 2 researchers (JW and SS). Any discrepancies were resolved by the third researcher (AG). Figure 1 depicts a flowchart of the process of selecting studies for inclusion.

## Data collection

The data was extracted from the included studies by 2 reviewers independently (JW and SS) under the following headings: author and publication year; types of anomalies; age group; types of clefts; results; and conclusions (Table 2). A modified version of the Newcastle–Ottawa Scale (NOS) was applied to evaluate the risk of bias.[25]

## Quality assessment

The modified version of NOS was applied to assess the quality of cross-sectional studies for the systematic review, specifically cohort studies (Table 3).[25,26] Each study that met the established criteria was classified as very good, good, satisfactory, or unsatisfactory, based on the number of stars received. In the present analysis, 3 studies were qualified as satisfactory, and the remaining 4 were rated as good.

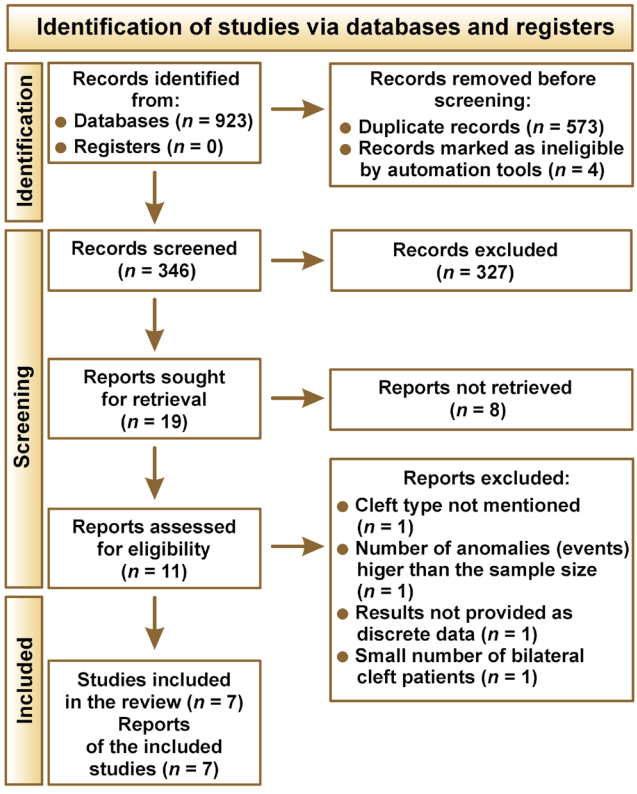


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the study

Table 1. Search databases and search strategies employed in the study

| Search database | Search strategy | Results |
|---|---|---|
| MEDLINE/PubMed® | (((((cleft) OR (unilateral)) AND (cleft)) OR (bilateral)) AND (cleft)) AND (dental anomalies[Text Word]) | 240 |
| EBSCOhost | cleft (title) AND dental anomalies (title) | 47 |
| Scopus | (((((cleft) OR (unilateral)) AND (cleft)) OR (bilateral)) AND (cleft)) AND (dental anomalies[Text Word]) | 636 |

**Table 2.** Characteristics of the included studies

| Study | Types of anomalies | Age group | Types of cleft | Results | Conclusions |
|---|---|---|---|---|---|
| Letra et al. 2007[16] | – agenesis<br>– microdontia<br>– ST<br>– malposition | 4–59 years (*M*: 17.3 years) | Cleft status was based on cleft completeness (comprised entirely of primary and secondary palates) and laterality (left, right, bilateral, and central in the cases involving median clefts or cleft palate only). | Agenesis on the right side was more frequently observed in cases of left unilateral clefts, and vice versa. The absence of maxillary left lateral incisors was significantly associated with unilateral right clefts, and vice versa. | The most notable observation was agenesis of the lateral incisor on the non-cleft side, which may suggest the presence of incomplete forms of bilateral clefts of the lip. |
| Wong et al. 2012[38] | – hypodontia<br>– ST<br>– taurodontism<br>– double tooth<br>– dens invaginatus<br>– microdontia | 12–16 years (*M*: 13.8 years) | – unilateral CLP<br>– bilateral CLP<br>– cleft lip<br>– cleft palate | Individuals with CLP had a statistically higher prevalence of hypodontia ($p < 0.001$), ST ($p < 0.01$) and microdontia ($p < 0.001$) compared to the non-CLP subjects. | Statistically higher prevalence of hypodontia, ST and microdontia was demonstrated in CLP children compared to the non-CLP children. |
| Germec Cakan et al. 2018[31] | – ST<br>– macrodontia<br>– microdontia | 14 ±6.4 years | – complete CLP (unilateral CLP, bilateral CLP and cleft palate)<br>– controls | There was a significant association between right unilateral CLP and right lateral incisor agenesis ($p = 0.0001$), left unilateral CLP and left lateral incisor agenesis ($p = 0.002$), and bilateral CLP and bilateral lateral incisor agenesis ($p = 0.0001$). Anterior ST were only detected in unilateral CLP groups (5–7.1%). | Dental anomalies manifest more frequently in patients with CLP compared to non-CLP subjects. A relationship has been observed between the cleft type and ipsilateral lateral incisor agenesis. |
| Camporesi et al. 2010[20] | – hypodontia<br>– ST<br>– abnormal shape and size<br>– enamel hypoplasia | 4 years and 2 months–16 years and 3 months (*M*: 10 years and 4 months) | – unilateral and bilateral CLP<br>– controls | The statistical analysis revealed significant differences in the prevalence of all dental anomalies compared with the control group, with the exception of second premolar agenesis. | In both unilateral and bilateral CLP subjects, the most prevalent missing teeth were lateral incisors. The dental anomalies occurred predominantly in the cleft area, thus suggesting that the effect of the cleft disturbance is more local than general on the dentition. |
| Al Jamal et al. 2010[19] | – agenesis<br>– ST<br>– microdontia<br>– taurodontism<br>– ectopic eruption<br>– dilaceration<br>– hypoplasia | 4–31 years (*M*: 11.5 years) | – unilateral CLP<br>– bilateral CLP | Dental anomalies were identified frequently in cleft lip and/or palate subjects. The prevalence of missing teeth was found to be 66.7% among the studied population. The most frequently missing tooth was the maxillary lateral incisor. Supernumerary teeth were found in 16.7% of subjects. | The prevalence of dental anomalies in patients with cleft lip and/or palate was higher than in the general population. However, larger samples are required to effectively determine the relationship between each dental anomaly and the cleft type. |
| Eslami et al. 2013[9] | – ST<br>– agenesis<br>– transposition<br>– tooth rotation<br>– peg laterals | 7–26 years | – unilateral CLP<br>– bilateral CLP | The frequency of missing maxillary lateral incisors was slightly higher in bilateral CLP (61.1%) than in unilateral clefts (60%). A non-significant difference was observed in the frequency of missing lateral incisors in the cleft area between right and left unilateral CLP ($p = 0.412$). However, there were significantly more cases of missing lateral incisors outside the cleft area in URCLP (20%) in comparison to ULCLP ($p = 0.015$). Bilateral CLP had a higher frequency of ST in the cleft area (2.8%) compared to unilateral clefts. | The prevalence of dental anomalies in the studied sample was higher compared to the general population. More anomalies were observed on the cleft side. |
| Sá et al. 2016[15] | – tooth agenesis<br>– giroversion<br>– microdontia<br>– tooth impaction<br>– ST<br>– transposition<br>– ectopic tooth<br>– accessory cusp | 12–45 years | – complete and incomplete unilateral CLP<br>– complete and incomplete bilateral CLP<br>– cleft lip<br>– complete and incomplete unilateral cleft lip<br>– complete and incomplete bilateral cleft lip | Tooth agenesis (47.1%) was the most prevalent anomaly. Agenesis was more frequent in complete unilateral CLP ($p < 0.0001$) and in complete bilateral CLP ($p = 0.0002$). | The present study revealed a high frequency of dental anomalies inside the cleft region in NSCL/P patients and further demonstrated that patients with complete unilateral CLP and incomplete bilateral CLP were more frequently affected by dental anomalies. |

*M* – mean; ST – supernumerary teeth; CLP – cleft lip and palate; NSCL/P – non-syndromic cleft lip with or without cleft palate; URCLP – unilateral right cleft and palate; ULCLP – unilateral left cleft and palate.

**Table 3.** Quality of the included studies assessed using the modified version of the Newcastle–Ottawa Scale (NOS)

| Study | Selection | Comparability | Outcome | Quality score |
|---|---|---|---|---|
| Letra et al.[16] | ★★★ | ★ | ★★ | 6 – satisfactory |
| Wong et al.[38] | ★★★★ | ★ | ★★ | 7 – good |
| Germec Cakan et al.[31] | ★★★★ | ★ | ★★ | 7 – good |
| Camporesi et al.[20] | ★★★★ | ★ | ★★ | 7 – good |
| Al Jamal et al.[19] | ★★★★ | ★ | ★★ | 7 – good |
| Eslami et al.[9] | ★★★ | ★ | ★★ | 6 – satisfactory |
| Sá et al.[15] | ★★ | ★ | ★★ | 5 – satisfactory |

## Synthesis of findings

The results of the studies were tabulated, and a meta-analysis was performed using RevMan 5.3 software (https://test-training.cochrane.org/online-learning/core-software-cochrane-reviews/review-manager-revman/download-revman-5), which synthesized the mean (*M*) and standard deviation (*SD*) values and depicted the results in the form of a forest plot. Statistics from 7 studies were analyzed, and the data was obtained, depending on the characteristic of effect size. For each study, discrete data was utilized to calculate the random risk ratio with the Mantel–Haenszel method. The heterogeneity of the included studies was investigated by inspecting study characteristics and using the $I^2$ statistic in cases where sufficiently similar studies were analyzed. As the measuring scale in all the included studies was different, the meta-analysis utilized the mean difference as the effect size. The calculations involved the division of the mean difference in each study by that study's *SD* to create an index (standardized mean difference). This index was found to be constant among studies. A funnel plot of studies with continuous data was plotted to assess publication bias for both dental anomalies (agenesis and ST between unilateral and bilateral CLP and for right and left unilateral CLP).

A meta-analysis was also performed to ascertain the prevalence of dental anomalies in patients with unilateral and bilateral clefts. The forest plot illustrated that the standard mean difference obtained for the prevalence of dental anomalies with unilateral and bilateral clefts as a whole was 1.23 (95% *CI*: 1.04–1.46). Patients with unilateral clefts demonstrated a higher prevalence of dental anomalies compared to those with bilateral clefts, with a *p*-value of 0.021 and low statistical heterogeneity ($I^2$ = 0%), which may be attributed to the fact that the included studies were conducted in a similar manner, with minimal variation in study design.

# Results

The search database yielded a total of 923 articles (Fig. 1). Duplicate studies and studies marked as ineligible by automation tools were removed and abstracts of the remaining 346 articles were screened. Of these, the full texts of 11 articles underwent screening. Seven articles fulfilled the inclusion criteria and were included in the present analysis. Four studies were excluded from the analysis due to the following reasons: the cleft type was not mentioned in the data; the number of anomalies (events) was higher than the sample size[27]; the results were not given as discrete data[28]; and there was a small number of bilateral cleft patients, which may have introduced bias.[17]

A random-effects meta-analysis was conducted to generate an overview of the difference between dental anomalies among patients with unilateral or bilateral CLP. Since the studies involved different populations across the globe, the random-effects meta-analysis was employed to account for the variance in the prevalence of caries. For a study to be included in the meta-analysis, it was required to provide information regarding sample size and discrete data for each group, along with either *SD*, standard error (*SE*), standard error of difference, or *p*-value. The meta-analysis was conducted using RevMan 5.3 software. The analysis involved studies that compared patients with unilateral and bilateral CLP in terms of commonly associated dental anomalies, namely A/MT and ST.

The sample size of individuals with ST in unilateral CLP was 786, and in bilateral CLP, it was 447. For agenesis, the sample size for unilateral CLP was 732 and 406 for bilateral CLP. The number of patients with ST and agenesis in left and right unilateral CLP was 39 and 196, respectively. The forest plot illustration of the random-effects meta-analysis of the included studies for ST and A/MT in patients with unilateral and bilateral CLP is presented in Fig. 2. The current analysis revealed the standard mean difference of 1.10 (95% confidence interval (*CI*): 0.69–2.06) for ST in patients with unilateral and bilateral CLP, and 0.89 (95% *CI*: 0.71–1.11) for A/MT in unilateral and bilateral CLP. The variation was statistically insignificant for the prevalence of ST in unilateral and bilateral CLP, as indicated by a *p*-value of 0.541, and there was low statistical heterogeneity among the included studies ($I^2$ = 29%, $p > 0.05$). The difference was also statistically insignificant in unilateral and bilateral CLP patients with A/MT, with a *p*-value of 0.301 and high statistical heterogeneity among the included studies ($I^2$ = 70%, p = 0.006).

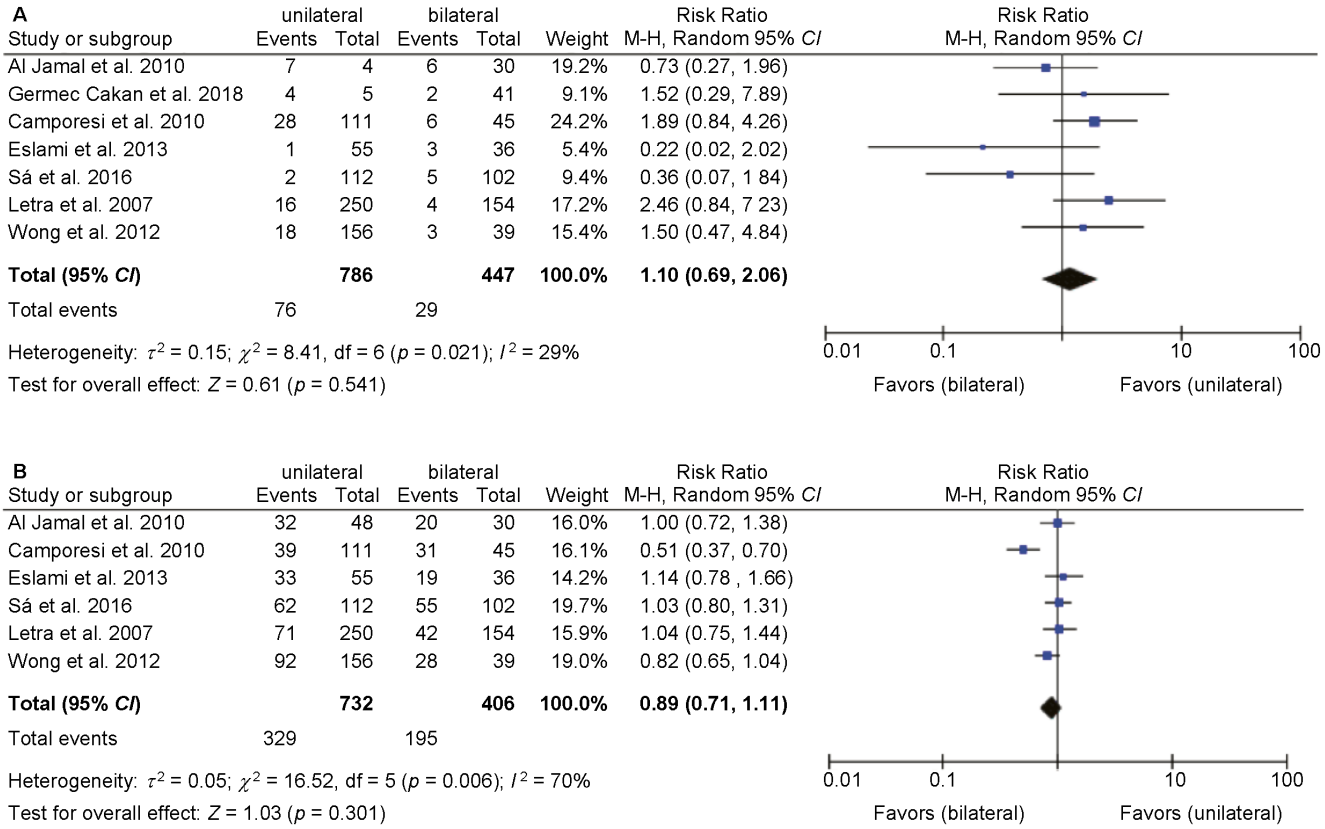


**Fig. 2.** Forest plot illustrating the random-effects meta-analysis of the included studies for supernumerary teeth (ST) and tooth agenesis/missing teeth (A/MT) in patients with unilateral cleft lip and palate (CLP) (A) and bilateral CLP (B)

*CI* – confidence interval.

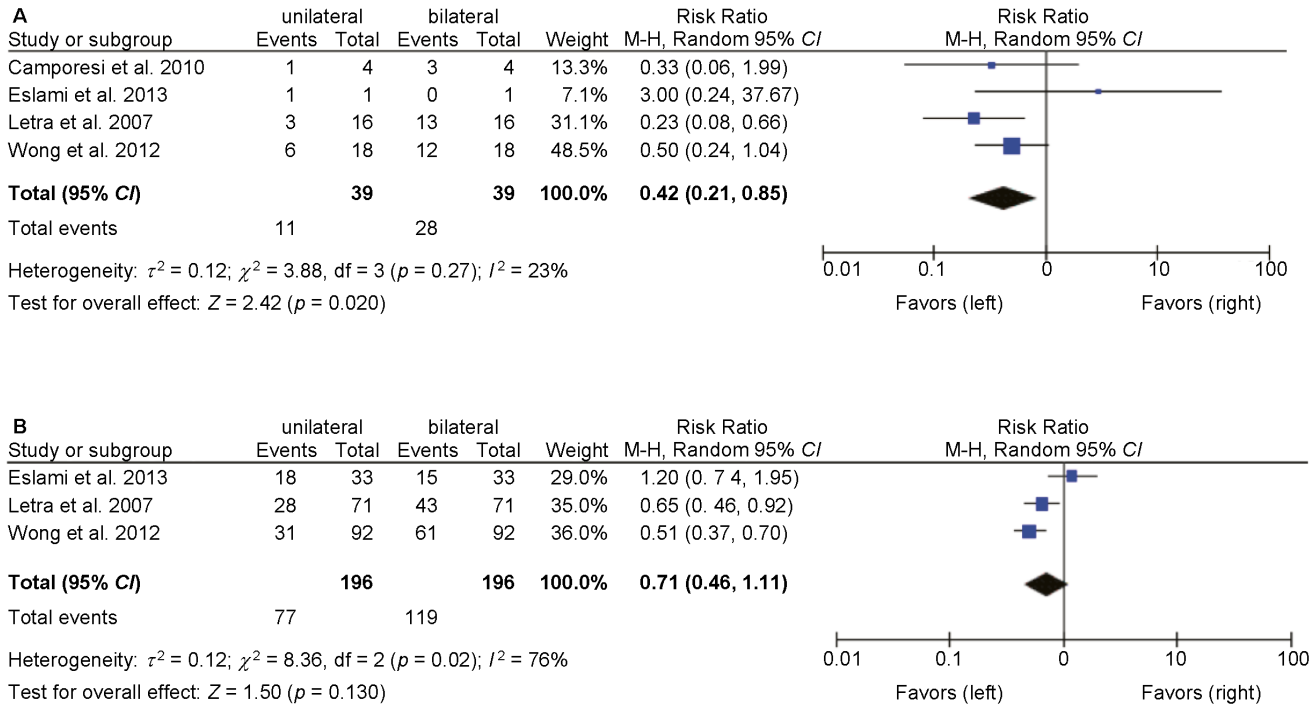


**Fig. 3.** Forest plot illustrating the random-effects meta-analysis of the included studies for ST and A/MT in patients with left unilateral CLP (A) and right unilateral CLP (B)

The forest plot illustration of the random-effects meta-analysis of the included studies for ST and A/MT in patients with left and right unilateral CLP is presented in Fig. 3. In the current analysis, the standard mean difference obtained for ST in patients with left and right unilateral CLP was 0.42 (95% *CI*: 0.21–0.85), and for A/MT in patients with left and right unilateral CLP, it was 0.71 (95% *CI*: 0.46–1.11). The variation was statistically significant for the prevalence of ST in patients with left or right unilateral CLP, with a *p*-value of 0.020, favoring left unilateral CLP. Low statistical heterogeneity was reported among the included studies, with $I^2 = 23\%$ ($p > 0.05$). On the other hand, the difference was statistically insignificant for the prevalence of A/MT in patients with left and right unilateral CLP, with a *p*-value of 0.130 and high statistical heterogeneity among the included studies ($I^2 = 76\%$, $p < 0.05$).

The results of the meta-analysis indicate that patients with left unilateral CLP have a higher prevalence of ST. On the contrary, the prevalence of A/MT was found to be statistically insignificant between patients with right and left unilateral CLP ($p > 0.05$). The quantitative analysis for A/MT and ST in unilateral and bilateral CLP patients yielded statistically insignificant results ($p > 0.05$).

## Discussion

The current review quantitatively analyzed the available literature to ascertain whether the prevalence of dental anomalies (A/MT and ST) is higher in patients with CLP. To the best of our knowledge, no review has explored the relationship between the occurrence of dental anomalies in unilateral and bilateral CLP patients and also between patients with right and left unilateral CLP. The results of the current meta-analysis demonstrate a statistically significant difference in the prevalence of ST in patients with left unilateral CLP ($p = 0.020$). These outcomes are similar to the results of previous studies.[9,29] On the other hand, the difference was statistically insignificant for ST in unilateral and bilateral CLP ($p = 0.541$). To date, the literature has proposed 2 types of hypotheses regarding the occurrence of ST in cleft patients. The first suggests that the odontogenic region of the lateral incisor originates from the medial nasal and maxillary processes, and that the non-fusion of these 2 processes results in 2 separate lateral incisors.[15,22] The other hypothesis suggests that ST arise from post-fusion rupture of the cleft in the lateral incisor area, and the tooth germ of the lateral incisor is separated into 2 teeth.[15,30]

The analysis of A/MT between unilateral and bilateral CLP patients, as well as between right and left unilateral CLP individuals, yielded statistically insignificant values ($p = 0.301$ and $p = 0.130$, respectively). However, the black diamond in the forest plot indicates that the bilateral CLP and left unilateral CLP groups are in favor, respectively. A high level of heterogeneity was observed in studies involving agenesis, indicating potential differences in study design, population type, age group, and surgical interventions across the included studies, with $I^2$ of 70% for unilateral and bilateral CLP, and 76% for right and left unilateral CLP. The studies that examined the prevalence of ST were similar in respect to the abovementioned attributes and reported a low level of heterogeneity, with $I^2$ values of 29% for unilateral and bilateral CLP and 23% for left and right unilateral CLP. Further clinical trials are necessary to reach a conclusive result.

Several theories have been advanced to explain the presence of dental agenesis in the vicinity of the affected region. These theories include low blood supply due to congenital conditions or surgery, low ectomesenchymal supply, and the osseous deficiency resulting from the cleft.[10,20,22] Sá et al. reported that lateral incisors are the most affected teeth and are more prevalent in individuals with unilateral complete CLP.[15] However, these findings differ from the results of the conducted meta-analysis. In the 12$^{th}$ month following birth, the permanent maxillary lateral incisors begin to calcify. Thus, the presence or absence of ST, microdontia, or malformation of lateral incisors may be attributed to the presence of a cleft, the intraoral environment generated by the cleft, and a lack of mesenchymal tissue. Letra et al. stated that the absence of the left or right lateral incisor was significantly associated with unilateral right or left clefts, respectively.[16] Research has indicated that genetic factors may contribute to the development of CLP and dental anomalies.[8,31,32] Furthermore, human studies revealed an association between genetic variations in *MSX1* and *PAX9* genes and tooth agenesis within and outside the cleft area.[31,33]

Marzouk et al. conducted a systematic review to determine whether individuals with non-syndromic orofacial clefts (OFCs) demonstrated an increased prevalence of dental abnormalities in comparison to those without OFCs.[34] The results indicated that individuals with OFCs are more likely to present with a range of dental abnormalities compared to their unaffected peers. Statistically significant associations were observed between OFCs and ST, developmental enamel defects, malposition and/or transposition, rotation, and impaction.[34]

Dental abnormalities manifest at a higher frequency among individuals with cleft palates compared to the general population. The observed differences in the prevalence of these abnormalities across studies can be attributed to ethnic variations, the diversity of the sample, or the severity of the cleft phenotype. However, a definitive conclusion has not been reached. In this analysis, the relationship between gender, cleft type and dental anomalies was not considered, as previous studies demonstrated no correlation between these variables.[23,29,31,34,35] Local factors, such as the cleft itself, and primary surgical procedures have been proposed as contributors in the development of dental anomalies. However, a conclusive statement regarding the involvement of surgical procedures

in influencing the development of anomalies in cleft patients could not be discussed at length, as the same factor was not considered in the included studies.[36,37] Additionally, although bilateral CLP is less common in the general population, the condition should be considered when conducting clinical studies in the future.

## Limitations

The study was subject to several limitations. Firstly, the population group and the type of dentition were heterogeneous, which may have affected the outcome, as the occurrence of dental anomalies may be more pronounced in a particular type of population. Secondly, the results of the review were not categorized by age or gender. Additionally, the oral hygiene practices adopted by patients with clefts are unclear. There is a need for randomized controlled trials based on patients with unilateral and bilateral CLP. Lastly, it was not specified whether the anomalies had been counted before or after the surgical intervention for the correction of CLP.

# Conclusions

The present analysis demonstrated that patients with left unilateral CLP are more susceptible to being associated with the presence of ST. There is a possible weak association between the type of unilateral and bilateral CLP concerning A/MT and ST in particular. However, in vivo studies with a similar study design and overall minimal heterogeneity are necessary to reach a definitive conclusion.

## Trial registration

The review protocol was registered with PROSPERO (identification No. CRD42022346399).

## Ethics approval and consent to participate

Not applicable.

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.


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Review

# Effect of the voxel size on the accuracy of endodontic length measurements using cone-beam computed tomography: A systematic review conducted according to the PRISMA guidelines and *Cochrane Handbook for Systematic Reviews of Interventions*

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## Abstract

**Background.** The accurate determination of the working length (WL) is imperative for endodontic success.

**Objectives.** Our objective was to systematically analyze the available evidence on the impact of voxel size variation on the estimation of WL using cone-beam computed tomography (CBCT).

**Material and methods.** An electronic search of the PubMed, Scopus, Embase, and Web of Science databases was conducted according to specific inclusion and exclusion criteria in March 2022. Studies published in English, comparing the influence of 2 or more voxel sizes on the CBCT assessments of WL in human teeth against physical or electronic methods qualified for inclusion. Multiple authors independently carried out study selection, data extraction and quality assessment.

**Results.** We included 4 studies involving the assessment of 220 teeth. There were some concerns with regard to the risk of bias in all studies, owing to methodological insufficiencies. Voxel sizes can affect the accuracy of CBCT measurements. All 4 studies reported that the voxel size in CBCT measurements was closely correlated with the estimation of WL. The smallest voxel sizes showed a greater correlation with the actual length (AL). Larger voxel sizes can reduce accuracy by ±0.05 mm. The differences may be clinically irrelevant. Cone-beam computed tomography assessments correlate strongly with the endodontic WL as measured by electronic apex locators (EALs), but are associated with a larger radiation dose in comparison with periapical radiographs.

**Conclusions.** Based on the limited evidence available, it can be stated with low certainty that voxel sizes may impact CBCT accuracy. However, the differences may be clinically irrelevant. The pre-existing CBCT scans may be useful in the estimation of WL, rather than additional periapical radiographs.

**Keywords:** accuracy, voxel, cone-beam computed tomography, endodontics, electronic apex locators

## Highlights

- Current studies suggest that the size of voxels may impact the accuracy of CBCT estimations of the working length (WL).
- The observed differences in voxel size do not reach statistical significance, indicating that the voxel size may have a minimal impact on CBCT-based WL measurements.
- While voxel size variations may affect CBCT estimations, these differences might be clinically irrelevant.
- In patients who already have CBCT scans, this data may offer additional insights for estimating WL without the need for extra periapical radiographs.

# Introduction

The long-term success of endodontic treatment depends on the proper technique and the complete elimination of microorganisms from the root canal system.[1] Several variables can affect the precise identification, disinfection and obturation of the root canal. The accurate determination of the working length (WL) is imperative for endodontic success.[2] A comprehensive knowledge of the entire root canal system and accurate diagnostic aids are necessary to determine the exact WL.[3] The most widely accepted description of the root canal is that the canal tapers apically from its wider coronal orifice to its apical constriction (the minor diameter) and widens in a funnel shape up to the apical foramen (the major diameter).[4,5] The apical constriction is usually 0.5-1.5 mm inside the apical foramen.[4] The endodontic WL is the distance from the coronal reference point to the anatomic reference point, i.e., the apical constriction, up to which the endodontic preparation is carried out.[6]

The exact location and morphology of the apical constriction is highly variable, making its exact identification in the root canal challenging.[7] The correct estimation of WL is required to ensure the proper instrumentation of the root canal system, to avoid iatrogenic injuries, such as perforation and/or the extrusion of debris or intervention into the periapical region, and to ensure complete obturation.[8] Over the years, several methods to identify the accurate WL have been employed, including and not limited to intracanal tactile sensation, preoperative radiographs, electronic apex locators (EALs), cone-beam computed tomography(CBCT), micro-CT, etc.[9–12]

For the longest period, endodontists relied on periapical radiographs for determining WL.[11,13] However, the reliability of the two-dimensional (2D) image of a three-dimensional (3D) structure has always been nebulous due to magnification errors, the superimposition of the surrounding anatomical structures, inter-operator variability, an angulation error, etc.[14,15] As a supplemental aid for the radiographic methods, EALs are being widely used due to the high accuracy of the device.[16–19] However, EALs are not infallible and may deliver unstable results, imprecise readings in the presence of metal restorations, etc.[12,20] As a result, it is advisable to use both radiographic as well as electronic methods for the determination of WL.

Cone-beam computed tomography provides the 3D images of the anatomical structures, overcoming the limitations inherent to conventional radiography.[8,21] It permits the 3D localization of structures without magnification errors, allowing rotation. This enables clinicians to view anatomic structures clearly around extraneous formations that would otherwise obstruct the view.

Cone-beam computed tomography can help assess the morphology of a tooth and its root canal.[22,23] Multiple studies have assessed the accuracy of CBCT, and determined CBCT to have higher accuracy in dentistry and by extension endodontics.[24,25]

Each CBCT 3D image is made up of volumetric pixels known as voxels, which are the 3D analogs of pixels.[26] A voxel is a unit of graphic information in 3D space. In this, it is similar to a pixel, which defines a unit of information in 2D space. Voxels are essentially 3D pixels in a cube shape, i.e., they are isometric.[27] Voxel sizes range from 0.075 $mm^3$ to 0.4 $mm^3$. An image resolution of 300 ppi would correspond to a pixel size of 0.085 mm.[28] Voxel sizes can influence the accuracy of measurements in CBCT scanning. Artifacts in the image expand in number with an increase in the voxel size. With a decreased voxel size, greater noise is evident, which can lead to errors in measurements.[29] The relationship between the voxel size and the radiation dose is inversely proportional, i.e., the smaller the voxel size, the higher the radiation dosage on the patient.[8,30] The comparison of CBCT assessments with various voxel settings can elucidate the impact of image quality on the accuracy and reliability of the measurements taken.[31]

This review aimed to systematically examine the available evidence on the effect of the voxel size on the accuracy of endodontic length measurements using CBCT.

# Methodology

## Focus question

This systematic review was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[32]

The focused question was "Does the voxel size and resolution influence the endodontic root canal measurement?"

## Search strategy

The inclusion criteria within the PICOS framework were as follows:

(P) Population: Human teeth;
(I) Intervention: CBCT scans at 2 or more voxel resolutions;
(C) Comparator: The endodontic WL determined physically with EAL;
(O) Outcome: Precision or accuracy in the endodontic WL measurement;
(S) Study type: Randomized controlled trials (RCTs), controlled clinical trials, cohort studies, in vitro, in vivo, and ex vivo studies published in English

Case reports, systematic reviews, opinion articles, letters to the editor, and articles in languages other than English were excluded.

The electronic databases of PubMed, Scopus, Embase, and Web of Science were searched for eligible studies in March 2022, with no restrictions placed on the start date. The U.S. National Institutes of Health (NIH) register of ongoing trials ClinicalTrials.gov (https://clinicaltrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform (https://trialsearch.who.int) were searched in April 2022. Forward citation tracking was conducted using Google Scholar. Three authors (S.B., B.R. and S.P.) independently reviewed the search results for study selection. Duplicates and nonrelevant articles were discarded. The researchers independently screened the titles and abstracts of the studies for their eligibility. The full-texts of relevant articles were examined for eligibility using the inclusion criteria, and a fourth author (M.C.) was consulted to make a final decision in case of any contention. A supplementary search of the references of the selected articles was conducted manually for additional eligible studies. The search strategy is depicted in Table 1.

## Data extraction

Data extraction was independently conducted by 2 authors (K.H.A. and G.M.) and verified by a third author (F.W.L.) for accuracy. The characteristics of each study, along with the author's name, the year of publishing, the country of origin, methodological aspects, the sample size, the treatment regimen, and duration, were extracted into a customized template manually.

## Assessment of study quality

The quality of the selected studies was independently assessed by 2 reviewers (S.B. and K.H.A.) using the a revised quality assessment tool for diagnostic accuracy studies (QUADAS-2).[33] Four specific domains were used to assess the validity of the studies, including 'sample selection', 'index test', 'reference standard', and 'flow and timing'. The response for each domain based on the signaling questions referred to a high, low or unclear risk of bias, or at a risk of bias. A negative answer in the signaling questions indicates potential bias, which is explored for a 'high' rating. The absence of pertinent information for rendering judgment resulted in a rating of 'unclear' risk of bias. The overall risk of bias was determined using the highest level of risk observed under the domains. Conflicts were resolved through a consensus.

## Methods used to assess the quality of evidence for the outcomes listed in the summary of findings

We followed the GRADE recommendations mentioned in *Cochrane Handbook for Systematic Reviews of Interventions* to assess each outcome.[34,35] The summary of findings is presented in Table 2. One review author (B.R.) applied the GRADE system, and the evidence ratings were applied after discussion with 2 other authors (F.W.L. and M.C.). The final rating was decided after the 3 review team members reached a consensus. Evidence for each outcome was graded as 'high quality' at the start in the case of RCTs. The risk of bias, the inconsistency of results, the indirectness of evidence, the imprecision of results, and publication bias were considered. Subsequently, the evidence rating was downgraded by 1 level for serious or 2 levels for very serious concerns regarding the study limitations, inconsistencies in the outcomes, the indirectness of evidence, the imprecision of effect estimates, or publication bias.

**Table 1.** Search strategy

| Database | Search strategy |
|---|---|
| PubMed | (voxel size) AND (cone beam computed tomography OR CBCT) AND (((endodontic) OR (root canal)) AND (length)) ("voxel" [All Fields] OR "voxels" [All Fields] OR "voxelization" [All Fields] OR "voxelized" [All Fields] OR "voxels" [All Fields]) AND ("endodontal" [All Fields] OR "endodontic" [All Fields] OR "endodontical" [All Fields] OR "endodontically" [All Fields] OR "endodontics" [MeSH Terms] OR "endodontics" [All Fields]) AND ("length" [All Fields] OR "lengths" [All Fields]) |
| Scopus | (ALL (voxel AND size ) AND ALL (( cone AND beam AND computed AND tomography) OR cbct) AND TITLE-ABS-KEY (root AND canal) AND ALL (length OR (working AND length) OR (actual AND length))) |
| Embase | voxel AND size AND cone AND beam AND computed AND tomography AND tooth AND root AND canal |
| Web of Science | voxel size (All Fields) AND CBCT OR cone beam computed tomography (All Fields) AND (root canal length) OR (working length) OR (root length) OR ((root canal) AND length) (All fields) |

Table 2. Quality assessment – summary of findings

| Outcome | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | Impact | Number of canals/studies | Certainty of evidence (GRADE) |
|---|---|---|---|---|---|---|---|---|
| Accuracy of the determination of WL | serious* | not serious | not serious | not serious | not serious | our confidence in the effect estimate is limited | 220/4 | low |

WL – working length. * Four studies showed some concerns regarding the risk of bias; the concerns regarding outcome measurement decreased our confidence in the estimate.

# Results

The initial search yielded 356 papers. After the removal of duplicates and the screening of titles and abstracts for eligibility, potentially relevant articles were identified. Thirteen full-text articles were selected for a complete review based on the inclusion criteria and the review objective. After evaluating the full texts of the articles, 9 articles were excluded based on the inclusion criteria. In the present review, 4 studies were included, all of which were ex vivo comparative studies.[36–39] The PRISMA flow diagram is shown in Fig. 1.

## Quality assessment

In terms of the overall risk of bias based on QUADAS-2, there were significant concerns regarding the risk of bias in the majority of studies. For the 'sample selection' domain, it was unclear whether the selection of the samples could have introduced bias (curved canals vs. straight canals). For the 'index test' domain, an unclear risk of bias was concluded, as it was not clear whether the accuracy tests were interpreted blindly to the reference standard. We judged the 'reference standard' domain to have an unclear risk of bias owing to inadequate details about the use of the reference standard and its interpretation. These methodological insufficiencies led to the overall rating of unclear risk of bias. The details of the risk of bias assessment, along with a summary, are presented in Fig. 2.[40]

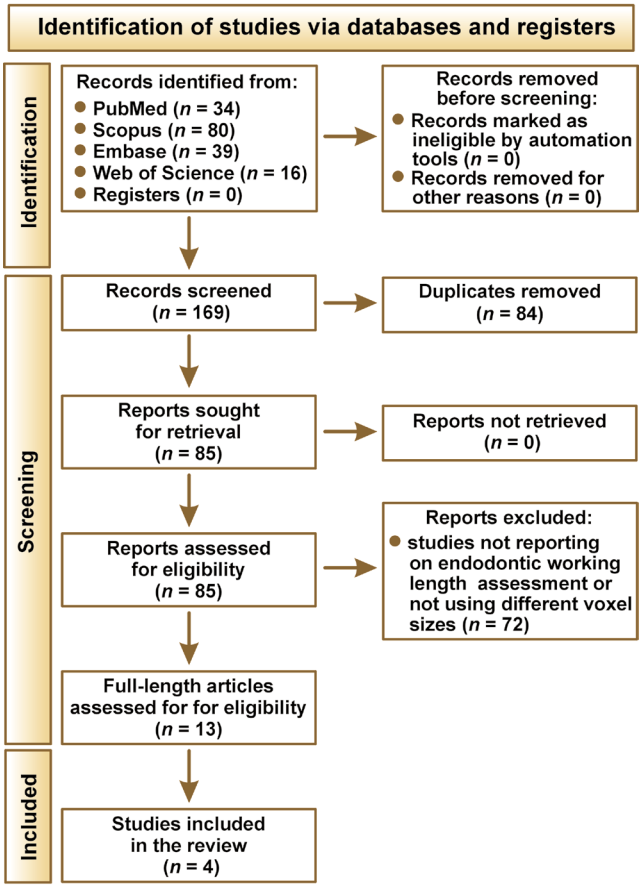


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the study

## Summary of the characteristics of selected studies

All the studies included in this review were from Asia. Three of these reports were from Turkey (Western Asia)[37–39] and one from Vietnam (Southeast Asia).[36] All reports used extracted human teeth ex vivo. A total of 220 canal WLs were assessed, out of which 70 regarded anterior teeth, 40 – maxillary central teeth[38] and 30 – mandibular anterior teeth.[37] The majority of teeth assessed were posterior teeth (30 premolars[39] and 120 molars[36]). Table 3 summarizes the characteristics of the included studies.

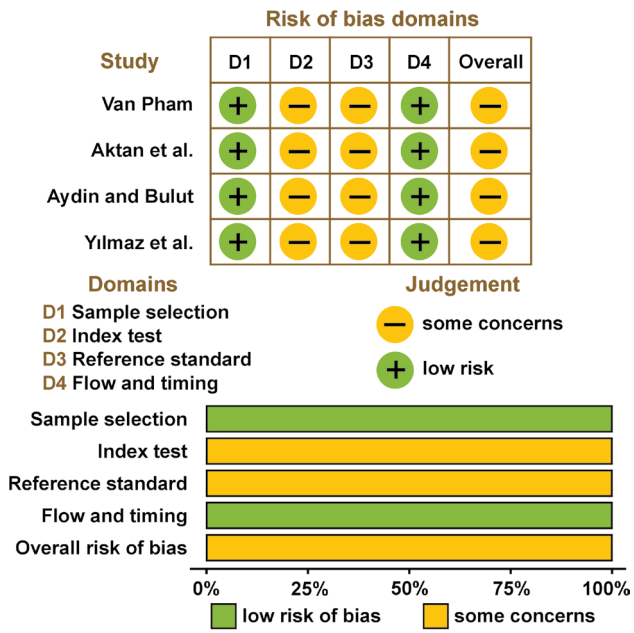


Fig. 2. Risk of bias assessment

**Table 3.** Characteristics of the selected studies

| Author(s) | Year | Country | Sample size | Study design | Intervention | CBCT WL assessment | Control | Outcome |
|---|---|---|---|---|---|---|---|---|
| Van Pham[36] | 2021 | Vietnam | 120 | 120 extracted molars<br><br>the CBCT images were taken and the canal length was measured using Romexis Viewer, and recorded as the conventional CBCT length (3D-CL)<br><br>the 3D Endo Software reconstructed automatically the 3D image of the canal system, and the canal length was recorded as the corrected length (3D-CL) | CBCT in 3 different voxel sizes: 0.075 $mm^3$ 0.100 $mm^3$ 0.150 $mm^3$ | the measurement made based on the best image of the entire length of the canal in the buccolingual view with the greatest curved angle<br><br>a line drawn from the occlusal reference to the apical foramen | a K-file #10 with an electronic digital caliper<br><br>EAL | at the largest voxel size, CBCT showed less accuracy than EAL by ±0.05 mm, at smaller sizes, CBCT showed greater accuracy<br><br>the 3D-PL (proposed length) measurements at a voxel size of 0.150 mm and the 3D-CL measurements at a voxel size of 0.100 mm agreed with AL |
| Aktan et al.[37] | 2016 | Turkey | 30 | 30 human mandibular anterior teeth<br><br>the arithmetic mean of the buccolingual and mesiodistal measurements was recorded as the CBCT WL | CBCT in 4 different voxel sizes: 0.100 $mm^3$ 0.150 $mm^3$ 0.200 $mm^3$ 0.400 $mm^3$ | the arithmetic mean of the buccolingual and mesiodistal measurements from coronal, sagittal, axial, and 3D images | a K-file with an electronic digital caliper | the mean absolute difference between AL and the CBCT scan measurements was 0.02 mm for the 0.2-$mm^3$ voxel size and HD resolution, 0.18 mm for the 0.4-$mm^3$ voxel size and HD resolution, 0.19 mm for the 0.2-$mm^3$ voxel size and LD resolution, and 0.26 mm for the 0.8-$mm^3$ voxel size and HD resolution<br><br>no significant differences were found between AL and CBCT measurements<br><br>the 0.4-$mm^3$ CBCT scans has a slightly lower reliability than the other voxel sizes |
| Aydin and Bulut[38] | 2021 | Turkey | 40 | 40 maxillary central teeth with straight root canals<br><br>each tooth was placed in the empty socket of a dry maxilla | CBCT in 2 different voxel sizes: 0.125 $mm^3$ 0.250 $mm^3$<br><br>EAL measurement with 2 different EALs | the measurements made in the reconstructed sections from the reference plane to artificial root perforation | a K-file #10 with an electronic digital caliper<br><br>EAL | electronic measurements provided greater values than AL, while CBCT measurement values were smaller than AL<br><br>no significant differences between the 2 voxel sizes were noted<br><br>the measurements taken at the 0.125-$mm^3$ voxel size was closer to AL |
| Yılmaz et al.[39] | 2017 | Turkey | 30 | 30 mandibular premolars<br><br>the CBCT images of the teeth inserted in the mandible were obtained | CBCT in 4 different voxel sizes: 0.080 $mm^3$ 0.125 $mm^3$ 0.160 $mm^3$ 0.250 $mm^3$ | the average of 2 measurements made from the buccal tip point to the radiographically visible apex | a K-file #15 with an electronic digital caliper<br><br>EAL | there were no significant difference between the average CBCT measurements obtained at 4 different voxel sizes<br><br>accuracy increased with smaller voxel sizes, without statistically significant differences |

CBCT – cone-beam computed tomography; EAL – electronic apex locator; AL – actual length; HD – high definition; LD – low definition.

## Comparator

The 4 studies varied in their estimation of WL. Three studies compared CBCT assessments to the measurements taken using a K-file and EALs.[36,38,39] One study only compared manual measurement and CBCT.[37]

The working length was measured using a K-file and digital calipers. Since they were all ex vivo studies, errors in the WL measurement were avoided, as it was possible to directly visualize the location of the tip of the K-file within the apex of the tooth. Three of these studies used the length from the occlusal reference point to the coronal most border of the apical foramen as a reference, while one study used the distance from the occlusal reference point to 1 mm short of the apical foramen.

The various EALs used in the studies were Propex Pixi,[36] DentaPort Root ZX.[38,39]

## CBCT systems and software

The studies differed in the radiographic systems used to capture CBCT data. Two studies used ProMax® 3D (Planmeca, Helsinki, Finland),[36,37] while the other two used the i-CAT CBCT system (Imaging Sciences International, Hatfield, USA)[38] and 3D Accuitomo 170 (J. Morita Tokyo, Tokyo, Japan).[39]

The studies used different software based on their CBCT systems to examine the CBCT data. Two studies assessed the CBCT images with the Planmeca Romexis® Viewer,[36,37] while the other two used the i-CATVision imaging software[38] or i-Dixel 2.0.[39] Only one study compared 2 different programs, i.e., Romexis Viewer and the 3D Endo™ Software (Dentsply Sirona, Johnson City, USA).[36]

For CBCT measurements, the teeth were embedded in various materials during scanning. Two studies used the sockets of the prepared dry maxilla[38] and mandible.[39] One study used plastic molds with wax and light impression silicone,[36] while the other study used the silicone putty.[37]

One study made the 3D reconstruction of the tooth to measure WL.[36]

## Characteristics of the intervention

All 4 studies used different voxel sizes to compare.[36–39] Overall, 9 different voxel sizes were evaluated [$mm^3$] – 0.075,[36] 0.080,[39] 0.100,[36,37] 0.125,[38,39] 0.150,[36,37] 0.160,[39] 0.200,[37] 0.250,[38,39] and 0.400.[37] A variable range of field of view (FOV) values [$mm^2$] were used in the selected studies – 40 × 40,[38,39] 50 × 50,[36] 50 × 80,[37] 60 × 60,[39] 80 × 80,[39] 80 × 100,[37] 100 × 100,[39] and 100 ×150.[37] Two studies mentioned the exposure time of the CBCT images,[38,39] which makes it easier to assess radiation exposure, while 2 studies failed to mention the exposure time.[36,37]

## Outcome assessment

Two of the studies had single observers assessing the data,[36,37] with only one of the 2 studies mentioning the repetition of the assessment to check for intra-observer reliability.[36] The other two studies had 2 different observers corroborating the data, with the assessment repeated after 1 month to check for intra-observer and inter-observer reliability.[38,39]

## Characteristics of the outcomes

Voxel sizes can affect the accuracy of CBCT measurements. All studies found that CBCT measurements were closely correlated with WL. The smallest voxel sizes showed a greater correlation with the actual length (AL).

At a voxel size of 0.150 $mm^3$, Aktan et al. found the measurements to be accurate in 50% of the cases, while they were short in 37% of the cases and long in 10% of the cases.[37] Van Pham found the accuracy of CBCT WL at a voxel size of 0.150 $mm^3$ to be 3%; CBCT assessments were short in 55.6% of the readings and long in 41.4% of the readings.[36] At a voxel size of 0.075 $mm^3$, the accuracy of CBCT WL determination with the proposed length (3D-PL) was 7.3%, while in 74.1% of the times CBCT assessed the value to be longer and in 18.5% of the times it was shorter. The corrected length (3D-CL) was accurate in 9.1% of the readings, while it was short in 55.9% of the readings and long in 34.9% of the readings.[36] At a voxel size of 0.080 $mm^3$, CBCT estimated WL short by a mean of 1.16 mm.[39]

As the voxel sizes increase, the correlation between the CBCT and AL values decreases. The 0.1-$mm^3$ voxel size was studied by Aktan et al.[37] and Van Pham.[36] The former group of researchers found the CBCT WL determination to be accurate in 70% of the measurements, while it was short in 17% of the measurements and long in 13% of the measurements.[37] Van Pham found the accuracy of CBCT WL at the 0.1-$mm^3$ voxel size to be 4.0% for 3D-CL; 3D-CL was short in 48.3% of the readings and long in 46.8% of the readings.[36]

For the 0.125-$mm^3$ voxel size, the means of the measurements were –1.19 mm,[39] and 0.19 ±1.89 (0.4 mm ARF) and 0.14 ± 0.41(1.0 mm ARF).[38]

At a voxel size of 0.160 $mm^3$, CBCT estimated WL short by a mean of 1.47 mm.[39] At a voxel size of 0.200 $mm^3$, the measurements were accurate in 53% of the cases, short in 30% of the cases and long in 17% of the cases.[37]

Two studies evaluated the accuracy of CBCT WL at the 0.25-$mm^3$ voxel size, and determined the mean difference to be –1.63 mm,[39] and 0.22 ±1.89 (for 0.4 mm ARP) and 0.21 ±0.61(for 1 mm ARP).[38] One study evaluated accuracy at the 0.4-$mm^3$ voxel size, and determined the readings to be accurate in 67% of the time, while it was short in 23% of the time and long in 10% of the time.[37]

Three studies found no statistically significant difference between AL and CBCT WL measurements

($p > 0.05$),[36–38] while one study found the difference to be statistically significant ($p < 0.05$).[39] Among the studies, 3 found no statistically significant differences in the CBCT WL measured at different voxel sizes ($p > 0.05$),[37–39] while one study found the differences between the voxel sizes to be statistically significant ($p < 0.05$).[36] The study comparing the direct CBCT WL measurement and the measurement of the 3D reconstruction found that the direct CBCT WL measurement (Romexis software) did not significant differed from AL ($p > 0.05$), whereas in the case of the 3D reconstructed tooth measurement, the difference from AL was statistically significant ($p < 0.05$).[36]

## Discussion

Maintaining an accurate WL during endodontic treatment is crucial to ensure therapeutic success and minimal post-operative complications. Conventional techniques involve the use of EAL, followed by a periapical radiograph with a file instrument. Technological advances have allowed greater precision in measurements. Research has shown that the CBCT assessment of WL is as accurate as in the case of EALs.[41–45] Cone-beam computed tomography provides a higher spatial resolution as compared to CT, making it better suited to examine the dental region and enabling the accurate visualization of the root canal morphology. Cone-beam computed tomography imparts a significantly lower radiation dose to the patient, aligning with the ALARA (As Low As Reasonably Achievable) principle, a cornerstone in clinical radiology. The quality CBCT images are predicated on the voxel size and the acquisition parameters. Our objective was to systematically analyze the available evidence on the impact of voxel size variation on the estimation of WL using CBCT.

Four studies that examined the influence of 2 or more voxel sizes on the CBCT assessments of WL in human teeth against physical (a K-file) or electronic methods (EALs) were included in this review. We found that image quality and the accuracy of CBCT measurements were affected by the voxel size used for imaging.[46–50] Smaller voxel sizes were correlated with greater precision.[36–39] While all studies found that there were differences between AL and CBCT WL assessments, these differences did not demonstrate statistical significance. The CBCT images obtained at different voxel sizes showed an underestimation (from −1.63 mm to −1.16 mm), with no distinction between various voxel sizes.[39] In comparison with CBCT, EALs showed less variation (−0.098 mm) from the direct measurement. Three studies found no statistically significant difference between AL and CBCT WL measurements.[36–38] Yılmaz et al dissented from this view and reported that there was a significant difference between the CBCT measurement and physical measurements.[39] This may be due to the fact that in a CBCT scan, the operator has to scroll through several sagittal views, negatively impacting repeatability. The accuracy of CBCT was not affected by perforations. The direct measurement of CBCT WL (Romexis software) showed no statistically significant difference with regard to AL; however, the measurements taken on a 3D reconstructed tooth showed significant differences from AL,[36] implying that the number of views may impact reliability. This is of paramount importance during scanning and reconstruction. Among the studies, 3 found no statistically significant differences in the CBCT WL measured at different voxel sizes,[37–39] while one study found the differences between the voxel sizes to be statistically significant.[36] Larger voxel sizes are associated with a decreased spatial resolution and can reduce accuracy by ±0.05 mm. Discrepancies less than 0.5 mm may not be clinically relevant.

The findings of our review show that CBCT measurements correlate strongly with endodontic WL as measured by EALs. This accords with earlier observations by Liang et al.[51] and Connert et al.[3] that CBCT is as accurate or more accurate than EALs. Lucena et al. dissented from this view, reporting that CBCT measurements were frequently shorter than AL by 0.59 mm.[52]

The results of this review are in agreement with the findings of Sherrard et al., who reported that CBCT tooth length and root length measurements were not significantly different as compared to physical methods, with the mean differences being ±0.3 mm.[53] Higher voxel sizes were correlated with greater inaccuracy.[53] Overall, the findings of this review are consistent with the previous literature, showing that a change in the voxel size during CBCT scanning impacts the accuracy of length and volume measurements, along with the quality of the models.[54–56] Low-certainty evidence indicates that while the size of voxels may affect the accuracy of the CBCT estimations of WL, the differences do not approach statistical significance.

### Overall completeness and applicability of evidence

Among the selected studies, only one study mentioned the radiation dosage experienced by the subject during CBCT imaging.[39] The effect of the voxel size on the radiation dose is a pertinent question in this regard. The radiation dose of CBCT is 43–50 μSv,[57] which is extremely high as compared to a periapical radiograph, i.e., 1–3 μSv.[58] The reduction of the voxel size for improving image quality will increase the radiation dosage the patients will be subjected to.[59,60] This may preclude the use of smaller voxel sizes. According to the American Association of Endodontists (AAE), the risks are too high in comparison with the benefits to make CBCT a routine screening tool.[61] Current recommendations by the European Society of Endodontology (ESE) suggest the use of EAL, followed by confirmation with a periapical radiograph.[62] The radiation dose and cost of CBCT screening

are considered disadvantages in their routine use for the estimation of WL. Diagnostic examinations should strive to follow the ALARA principle and use the lowest reasonably achievable dose of radiation.[30]

All studies included in this review found a strong correlation between a smaller voxel size and accuracy. Similar to the voxel size affecting the radiation dose, the FOV chosen may impact the effective radiation dose and the quality of the images, directly affecting the spatial resolution and accuracy of the images.

Several other factors may have impacted image acquisition, quality and measurements. Each study used different software. Similarly, the simulated clinical conditions during scanning varied with each study. Two studies used human dry maxilla[38] and mandible,[39] while the remaining studies used wax[36] and silicone.[37] This may have prevented artefacts in the image due to absence of motion and contralateral structures. The selected teeth varied among the studies, with only one study using multirooted teeth with curved canals. It is unclear whether these factors may have affected accuracy.[63] The acquisition parameters (the duration of exposure, voltage and amperage) may impact the overall accuracy of measurements.[64]

The CBCT imaging has the advantage of archiving and communication in medicine. The DICOM models of CBCT scans can be shared between specialists to facilitate communication and treatment planning. In the case of patients having earlier relevant CBCT scans, it may be prudent to use these for the estimation of WL rather than subject a patient to further periapical radiographs. This review also highlights a dearth of studies in this area of concern. Overall, there was a paucity of well-designed studies examining the accuracy of CBCT in endodontic length and volume measurements.

## Quality of evidence

The certainty for the evidence was downgraded by 2 steps, once for bias and once due to all studies being non-randomized. We found the quality of evidence for the outcome to be low due to the risk of bias. It could be argued that the use of EALs and physical measurements with a K-file and digital calipers should be assessed as high quality. However, there are concerns regarding the inconsistency of results across a small number of included studies. Three studies had low sample sizes. With only 4 studies included, there may be a large potential impact if one study differs in size. We urge a cautious interpretation of these results due to the small number of studies and since there are negative effects for CBCT with regard to the radiation dose. Several factors limited the interpretation of the data, including the lack of a uniform gold reference standard. The majority of studies used EALs for the determination of WL. While the available evidence on their accuracy is short with a considerable risk of bias, they can predict WL.[12] A combination of methods to assess WL may be more reliable than a single technique alone. In this regard, EALs may be combined with the patient's pre-existing CBCT data for accuracy.

The strength of this review is the comprehensive searche, and stringent adherence to the inclusion and exclusion criteria. Multiple authors independently conducted study selection, data extraction and quality assessment to minimize the selection bias. A limitation of our review is that only English language articles were considered for selection due to the lack of availability of translational resources. Excluding languages other than English may have introduced the language bias.

# Conclusions

Based on the limited research available, there is low-certainty evidence suggesting that the size of voxels may affect the accuracy of the CBCT estimations of WL. However, these differences do not approach statistical significance and may not be clinically relevant. In the case of patients with the pre-existing CBCT scans, the data may provide additional information for WL estimation rather than additional periapical radiographs.

## Ethics approval and consent to participate

Not applicable.

## Data availability

The datasets supporting the findings of the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.


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Review

# Efficacy of botulinum toxin type A in bruxism management: A systematic review

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## Abstract

Botulinum toxin type A (BTX-A) injections have emerged as a promising alternative for the management of bruxism. In this context, a systematic review of randomized controlled trials on the impact of BTX-A on patients with bruxism was conducted. A literature search of multiple online electronic databases (PubMed®, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL)) was undertaken from their inception to February 1, 2024. The Medical Subject Headings (MeSH) included "Botulinum Toxins", "Botulinum Toxins, Type A", "Bruxism", and "Sleep Bruxism", which were combined with the Boolean operators "AND" and "OR". The methodological quality of each included study was assessed using the Joanna Briggs Institute (JBI) critical appraisal tool. Reducing muscle pain and activity were assessed as primary outcomes, while the quality of sleep was considered as a secondary outcome. Twelve articles met the inclusion criteria. The risk of bias was low in 10 studies and moderate in 2. Bilateral injections of BTX-A into the masseter, temporalis and medial pterygoid muscles were compared to saline injections, the use of occlusal splints and conventional treatment. Of the 12 studies, 6 reported a reduction in muscle activity recorded by rhythmic masticatory muscle activity (RMMA) and electromyography (EMG) after the administration of BTX-A. In addition, 3 studies indicated that the intensity of muscle pain, measured using the visual analogue scale (VAS), decreased significantly in individuals with bruxism who received BTX-A. Finally, 1 study highlighted improved sleep quality in patients with bruxism who were rehabilitated with a single-arch implant overdenture and received either BTX-A or occlusal appliances. Botulinum toxin type A can effectively reduce symptoms of bruxism. However, the included studies exhibited heterogeneity and methodological differences. Long-term follow-up studies with large sample sizes and the incorporation of repeated injections are necessary to further validate the findings.

**Keywords:** therapeutics, systematic review, botulinum toxin, sleep bruxism

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## Highlights

- Botulinum toxin type A may be effective in the management of bruxism.
- Studies suggest low doses of BTX-A as an alternative treatment for bruxism.
- Further prospective, long-term studies are needed to determine optimal parameters of BTX-A injections.

# Introduction

Bruxism is a topic of interest in oral medicine.[1] Lobbezoo et al. defined bruxism as "a masticatory muscle activity that occurs during sleep (characterized as rhythmic or non-rhythmic) and wakefulness (characterized by repetitive or sustained tooth contact and/or by bracing or thrusting of the mandible)".[2] Research has demonstrated that bruxism can have harmful effects on various structures within the mouth and contribute to tooth wear, damage to periodontal tissue, myofascial pain, headache, and muscular or joint problems.[3] Two different categories of bruxism have been identified, namely sleep bruxism and awake bruxism, observed during sleep and wakefulness, respectively.[2,4] Lobbezoo et al. have emphasised the role of the masticatory muscles during sleep and wakefulness in provoking potential clinical consequences.[2] Sleep bruxism is no longer considered as a parafunction or a disease but rather as a behavior.[5] Classifications and definitions of bruxism have varied widely over the decades, along with the assessment tools and diagnostic criteria.[2,6] Non-instrumental (e.g., questionnaires, oral history, clinical examinations, and diaries), semi-instrumental (e.g., ecological momentary assessment) and instrumental (e.g., electromyography recordings, polysomnography records) approaches have been implemented to diagnose the condition.[4] In addition, a grading system has been proposed to determine the degree of validity of these means of assessment in order to facilitate therapeutic approaches.[2] Several treatment options are available for the management of bruxism, including occlusal splints, biofeedback, cognitive-behavioral approaches and pharmacological methods.[7] Among these, occlusal splints are typically the preferred method for protecting teeth and dental prostheses from damage.[7] However, there is insufficient evidence to support the effectiveness of occlusal splints in reducing sleep bruxism.[8] Recently, local injections of botulinum toxin (BTX) have been increasingly used in the treatment of movement disorders and have received the attention for its efficacy in treating bruxism.

Botulinum toxin, also known by the brand name Botox, is an anaerobic bacterial endotoxin produced by the *Clostridium botulinum* bacterium.[8] It has been the subject of research since the late 1970s regarding its therapeutic potential in the management of various neuromuscular disorders.[9] Botulinum toxin blocks the action of neuromuscular transmission, which leads to muscle relaxation and decreased muscle contractions. A recent systematic review has shown the efficiency of BTX in treating refractory myofascial pain associated with temporomandibular disorders (TMD) by alleviating pain and increasing the pressure pain threshold.[10] Since bruxism is a behavior characterized by repetitive masticatory muscle activity that may lead to TMD, researchers have proposed the administration of BTX injections to mitigate bruxism by reducing the contractions of the masseter muscles.[9] Despite the widespread use of BTX in clinical practice, the efficacy and safety of this approach in the treatment of bruxism have not been fully established. Previous systematic reviews on the subject have included articles with subjective outcome values, such as reported pain reduction, instead of objective reduction of muscular forces and/or episodes of bruxism.[7,11–15] As a result, the conclusions that could be drawn from these reviews were limited to more subjective interpretations. It is therefore important to conduct a novel review in order to obtain more reliable and consensus-based results. This objective can be achieved by incorporating newly published articles that have not been systematically reviewed in a scientifically rigorous manner. Hence, this systematic review was carried out as an attempt to evaluate the efficacy of botulinum toxin type A (BTX-A) in the treatment of bruxism.

# Material and methods

## Protocol and eligibility criteria

The present study adhered to the guidelines established by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[16] The review protocol was registered with PROSPERO (identification No. CRD42023472755).

The inclusion criteria were established in accordance with the PICOS criteria, as follows: P (population) = patients diagnosed with primary bruxism; I (intervention/exposure) = injection of BTX-A; C (comparison): patients with primary bruxism receiving placebo injections or treated by conventional therapies or with a lower dose of BTX-A; O (outcome): decrease of pain and/or muscle activity; S (study design): randomized clinical trials (RCTs) written in English. The review question posed was: "Is BTX-A effective in reducing symptoms of primary bruxism?".

The present study was conducted with no restrictions applied concerning setting, country, or period of the study. Studies that did not share the purpose of this systematic review, as well as studies reported in proceedings, books, dissertations, theses, and monographs, were excluded from consideration. Studies not fully published and those with data associated with other health problems and with secondary bruxism caused by psychological or neurological disorders were also excluded from the analysis.

## Search strategy

A comprehensive electronic search of the PubMed®, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) databases was conducted by 2 independent reviewers (GO and MK) to identify studies assessing the efficacy of BTX-A in the management of bruxism. The following Medical Subject Headings (MeSH) were used: "Botulinum Toxins", "Botulinum Toxins, Type A", "Bruxism", and "Sleep Bruxism" combined with the Boolean operators "AND" and "OR", as follows: ("Bruxism"[MeSH] OR "Sleep Bruxism"[MeSH]) AND ("Botulinum Toxins"[MeSH] OR "Botulinum Toxins, Type A"[MeSH]).

Disagreements among reviewers regarding the final inclusion of articles were resolved by consensus. The search was limited to articles published in English language before February 1, 2024.

## Study selection

Two investigators (SY and GO) used the EndNote™ software, v. 9.0 (Clarivate™, London, UK) to eliminate duplicates and perform the initial screening of the articles based on their titles and abstracts. Subsequently, the full texts of eligible articles were assessed according to the established inclusion criteria. Any discrepancies between the 2 reviewers were resolved by the third reviewer (MK).

## Data extraction

The data from the included studies was extracted in a specified format, including the population, the parameters being investigated, the periods of parameter collection, and the significant findings. The extracted data was then reviewed and analyzed by 2 authors (SY and GO). Subsequently, it was verified by the third author (MK). Any divergence in data collection was resolved through consensus.

## Methodological quality assessment

The quality of the included studies was assessed according to the Joanna Briggs Institute (JBI) critical appraisal tool for the assessment of risk of bias for randomized controlled trials.[17] The tool encompasses 13 items: randomization component; allocation concealment; similarity of treatment groups at baseline; blinding of participants; blinding of personnel; blinding of outcome assessors; groups treated identically other than the intervention of interest; follow-up; intention to treat; similar way of outcome measurement; reliable way of outcome measurement; statistical analysis; and trial design.

The methodological quality and risk of bias of each included study were analyzed independently by 2 authors (SY and OG). The reliability was scored as "yes", "no", "unclear", or "not applicable". In case of discrepancy, the third author (MK) reviewed the studies to reach a consensus.

The risk of bias in the studies was categorized as low ("yes" scores ≥70%), moderate ("yes" scores between 50% and 69%) or high ("yes" scores ≤49%).[18]

# Results

## Search results

The search of the electronic databases yielded a total of 647 articles published between 2008 and 2024. After the elimination of duplicates, 569 papers remained for further consideration. In the first phase of the study, the titles and abstracts of these articles were reviewed, resulting in the selection of 23 studies.[3,8,9,19–38] No additional paper was added after screening the reference lists of the 23 articles. In phase 2, the texts of the articles were read in full, with 11 papers excluded.[28–38] Ultimately, 12 studies[3,8,9,19–27] were included in the systematic review (Fig. 1).

## Methodological quality assessment results

The methodological quality of the included studies was assessed using the JBI critical appraisal checklist, with 10 articles classified as low risk of bias and the remaining 2 papers classified as moderate risk of bias. The final score ranged from 61% to 100% (Table 1). All studies reported data on the following items: 1 (i.e., randomization component); 7 (i.e., groups treated identically other than the intervention of interest); 8 (i.e., follow-up); 9 (i.e., intention to treat); 10 (i.e., similar way of outcome measurement); 11 (i.e., reliable way of outcome measurement); and 13 (i.e., trial design).

## Study characteristics

After the selection of 12 articles,[3,8,9,19–27] the following information was extracted: first author; year of publication; study period; study design; follow-up duration; diagnosis of bruxism; inclusion and exclusion criteria; sample size; age and sex of participants; collected data and how they were assessed; and characteristics of BTX-A injection (Table 2). The included studies were published

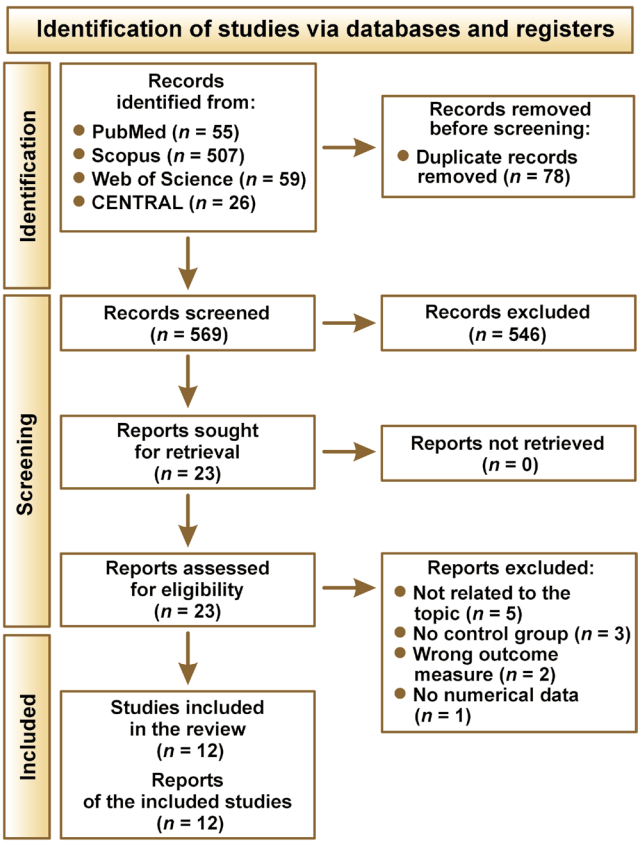


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the study

CENTRAL – Cochrane Central Register of Controlled Trials.

between 2008[26] and 2024.[19] They were conducted in Saudi Arabia,[19,20] Egypt,[25] Turkey,[23] Australia,[21] the United States,[27] South Korea,[3,8,24] Italy,[26] India,[9] and Syria.[22] All studies were RCTs. The sample size ranged from 12[24] to 50[20] subjects, with 3 studies reporting a sample size calculation.[19,22,25] Ten studies[3,8,19,21–27] included both males and females and 1 study included females only.[20] Additionally, 1 study did not report any information related to sex.[9] The mean age of the study participants ranged from 25[3,24] to 58[25] years. The duration of follow-ups varied from 4 weeks[3] to 12 months.[20,25]

## Diagnosis of bruxism

The included studies showed different approaches to bruxism diagnosis through a combination of both subjective and objective criteria. These methods included the evaluation of clinical signs and symptoms (such as muscle pain, tooth grinding, attrition in occlusal surfaces of posterior teeth), medical questionnaire and electromyography (EMG). Patients were diagnosed with definite bruxism in 9 studies.[3,9,19–21,23,25–27] Two studies[21,27] applied the International Classification of Sleep Disorders – Third Edition (ICSD-3), whereas "The international consensus on the definition and the diagnosis of bruxism" by Lobbezoo et al. was followed in 1 study.[19]

## Outcome assessment

Different bruxism characteristics were evaluated, including muscle pain[19–23,26,27] and muscular activity.[22] Pain intensity was measured using the visual analogue scale (VAS)[9,19–23,26,27] and the short-form McGill Pain Questionnaire.[21] Muscular activity was recorded through rhythmic masticatory muscle activity (RMMA),[3,8] EMG,[3,8,21,22,24,27] bruxism index (BI),[21] and bite force.[23] Bruxism symptoms were also investigated using various questionnaires.[21]

The secondary outcome was the participants' quality of sleep. The Epworth Sleepiness Scale (ESS)[21,27] and the Pittsburgh sleep quality index (PSQI)[25,27] were used to evaluate this outcome.

## BTX-A injection

Botulinum toxin type A was injected in all subjects in the included studies. Among the 12 RCTs, in 4[8,19,22,24] and 2 trials,[26,27] respectively, bilateral injections were administered into the masseter muscles and both the masseter and temporalis muscles. Controls received placebo injections of isotonic saline. Cruse et al. extended their comparisons to include bilateral injections into the masseter, temporalis and medial pterygoid muscles, with a control group receiving saline injections.[21] On the other hand, bilateral injections of BTX-A into the masseter muscles were compared to occlusal splints[23] and conventional treatments for bruxism, which included behavioral strategies, occlusal splints and pharmacological treatment.[20] Only 1 investigation compared bilateral BTX-A injection in the masseter muscles alone with combined injections in the masseter and temporalis muscles.[3] Jadhao et al. included 3 groups and compared bilateral BTX-A injections into the masseter and temporalis muscles to a control group.[9] The control group received saline injections, and a second control group was not subjected to any intervention.[9] Finally, a study by Ali et al. used bilateral injections of BTX-A into the masseter and temporalis muscles and compared it to conventional occlusal stents and a second control group that did not receive any intervention (patients were instructed to only remove the overdenture at night).[25]

The total dosage of BTX-A injections administered to the masseter muscles ranged from 20 mouse units (MU)[22] to 120 MU.[27] In the temporalis muscles, the dosage ranged from 30 MU[21] to 80 MU.[27] Cruse et al. injected 15 MU into each medial pterygoid muscle (Table 2).[21]

## Efficacy of botulinum toxin in the management of bruxism

The main results of the published studies assessing the impact of BTX-A on bruxism are presented in Table 3.

**Table 1.** Quality scoring of the analyzed articles according to the Joanna Briggs Institute (JBI) critical appraisal checklist

| Study | Item | | | | | | | | | | | | | Score [%] | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | | |
| Shehri et al. 2022[22] | Y | Y | Y | Y | N/A | Y | Y | Y | Y | Y | Y | Y | Y | 92 | low |
| Cruse et al. 2022[21] | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | 100 | low |
| Ali et al. 2021[25] | Y | Y | Y | N/A | N/A | Y | Y | Y | Y | Y | Y | Y | Y | 84 | low |
| Alwayli et al. 2024[19] | Y | Y | Y | Y | Y | N/A | Y | Y | Y | Y | Y | Y | Y | 92 | low |
| Kaya and Ataoglu 2021[23] | Y | U | Y | N/A | N/A | U | Y | Y | Y | Y | Y | Y | Y | 69 | moderate |
| Shim et al. 2020[8] | Y | U | Y | U | U | U | Y | Y | Y | Y | Y | U | Y | 61 | moderate |
| Ondo et al. 2018[27] | Y | U | Y | Y | Y | U | Y | Y | Y | Y | Y | Y | Y | 84 | low |
| Jadhao et al. 2017[9] | Y | U | Y | Y | Y | U | Y | Y | Y | Y | Y | Y | Y | 84 | low |
| Al-Wayli 2017[20] | Y | Y | Y | N/A | N/A | U | Y | Y | Y | Y | Y | Y | Y | 77 | low |
| Shim et al. 2014[3] | Y | U | U | Y | U | Y | Y | Y | Y | Y | Y | Y | Y | 77 | low |
| Lee et al. 2010[24] | Y | U | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | 92 | low |
| Guarda-Nardini et al. 2008[26] | Y | U | Y | Y | Y | U | Y | Y | Y | Y | Y | U | Y | 77 | low |

Y – yes; N – no; N/A – not applicable; U – unclear; item 1 – randomization component?; item 2 – allocation concealment?; item 3 – treatment group similar at baseline?; item 4 – blinding of participants?; item 5 – blinding of personnel?; item 6 – blinding of outcome assessors?; item 7 – groups treated identically other than the intervention of interest?; item 8 – follow-up?; item 9 – intention to treat?; item 10 – similar way of outcome measurement?; item 11 – reliable way of outcome measurement?; item 12 – statistical analysis?; item 13 – trial design?

## Myofascial pain or jaw stiffness

Three studies[20,22,27] indicated a significant reduction in pain scores in the BTX-A group compared to the placebo group, while 1 investigation[20] reported the same reduction in the treatment group compared to conventional treatments. On the other hand, 5 studies demonstrated the efficacy of BTX-A in addressing bruxism-related myofascial pain symptoms.[19,20,22,23,26] Specifically, Guarda-Nardini et al. observed a significant pain reduction during chewing after 6 months in individuals with bruxism who received BTX-A, as compared to those who received a placebo.[26] In addition, Kaya and Ataoglu reported that both occlusal splints and BTX-A were effective in alleviating pain associated with bruxism.[23] However, BTX-A was found to be slightly less effective in pain reduction compared to occlusal splints. Notably, BTX-A injections still provided a significant reduction in pain symptoms, making them a viable and alternative treatment option.[23] Two other studies[21,27] reported contradictory results in terms of pain reduction following the injection of BTX-A. No evidence was found for change in pain intensity as measured by the short-form McGill Pain Questionnaire[21] or the VAS[21,27] compared to the control group and before injection.

## Muscle activity

Three studies[3,9,22] demonstrated the efficacy of BTX-A injections for sleep bruxism, as evidenced by the reduction in the intensity of both the masseter and temporalis muscles in comparison to the control groups. However, this reduction was observed only in the masseters in 2 other studies.[8,24] Three studies reported that the administration of BTX-A into the masseter muscle[8,24] and into both the temporalis and masseter muscles[3] reduced muscle activity compared to the baseline. On the other hand, Kaya and Ataoglu reported that BTX-A administration effectively increased the relaxation of the masseter muscles.[23] The study demonstrated that BTX-A injections offer a promising approach to alleviate muscle-related pain and discomfort in patients with bruxism, providing a potential alternative for those who may not be able to use traditional occlusal splints or who have contraindications for other treatments.[23] Cruse et al. demonstrated a decrease in BI in the masticatory muscles evaluated by EMG between the experimental and control groups.[21]

**Table 2.** Main characteristics and methodological aspects of studies on the efficacy of botulium toxin type A (BTX-A) in the treatment of bruxism

| Study | Publication city (country) | Publication year | Study period | Study design | Follow-up duration | Diagnosis of bruxism | Inclusion criteria | Exclusion criteria |
|---|---|---|---|---|---|---|---|---|
| Shehri et al.[22] | Damascus (Syria) | 2022 | 2021 | parallel RCT | 6 months | – bruxism questionnaire<br>– clinical examination | – pain in the masseter<br>– age: 18–40 years<br>– tooth grinding<br>– attrition in occlusal surface of posterior teeth | – loss of 2 or more posterior teeth<br>– fixed or movable prosthodontics for more than 4 dental units<br>– advanced malocclusion<br>– TMD<br>– orofacial pain<br>– insomnia<br>– known BTX-A allergy<br>– pregnancy<br>– neuromuscular disease<br>– hemorrhagic disease<br>– antibiotic treatment<br>– infectious lesion at injection site<br>– respiratory ailments causing night time coughing |
| Cruse et al.[21] | Melbourne (Australia) | 2022 | 2017–2020 | crossover RCT | 12 weeks | ICSD-3 | BI > 5 | – medications affecting muscle relaxation<br>– previous jaw trauma<br>– orofacial pain<br>– neuromuscular disease<br>– pregnancy<br>– previous or current BTX-A injection for bruxism |
| Ali et al.[25] | Giza (Egypt) | 2021 | 2019–2020 | parallel RCT | 12 months | at least one of the bruxism signs/symptoms | – natural dentition in 1 arch<br>– at least 6 anterior teeth<br>– maximum 1/2 premolar/molar missing in any quadrant<br>– single implant-retained overdentures loaded 1 year before the study | – previous bruxism management<br>– medical condition that would affect TMJ, such as radiation, osteoarthritis or trauma |
| Alwayli et al.[19] | Riyadh (Saudi Arabia) | 2024 | 2017–2019 | parallel RCT | 24 weeks | – 2013 protocol by Lobbezoo et al.[6]<br>– bruxism questionnaire | – no systemic pathologies<br>– moderate/severe pain in the masseters and TMJ area<br>– age: 20–60 years<br>– tooth grinding<br>– ccclusal wear of posterior and anterior teeth | – dentures<br>– implants<br>– use of orthodontic appliances<br>– orofacial pain<br>– insomnia<br>– known BTX-A allergy<br>– pregnancy<br>– neuromuscular disease<br>– bleeding disorder<br>– antibiotic therapy<br>– respiratory ailments causing night time coughing<br>– infectious lesion at injection site<br>– previous bruxism treatment |
| Kaya and Ataoglu[23] | Istanbul (Turkey) | 2021 | 2017 | parallel RCT | 6 months | clinical diagnosis | – age: 18–65 years<br>– absence of systemic diseases<br>– myofascial pain in the masseter during palpation | – use of systemic steroids, immunosuppressive drugs or non-steroidal anti-inflammatory drugs within the last 7–10 days<br>– use of occlusal splints within the last 6 months<br>– removable or fixed prosthesis<br>– missing teeth<br>– TMJ surgery<br>– patients who received physiotherapy for TMJ within the last 6 months<br>– patients with occlusal etching<br>– pregnant and nursing women |
| Shim et al.[8] | Seoul (South Korea) | 2020 | 2017 | parallel RCT | 12 weeks | clinical signs and symptoms of sleep bruxism | – tooth grinding at least 3 nights/week<br>– morning jaw stiffness<br>– presence of tooth wear<br>– moderate to severe wear facets on the occlusal splint | – severe obstructive sleep apnea on polysomnography<br>– BTX-A injection in the past year<br>– medications affecting muscle relaxation<br>– infectious lesion at injection site<br>– known BTX-A allergy<br>– neuromuscular disease<br>– pregnancy |

| Sample size calculation | Participants (M/F), *n* | Age [years] | Intervention | Comparison | Collected data | Equipment | Injection position | BTX-A dosage (per side) |
|---|---|---|---|---|---|---|---|---|
| yes | 20 (7/13) | 29.81 ±7.12[a] | BTX-A | saline | – pain intensity<br>– muscular activity | – EMG<br>– VAS | masseter (2 points) | 20 MU (10 MU) |
| NR | 22 (8/14) | 42.10 ±13.98[a] | BTX-A | saline | – BI<br>– pain intensity<br>– headache | – EMG<br>– bruxism questionnaire<br>– SF McGill Pain Questionnaire<br>– VAS + pain rating scale<br>– HIT-6<br>– ESS | – masseter (1 point)<br>– temporalis muscle (3 points)<br>– medial pterygoid muscle (1 point) | – group A: 60 MU (masseter: 30 MU)<br>– group B: 90 MU (masseter: 30 MU, temporalis muscle: 15 MU)<br>– group C: 120 MU (masseter: 30 MU, temporalis muscle: 15 MU, medial pterygoid muscle: 15 MU) |
| yes | 42 (20/22) | group 1: 58.70 ±9.20[a]<br>group 2: 57.48 ±8.30[a]<br>group 3: 53.70 ±6.30[a] | BTX-A + overdenture | – no overdenture at night<br>– overdenture at night + conventional occlusal stents | – patient satisfaction<br>– subjective sleep quality<br>– prosthodontic complications | – PSQI<br>– TMD/numeric scales | masseter (3 points) | 50 MU (25 MU) |
| yes | 40 (16/24) | 21–52[b] | BTX-A | saline | – pain intensity<br>– subjective efficacy of the treatment<br>– subjective tolerability of the treatment | – VAS<br>– questionnaire on the subjective efficacy and tolerability of the treatment | masseter (4 points) | 40 MU (20 MU) |
| NR | 40 (7/33) | 26.3 (21–52)[c] | BTX-A | occlusal splints | – pain intensity<br>– maximum bite force<br>– functional movement | – FlexiForce pressure sensor<br>– VAS | masseter (3 points) | 48 MU (24 MU) |
| NR | 23 (10/13) | placebo group: 28.90 ±8.13[a]<br>BTX-A group: 32.46 ±9.94[a] | BTX-A | saline | – sleep duration<br>– sleep efficacy/latency<br>– apnea-hypopnea index<br>– periodic limb movement<br>– RMMA episodes<br>– EMG variables | – EMG<br>– audio-video polysomnography | masseter (2 points) | 50 MU (25 MU) |

| Study | Publication city (country) | Publication year | Study period | Study design | Follow-up duration | Diagnosis of bruxism | Inclusion criteria | Exclusion criteria |
|---|---|---|---|---|---|---|---|---|
| Ondo et al.[27] | Texas (USA) | 2018 | 2009–2011 | parallel RCT | 8 weeks | – ICSD-3<br>– bruxism signs in polysomnography<br>– EMG | – diagnosis of bruxism<br>– subjective symptoms associated with bruxism | – cranial dystonia<br>– severe obstructive sleep apnea on polysomnography with the apnea-hypopnea index >30/h |
| Al-Wayli[20] | Riyadh (Saudi Arabia) | 2017 | 2010–2011 | parallel RCT | 12 months | – diagnostic grading system of bruxism<br>– bruxism questionnaire<br>– clinical examination | – moderate to severe pain in the masseter muscles and TMJ area related to bruxism<br>– age: 20–60 years<br>– tooth grinding<br>– occlusal surface attrition of posterior teeth | – orofacial pain<br>– insomnia<br>– known BTX-A allergy<br>– pregnancy<br>– neuromuscular disease<br>– bleeding disorders<br>– antibiotic therapy<br>– respiratory ailments causing night time coughing<br>– infectious skin lesion at injection site |
| Shim et al.[3] | Seoul (South Korea) | 2014 | NR | parallel RCT | 4 weeks | – history of tooth grinding occurring ≥3 nights/week<br>– morning jaw stiffness<br>– tooth wear<br>– use of an oral splint | – self-reported bruxism activity<br>– moderate to severe wear facets on the oral splint<br>– RMMA at the baseline polysomnography recordings | – previously received BTX-A injection into the masseter and temporalis muscles<br>– medications affecting muscle relaxation<br>– infectious skin lesion at injection site<br>– known BTX-A allergy<br>– neuromuscular disease<br>– pregnancy |
| Jadhao et al.[9] | Hingoli (India) | 2017 | NR | parallel RCT | 6 months | screening-oriented clinical diagnostic criteria | – grinding or bruxing sounds during sleep 5 nights per week<br>– tooth wear and shiny spots on restorations or masseter hypertrophy or evidence of morning masticatory muscle fatigue and pain | – heart disease<br>– mental illness<br>– systemic disorders<br>– treated for bruxism and/or TMD in the 6 months prior to the study<br>– neuromuscular disease<br>– hypersensitivity to BTX-A<br>– diseases that could cause joint imbalance |
| Lee et al.[24] | Seoul (South Korea) | 2010 | NR | parallel RCT | 12 weeks | – medical questionnaire<br>– EMG | – tooth grinding<br>– healthy participants<br>– age: 20–30 years | – TMD<br>– orofacial pain<br>– insomnia<br>– known BTX-A allergy<br>– pregnancy<br>– neuromuscular disease<br>– bleeding disorders<br>– antibiotic therapy<br>– respiratory ailments causing night time coughing<br>– infectious skin lesion at injection site |
| Guarda-Nardini et al.[26] | Padua (Italy) | 2008 | NR | parallel RCT | 6 months | screening-oriented clinical diagnostic criteria | – grinding or bruxing sounds during sleep for the past 6 months<br>– tooth wear and shiny spots on restorations or morning masticatory muscle fatigue and pain or masseter hypertrophy or myofascial pain of the masticatory muscles | – treated for bruxism and/or TMD in the 6 months prior to the study<br>– neuromuscular disease<br>– hypersensitivity to BTX-A |

NR – not reported; RCT – randomized clinical trial; ICSD-3 – International Classification of Sleep Disorders – Third Edition; EMG – electromyography; BI – bruxism index; TMJ – temporomandibular joint; RMMA – rhythmic masticatory muscle activity; TMD – temporomandibular disorders; VAS – visual analogue scale; HIT-6 – headache impact test; ESS – Epworth Sleepiness Scale; PSQI – Pittsburgh sleep quality index; SF – short-form; [a] mean (*M*) ± standard deviation (*SD*); [b] minimum–maximum; [c] *M* (minimum–maximum).

| Sample size calculation | Participants (M/F), *n* | Age [years] | Intervention | Comparison | Collected data | Equipment | Injection position | BTX-A dosage (per side) |
|---|---|---|---|---|---|---|---|---|
| NR | 23 (4/19) | 47.4 ±16.9[a] | BTX-A | placebo | – pain intensity<br>– sleep efficiency<br>– bruxism questionnaire<br>– clinical global impression<br>– polysomnography data | – EMG<br>– VAS<br>– polysomnography<br>– bruxism questionnaire<br>– HIT-6<br>– PSQI<br>– ESS<br>– anxiety scale | – masseter (2 points)<br>– temporalis muscle (3 points) | 200 MU (masseter: 60 MU, temporalis muscle: 40 MU) |
| NR | 50 (0/50) | 45.5 ±10.8[a] | BTX-A | behavioral strategies, occlusal splints and pharmacological measures | pain intensity | VAS | masseter (3 points) | 40 MU (20 MU) |
| NR | 20 (7/13) | 25.8 ±5.1[a] | BTX-A in the masseters | BTX-A in the masseter and temporalis muscles | – RMMA<br>– orofacial activity<br>– frequency of episodes, bursts per episode, episode duration<br>– peak amplitude of EMG activity<br>– sleep variables | – EMG<br>– audio-video polysomnography | – masseter (3 points)<br>– temporalis muscle (3 points) | – 50 MU (masseter: 25 MU)<br>– 100 MU (masseter: 25 MU, temporalis muscle: 25 MU) |
| NR | 24 (NR/NR) | 20–35[b] | BTX-A | – saline<br>– no injections | – pain intensity<br>– subjective efficacy of the treatment<br>– duration of clenching and releasing<br>– asymmetry index for occlusal force | – VAS<br>– I-Motion occlusal force analyzer | – masseter (4 points)<br>– anterior temporalis muscle (3 points) | 100 MU (masseter: 30 MU, anterior temporalis muscle: 20 MU) |
| NR | 12 (7/5) | M: 25.0 ±2.35[a]<br>F: 24.8 ±0.83[a] | BTX-A | saline | – EMG bruxism events<br>– subjective symptoms of bruxism | – EMG<br>– bruxism questionnaire | – masseter (3 points)<br>– temporalis muscle (3 points) | 80 MU (40 MU) |
| NR | 20 (10/10) | 25–45[b] | BTX-A | saline | – pain intensity<br>– mastication efficiency<br>– maximum mouth opening<br>– functional limitation during usual jaw movements<br>– subjective efficacy of the treatment<br>– treatment tolerance | – VAS<br>– questionnaire on the subjective efficacy of the treatment | – masseter (4 points)<br>– anterior temporalis muscle (3 points) | 100 MU (masseter: 30 MU, anterior temporalis muscle: 20 MU) |

**Table 3.** Main results of studies on the efficacy of botulinum toxin type A (BTX-A) in the treatment of bruxism

| Study | Results | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | sleeping (TG vs. CG) | | | | | | | pain (TG vs. CG) | | | | | | | muscle activity (TG vs. CG) | | | | | |
| Shehri et al. 2022[22] | tool | $T_0$ | 2W | 1M | 3M | 4M | 6M | tool | $T_0$ | 2W | 1M | 3M | 4M | 6M | tool | $T_0$ | 2W | 3M | 6M | |
| | – | – | – | – | – | – | – | VAS[a] | 8.6 ±1.3<br>8.5 ±1.1 | 2.8 ±1.5†<br>8.0 ±1.0* | 1.3 ±1.3†<br>8.1 ±1.1* | 2.4 ±2.0†<br>8.4 ±1.0* | 4.7 ±1.0†<br>8.3 ±0.7* | 6.1 ±1.0†<br>8.6 ±0.5* | EMG of RM[a] [μV] | 596.4 ±363.0<br>533.1 ±226.2 | 258.8 ±160.4<br>515.6 ±248.1* | 257.3 ±160.8<br>528.7 ±274.9* | 539.9 ±316.2<br>574.6 ±251.8 | |
| | – | – | – | – | – | – | – | – | – | – | – | – | – | – | EMG of LM[a] [μV] | 694.7 ±360.8<br>645.8 ±193.9 | 328.8 ±181.0<br>620.1 ±205.9* | 336.1 ±188.6<br>623.7 ±236.1* | 700.6 ±387.8<br>647.8 ±233.7 | |
| | Conclusion: Injecting 10 MU of BTX-A into the masseter muscle reduced muscle activity and pain symptoms associated with nocturnal bruxism. | | | | | | | | | | | | | | | | | | | |
| Cruse et al. 2022[21] | tool | $T_0$ | 4W | 12W | | | | tool | $T_0$ | 4W | 12W | | | | tool | $T_0$ | 4W | 12W | | |
| | BI[a] | 8.3 ±2.9<br>8.3 ±2.9 | 6.7 ±4.1<br>8.3 ±4.1* | 7.4 ±3.5<br>7.7 ±3.5 | | | | VAS[a] | 56.9 ±26.7<br>56.9 ±26.7 | 41.9 ±26.6<br>46.9 ±28.8 | 44.6 ±27.1<br>53.9 ±29.9 | | | | – | – | – | – | | |
| | ESS[a] | 7.5 ±4.8<br>7.5 ±4.8 | 6.6 ±4.6<br>7.1 ±4.8 | 6.8 ±4.5<br>7.4 ±4.8 | | | | SF McGill[a] | 2.9 ±1.3<br>2.9 ±1.3 | 2.2 ±1.1<br>2.5 ±1.4 | 2.1 ±1.2<br>2.6 ±1.3 | | | | – | – | – | – | | |
| | – | – | – | – | | | | PRI[a] | 16.2 ±10.6<br>16.2 ±10.6 | 12.6 ±8.8<br>13.1 ±10.6 | 14.3 ±12.5<br>14.8 ±10.1 | | | | – | – | – | – | | |
| | Conclusion: Targeted BTX-A injection is safe and effective in the treatment of bruxism. | | | | | | | | | | | | | | | | | | | |
| Ali et al. 2021[25] | tool | $T_0$ | 3M | 6M | 9M | 12M | | tool | $T_0$ | 3M | 6M | 9M | 12M | | tool | $T_0$ | 3M | 6M | 9M | 12M |
| | PSQI[a] | 7.9 ±2.2<br>8.2 ±1.5<br>8.3 ±1.8 | 6.2 ±2.3†<br>6.8 ±2.9†<br>7.7 ±3.4* | 5.9 ±2.1<br>6.6 ±3.0<br>8.2 ±1.2* | 5.2 ±1.9<br>7.1 ±2.1<br>7.8 ±1.5* | 5.0 ±2.1<br>6.9 ±1.7<br>8.3 ±1.8* | | – | – | – | – | – | – | | – | – | – | – | – | – |
| | Conclusion: BTX-A and occlusal appliances are effective in improving sleep quality of patients with bruxism rehabilitated with a single-arch implant overdenture. | | | | | | | | | | | | | | | | | | | |
| Alwayli et al. 2024[19] | tool | $T_0$ | 2W | 8W | 24W | | | tool | $T_0$ | 2W | 8W | 24W | | | tool | $T_0$ | 2W | 8W | 24W | |
| | – | – | – | – | – | | | VAS[a] | 6.8 ±0.1<br>7.0 ±0.4 | 4.1 ±0.6†<br>5.2 ±0.4* | 2.2 ±0.6†<br>5.2 ±0.4* | 0.1 ±0.4†<br>5.2 ±0.4* | | | – | – | – | – | – | |
| | Conclusion: BTX-A could reduce the pain associated with nocturnal bruxism in affected patients. | | | | | | | | | | | | | | | | | | | |
| Kaya and Ataoglu 2021[23] | tool | 2W | 6W | 3M | 6M | | | tool | 2W | 6W | 3M | 6M | | | tool | 2W | 6W | 3M | 6M | |
| | – | – | – | – | – | | | VAS[a] | 2.9 ±0.5†<br>2.0 ±0.3† | 3.3 ±0.5†<br>1.8 ±0.4† | 2.4 ±0.4†<br>2.2 ±0.5† | 2.1 ±0.5†<br>2.5 ±0.4† | | | BF[a] | 57 ±14†<br>−8 ±17 | 66 ±16.4†<br>−43 ±22.6 | 13 ±17<br>−34 ±22 | −40 ±21<br>−52 ±23† | |
| | Conclusion: A low dose of BTX-A can be considered an alternative treatment for patients who cannot use occlusal splints. | | | | | | | | | | | | | | | | | | | |
| Shim et al. 2020[8] | tool | $T_0$ | 4W | 12W | | | | tool | $T_0$ | 4W | 12W | | | | tool | $T_0$ | 4W | 12W | | |
| | – | – | – | – | | | | – | – | – | – | | | | MVC[a] [μV] | 89.2 ±55.9<br>118.0 ±94.7 | 38.1 ±20.6‡<br>106.5 ±105.9* | 36.7 ±24.4‡<br>92.0 ±109.8* | | |
| | – | – | – | – | | | | – | – | – | – | | | | RMMA[a] [μV] | 88.0 ±70.2<br>71.5 ±46.9 | 29.8 ±13.9‡<br>62.8 ±33.0* | 37.2 ±23.8‡<br>61.4 ±50.9* | | |
| | Conclusion: A single BTX-A injection can be an effective management option for sleep bruxism, as it has been shown to reduce the intensity of masseter muscle activity. | | | | | | | | | | | | | | | | | | | |
| Ondo et al. 2018[27] | tool | $T_0$ | 4W | | | | | tool | $T_0$ | 4W | | | | | tool | $T_0$ | 4W | | | |
| | ESS[a] | 8.8 ±0.3<br>10.0 ±2.9 | 8.1 ±4.9<br>8.8 ±3.0 | | | | | VAS[a] | – | 65.0 ±19.6<br>44.2 ±14.3* | | | | | – | – | – | | | |
| | PSQI[a] | 19.3 ±8.3<br>18.6 ±6.6 | 14.3 ±8.7<br>13.7 ±6.8 | | | | | – | – | – | | | | | – | – | – | | | |
| | Conclusion: BTX-A is an effective and safe treatment for sleep bruxism. | | | | | | | | | | | | | | | | | | | |

| Study | Results | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | sleeping (TG vs. CG) | | | | | pain (TG vs. CG) | | | | | muscle activity (TG vs. CG) | | | | |
| Jadhao et al. 2017[9] | tool | $T_0$ | 1W | 3M | 6M | tool | $T_0$ | 1W | 3M | 6M | tool | 1W | 3M | 6M | |
| | – | – | – | – | – | VAS[a] | 3.8 ±1.1<br>4.0 ±0.8 | 3.5 ±1.2<br>3.8 ±0.9 | 3.2 ±1.8<br>4.1 ±0.6 | 3.0 ±0.9<br>3.8 ±1.0 | BF[a] | −32.4 ±7.8<br>−5.8 ±5.4* | −37.6 ±10.9<br>−11.3 ±6.0* | −30.1 ±12.3<br>−24.3 ±7.9 | |
| | – | – | – | – | – | VAS when chewing[a] | 3.1 ±1.3<br>4.1 ±1.5 | 3.5 ±1.2<br>3.8 ±0.9 | 3.2 ±1.8<br>4.1 ±0.6 | 3.0 ±0.9<br>3.8 ±1.0 | – | – | – | – | |
| | Conclusion: The efficacy of BTX-A in the treatment of bruxism was demonstrated by a significant reduction in myofascial pain symptoms. | | | | | | | | | | | | | | |
| Al-Wayli 2017[20] | tool | $T_0$ | 3W | 2M | 6M | 12M | tool | $T_0$ | 3W | 2M | 6M | 12M | tool | $T_0$ | 3W | 2M | 6M | 12M |
| | – | – | – | – | – | – | VAS[a] | 7.1 ±0.7<br>7.5 ±0.7 | 4.6 ±0.6<br>5.4 ±0.6* | 2.5 ±0.6<br>4.3 ±0.5* | 0.2 ±0.5<br>2.1 ±0.7* | 0.2 ±0.5<br>2.1 ±0.7 | – | – | – | – | – | – |
| | Conclusion: BTX-A injection reduced the mean pain score and the number of bruxism events by decreasing the activity of the masseter muscles. | | | | | | | | | | | | | | | | | |
| Guarda-Nardini et al. 2008[26] | tool | $T_0$ | 1W | 1M | 6M | | tool | $T_0$ | 1W | 1M | 6M | | tool | $T_0$ | 1W | 1M | 6M | |
| | – | – | – | – | – | | VAS[a] | 5.0 ±3.6<br>3.9 ±2.9 | 4.6 ±3.6<br>3.0 ±2.5 | 2.5 ±2.7<br>3.7 ±2.7 | 3.6 ±2.9<br>4.1 ±2.8 | | – | – | – | – | – | |
| | – | – | – | – | – | | VAS when chewing[a] | 6.2 ±2.8<br>4.1 ±2.9 | 5.2 ±3.0<br>3.8 ±2.8 | 3.6 ±2.3<br>3.7 ±2.7 | 3.6 ±2.4‡<br>4.7 ±2.8 | | – | – | – | – | – | |
| | Conclusion: BTX-A injection reduced myofascial pain symptoms in individuals with bruxism. | | | | | | | | | | | | | | | | | |
| Shim et al. 2014[3] | tool | $T_0$ | 4W | | | | tool | $T_0$ | 4W | | | | tool | $T_0$ | 4W | | | |
| | – | – | – | | | | – | – | – | | | | MVC MM[b] [μV] | 223.1 (81.2–333.8)<br>216.3 (39.0–800.5) | 78.0 (34.2–169.1)‡<br>43.1 (26.7–130.1)‡ | | | |
| | – | – | – | | | | – | – | – | | | | MVC TM[b] [μV] | 226.3 (104.9–432.9)<br>169.7 (105.5–515.5) | 104.4 (40.2–218.2)‡<br>171.0 (64.7–414.0)* | | | |
| | – | – | – | | | | – | – | – | | | | RMMA MM[b] [μV] | 215.7 (114.3–390.9)<br>290.5 (31.1–741.6) | 72.3 (32.9–98.9)‡<br>72.4 (29.4–141.6)‡ | | | |
| | – | – | – | | | | – | – | – | | | | RMMA TM[b] [μV] | 306.4 (161.0–377.7)<br>277.6 (87.4–553.5) | 83.0 (17.2–283.4)‡<br>194.8 (45.0–383.9)* | | | |
| | Conclusion: A single BTX-A injection is an effective strategy for controlling sleep bruxism for at least 1 month. | | | | | | | | | | | | | | | | | |
| Lee et al. 2010[24] | tool | $T_0$ | 4W | 8W | 12W | | tool | $T_0$ | 4W | 8W | 12W | | tool | $T_0$ | 4W | 8W | 12W | |
| | – | – | – | – | – | | – | – | – | – | – | | MVC20 MM (E/H)[a] | 2.8 ±1.9<br>2.5 ±1.3 | 0.1 ±0.3‡<br>2.2 ±1.1* | 0.3 ±0.3‡<br>2.5 ±1.4* | 0.3 ±0.2‡<br>2.7 ±1.4* | |
| | – | – | – | – | – | | – | – | – | – | – | | MVC20 TM (E/H)[a] | 2.3 ±1.2<br>1.8 ±1.5 | 2.5 ±2.5<br>1.8 ±1.6 | 2.2 ±0.8<br>2.0 ±1.6 | 1.9 ±1.0<br>1.7 ±1.5 | |
| | – | – | – | – | – | | – | – | – | – | – | | MVC10 MM (E/H)[a] | 5.0 ±2.3<br>4.7 ±1.2 | 0.6 ±0.6‡<br>4.1 ±1.3* | 1.3 ±1.1‡<br>4.1 ±0.9* | 1.7 ±1‡<br>4.4 ±1.5* | |
| | – | – | – | – | – | | – | – | – | – | – | | MVC10 TM (E/H)[a] | 4.2 ±2.2<br>3.2 ±1.8 | 4.4 ±3.1<br>3.0 ±1.3 | 4.3 ±1.7<br>3.3 ±1.8 | 4.8 ±2.6<br>3.6 ±2.1 | |
| | Conclusion: The injection of BTX-A into the masseter muscles reduced the number of bruxism events during sleep. | | | | | | | | | | | | | | | | | |

[a] *M* ±*SD*; [b] median (*Me*) (1st quartile–3rd quartile); * $p < 0.05$ (treatment group (TG) vs. control group (CG)); † $p < 0.05$ ($T_n$ vs. $T_{n-1}$: comparison between the measure made at a period n and the preceding period); ‡ $p < 0.05$ ($T_n$ vs. $T_0$: comparison between the measure made at a period n and the baseline); M – month; W – week; LM – left masseter; RM – right masseter; PRI – pain rate index; BF – bite force; MVC – maximal voluntary clenching; MVC20 – EMG amplitude exceeding 20% MVC; MVC10 – EMG amplitude exceeding 10% MVC; MM – masseter muscle; TM – temporalis muscle; E/H – events per hour.

### Sleep variables

Ali et al. reported that BTX-A and occlusal appliances effectively improve sleep quality in patients with bruxism who have been rehabilitated with a single-arch implant overdenture, as compared to the control group and the values registered prior to the injection.[25]

# Discussion

The present systematic review included 12 RCTs[3,8,9,19–27] that reported the effects of BTX-A on primary bruxism. Although BTX-A doses and injection sites varied widely between the studies, a promising conclusion was retained: BTX-A injection can be an effective management strategy for bruxism.

## Scope of the study

Bruxism is defined as repetitive masticatory muscle activity, which refers to the involuntary and non-functional grinding or clenching of teeth, occurring during sleep or while awake.[2,32] Bruxism is a behavior that may have several etiologies.[5,30] Central nervous system involvement in the pathophysiology of bruxism has been demonstrated, with a role of brain neurotransmitters,[39] including the serotoninergic pathway.[40] Bruxism affects the quality of sleep and muscle activity, causes pain in the teeth, temporomandibular joints and mastication muscles, as well as leads to tooth decay.[3] Despite the existence of various therapeutic modalities, including pharmacological and non-pharmacological approaches, none of these techniques has been fully effective for bruxism management.[21,36] Firstly, behavioral approaches necessitate that the patient be conscientious and observant. The latter is imperative for massage sessions.[14] Secondly, pharmacological treatment involves the administration of various drugs, such as clonazepam, clonidine, buspirone, clozapine, gabapentin, and amitriptyline.[41] Although these molecules are effective in reducing bruxism pain, many drug interactions in patients with other diseases contraindicate their use.[42] Particular care should be taken when prescribing these medications due to their potential adverse effects.[41] Moreover, de Baat et al. concluded that "there are insufficient evidence-based data to draw definite conclusions concerning medications attenuating sleep bruxism and/or awake bruxism".[41] Additionally, given that bruxism is a condition that causes phasic or tonic masticatory muscle activity, the use of splints has been explored as a means of mitigating muscle contractions.[29] A recent systematic review has concluded that there is an absence of sufficient evidence to prove the effectiveness of occlusal splints in the treatment of sleep bruxism, thus recommending a multidisciplinary approach encompassing the use of occlusal splints in conjunction with complementary therapies, such as massage therapy.[43] Over the last 2 decades, an increasing number of studies have explored the efficacy of BTX-A in mitigating nocturnal bruxism, with encouraging outcomes reported.[22] In addition, patients may exhibit a higher motivation for BTX-A injections compared to the nocturnal use of splints or repeated psychotherapy sessions.[14]

## Efficacy of BTX-A injection

The present review provides a summary of the current evidence regarding the efficacy of BTX-A in the targeted management of bruxism. The studies included in this systematic review reported a short-term assessment that consolidated the analgesic effect of BTX-A; only 2 studies reported a follow-up of more than 6 months after the end of the intervention.[20,25] However, of the 12 studies, only 6 reported a reduction of muscle activity after administering BTX-A.[3,8,9,21,22,24] Nevertheless, this reduction was observed in the masseter muscles, and not in the temporalis muscles, in 1 study.[24] Shim et al. found that the injection of BTX-A to the muscles reduced their activity in the temporalis muscles, but not in the masseters.[3] In addition, 3 studies[19,22,27] indicated that the intensity of muscle pain significantly decreased in patients with bruxism who received BTX-A. Finally, 1 study highlighted that patients with bruxism experienced enhanced sleep quality following the administration of BTX-A.[25]

The heterogeneity of the results may be attributed to methodological differences among the included studies, which precluded the possibility of conducting a meta-analysis to synthesize the data. Three remarks related to the differences regarding the BTX-A injection should be highlighted. First, concerns have been raised about the usefulness of injecting areas other than the masseter muscles. The masseters are the principal muscles responsible for both grinding and clenching movements observed during bruxism.[44] Secondly, the variability concerned doses which ranged from 20 MU[22] to 120 MU[27] and from 30 MU[21] to 80 MU[27] for masseter and temporalis muscles, respectively. In addition, the dosage of BTX-A products is influenced by their formulation.[45] For example, 1 MU of Botox (Allergan Aesthetics, Irvine, USA) is equivalent to 3–5 MU of Dysport® (Ipsen, London, UK).[46] Thirdly, the varied frequency of injections could possibly lead to different results. Ali et al. opted for repetitive injections every 3 months,[25] despite the fact that recent studies have demonstrated the longevity of toxin action for months after its single use.[47] In fact, the attenuation of symptoms was still significant 12 months later despite the unique intervention in 1 study.[20]

In this context, future studies should ascertain the optimum characteristics of BTX-A injections for individuals with bruxism. The authors of the present study recommend that injections be administered exclusively into the masseter muscles, with ultrasound assistance. The principal advantage of this technique is the quantification of muscle thickness.[30] In addition, musculoskeletal ultrasound is

a useful guidance for interventional procedures, has high spatial resolution, allows for serial evaluations, and is widely available.[48] A maximum dose of 100 MU of BTX-A is proposed per dental session.[49] Larger doses can cause side effects such as dysphagia, dysphonia, dry mouth, headache, and nervous atrophy.[50] In addition, sensitivity and mild cutaneous reactions at injection site are frequently observed.[50] Animal studies reported the possible systemic adverse effects after the injection of BTX-A, which include transient weakness, fatigue, nausea, and pruritus.[51] These effects are presumed to result from BTX-A diffusion into the bloodstream.[51] However, the studies included in this systematic review did not report any side effects. Therefore, the injection of BTX-A may be considered safe for the management of pain in patients with bruxism.[20,21]

## Biological mechanisms underlying the effects of BTX-A injection

Botulinum toxin, recognized as the most potent neurotoxin, is produced by *C. botulinum*.[20] The present systematic review revealed that BTX-A may be efficacious in managing symptoms of bruxism. Botulinum toxin acts as a muscle relaxant and provides an analgesic effect in neuromuscular disorders.[47] Additionally, it reduces bruxism pain through 2 mechanisms.[52,53] The first mechanism involves the antinociceptive effects of BTX-A. Studies have highlighted that BTX-A impedes the release of substance P and calcitonin gene-related peptide (CGRP).[52,53] Moreover, based on the examination of mechanical sensitivity of dural afferents, BTX-A has been shown to reduce the activity of mechanosensitive receptors and the transient receptor potential ankyrin 1 (TRPA1) channel. These processes elucidate the antinociceptive activity of BTX-A.[47] The second mechanism involves the masseter muscle, which is induced to a state of rest by BTX-A injection. The final mechanism involves the reduction of exocytotic release of acetylcholine among the motor nerve terminals by inhibiting the fusion of synaptic vesicles with the pre-synaptic membrane at the neuromuscular junction.[54] This mechanism stems from hydrolysis of synaptosomal-associated protein 25 (SNAP-25), a vital component within the vesicle docking system responsible for exocytosis.[54] It is an integral part of the SNARE (soluble N-ethylmaleimide-sensitive factor attachment protein receptor) complex, which plays a crucial role in facilitating the docking and fusion of synaptic vesicles.[55] Consequently, the source of muscle contraction is blocked.[47] Based on these 2 theories, the efficacy of BTX-A was tested in several pathologies that cause increased painful muscle tone, and it might be useful to manage bruxism and myofascial pain.[47,52] In addition, some studies indicated that the BTX-A effect persists for months after its single use.[47] The principal contributing factor is the BTX-A protease, which has the capacity to escape from cellular degradation mechanisms and survive in the cell cytoplasm.[47]

Despite the recent biological findings, no study has yet reported on the efficacy of BTX-A injections for reducing pain with a constant and long-lasting effect following a single injection. Patients were followed up for short periods, whereas bruxism is a chronic condition. Longer follow-up observations are necessary to determine the long-term effectiveness of BTX-A in treating bruxism. Therefore, upcoming controlled clinical studies should extend their observation periods to more than 4 months.

## Discussion of the methodology

The evaluation of treatment efficacy or preventive interventions is more rigorous through RCTs.[56] In effect, a low score of risk of bias was attributed to 83% of the included studies. As systematic reviews have the risk of being affected by bias at the level of individual studies, the validity of these studies is necessary to estimate when conducting this type of review.[57,58] Indeed, the true intervention effect may be over- or underestimated.[57]

The included studies employed a variety of tools and methods for bruxism diagnosis, a factor that can introduce discrepancies. None of the included studies mentioned the depth of the BTX-A injection.[3,19,20,22,27] The primary outcome assessment of patients in the included studies focused on bruxism characteristics, which were evaluated using various assessment tools. Initially, muscle pain was assessed and analyzed. To this end, 8 studies employed VAS, a unidimensional pain rating scale,[9,19–23,26,27] while only 1 study used the short-form McGill Pain Questionnaire,[21] a multidimensional questionnaire that provides a description of pain aspects in adults with chronic pain.[21,59]

In order to assess the impact of BTX-A injection on patients' quality of life, 3 studies considered sleep quality as a secondary outcome and used ESS and/or PSQI for evaluation.[21,25,27] Although ESS is a valid tool commonly used to measure sleepiness, it is important to consider its limitations in order to avoid bias.[31] Recent studies have demonstrated the clinical application of PSQI and its efficacy in sleep measurement.[60]

## Limitations

The current systematic review is subject to 4 limitations. The first limitation concerns the number of patients included in the studies, which varied between 12 and 50. In fact, only 3 studies reported on the method of sample size calculation.[19,22,25] While the results of studies are promising, the quality level of the evidence is not high enough to provide explicit guidelines for bruxism. Consequently, upcoming studies should include a sufficient sample size to ensure the representativeness of the studied population and to minimize the risk of bias.[61] The second limitation is related to the assessment of bruxism characteristics. Only 3 studies evaluated the quality of sleep,[21,25,27] while the

muscle activity was assessed in 6 studies.[3,8,9,22–24] Future works should formulate common criteria for the assessment of bruxism to ensure the attainment of conclusive results. Thirdly, the included RCTs explored events related to pain and bruxism only. Subsequent studies should also evaluate the alleviation of bruxism complications after BTX-A injections, such as tooth wear.[7] Fourthly, concerning control groups, it would be preferable to opt for traditional therapies rather than placebo injections. In fact, this comparison allows for widening the gap between the 2 therapeutic approaches and, thus, emphasizes the effect of BTX-A injections. From an ethical standpoint, even if control patients are engaged in research activities, it is advisable to recommend a standard therapy to them in order to alleviate their pain, even if only minimally.

# Conclusions

This study investigated the impact of BTX-A injections on patients diagnosed with bruxism. A comprehensive review of the relevant literature revealed that BTX-A may be effective in the treatment of bruxism. Therefore, low doses of BTX-A may be an alternative treatment option for patients with bruxism, especially in the absence of well-established treatments. Further prospective and long-term follow-up studies, taking into account the potential need for repeated injections, should be conducted.

## Trial registration

The protocol of the review was registered with PROSPERO (identification No. CRD42023472755).

## Ethics approval and consent to participate

Not applicable.

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.


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Review

# Clear aligners: A network and bibliometric analysis of 50 pivotal articles

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D – writing the article; E – critical revision of the article; F – final approval of the article

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## Abstract

**Background.** A bibliometric analysis uses statistical and mathematical methods to analyze the published literature, extracting meaningful information that helps to identify trends, assess research impact, and visualize key data patterns through graphs and trendlines.

**Objectives.** The aim of the study was to list the top 50 papers on clear aligners, evaluate them critically and apply a bibliometric analysis to investigate the achievements and prospects in this field of study.

**Material and methods.** A computerized database search (Scopus) was conducted on September 24, 2023, to find articles on clear aligners published in the scientific literature between 2013 and 2023. The top 50 cited manuscripts were chosen. Author-based characteristics were obtained from the Scopus database. The dataset from Clarivate™ InCites Benchmarking & Analytics™ and Journal Citation Reports (JCR) was used to determine parameters based on journals and articles. To improve the visual analysis, the keywords were collected systematically from the chosen articles.

**Results.** The database search produced a directory of the 50 most often cited articles out of 1,405 papers. Of the 50 most frequently cited works on clear aligners, 35 (70.0%) were original research studies and 15 (30.0%) were reviews. The keyword-network analysis indicated 'removable orthodontic appliance' as the most important and repetitive keyword.

**Conclusions.** The results of the present bibliometric study indicated that clear aligner therapy (CAT)-related papers received increasing citations. The study determined the most influential articles by highlighting their authors and the journals in which the papers were published.

**Keywords:** bibliometric analysis, orthodontics, network analysis, clear aligner, clear aligner treatment

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## Highlights

- The number of research papers on dental aligners and their citations have been steadily increasing year over year.
- Advancement in clear aligner therapy (CAT) relies heavily on well-designed RCTs, yet these make up only a small percentage of the top 50 most cited CAT studies.
- Many studies, particularly in vitro and laboratory-based studies, contribute only slightly to the scientific evidence.
- Three major journals account for 54% of all CAT publications.
- According to the keyword co-occurrence network (KCN), the primary research areas with regard to CAT are biomechanics, the physical characteristics of materials, the predictability of tooth movements, and the impact of CAT on periodontal health.

# Introduction

Since Dr. H. Kesling developed a set of thermoplastic tooth positioners to gradually achieve teeth alignment in 1946, clear aligners have been used in orthodontics.

The introduction of new materials, dental attachments, tooth movement staging, interproximal enamel reduction, and the use of inter-arch elastics to handle several kinds of malocclusion have all contributed to a significant change in the handling over the last 15 years.[1–6]

Nowadays, clear aligner therapy (CAT) is an effective alternative to the conventional fixed appliances (FA) in orthodontics because of rapid advancement in technology and computer-aided design and manufacturing (CAD/CAM).[7–9]

Adult patients prefer clear aligners for their comfort and esthetics. This is why the demand for aligners has greatly increased. All over the world, there are numerous brands of clear aligners, each with distinctive features and efficacy.[3,10–12]

As a consequence of the technological progress, there have been a lot of research projects and publications regarding clear aligners, which may make it more difficult for researchers to obtain accurate data.[13,14]

Citations indicate a relationship between authors, research teams, study subjects, or nations. They are a tool for measuring the influence and frequently the quality of a publication in a certain field. Furthermore, mapping bibliometric networks with a graphical analysis can offer a clear and thorough summary of a sizable dataset.[15]

A bibliometric analysis is a mathematical and statistical method of quantitative measurement to assess the quality of publications within a scientific research area. Several details on authors, journals and articles might be highlighted through this process; moreover, a visual network analysis might be provided for the keywords of these articles.[16]

As far as we know, network and bibliometric analyses have been used in different dentistry fields, although surveys on clear aligners have not been carried out recently.[15,17]

Thus, the goal of the present study was to carry out a bibliometric analysis of the 50 most often cited articles on clear aligners to allow a clearer view and to improve research on this topic.

# Material and methods

## Search strategy

On September 24, 2023, two authors independently conducted a database search to find papers on clear aligners published in the scientific literature considering the last 10 years (from 2013 to 2023), as shown in Fig. 1.

The keywords used in the Scopus database (Elsevier, Amsterdam, the Netherlands) for the advanced search were: ("orthodontic" OR "orthodontic treatment" OR "orthognathic") AND ("clear aligner" OR "attachments" OR "3d printed aligner" OR "digital set up" OR "digital planning" OR "customized aligner" OR " thermoforming aligner" OR "digital models" OR "clear aligner treatment" OR "clear aligner therapy" OR "invisible orthodontics"). Scopus was chosen to narrow the publication time of papers and locate all possibly relevant research, independent of the kind of publishing. As reported in the literature, Scopus allows access to articles in all fields.[18] The database is easy to search and covers more journals than PubMed® and the Web of Science, adding more precise information regarding citations and authors.

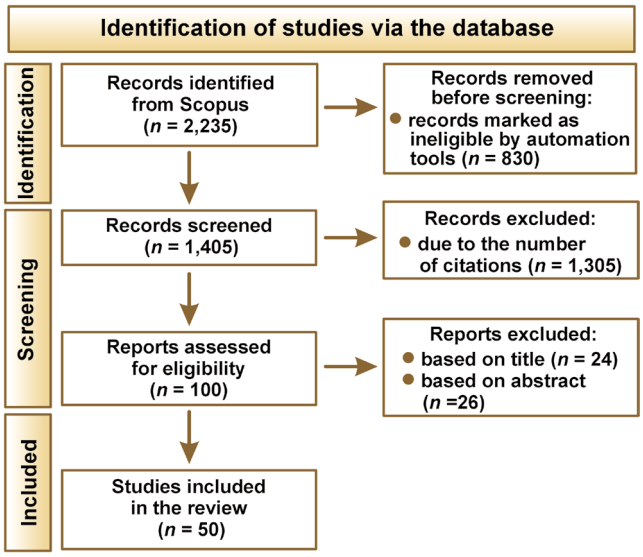


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the study

Each author downloaded the complete records of the publications retrieved from Scopus into a Microsoft Excel spreadsheet (Microsoft Corp., Redmond, USA). At this stage, the papers were independently screened by 2 reviewers (A.F and F.D.) according to titles and abstracts to determine the eligibility of the studies, excluding any papers that did not directly relate to clear aligners. In case of disagreement, a third reviewer contributed to reaching a consensus (V.G.). The 2 authors then carried out full-text screening. All the articles not concerning clear aligners were excluded. Therefore, out of the remaining papers, only the 50 papers on clear aligners most often cited in the literature were included in the bibliometric analysis.

The sample comprised papers on all types of clear aligners, regardless of the brand.

## Data extraction

### Article-based bibliometric parameters

The following article-based bibliometric data was extracted using the Scopus database: title; author(s); journal; keywords; publication year; study design; total number of citations; and the mean number of citations/year.

### Journal-based bibliometric parameters

The journal-based bibliometric data listed below was gathered using Clarivate™ InCites Benchmarking & Analytics™ and Journal Citation Reports (JCR): the 2022 Journal Impact Factor (JIF), an indicator of the importance of a journal, derived from the data indexed in the Web of Science Core Collection (if available); quartile with regard to the category "Dentistry, Oral Surgery & Medicine"; Eigenfactor Score (EF), measuring the number of times the articles from the journal published in the past 5 years have been cited in the JCR year; Normalized Eigenfactor Score (nEF), using journal year rescaling; Article Influence Score (AI), which normalizes EF by determining the average influence of the journal's articles over the first 5 years after publication; 5-Year Journal Impact Factor (5-JIF), considered as the average number of times the articles from the journal published in the past 5 years have been cited in the JCR year; and Immediacy Index, the count of citations in the current year to the journal that reference content in this same year.

### Author-based bibliometric parameters

With the help of the Scopus database, the following author-based bibliometric parameters were extracted: name; affiliation; country; H-index; number of articles among the top 50 articles about clear aligners; and number of citations of the papers which made up the top 50 articles about clear aligners.

# Results

## Articles

From the research query, 2,235 papers were found. With regard to the years 2013–2023, 1,405 papers were found through applying a limiting filter; they were collected from the most cited to the least cited ones.

Table 1 details the top 50 articles on clear aligners.[1,2,4–10,13,14,19–57]

Of the 50 articles, 24 were about Invisalign® (Align Technology, San Jose, USA), while the remaining 26 were about unspecified clear aligners.

A total of 35 (70%) articles were original articles, and the remaining 15 (30%) were reviews. Among the 35 original papers, 14 were prospective studies, with 2 RCTs (28%), 12 were retrospective studies (24%), 6 were in vitro studies (12%), 2 were finite element analysis studies (4%), and 1 study had a cross-sectional design (2%). Among the reviews, 7 were systematic reviews (14%), 6 were reviews (12%), and only 2 were meta-analyses (4%). Further details are shown in Fig. 2.

The oldest article was from 2013 and the most recent papers were from 2021. The year 2020 was the publication year for as many as 11 papers, whereas 2015 was the year with the greatest number of citations (Fig. 3). The most often cited paper about clear aligners has collected 289 citations and was published by *Angle Orthodontist* in 2015; it is a systematic review titled: "Efficacy of clear aligners in controlling orthodontic tooth movement: A systematic review".[4] The second most often cited article is titled "Treatment outcome and efficacy of an aligner technique – regarding incisor torque, premolar derotation, and molar distalization"; it is a retrospective study published in 2014 by *BMC Oral Health*, which has been cited 144 times.[14] The third article is a retrospective study reporting 113 citations; it is titled "Forces and moments generated by removable thermoplastic aligners: Incisor

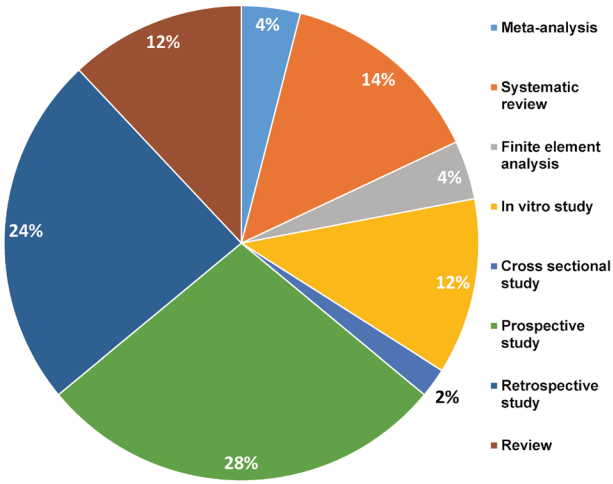


Fig. 2. Study design distribution for the 50 most cited articles on clear aligner therapy (CAT)

**Table 1.** The 50 most cited articles on clear aligners therapy (CAT)

| Ranking | Title | Author(s) | Journal | Publication year | Study design | Total number of citations | Mean number of citations/year |
|---|---|---|---|---|---|---|---|
| 1 | Efficacy of clear aligners in controlling orthodontic tooth movement: A systematic review[4] | Rossini G, Parrini S, Castroflorio T, Deregibus A, Debernardi CL | Angle Orthodontist | 2015 | systematic review | 289 | 32.1 |
| 2 | Treatment outcome and efficacy of an aligner technique – regarding incisor torque, premolar derotation and molar distalization[14] | Simon M, Keilig L, Schwarze J, Jung BA, Bourauel C | BMC Oral Health | 2014 | retrospective study | 144 | 14.4 |
| 3 | Forces and moments generated by removable thermoplastic aligners: Incisor torque, premolar derotation, and molar distalization[13] | Simon M, Keilig L, Schwarze J, Jung BA, Bourauel C | American Journal of Orthodontics and Dentofacial Orthopedics | 2014 | retrospective study | 113 | 11.3 |
| 4 | Clear aligners in orthodontic treatment[19] | Weir T | Australian Dental Journal | 2017 | review | 109 | 15.6 |
| 5 | Has Invisalign improved? A prospective follow-up study on the efficacy of tooth movement with Invisalign[7] | Haouili N, Kravitz ND, Vaid NR, Ferguson DJ, Makki L | American Journal of Orthodontics and Dentofacial Orthopedics | 2020 | prospective study | 99 | 24.8 |
| 6 | Efficiency, effectiveness and treatment stability of clear aligners: A systematic review and meta-analysis[8] | Zheng M, Liu R, Ni Z, Yu Z | Orthodontics and Craniofacial Research | 2017 | systematic review and meta-analysis | 90 | 12.9 |
| 7 | Initial force systems during bodily tooth movement with plastic aligners and composite attachments: A three-dimensional finite element analysis[20] | Gomez JP, Peña FM, Martínez V, Giraldo DC, Cardona CI | Angle Orthodontist | 2015 | finite element analysis | 88 | 9.7 |
| 8 | Periodontal health during clear aligners treatment: A systematic review[21] | Rossini G, Parrini S, Castroflorio T, Deregibus A, Debernardi CL | European Journal of Orthodontics | 2015 | systematic review | 84 | 9.3 |
| 9 | Effectiveness of clear aligner therapy for orthodontic treatment: A systematic review[9] | Robertson L, Kaur H, Fernandes Fagundes NC, Romanyk D, Major P, Mir CF | Orthodontics and Craniofacial Research | 2020 | systematic review | 77 | 19.3 |
| 10 | A comparison of treatment effectiveness between clear aligner and fixed appliance therapies[23] | Ke Y, Zhu Y, Zhu M | BMC Oral Health | 2019 | systematic review | 74 | 14.8 |
| 11 | Accuracy of clear aligners: A retrospective study of patients who needed refinement[22] | Charalampakis O, Iliadi A, Ueno H, Oliver DR, Kim KB | American Journal of Orthodontics and Dentofacial Orthopedics | 2018 | retrospective study | 74 | 12.3 |
| 12 | Analysis of pain level in cases treated with Invisalign aligner: Comparison with fixed edgewise appliance therapy[24] | Fujiyama K, Honjo T, Suzuki M, Matsuoka S, Deguchi T | Progress in Orthodontics | 2014 | prospective study | 71 | 7.1 |
| 13 | The predictability of transverse changes with Invisalign[25] | Houle JP, Piedade L, Todescan R Jr., Pinheiro FH | Angle Orthodontist | 2017 | retrospective study | 70 | 10.0 |
| 14 | A systematic review of the accuracy and efficiency of dental movements with Invisalign®[10] | Galan-Lopez L, Barcia-Gonzalez J, Plasencia E | Korean Journal of Orthodontics | 2019 | systematic review | 66 | 13.2 |
| 15 | Periodontal health status in patients treated with the Invisalign® system and fixed orthodontic appliances: A 3 months clinical and microbiological evaluation[26] | Levrini L, Mangano A, Montanari P, Margherini S, Caprioglio A, Abbate GM | European Journal of Dentistry | 2015 | prospective study | 63 | 7.0 |
| 16 | Mechanical and geometric properties of thermoformed and 3D printed clear dental aligners[27] | Jindal P, Juneja M, Siena FL, Bajaj D, Breedon P | American Journal of Orthodontics and Dentofacial Orthopedics | 2019 | in vitro study | 62 | 12.4 |
| 17 | Periodontal health during orthodontic treatment with clear aligners and fixed appliances: A meta-analysis[28] | Jiang Q, Li J, Mei L, Du J, Levrini L, Abbate GM, Li H | Journal of the American Dental Association | 2018 | meta-analysis | 57 | 9.5 |

| Ranking | Title | Author(s) | Journal | Publication year | Study design | Total number of citations | Mean number of citations/year |
|---|---|---|---|---|---|---|---|
| 18 | Effects of variable attachment shapes and aligner material on aligner retention[29] | Dasy H, Dasy A, Asatrian G, Rózsa N, Lee HF, Kwak JH | Angle Orthodontist | 2015 | in vitro study | 56 | 6.2 |
| 19 | Clear aligners generations and orthodontic tooth movement[30] | Hennessy J, Al-Awadhi EA | Journal of Orthodontics | 2016 | prospective study | 55 | 6.8 |
| 20 | Variables affecting orthodontic tooth movement with clear aligners[31] | Chisari JR, McGorray SP, Nair M, Wheeler TT | American Journal of Orthodontics and Dentofacial Orthopedics | 2014 | prospective study | 50 | 5.0 |
| 21 | Comparison of achieved and predicted tooth movement of maxillary first molars and central incisors: First premolar extraction treatment with Invisalign[32] | Dai FF, Xu TM, Shu G | Angle Orthodontist | 2019 | retrospective study | 47 | 9.4 |
| 22 | Salivary concentrations of Streptococcus mutans and Lactobacilli during an orthodontic treatment. An observational study comparing fixed and removable orthodontic appliances[33] | Mummolo S, Tieri M, Nota A, Caruso S, Darvizeh A, Albani F, Gatto R, Marzo G, Marchetti E, Quinzi V, Tecco S | Clinical and Experimental Dental Research | 2020 | prospective study | 46 | 11.5 |
| 23 | Salivary levels of Streptococcus mutans and Lactobacilli and other salivary indices in patients wearing clear aligners versus fixed orthodontic appliances: An observational study[34] | Mummolo S, Nota A, Albani F, Marchetti E, Gatto R, Marzo G, Quinzi V, Tecco S | PLoS One | 2020 | prospective study | 46 | 11.5 |
| 24 | Accuracy of interproximal enamel reduction during clear aligner treatment[2] | De Felice ME, Nucci L, Fiori A, Flores-Mir C, Perillo L, Grassia V | Progress in Orthodontics | 2020 | retrospective study | 45 | 11.3 |
| 25 | Impact of molar teeth distalization with clear aligners on occlusal vertical dimension: A retrospective study[35] | Caruso S, Nota A, Ehsani S, Maddalone E, Ojima K, Tecco S | BMC Oral Health | 2019 | retrospective study | 44 | 8.8 |
| 26 | The oral microbiota changes in orthodontic patients and effects on oral health: An overview[36] | Contaldo M, Lucchese A, Lajolo C, Rupe C, Di Stasio D, Romano A, Petruzzi M, Serpico R | Journal of Clinical Medicine | 2021 | review | 39 | 13.0 |
| 27 | Clear aligner orthodontic therapy of rotated mandibular round-shaped teeth: A finite element study[37] | Cortona A, Rossini G, Parrini S, Deregibus A, Castroflorio T | Angle Orthodontist | 2020 | finite element analysis | 39 | 9.8 |
| 28 | Design of the Invisalign system performance[38] | Morton J, Derakhshan M, Kaza S, Li C | Seminars in Orthodontics | 2017 | review | 39 | 5.8 |
| 29 | Prevalence and severity of apical root resorption during orthodontic treatment with clear aligners and fixed appliances: A cone beam computed tomography study[39] | Li Y, Deng S, Mei L, Li Z, Zhang X, Yang C, Li Y | Progress in Orthodontics | 2020 | retrospective cohort study | 38 | 9.5 |
| 30 | Clear aligner treatment: Different perspectives between orthodontists and general dentists[1] | d'Apuzzo F, Perillo L, Carrico CK, Castroflorio T, Grassia V, Lindauer SJ, Shroff B | Progress in Orthodontics | 2019 | cross-sectional study | 38 | 7.6 |
| 31 | Which orthodontic appliance is best for oral hygiene? A randomized clinical trial[40] | Chhibber A, Agarwal S, Yadav S, Kuo CL, Upadhyay M | American Journal of Orthodontics and Dentofacial Orthopedics | 2018 | prospective study (RCT)l | 37 | 6.2 |
| 32 | YouTube as a source of information about orthodontic clear aligners[41] | Ustdal G, Guney AU | Angle Orthodontist | 2020 | review | 36 | 9.0 |
| 33 | Efficiency of upper arch expansion with the Invisalign system[42] | Zhou N, Guo J | Angle Orthodontist | 2020 | retrospective study | 36 | 9.0 |
| 34 | Movement of anterior teeth using clear aligners: A three-dimensional, retrospective evaluation[44] | Tepedino M, Paoloni V, Cozza P, Chimenti C | Progress in Orthodontics | 2018 | retrospective study | 35 | 5.8 |

| Ranking | Title | Author(s) | Journal | Publication year | Study design | Total number of citations | Mean number of citations/year |
|---|---|---|---|---|---|---|---|
| 35 | Root resorption during orthodontic treatment with Invisalign®: A radiometric study[43] | Gay G, Ravera S, Castroflorio T, Garino F, Rossini G, Parrini S, Cugliari G, Deregibus A | Progress in Orthodontics | 2017 | prospective study | 35 | 5.0 |
| 36 | Direct 3D printing of clear orthodontic aligners: Current state and future possibilities[46] | Tartaglia GM, Mapelli A, Maspero C, Santaniello T, Serafin M, Farronato M, Caprioglio A | Materials | 2021 | review | 34 | 11.3 |
| 37 | Pain level between clear aligners and fixed appliances: A systematic review[47] | Cardoso PC, Espinosa DG, Mecenas P, Flores-Mir C, Normando D | Progress in Orthodontics | 2020 | systematic review | 34 | 8.5 |
| 38 | Colour stabilities of three types of orthodontic clear aligners exposed to staining agents[45] | Liu CL, Sun WT, Liao W, Lu WX, Li QW, Jeong Y, Liu J, Zhao ZH | International Journal of Oral Science | 2016 | in vitro study | 34 | 4.3 |
| 39 | Forces and moments delivered by PET-G aligners to an upper central incisor for labial and palatal translation[48] | Elkholy F, Panchaphongsaphak T, Kilic F, Schmidt F, Lapatki BG | Journal of Orofacial Orthopedics | 2015 | in vitro study | 34 | 3.8 |
| 40 | Thickness of orthodontic clear aligners after thermoforming and after 10 days of intraoral exposure: A prospective clinical study[49] | Bucci R, Rongo R, Levatè C, Michelotti A, Barone S, Razionale AV, D'Antò V | Progress in Orthodontics | 2019 | prospective study | 33 | 6.6 |
| 41 | In vitro cytotoxicity of different thermoplastic materials for clear aligners[50] | Martina S, Rongo R, Bucci R, Razionale AV, Valletta R, D'Antò V | Angle Orthodontist | 2019 | in vitro study | 33 | 6.6 |
| 42 | Invisible orthodontics part 1: Invisalign[51] | Malik OH, McMullin A, Waring DT | Dental Update | 2013 | review | 33 | 3.0 |
| 43 | Comparison of pain perception, anxiety, and impacts on oral health-related quality of life between patients receiving clear aligners and fixed appliances during the initial stage of orthodontic treatment[52] | Gao M, Yan X, Zhao R, Shan Y, Chen Y, Jian F, Long H, Lai W | European Journal of Orthodontics | 2021 | prospective study | 31 | 10.3 |
| 44 | Outcomes of clear aligner treatment with and without Dental Monitoring: A retrospective cohort study[55] | Hansa I, Katyal V, Ferguson DJ, Vaid N | American Journal of Orthodontics and Dentofacial Orthopedics | 2021 | retrospective study | 30 | 10.0 |
| 45 | Incidence of white spot lesions among patients treated with clear aligners and traditional braces[53] | Buschang PH, Chastain D, Keylor CL, Crosby D, Julien KC | Angle Orthodontist | 2019 | prospective study | 30 | 6.0 |
| 46 | Changes in roughness and mechanical properties of Invisalign® appliances after one- and two-weeks use[54] | Papadopoulou AK, Cantele A, Polychronis G, Zinelis S, Eliades T | Materials | 2019 | prospective study | 30 | 6.0 |
| 47 | Class II malocclusion correction with Invisalign: Is it possible?[57] | Patterson BD, Foley PF, Ueno H, Mason SA, Schneider PP, Kim KB | American Journal of Orthodontics and Dentofacial Orthopedics | 2021 | retrospective study | 29 | 9.6 |
| 48 | Forces and moments generated by aligner-type appliances for orthodontic tooth movement: A systematic review and meta-analysis[6] | Iliadi A, Koletsi D, Eliades T | Orthodontics and Craniofacial Research | 2019 | systematic review | 29 | 5.8 |
| 49 | A randomized clinical trial comparing mandibular incisor proclination produced by fixed labial appliances and clear aligners[56] | Hennessy J, Garvey T, Al-Awadhi EA | Angle Orthodontist | 2016 | prospective study (RCT) | 29 | 3.6 |
| 50 | Mechanical properties of thermoplastic polymers for aligner manufacturing: In vitro study[5] | Tamburrino F, D'Antò V, Bucci R, Alessandri-Bonetti G, Barone S, Razionale AV | Dentistry Journal | 2020 | in vitro study | 28 | 7.0 |

RCT – randomized controlled trial.

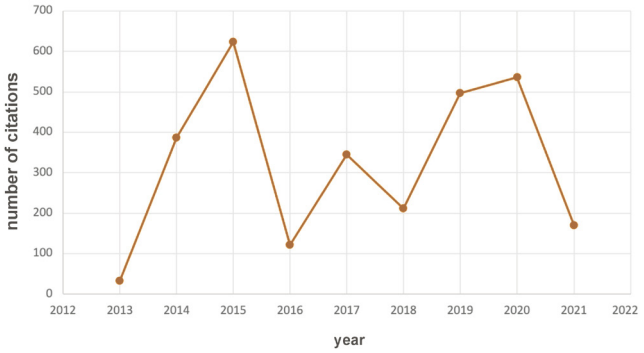


Fig. 3. Total citations per year (2013–2021)

torque, premolar derotation, and molar distalization" and was published by *American Journal of Orthodontics and Dentofacial Orthopedics* in 2014.[13]

Further details are shown in Table 1.

## Number of citations

The 50 articles obtained a total of 2,862 citations. As shown in Fig. 3, 2015 was the year with the greatest number of citations, when an important systematic review headed "Efficacy of clear aligners in controlling orthodontic tooth movement: A systematic review" was published.[4] The article with the greatest average number of citations per year (32.1) is the first on the list, published in 2015 and it is a systematic review.[4] However, the article titled "Has Invisalign improved? A prospective follow-up study on the efficacy of tooth movement with Invisalign" was published in 2020 and had a mean of 24.75 citations per year.[7]

## Journals

Table 2 shows that the top 50 referenced papers on clear aligners were published in 20 different scientific journals. *Angle Orthodontist* had the most citations of any scientific journal ($n$ = 753; 26.31% of total citations). This journal also published the most manuscripts from among the 50 most referenced papers ($n$ = 11; 22%).

Furthermore, Table 2 illustrates the range of the 2021 JIF from 24.9 (*International Journal of Oral Science*) to 1.0 (*Australian Dental Journal*) for the scientific journals which published the 50 most often cited articles on clear aligners in the Web of Science, while the 5-JIF varied between 13.7 (*International Journal of Oral Science*) and 1.16 (*Seminars in Orthodontics*). Out of the 20 scientific journals, 80% were in the category "Dentistry, Oral Surgery & Medicine", according to the JCR dataset.

Further details are shown in Table 2.

Table 2. Journals which published the 50 most cited articles on clear aligner therapy (CAT) ranked in descending order according to the total number of citations

| Ranking | Journal | JIF (2021) | Quartile | EF | nEF | AI | 5-JIF | Immediacy Index | Number of manuscripts | Number of citations |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Angle Orthodontist | 2.7 | Q2 | 0.00401 | 0.86338 | NA | 3.212 | 0.683 | 11 | 753 |
| 2 | American Journal of Orthodontics and Dentofacial Orthopedics | 2.7 | Q2 | 0.00630 | 1.35622 | 0.742 | 3.345 | 0.579 | 8 | 494 |
| 3 | Progress in Orthodontics | 3.2 | Q2 | 0.00177 | 0.38166 | 0.866 | 3.782 | 0.220 | 8 | 329 |
| 4 | BMC Oral Health | 3.7 | Q3 | 0.00831 | 178.663 | NA | 3.916 | 0.419 | 3 | 262 |
| 5 | Orthodontics and Craniofacial Research | 3.0 | Q2 | 0.00121 | 0.14161 | NA | 1.954 | 0.433 | 3 | 196 |
| 6 | European Journal of Orthodontics | 3.1 | Q2 | 0.00314 | 0.67639 | 0.799 | 3.166 | 1.000 | 2 | 115 |
| 7 | Australian Dental Journal | 1.0 | Q3 | 0.00265 | 0.30928 | NA | 1.731 | 0.269 | 1 | 109 |
| 8 | Korean Journal of Orthodontics | 1.4 | Q4 | 0.00109 | 0.23432 | 0.544 | 2.043 | 0.415 | 1 | 66 |
| 9 | Materials | 3.7 | Q3 | 0.07687 | 16.52407 | 0.541 | 4.042 | 0.835 | 2 | 64 |
| 10 | European Journal of Dentistry | 3.1 | Q2 | 0.00314 | 0.67639 | 0.799 | 3.166 | 1.000 | 1 | 63 |
| 11 | Journal of the American Dental Association | 3.7 | Q2 | 0.00451 | 0.97067 | 1.064 | 4.065 | 1.556 | 1 | 57 |
| 12 | Journal of Orthodontics | NA | NA | 0.00084 | 0.18110 | 0.442 | NA | NA | 1 | 55 |
| 13 | Clinical and Experimental Dental Research | NA | NA | 0.00096 | 0.20750 | 0.330 | NA | NA | 1 | 46 |
| 14 | PLoS One | 3.8 | NA | 0.84726 | 182.12875 | 0.974 | 4.069 | 0.801 | 1 | 46 |
| 15 | Journal of Clinical Medicine | 5.0 | NA | 0.07171 | 15.41548 | 1.084 | 5.098 | 0.792 | 1 | 39 |
| 16 | Seminars in Orthodontics | 1.3 | Q4 | 0.00047 | 0.10135 | 0.311 | 1.156 | 1.250 | 1 | 39 |
| 17 | International Journal of Oral Science | 24.9 | Q1 | 0.00411 | 0.88483 | 2.629 | 13.721 | 0.952 | 1 | 34 |
| 18 | Journal of Orofacial Orthopedics | 2.3 | Q3 | 0.00098 | 0.21107 | 0.477 | 2.249 | 0.125 | 1 | 34 |
| 19 | Dental Update | – | – | – | – | – | – | – | 1 | 33 |
| 20 | Dentistry Journal | NA | Q2 | 0.0017 | 0.35702 | NA | NA | NA | 1 | 28 |

JIF – Journal Impact Factor; EF – Eigenfactor Score; nEF – Normalized Eigenfactor Score; AI – Article Influence Score; 5-JIF – 5-Year Journal Impact Factor. NA – data not available. Quartiles refer to the category "Dentistry, Oral Surgery & Medicine" in the Web of Science.

## Authors, institutions and countries

To identify the most productive authors on the topic, information about all authors (201) was downloaded from Scopus and imported into an Excel file. Among the most productive authors, G. Rossini, M. Simon, J. Hennessy, and S. Mummolo were listed as the first authors twice.

## Keywords network analysis

Based on the cooccurrence map of keywords, concepts like "clear aligners", "orthodontic tooth movement" and "removable orthodontic appliance" occupied the larger and centrally positioned nodes (Fig. 4).

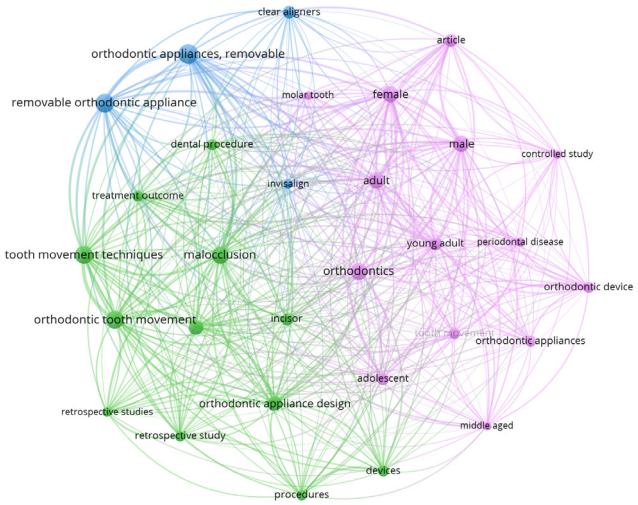


Fig. 4. Keyword co-occurrence network (KCN)

# Discussion

This bibliometric analysis aimed to update the previous analysis,[15] expanding the research to clear aligners in general. A sample size of 50 articles was chosen following other comparable publications[15] to obtain an adequate amount of information and to create a graph with significant trendline data. The last 10 years have been chosen to analyze the most recent articles of greater interest for clinicians and researchers.

It is worth noting that the most cited type of article is a systematic review, a product that is at the apex of scientific evidence, and is therefore a reference for researchers and clinicians. The same type of article in the previous bibliometric analysis reached the 3rd rank with 83 citations.[15] The particular systematic review sums up the literature on the efficacy of clear aligners.[4] At the 2nd and 3rd place, there are two retrospective clinical studies.[13,14] They focus on the predictability of critical movements with aligners.

It is important to observe that the 50 most cited articles do not include articles of great scientific interest, which, being recent, still have to reach many citations to fall into the first 50.[58–61] The year 2015 was the year with the greatest number of citations, although 2020 featured a high number of citations as well, almost equal to 2015, despite a short time span between 2020 and 2023, which was probably related to the high number of articles published. The results show that the pandemic period was very advantageous for scientific production.

Time may affect the citation ranking of articles. Thus, at the top of the list may be the oldest studies, while high-quality original articles published in recent years may be underrated. For this reason, the average number of citations per year was calculated.

There is a wide range of journals in which the articles were published (20). This shows that no journal has developed a specificity in the subject. On the one hand, the dispersion of scientific production is a limitation; on the other hand, it creates diversification in the advertising field.

It is challenging to figure out the function of each author who contributed to the top 50 publications mentioned, which showed an average of more than 4 authors per piece. We evaluated each author's overall number of citations, the total number of papers they had published, their standing in the author list, and the connection between

Table 3. Ten authors contributing to the 50 most cited articles on clear aligner therapy (CAT)

| Ranking | Author | Affiliation | Country | H-index | Number of articles | First author | Co-author | Last author | Citations |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Castroflorio T | University of Turin | Italy | 26 | 5 | 0 | 4 | 1 | 39 |
| 2 | Jung BA | University Hospital Freiburg | Germany | 13 | 2 | 0 | 2 | 0 | 38 |
| 3 | Deregibus A | University of Turin | Italy | 24 | 4 | 0 | 3 | 1 | 35 |
| 4 | Rossini G | University of Turin | Italy | 15 | 4 | 2 | 2 | 0 | 34 |
| 5 | Parrini S | University of Turin | Italy | 10 | 4 | 0 | 4 | 0 | 33 |
| 6 | Debernardi CL | University of Turin | Italy | 18 | 2 | 0 | 0 | 2 | 32 |
| 7 | Bourauel C | University of Bonn | Germany | 39 | 2 | 0 | 0 | 2 | 29 |
| 8 | Kravitz ND | private practice | USA | 17 | 1 | 0 | 1 | 0 | 26 |
| 9 | Wheeler TT | University of Florida | USA | 24 | 1 | 0 | 0 | 1 | 21 |
| 10 | Keilig L | University of Bonn | Germany | 22 | 2 | 0 | 2 | 0 | 19 |

productivity and the researcher's level of expertise. The bibliometric indicator under consideration is the H-index, which measures the effectiveness of a scientist's studies while considering the publication volume and visibility.

Nearly all of the most often quoted pieces were from Central Europe, but there were also some from the USA and China. In most cases, citations come from institutions that are located in the author's country of origin. The top 2 institutions with the most citations are both in Central Europe – in Germany (University Hospital Freiburg) and Italy (University of Turin). Neal D. Kravitz is renowned in the USA for garnering numerous awards from his private practice. Half of the top 10 authors on the list are Italian authors who are affiliated with the University of Turin.

Table 3 provides more information.

A keyword co-occurrence network (KCN) is a useful tool for mapping to investigate the connections between keywords in the literature, and comprehend the knowledge structure and components of a scientific area.[16,17] Keywords are a set of terms that allow correct indexing in computerized databases, facilitating research in the scientific literature.

The required minimum quantity of keyword occurrences in the analysis dataset was set at 7. The occurrences of each keyword and the overall strength of the link were tabulated. The keywords were mapped using VOSviewer (Centre for Science and Technology Studies, Leiden University, the Netherlands). The nodes of the generated network stand for keywords, while their edges indicate keyword associations. Similar keywords were grouped in clusters of the same color. The sizes of the nodes indicate how frequently the terms occur. The degree of connection between the nodes is indicated by the thickness and length of the lines.

Keywords like "clear aligners", "orthodontic tooth movement" and "removable orthodontic appliance" occupied the larger and centrally positioned nodes. The keyword "removable orthodontic appliance" had significant weight in the keyword map. This orthodontic appliance has become widespread among adult patients, as it is comfortable, esthetic and allows more practical oral hygiene. This is why the keyword "periodontal disease" also carries significant weight. The term "orthodontic tooth movement" was mentioned in multiple research investigations that looked into the predictability of particular results. The term "clear aligner" was used frequently, indicating that there is increasing interest in testing this kind of device, while the presence of the term "Invisalign" was reduced, since the selected articles concerned treatment with any type of clear aligners (Fig. 4).

## Limitations

The main issue is that the bibliometric analysis is very variable over time. The results may change, depending on the month.

The articles have been sorted in descending order according to the number of citations, but this parameter is not sufficient to assess the value of an article.

Citations are affected by time, so high-quality but more recent articles may be underreported.

Also, there may be a bias due to self-citations.

Furthermore, another important limitation is the challenge of evaluating researchers' contributions accurately. It would be essential to evaluate the actual contribution.

# Conclusions

The results of the present bibliometric study indicated that CAT-related papers received increasing citations. The study determined the most influential articles by highlighting their authors and the journals in which the papers were published.

## Ethics approval and consent to participate

Not applicable.

## Data availability

The datasets supporting the findings of the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.


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Review

# Mechanism and clinical aspects of sodium hypochlorite accidents: A narrative review

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## Abstract

Sodium hypochlorite (NaOCl) solution is a widely used irrigant in endodontics. However, it is highly cytotoxic and can have destructive effects on surrounding tissues when it is not confined to the root canal during irrigation. The extrusion of NaOCl beyond the confines of the root canal into the surrounding tissues or anatomical spaces is known as a NaOCl accident. The NaOCl accident is a serious iatrogenic mishap that can lead to severe tissue damage and complications, which can be life-threatening and/or cause long-term or permanent consequences with medico-legal implications. Therefore, this narrative review was conducted to provide clinicians with a comprehensive understanding of the mechanism and clinical aspects of NaOCl accidents. A literature search was conducted in various online databases using specific Medical Subject Headings (MeSH) and key search terms. The review included all categories of articles dealing with the NaOCl accident and available as full text. Additionally, a manual method of search was conducted by screening references of the included articles. Duplicate articles and articles available only as abstracts were excluded from the review. The included articles were reviewed, analyzed and discussed according to the following sections: causative factors; mechanism; clinical categorization; clinical manifestations; diagnosis, including history, clinical assessment and examination, clinical investigation, and differential diagnoses; and treatment planning of NaOCl accidents. This would enable clinicians to recognize and manage NaOCl accidents in the best possible manner and minimize their serious consequences. Future research should prioritize the identification of solutions or measures to address the challenges associated with conducting clinical or in vivo studies on NaOCl irrigation and extrusion.

**Keywords:** accident, endodontics, root canal irrigants, root canal therapy, sodium hypochlorite

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## Highlights

- A sodium hypochlorite accident is an iatrogenic incident with the potential for severe complications and medico-legal consequences.
- Clinicians must understand the causes, mechanisms, clinical categorization, manifestations, diagnosis, and treatment of NaOCl accidents for effective management and recovery.
- Future research should investigate the dynamics of NaOCl irrigation and extrusion in clinical settings to achieve higher levels of evidence.

# Introduction

Sodium hypochlorite (NaOCl) solution is one of the most widely used irrigants in endodontics due to its capacity to dissolve pulpal tissues and remove smear layer, as well as because of its antimicrobial effects, lubrication properties and low viscosity.[1–5] It is also inexpensive and easily available, with a reasonable shelf life.[2,6] Sodium hypochlorite solution is used in concentrations ranging from 0.5% to 6.0%.[7,8] Although NaOCl is an effective irrigant, its efficacy also depends on the irrigant delivery and activation techniques used. The efficacy of NaOCl has been shown to increase with mechanical or machine-assisted techniques when compared with manual or conventional techniques, despite some variations and limitations among the former.[9] Sodium hypochlorite has certain drawbacks, such as high surface tension, unpleasant odor, as well as discoloring and corrosive effects on endodontic instruments.[1,2,10–14] The corrosive effect of NaOCl can affect the mechanical properties of endodontic instruments and contribute to instrument separation, which is a concern considering the role of nickel–titanium (Ni-Ti) rotary files in modern endodontics. However, a study reported no significant effect of NaOCl on the fracture resistance of Ni-Ti rotary files despite employing a higher concentration of NaOCl (5.25%) at different temperatures.[15] The major concern with NaOCl has been its cytotoxicity, including its tendency to cause cellular (chromosomal) abnormalities at all concentrations.[1,16–21] Sodium hypochlorite is highly cytotoxic to all living tissues, with the exception of heavily keratinized epithelia.[17] The cytotoxic effects of NaOCl include severe inflammation, rapid hemolysis, ulceration, inhibition of neutrophil migration, destruction of endothelial and fibroblast cells, and degradation of cancellous bone.[17–20] This can result in severe damage to both soft and hard tissues.[17,19]

A NaOCl accident is an irrigant mishap, which mainly refers to the extrusion of NaOCl beyond the confines of a root canal into the surrounding periapical or periradicular tissues and/or tissue spaces.[11,22] It can lead to extensive tissue damage, life-threatening situations, and residual or long-term complications.[23–27] Therefore, from the perspectives of clinicians or operators, NaOCl accidents can have medico-legal implications and be associated with malpractice.[28,29] A recent clinical study by Özdemir et al. demonstrated a low rate of NaOCl extrusion and accidents during root canal irrigation with NaOCl.[30] However, it is reported that many practitioners have experienced the NaOCl accident at least once in their career.[31,32] Therefore, it is very important for a clinician or an operator to be completely aware of various aspects of NaOCl accidents to thoroughly understand, manage or prevent them and avoid their associated consequences, including potential medico-legal issues. The purpose of this article is to provide a comprehensive narrative review of the mechanism and clinical aspects of NaOCl accidents, including their causative factors, categorization, manifestations, diagnosis, and treatment planning.

# Material and methods

This narrative review was performed following a thorough electronic and manual literature search. The electronic search was conducted in PubMed®/MEDLINE, Web of Science, Google Scholar, Cochrane, Scopus, LILACS, ScienceDirect, and Crossref databases using specific Medical Subject Heading (MeSH) and key search terms, which included "sodium hypochlorite", "irrigant", "irrigation", "rinse", "root canal", "apical", "periapical", "tissue", "accidental", "inadvertent", "extrusion", "extravasation", "injection", "iatrogenic", "error", "mishap", "accident", "adverse effect", "complication", "dentistry", and "endodontics". These terms were used with Boolean operators to search for articles on NaOCl accidents and irrigant-related mishaps. No language restrictions were applied and the articles published up to August 2023 were searched. All categories or types of articles, such as case reports, case series, original studies, and reviews, available as full text, were included in this review. Additionally, a manual search was performed by screening the references of the included articles. Duplicate articles and articles available only as abstracts were excluded from this review. The included articles were reviewed in depth, and relevant details were extracted, compiled, analyzed, interpreted, and discussed under the following sections: causative factors; mechanism; clinical categorization; clinical manifestations; diagnosis, including history, clinical assessment and examination, clinical investigation, and differential diagnoses; and treatment planning of NaOCl accidents.

# Discussion

## Causative factors for NaOCl accidents

Although a NaOCl accident is considered an iatrogenic mishap mainly caused by the clinician or operator, it occurs in the presence of various contributing or predisposing factors related to the patient (host), tooth, operator, and irrigant (NaOCl).[25,33] The major contributing factors are employing positive pressure or conventional irrigation technique (syringe and needle) and delivering NaOCl in solution form and/or in large amount or volume into the root canal through an open-ended needle or a tightly binding or wedged needle with higher irrigation force, apical irrigation pressure, or NaOCl flow rate during irrigation in a tooth with a large periapical lesion, open or immature apex, wider apex due to resorption, perforation, over-instrumentation, or greater apical patency, larger apical preparation, root defect due to resorption, perforation, or fracture, apical fenestration, close proximity to maxillary sinus, or any iatrogenic error.[25,31–34]

Presently, clinical evidence on the causes for NaOCl accidents is primarily based on case reports, case series, retrospective and observational studies, few studies in the form of surveys, and a couple of systematic reviews on the published case reports and case series.[25,28–31,34–36] Although an observational clinical study reported no statistically significant correlation of demographic characteristics of patients and the preoperative status of teeth to NaOCl extrusion,[30] female sex and non-vital teeth with periapical lesions have been identified as risk factors for NaOCl accidents.[25,31,33,34] Although the NaOCl accidents are mainly caused by the extrusion of NaOCl due to operator factors such as technique, force, pressure, and flow rate employed during NaOCl irrigation, the available clinical data on NaOCl irrigation and extrusion remains limited. Moreover, the data obtained from in vitro studies is inconsistent and not sufficiently conclusive to be extrapolated to a clinical scenario.[30,33–36] Although more clinical research is required on NaOCl irrigation and extrusion, there are many challenges related to the sample size, standardization of predisposing factors, objective measurement of irrigation factors (i.e., force or pressure), tissue back pressure, volume of extruded NaOCl, determination of the extent of tissue damage, and ethical dilemma due to the absence of an antidote to NaOCl and the dearth of data on the volume of NaOCl that could be considered safer upon extrusion.[36]

## Mechanism of NaOCl accidents

The extrusion of NaOCl beyond the confines of the root canal can be categorized as either active or passive. Active extrusion occurs when NaOCl is forced under pressure and is mostly responsible for a NaOCl accident.[37–39] On the other hand, passive extrusion happens when NaOCl seeps or leaches out of the root canal without the application of force or pressure.[32,38,40–42] The likelihood of passive extrusion of NaOCl is increased in cases involving an open, immature or widened apex due to root resorption or overinstrumentation, which provides larger apical access for NaOCl seepage. Both active and passive extrusion of NaOCl can lead to a NaOCl accident, exhibiting different mechanisms and manifestations.

As a result of active extrusion, a NaOCl accident occurs following the cascade mechanism:

- extrusion of NaOCl under high force or pressure into the periapical tissues through a patent apical foramen[22,41];
- infusion of extruded NaOCl into the surrounding vasculature. This process requires intact and open blood vessels and a vascular pressure lower than the pressure of extruded NaOCl, as infusion of NaOCl takes the path of least resistance. The infusion of extruded NaOCl occurs in the veins rather than the arteries because the venous pressure is always lower than the arterial pressure in the vasculature. Thus, when the apical pressure extruding NaOCl into the periapical tissues exceeds the venous pressure in the facial vasculature, infusion of NaOCl ensues. The infusion of extruded NaOCl into the venous vasculature can occur through direct or indirect means. Hypothetically, a direct infusion of NaOCl requires intact pulpal and/or periapical vasculature. However, in the absence of such vasculature, the direct infusion of NaOCl may not occur in teeth with pulpal and/or periapical pathology or those undergoing root canal therapy (RCT). Interestingly, a direct infusion of NaOCl into the pulpal vasculature remains possible in vital teeth undergoing endodontic therapy. However, venous congestion in an inflamed pulp and/or pulp extirpation, which often precedes a major part of irrigation, can limit any such potential. Therefore, an indirect infusion of NaOCl into the vasculature occurs when extruded NaOCl reaches the intraosseous or bone marrow space, which contains a network of sinusoids acting like a sponge and a higher intraosseous blood pressure compared to the central venous pressure. Thus, extruded NaOCl is immediately absorbed into the intraosseous or bone marrow space, reaching the venous vasculature due to a higher to lower pressure gradient[22];
- draining of the infused NaOCl through the venous vasculature directly into the pterygoid plexus. However, in the presence of anatomical variations in the facial venous vasculature, the infused NaOCl reaches the facial veins instead of draining into the pterygoid plexus. Apart from releasing chemical mediators, the infused NaOCl causes damage to the vessels and increases vascular permeability. Thus, the infused NaOCl indirectly comes into contact with surrounding soft tissues, leading to a NaOCl accident with typical signs and symptoms.[22,43,44]

In accordance with the abovementioned mechanism, NaOCl accidents mainly occur in instances of active extrusion of NaOCl under force or pressure. However, it has been established that a NaOCl accident may not occur in every patient, even in cases where similar irrigation methods are employed. Two theories have been advanced to explain this phenomenon, namely the threshold theory and the compliance theory.

According to the initially proposed threshold theory, a NaOCl accident occurs only if active extrusion takes place, with the irrigation pressure near the apical foramen exceeding a threshold of back pressure offered by the surrounding tissues. Therefore, when the pressure is below this threshold, a NaOCl accident may not occur, despite forceful irrigation.[22,32,45–48] However, this theory has certain limitations which are related to the size of pressure sensors employed in the studies, lack of validity for the positive back pressure concept as the influx of fluid into an empty root canal does not occur, absence of consistency in the values of back pressure at the apical foramen, and findings reporting that conventional irrigation pressure can actually exceed the stated thresholds.[32] Therefore, the compliance theory has been proposed as an alternative concept. According to this theory, back pressure is not constant and is influenced by the differences in the anatomy of the periapical tissues.[31,32,34,42] Therefore, the compliance of the periapical tissues plays a crucial role in back pressure offered toward the extrusion of NaOCl.[32,42] Thus, a classic NaOCl accident occurs only when NaOCl is extruded with a pressure that exceeds the pressure from the surrounding tissues and the vasculature and is infused into the venous blood flow.

The aforementioned mechanism and theories explain why NaOCl accidents are less prevalent despite the common nature of RCT.[22] This mechanism also clarifies why NaOCl accidents with classic features may not occur in cases of passive extrusion of NaOCl into the periapical tissues.[22,32,42] However, in the event of passive extrusion, NaOCl can still come into contact with the periapical tissues, exerting a direct cytotoxic effect on them, even though cortical bone is generally resistant to the effects of NaOCl.[19] This situation can lead to a NaOCl accident without typical signs and symptoms. Although classic features of a NaOCl accident may not manifest, extrusion of even a small amount of NaOCl can lead to pain. Sodium hypochlorite extrusion is one of the contributing factors for postoperative or post-treatment endodontic pain. Similarly, passive or active extrusion of NaOCl into an empty or surrounding anatomical space, such as the maxillary sinus, can result in a NaOCl accident without typical manifestations. Additionally, when NaOCl is extruded into the surrounding soft tissues due to iatrogenic errors, such as perforation, or directly into a soft tissue space, such as the buccal and infraorbital spaces, through the periapical area or bone fenestration, NaOCl directly exerts its cytotoxic effect, actively destroying surrounding soft tissues and creating its own planes. This spread may occur in a haphazard or unpredictable manner, accompanied by symptomatology that is less typical of NaOCl extrusion into the periapical tissues.[31,49,50] The various types of NaOCl extrusion and various pathways for extrusion can influence the mechanism and manifestations of NaOCl accidents. These pathways have been schematically depicted in Fig. 1.

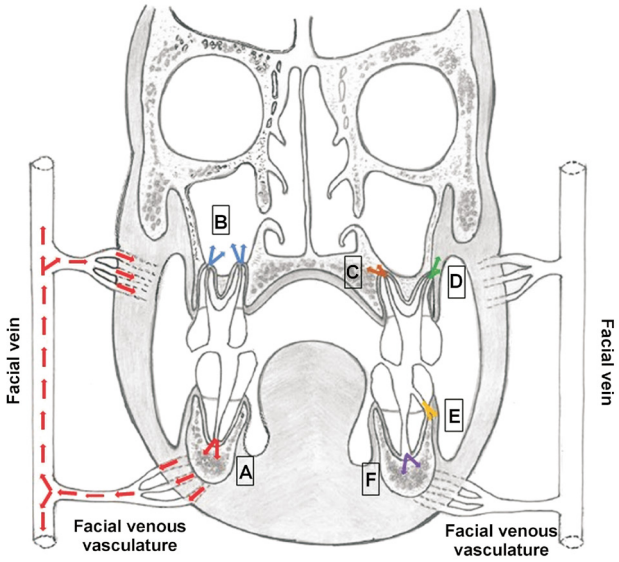


Fig. 1. Schematic illustration depicting types and pathways of sodium hypochlorite (NaOCl) extrusion that influence the mechanism and manifestations of NaOCl accidents

A – active extrusion of NaOCl via root apex into hard tissues (periapical tissues) with an indirect (hematogenous) pathway via facial vein to surrounding tissues (red arrows); B – active extrusion of NaOCl via root apex into an anatomical space (maxillary sinus) with a direct pathway to surrounding tissues (blue arrows); C – active extrusion of NaOCl via root apex into hard tissues (periapical tissues) with a direct pathway to surrounding tissues (orange arrows); D – active extrusion of NaOCl via bony defect (e.g., apical fenestration) into soft tissues or fascial spaces with a direct pathway to surrounding tissues (green arrows); E – active extrusion of NaOCl via root defect (e.g., root fracture or iatrogenic root perforation) and a direct pathway into the surrounding soft tissues (yellow arrows). Similarly, active extrusion into hard tissues (periradicular tissues) with an indirect pathway to surrounding tissues can occur if the defect is located beyond the cervical third of the root; F – passive extrusion of NaOCl via root apex (e.g., open apex) into hard tissues (periapical tissues) (purple arrows). Similar tendencies may also exist for passive extrusion of NaOCl via root apex into an anatomical space (maxillary sinus) or via root defect into soft tissues or tissue spaces.

## Clinical categorization and manifestations of NaOCl accidents

Sodium hypochlorite accidents can be broadly categorized based on their manifestations and the mode and site of extrusion (Table 1).[22] Their clinical manifestations may be further categorized based on various factors (Table 2).[51]

Table 1. Clinical categorization of sodium hypochlorite (NaOCl) accidents

| Basis | Category |
|---|---|
| Mode of NaOCl extrusion | • NaOCl accident due to active extrusion:<br>– direct pathway to the surrounding tissues<br>– indirect pathway to the surrounding tissues (hematogenous route)<br>• NaOCl accident due to passive extrusion |
| Site of NaOCl extrusion | • NaOCl accident due to extrusion into the surrounding soft tissues or fascial spaces and hard tissues (such as periapical and periradicular tissues)<br>• NaOCl accident due to extrusion into the surrounding or anatomical tissue spaces (such as the maxillary sinus) |
| Manifestations depending on the mode and site of NaOCl extrusion | • NaOCl accident with classic or typical manifestations<br>• NaOCl accident with non-classic or non-typical manifestations |

Table 2. Categorization of clinical manifestations of sodium hypochlorite (NaOCl) accidents

| Basis | Category |
|---|---|
| Site of clinical manifestations | • local manifestations:<br>– intraoral features<br>– extraoral features<br>• systemic manifestations |
| Duration or time required for the onset or persistence of clinical manifestations | • short-term manifestations:<br>– immediate or early features<br>– later or delayed features<br>• long-term or residual manifestations |
| Extent of clinical manifestations | • mild manifestations<br>• moderate manifestations<br>• severe manifestations |

## NaOCl accident due to NaOCl extrusion into the surrounding tissues

Accidents involving NaOCl typically result from the extrusion of NaOCl into the surrounding soft tissues or fascial spaces and hard tissues, including periapical and periradicular tissues. Documented cases of accidents involving NaOCl under this category have been reported in both permanent and primary teeth.[25,34] However, the number of cases involving primary teeth is limited.[49,52–58] The clinical manifestations and management of NaOCl accidents do not differ significantly between permanent and primary teeth.

### Local manifestations

#### Short-term manifestations

Short-term manifestations include both soft tissue and hard tissue manifestations with intraoral and extraoral features.

Immediate or early features occur immediately after NaOCl extrusion, although in some cases, they may manifest after few hours.[59] They are mainly due to soft tissue damage following a NaOCl accident. Sudden pain, profuse bleeding from the root canal, immediate swelling, and ecchymosis are the characteristic features of NaOCl extrusion into the periapical tissues.[25,60] The intensity of pain varies depending on the extent of the NaOCl accident, pain threshold of the patient, and whether anesthesia was administered during RCT. Some patients treated under local anesthesia (LA) may not experience pain immediately.[61] Otherwise, pain would be severe even if the patient was anesthetized.[62] With NaOCl spreading rapidly over a wide region, pain management becomes difficult because symptoms from distant anatomic structures will continue to cause discomfort. This phenomenon also explains the extreme pain experienced during NaOCl accidents, despite the implementation of adequate LA prior to treatment initiation.[31,63] The profuse bleeding from the canal, including the gingival margin,[50,64] is due to the body's reaction to NaOCl.[63] The extruded NaOCl affects vascular permeability by damaging the vessels and releasing chemical mediators. This results in interstitial hemorrhage, causing immediate swelling, severe bleeding from the canal, and ecchymosis.[43,44]

Swelling manifests as both large and diffuse, appearing within minutes to hours after the extrusion. It extends intra- and extraorally,[65] and may lead to difficulty in the opening of the eye on the affected side.[59,66,67] The distended soft tissues cause a sensation of tightness and contribute to pain.[60] Swelling may also manifest as emphysema with crepitus due to the use of positive pressure irrigation with open-ended needles to deliver NaOCl or extrusion of compressed air or hydrogen peroxide along with NaOCl,[56,68,69] as well as oxygen liberation into the tissues because of the oxidizing ability of NaOCl.[66,69]

Ecchymosis is another salient feature of NaOCl accidents and can be broadly categorized considering its location and extent (Table 3).[22] Ecchymosis typically manifests extraorally and unilaterally along the angle of the mouth and around the periorbital region of the affected side, following the course of the facial superficial venous vasculature. This is attributed to the mechanism of NaOCl accidents, where extruded and systemically absorbed NaOCl eventually reaches the facial vein, causing extraoral ecchymosis.[22] Due to the same reason, NaOCl accidents typically manifest with a similar pattern of extraoral ecchymosis, irrespective of the tooth involved.[22] Most often, extraoral ecchymosis does not manifest in the cheek or middle third of the face because the malar fat pad and zygomatic muscles cover the facial venous vasculature, concealing the area of underlying interstitial hemorrhage.[22] Occasionally, ecchymosis may manifest intraorally[22,23]

Table 3. Categorization of ecchymosis following a sodium hypochlorite (NaOCl) accident

| Basis | Category |
|---|---|
| Site of involvement | • intraoral ecchymosis<br>• extraoral ecchymosis |
| Side of involvement | • unilateral ecchymosis<br>• bilateral ecchymosis |
| Extent of involvement | • grade 1: ecchymosis is not observed<br>• grade 2: ecchymosis is evident, involving the angle of the mouth and the periorbital region (facial ecchymosis)<br>• grade 3: ecchymosis is evident, involving the regions of grade 2 and extending into the neck region (facial and cervical ecchymosis)<br>• grade 4: ecchymosis is observed, involving the regions of grade 3 and extending into the chest area (facial, cervical and mediastinal ecchymosis) |

or be observed bilaterally by crossing the midline[70] or extending to the contralateral periorbital region due to any communication between left and right anterior facial veins.[49,55,69] The extent of ecchymosis depends on the amount of loose tissue present in the surrounding area.[70] However, ecchymosis does not manifest in the intraoral soft tissues around the apical area of the involved tooth, as intravenous infusion of extruded NaOCl into the local circulation is least likely due to the lack of pulpal and/or periapical blood supply in relation to the involved tooth.[22]

Later or delayed features manifest within 24–48 h or several days after the NaOCl accident. These include life-threatening airway obstruction due to Ludwig's angina,[23,24] dysphagia,[71] dysphonia, drooling saliva,[23] trismus,[23,72] purulent discharge from periapical tissues or necrotic soft tissues due to secondary infection,[60,66,73–75] ulceration,[65] formation of a fistula with ulceration,[76] hard tissue damage in the form of demineralization and necrosis of bone,[19,77] neurological complications such as altered sensation,[69] residual anesthesia, paresthesia, and loss of sensory and/or motor functions affecting speech and swallowing due to the involvement of the trigeminal, infraorbital,[78] or isolated facial nerves,[44,64–66,68,70,72–74,76,79–84] and ophthalmological complications such as eye pain, blurring of vision, blepharospasm,[78] diplopia, and corneal patchy coloration.[62,73]

**Long-term or residual manifestations**

Long-term or residual effects may persist for many months or years. They include neurological deficits manifesting as persistent or permanent paresthesia,[76,85,86] as well as permanent damage to mimic musculature, trigeminal nerve weakness,[78,82,87,88] ocular damage,[87] hypertrophied or excessive granulation tissue and fibrosis with or without a foreign body-like reaction,[27,44,77,89] mucosal or facial tissue scarring,[49,65,90] facial atrophy,[61,88] facial discoloration,[91] cosmetic deformity,[25,44,64,73,74] and damage to the permanent tooth follicle in case of a NaOCl accident in a primary tooth.[92,93]

## NaOCl accident due to extrusion of NaOCl into the surrounding anatomical spaces

The extrusion of NaOCl into the surrounding anatomical spaces involves tissue spaces, such as the maxillary sinus. Although the risk of extrusion of NaOCl into the maxillary sinus is higher, only few cases have been documented in comparison to extrusion of NaOCl into soft and hard tissues (periapical and periradicular tissues). The literature has documented such cases only in the context of permanent teeth.[37,74,87,89,94–97] The clinical features of extrusion of NaOCl into the maxillary sinus also differ from those of extrusion of NaOCl into soft and hard tissues. The extrusion of NaOCl into the maxillary sinus generally manifests with non-classic or non-typical features.

### Local manifestations

**Short-term manifestations**

Immediate or early features include dripping of extruded NaOCl with a taste of chlorine from the nose or throat due to its flowing from the nostrils, a burning sensation in the maxillary sinus, epistaxis, blood or blood-stained fluid dripping in the throat, breathing disturbances, and sinusitis or sinus congestion.[37,77,89,95–97] Classic or typical features such as severe pain, swelling, ecchymosis, and bleeding from the canal may not be seen, as NaOCl extruded into the maxillary sinus, which is not an enclosed space, may be evacuated from the nostrils with limited time of contact in the sinus.[25,37,68,89,94–97] Nevertheless, few cases with immediate severe pain and swelling have been reported.[77,95,97] Symptoms such as the taste of chlorine and NaOCl running down through the nose and throat can also manifest with the extrusion of NaOCl into the periapical tissues of maxillary incisors due to their proximity to the nasal cavity or floor.[83]

Later or delayed features consist of any necrosis or sequestration of surrounding or adjacent bone and associated features.[77,87]

**Long-term or residual manifestations**

Long-term manifestations include hypertrophy or thickening of sinus lining, neurological complications such as paresthesia due to infraorbital nerve damage, ocular complications such as dystonia of the eye and enophthalmos due to damage to the orbital floor, mobility of the tooth, and oroantral fistula or communication as an associated complication following the extraction of the involved tooth.[77,87,89]

## Systemic manifestations of NaOCl accidents

NaOCl accidents with systemic involvement are rarely reported, and the tendency for systemic involvement seems to be limited to cases of grade 4 ecchymosis extending to the cervical and mediastinal areas.[22] However, a NaOCl accident can potentially lead to systemic manifestations in a medically compromised patient.[26] Barbas et al. reported the death of a patient due to systemic involvement following NaOCl irrigation during RCT in a maxillary tooth.[98] The irrigation with NaOCl was identified as the probable cause of the patient's sudden coma and subsequent death, despite their reported health status. Based on the available circumstantial evidence, the death was attributed to an acute rise in blood pressure and intracerebral hemorrhage resulting from severe pain and/or sudden trigeminal nerve stimulation following the irrigation with NaOCl, which may have been extruded through the root apex. The reported symptoms prior to the patient's unresponsiveness were indicative of a NaOCl accident.[98]

## Diagnosis of NaOCl accidents

The diagnosis of NaOCl accidents involves history, clinical assessment and examination, clinical investigations, and differential diagnoses.

### History

The majority of NaOCl accidents are reported during the RCT itself (under primary care). However, when such cases are referred or reported to secondary care (i.e., oral and maxillofacial surgery unit, emergency unit, hospital, or medical and/or dental specialist), they could be either an immediate or early referral with all the classic or non-classic signs and symptoms or complications, or a delayed referral, with features of residual or long-term effects.[51,77,87–89] In such cases, a comprehensive history of RCT, along with the rapid or sudden onset of salient features such as pain and swelling during the procedure, prevailing signs and symptoms, and clinical and radiological examination, would facilitate the diagnosis.

### Clinical assessment and examination

The intensity of pain should be assessed using the numeric rating scale or the visual analogue scale. These instruments facilitate the categorization of the extent of a NaOCl accident and, consequently, the formulation of a treatment plan. They also serve as a baseline record to monitor the progress and management of a NaOCl accident.[51,99] Although pain evaluation using these scales is subjective, it can still be considered a useful tool for the assessment of the extent of pain.[100] In cases where patients are already experiencing significant discomfort, and where time is of the essence in managing a NaOCl accident, these scales can be instrumental in rapidly evaluating pain and mitigating further distress to the patient. They can facilitate the immediate initiation of emergency measures to control pain and other symptoms.

Vital signs must be meticulously monitored, particularly in cases where systemic involvement is observed following substantial extrusion and infusion of NaOCl into the vasculature. This is needed to monitor the patient's well-being, as systemic involvement can be life-threatening.[98]

The extraoral examination consists of facial, airway, neurological, and ophthalmologic assessment. The facial assessment involves the observation of any asymmetry, swelling or ecchymosis. The airway assessment is crucial for detecting signs such as high-pitched wheezing (stridor), hoarseness, coughing, difficulty swallowing, and labored or rapid breathing, which would necessitate emergency intervention. The neurological assessment involves the examination of cranial nerves, particularly the trigeminal and facial nerves, to assess sensory and/or motor functions in the affected area.[23,27,51,99] The examination of nerves should be performed once the anesthetic effect has worn off.[25] The ophthalmologic assessment is of critical importance, especially in cases of NaOCl accidents involving the maxillary region, to avoid ocular complications.[87,99]

The intraoral examination involves the assessment of the treated tooth, sensory and/or motor functioning of nerves in the affected area, as well as any associated swelling, ecchymosis, ulceration,[65] or necrosis of soft and hard tissues.[77] The involved tooth and the associated gingiva are usually tender to percussion.[51] Additionally, the presence of a chlorine odor in the affected area can assist in the diagnosis of patients who have been referred with a NaOCl accident.[76,79]

### Clinical investigation

The clinical investigation involves the radiological assessment using periapical radiography,[65] dental panoramic tomography,[72] cone beam computed tomography (CBCT) or dental volumetric tomography (DVT),[89,101] computed tomography (CT),[49,69,77,86,87] and magnetic resonance imaging (MRI).[64] Since conventional radiographs have certain limitations,[32,71] advanced imaging techniques such as CBCT or DVT, CT, and MRI have been suggested depending on the extent of damage following a NaOCl accident.[32,51] These advanced techniques also allow for preoperative identification of predisposing factors for NaOCl accidents, three-dimensional visualization of the affected area, revealing the cause of an accident, and reduction of time spent in assessing the prognosis of the involved tooth, particularly in a referred case of a NaOCl accident.[60,101] In CBCT, the affected region shows the presence of multiple round or ovoid air-bubble-like voids and low-density areas within the soft tissues.[60] Computed

tomography and MRI are suitable for the assessment of affected areas in relation to the maxillary sinus.[77,102] Nasal endoscopy, or nasoscopy, is also recommended in cases of NaOCl extrusion into the maxillary sinus.[77,86,87,97] Medical or laboratory investigations including blood and urine analysis can be considered in cases of systemic manifestations following a NaOCl accident.[103–105]

### Differential diagnoses

The following conditions must be ruled out while diagnosing NaOCl accidents, especially in referred cases:

– mucosal injury with salicylate or other chemicals or solvents, particularly in cases of intraoral ulceration.[105,106] Similarly, in the presence of features such as pain, intraoral ulceration, soft and hard tissue necrosis, and paresthesia, the exclusion of any seepage of NaOCl during RCT is imperative. The absence of immediate pain and swelling during NaOCl irrigation and extraoral ecchymosis may assist as differentiating features[107–109];
– extrusion of other irrigants such as hydrogen peroxide, chlorhexidine, ethylenediaminetetraacetic acid, and citric acid. When a regimen of multiple irrigants is employed during RCT, a similar potential for extrusion exists. Extrusion of other irrigants can also lead to signs and symptoms such as pain, swelling, ulceration, and paresthesia, which are similar to those caused by a NaOCl accident. However, features such as crepitus and the absence of facial ecchymosis may facilitate a differential diagnosis. The management of extrusion of these irrigants is based on similar principles[110–112];
– injury due to inadvertent injection or extrusion of gutta percha solvents such as xylene and chloroform, particularly in a patient undergoing endodontic retreatment[113,114];
– direct injection of NaOCl instead of LA into the surrounding tissues of the oral cavity. This iatrogenic error can manifest with signs and symptoms analogous to those associated with NaOCl accidents, including pain, swelling, ulceration, and paresthesia. However, facial ecchymosis, a salient feature of NaOCl accidents, is mostly absent. Since the LA step generally precedes the irrigation procedure during RCT, confirming this may assist in ruling out the possibility of direct injection of NaOCl. However, when LA is administered during root canal cleaning and shaping and the irrigation procedure, direct injection of NaOCl into the surrounding tissues must be considered under differential diagnoses. The protocols for managing NaOCl accidents and direct injection of NaOCl are similar[102,105,115–117];
– orofacial infection such as an acute periapical abscess with cellulitis.[51,80,81,90] However, the presence of features such as history of pain and swelling that develops suddenly during RCT, facial bruising or ecchymosis, and sensory or motor deficit help to rule out such an infection[80,81,90,118,119];
– allergic or immediate hypersensitivity reaction to household products, medications, local anesthetics, and rubber dam.[24,118,120] The absence of history of such allergic reactions, the presence of intense pain and the clinical features that are mostly seen unilaterally on the side corresponding to the treated tooth, the absence of breathing difficulties or cardiorespiratory manifestations, and the lack of itching and/or rashes on the skin facilitate in ruling out an allergic reaction[24,105,118,121];
– air or tissue emphysema. The presence of immediate and intense pain, swelling mostly confined to the affected side, and the absence of crepitus and erythema help to rule out air or tissue emphysema[121];
– hematoma formation[121];
– angioneurotic edema. Although it could be rapid in its onset, facial swelling is typically bilateral and may involve other areas of the body, manifesting as urticaria and skin rashes. The absence of these features, the absence of a history of recurring episodes of such facial swelling, and the occurrence of signs and symptoms during or following RCT would assist in ruling out angioneurotic edema[120,121];
– interappointment and post-treatment endodontic pain or flare-up. These must be considered under the differential diagnoses in the presence of iatrogenic errors, such as overinstrumentation, and when signs and symptoms, such as pain and swelling following a NaOCl accident, start to appear late.[100,122]

## Treatment planning for NaOCl accidents

Following confirmation or diagnosis of a NaOCl accident, it can be clinically categorized based on its manifestations and extent. The extent of a NaOCl accident is influenced by various factors, including the host, the site of extrusion, the concentration and amount or volume of extruded NaOCl, the spatial location of the fluid introduction, and proximity to vital anatomic structures.[41,68,73,123] Sodium hypochlorite accidents can be categorized into mild, moderate and severe. The categorization and treatment planning for NaOCl accidents can be carried out in the following manner.

### Mild category

Mild NaOCl accidents are characterized by pain at the lower end of the pain scale and are localized to the tooth undergoing RCT. These accidents result in swelling less than 30% relative to the contralateral side and localized ecchymosis. The management of this condition can be performed under primary care[51] or on an outpatient basis in a hospital.[84]

### Moderate category

Moderate NaOCl accidents are characterized by an increase in pain, with an intensity in the mid-range on a pain scale, swelling up to 50% relative to the contralateral

side, diffuse ecchymosis, intraoral ulceration adjacent to the treated tooth, and cosmetic deformity. Such cases require management under secondary care in a maxillofacial unit[51,99] or emergency unit, or on an outpatient basis in a hospital.[84]

### Severe category

The severe category of NaOCl accidents is characterized by intense pain at the higher end of the pain scale, swelling greater than 50% relative to the contralateral side, diffuse ecchymosis, intraoral ulceration and necrosis of soft tissues, compromised airway, neurological and ophthalmological complications, and cosmetic deformity. Severe cases must be managed under secondary care in a maxillofacial unit or emergency unit[51,99] or on an inpatient basis with hospitalization and intensive care.[23,24,26]

A comprehensive diagnosis involving history, clinical assessment and examination, and clinical investigations, as well as the categorization of manifestations and their extent would assist clinicians in decision-making to manage NaOCl accidents and minimize their consequences (Fig. 2). The management and prevention of NaOCl accidents will be addressed as a separate topic, given the extent of content to be reviewed and discussed.

## Conclusions

A NaOCl accident is a serious iatrogenic mishap with potential medico-legal consequences. Although clinicians must implement measures to prevent it, an element of risk exists during root canal irrigation with NaOCl. Therefore, dental professionals must thoroughly understand and be aware of various aspects of NaOCl accidents. This narrative review was conducted to elucidate the mechanism and clinical aspects of NaOCl accidents. It provides clinicians with a detailed overview of the causes, mechanism, clinical categorization, clinical manifestations, diagnosis, and treatment planning of NaOCl accidents, thereby enabling them to manage NaOCl accidents in the most optimal manner and minimize or avert their serious consequences, including medico-legal implications. However, this narrative review is based on the currently available clinical evidence on NaOCl irrigation and NaOCl accidents or extrusion in the endodontic literature, which is considered to be limited. Hence, there is a need to accumulate higher-level evidence through additional clinical studies on NaOCl irrigation and extrusion. Future research should prioritize the identification of solutions or measures to address the challenges associated with conducting clinical or in vivo studies on NaOCl irrigation and extrusion.

## Ethics approval and consent to participate

Not applicable.

## Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

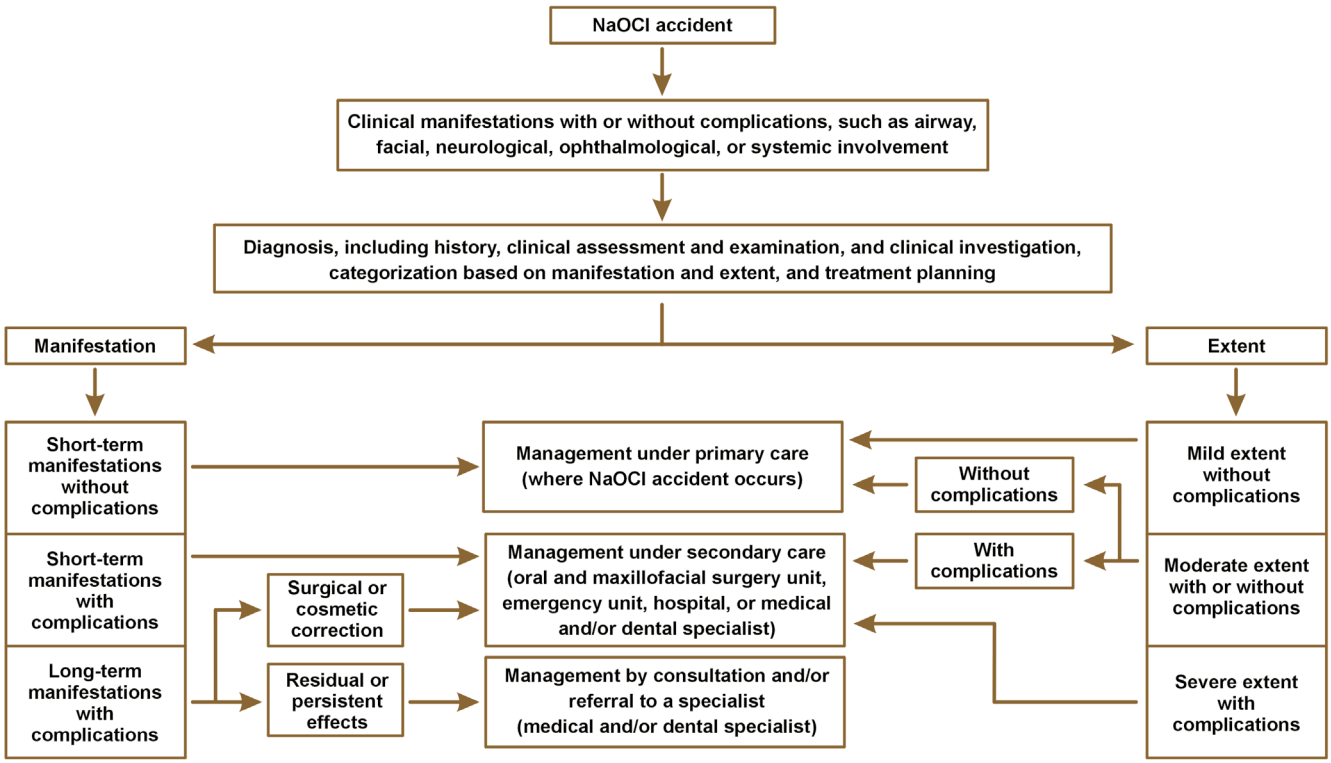


Fig. 2. Flowchart depicting the clinical decision-making process concerning treatment planning and management of sodium hypochlorite (NaOCl) accidents

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.

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Research letter

# Single intra-articular administration of injectable platelet-rich fibrin (I-PRF) in alleviating temporomandibular joint pain: A pilot clinical trial

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## Abstract

**Background.** Intracapsular injections are a recognized therapeutic method for temporomandibular joint (TMJ) pain and limited mandibular mobility. Among many injectables, injectable platelet-rich fibrin (I-PRF) is noteworthy for its safety, promising clinical results and potential regenerative effects. The minimal invasiveness of a single injection makes it attractive as compared to arthrocentesis or a series of administrations.

**Objectives.** This single-arm, open-label clinical trial aimed to verify the research hypothesis that a single administration of I-PRF into TMJ relieves articular pain.

**Material and methods.** The study sample included adults with a history of TMJ articular pain treatment. A single injection of I-PRF into the affected TMJ was performed. Each patient assessed (1) articular pain within the last 7 days, (2) the articular pain provoked by a physical examination, (3) muscular pain, (4) headache, and (5) neck pain before and 14 days after the intervention. The investigator measured (6) pain-free and (7) maximal voluntary mandibular abduction.

**Results.** The study sample included 33 patients and 44 TMJs. No adverse events were observed at the recipient sites (TMJs). The treatment reduced the spontaneous articular pain by 0.5 ±1.5 and the provoked articular pain by 1.2 ±1.9 visual analog scale (VAS) points, with the differences being statistically significant ($p < 0.05$). Improvement was observed in 39–48% of Wilkes II–V patients, and 5–14% experienced deterioration up to 2 VAS points. Mandibular mobility decreased by an average of 1–2 mm, and no statistically significant effect on muscle pain, headache or neck pain was recorded.

**Conclusions.** A single intra-articular injection of I-PRF into TMJ brings statistically significant articular pain relief, regardless of the assessment method. In non-respondents, subsequent administrations may be considered.

**Keywords:** temporomandibular joint, temporomandibular disorders, intra-articular injections, injectable platelet-rich fibrin, I-PRF

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## Highlights

- A single injection of I-PRF into the articular cavity of TMJ brings statistically significant joint pain relief, regardless of the examination method used.
- The promising results of I-PRF intra-articular injections, coupled with the absence of reported complications, make it a compelling option for patients suffering from TMJ pain.
- A single injection of I-PRF into TMJ does not show a statistically significant effect on muscle pain, headache and neck pain.

# Introduction

Temporomandibular joint (TMJ) pain is an interdisciplinary problem affecting 14.6–21.1% of the Polish population.[1–3] A single TMJ is divided by an articular disc and the articular surfaces are covered with cartilage, constantly absorbing friction and loads. The overload and microtrauma of the joint surfaces induce inflammation. The secretion of pro-inflammatory cytokines into the joint cavities deteriorates the composition of the synovial fluid, further intensifying the inflammation and, consequently, causing damage to the articular cartilage cells, leading to the degradation of the joint surfaces, which is related to age and gender.[4,5] Degeneration can lead to the pain, stiffness and limited mobility of the joints.[6]

The treatment of TMJ pain should be preceded by meticulous and properly directed diagnostics, with regard to the presence of etiological factors, which include those of a psychological nature, systemic diseases and local problems, such as injuries or their consequences.[7–12] While the priority is to exclude the etiological factors of TMJ pain, symptomatic treatment is used in cases of diagnostic difficulties, contraindications to causal treatment and advanced degeneration. Among the surgical methods, the least invasive is intra-articular injections, which, according to the current state of knowledge, are expected not only to relieve pain, but also stimulate the regeneration of the articular surfaces.[13,14]

Injectable platelet-rich fibrin (I-PRF) is an autologous blood product containing platelets, growth factors and leukocytes.[15] So far, it has been successfully used in treating wounds, especially intraoral ones, and in regenerative medicine.[15,16] The intra-articular administration of I-PRF has been shown to stimulate the regeneration of the cartilage cells and stop the degradation of the joint surfaces.[17,18] It is worth noting, however, that the intra-articular injection of I-PRF is a relatively new technique, and its exact effect on the articular cartilage is still being studied.[14]

The demonstrated long-term effect of I-PRF on the cartilage tissue justifies administering this self-derived preparation into the cavities of TMJs.[14,19] Intra-articular intervention is reserved primarily for severe TMJ pain, not responding to less invasive treatment. Immediate pain relief from hyaluronic acid or platelet-rich plasma (PRP) administered in one session using a single injection has been confirmed.[20,21] The effectiveness of I-PRF in the ad hoc articular pain relief is also presumed, but this needs to be proven.

This study aimed to verify the research hypothesis that a single administration of I-PRF into the TMJ cavity has an analgesic effect.

# Material and methods

The study was designed as a single-arm, open-label clinical trial. It was conducted following the Declaration of Helsinki, and the protocol was approved by the Ethics Committee at the Świętokrzyska Chamber of Physicians, Kielce, Poland (1/2022-VIII). Informed consent to treatment and to participate in the study was obtained from each patient before enrollment in the study. The study protocol was registered in the ClinicalTrials.gov database: NCT05883982. This report was prepared under the CONSORT guidelines.[22]

The patients were recruited from among those diagnosed with TMJ pain and referred for intra-articular I-PRF injections by orthodontists and prosthodontists. A maxillofacial surgeon (M.S.) confirmed articular pain attributed to the presence of arthritis, disc displacement or degenerative joint disease under the International Classification of Orofacial Pain (ICOP) 2020 protocol (diagnoses 3.2.1 to 3.2.3).[23] The detailed inclusion and exclusion criteria are presented in Table 1. Due to the pilot nature of the study, the patients interrupted their current treatment for only 2 weeks. The study was conducted solely at the Maxillofacial Surgery Clinic, NZOZ (non-public health service institution) Ars Medica in Kielce, Poland.

Venous blood was collected into a vacuum tube. Then, I-PRF was acquired according to the protocol for the iFuge D06 centrifuge (Neuation Technologies, Kalol, India): 630 rpm, 3 min. After skin disinfection, approx. 0.4 mL of I-PRF was administered to the upper TMJ compartment, each time by the same operator (M.S.). The TMJ area was not priorly injected with a local anesthetic.

The patients subjectively rated the greatest pain intensity over the last 7 days on an 11-point (0–10) visual analog

**Table 1.** Inclusion and exclusion criteria for the participation in the study

| Category | Inclusion criteria | Exclusion criteria |
|---|---|---|
| Demographics | 18 years or older | none |
| Main diagnosis | unilateral or bilateral TMJ pain attributed to arthritis, disc displacement or degenerative joint disease | TMJ ankylosis |
| Other diagnoses | not applicable | bleeding diathesis, mental illness or preauricular skin disease of the affected side |
| Previous treatment | possibility of interrupting the current TMD treatment | TMJ prosthesis |
| Consent | informed written consent | withdrawal of consent at any stage |

TMJ – temporomandibular joint, TMD – temporomandibular joint disorders.

scale (VAS). The exception was the assessment of the pain provoked by a physical examination, which concerned the severity of pain immediately after the examination. Each type of pain was defined for a specific side of the body, and therefore assigned to a specific TMJ. The range of mandibular abduction was examined between the points of incision superius and incision inferius or their equivalents in prosthetic restorations.

Changes in the spontaneous and provoked TMJ pain were the primary outcomes of this study, and the rest were secondary outcomes. The initial assessment of symptom severity as well as the intervention were carried out at the first and sole examination at the second medical appointment.

The size of the sample resulted from the recruitment time. Sample power calculations were performed based on reference results of Albilia et al. (33/48 respondent TMJs).[19]

The values of the following variables were collected: muscle, head and neck pain; spontaneous and provoked TMJ pain; and painless and maximal volunteer mandibular abduction. The following were calculated: extremes; decreased, non-changed and increased cases; extreme, median (*Me*) and mean (*M*) differences. The subgroups were created depending on the treatment response and the Wilkes stage.

The following software was used: Sample Size Calculator (https://clincalc.com/stats/samplesize.aspx; ClinCalc, Chicago, USA); MedCalc (MedCalc Software, Ostend, Belgium); Microsoft Office (Microsoft Corporation, Redmond, USA); Google Workspace (Google, Mountain View, USA); and LibreOffice (The Document Foundation, Berlin, Germany).

## Results

Recruitment lasted from January 1 to June 30, 2023. The intervention and follow-up dates varied among the patients, but each patient was included in the study for 14 days. Of the 34 patients admitted during the recruitment period, one was rejected after completing the 1st questionnaire and after the 1st physical examination. In the discussed case, habitual dislocation of the mandible was diagnosed.

Ultimately, the study group consisted of 33 patients and 44 TMJs. The study group included 25 women and 8 men, all Polish. Particular diagnoses in the Wilkes scale concerned the following numbers of joints: Wilkes II – 29 joints; Wilkes III – 4 joints; Wilkes IV – 9 joints; and Wilkes V – 2 joints. The following comorbidities were diagnosed: general osteoarthritis – 6 patients; and ankylosing spondylitis – 1 patient. The entire sample was included in the analyses. The sample power was 80%.

Two weeks after the administration of I-PRF, the spontaneous pain decreased in 17 (38.6%) TMJs, no change was observed in 21 (47.7%) TMJs, and the pain worsened in 6 (13.6%) TMJs. The average change in pain intensity expressed on an 11-point VAS was –0.45 ±1.47. The decrease in the intensity of subjective pain reported by the patients was statistically significant ($p < 0.05$) (Fig. 1).

In the group of 27 non-respondent TMJs, there was no change in the intensity of the spontaneous joint pain or an increase to a maximum of 2 VAS points (4 joints in 4 different patients). The average change in the non-respondent TMJs was 0.37 ±0.74 VAS points (*Me* = 0).

In the 17 respondent TMJs, the maximum improvement was –6 VAS points in 1 joint in a patient treated bilaterally. Contralaterally, an improvement of –4 VAS points was observed in the same patient. The average improvement among the respondent TMJs was –1.76 ±1.39 points on the VAS scale (*Me* = –1).

In the subgroup of 29 Wilkes II TMJs, the change in spontaneous pain intensity was from –6 to 2 VAS points. Improvement occurred in 11 TMJs, no changes were observed in 12 TMJs, and deterioration occurred in 6 TMJs. The average change in pain intensity was –0.34 ±1.67 VAS points (*Me* = 0) and was not statistically significant ($p = 0.280$).

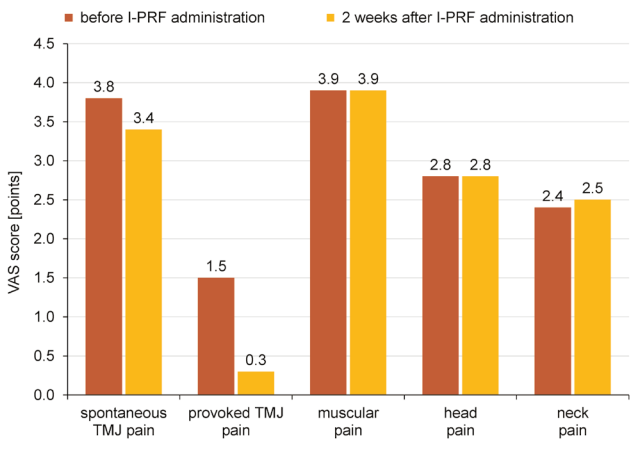


**Fig. 1.** Mean pain scores (visual analog scale – VAS)
I-PRF – injectable platelet-rich fibrin.

In the subgroup of 15 Wilkes III–V TMJs, the change in spontaneous pain intensity ranged from –3 to 0 VAS points. There was improvement in 6 TMJs, there were no changes in 9 TMJs, and the pain did not worsen in any TMJ. The average change in the intensity of the unprovoked pain was –0.67 ±0.98 VAS points (*Me* = 0) and was statistically significant ($p < 0.05$).

Articular pain assessed by the patient immediately after the physical examination decreased after I-PRF administration and 2 weeks of follow-up in 21 (47.7%) TMJs, remained unchanged in 21 (47.7%) TMJs, and worsened in 2 (4.5%) TMJs. On average, the pain provoked by the examination changed by –1.16 ±1.90 ($p < 0.05$) (Fig. 1).

Of the 23 non-respondent TMJs, 2 showed a deterioration of 1 and 2 VAS points. The first patient showed no contralateral change in the provoked pain domain and no change bilaterally in the spontaneous pain. The other patient was injected unilaterally and showed an improvement of –1 VAS point in the assessment of the spontaneous pain.

The respondent TMJs showed a decrease in the provoked pain up to –8 VAS points in a patient injected unilaterally. The same patient rated the spontaneous joint pain both before and after the intervention at 10 VAS points, which showed no change in this domain. The mean improvement in the joint pain measured after the physical examination in the group of the respondent TMJs was –2.57 ±1.89 (*Me* = –2).

In the Wilkes II subgroup, the provoked articular pain score varied from –4 to 1 VAS points. Improvement concerned 14 TMJs, in 14 TMJs there were no changes in pain intensity, and 1 case of deterioration was observed. The average improvement was –0.86 ±1.22 VAS points (*Me* = 0) and was statistically significant ($p < 0.05$).

In the Wilkes III–V subgroup, the articular pain score varied from –8 to 2 VAS points after the physical examination. Improvement concerned 7 TMJs, 7 TMJs showed no changes in pain intensity, and 1 case of deterioration was recorded. The average improvement was –1.73 ±2.76 VAS points (*Me* = 0). It was statistically significant ($p < 0.05$).

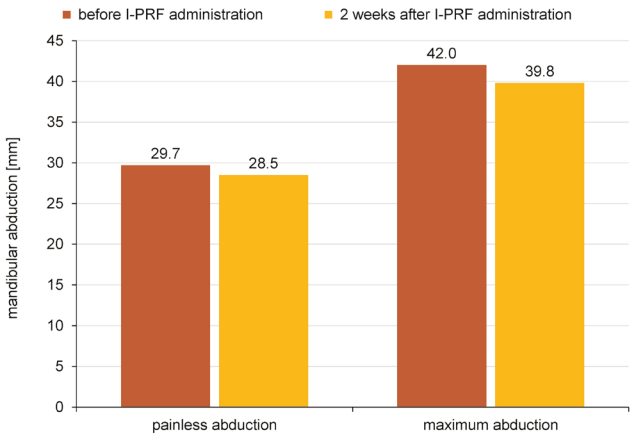


Fig. 2. Mean mandibular abduction [mm]

The mean pain intensity values for the masticatory muscles, head and neck were 3.86 ±2.47 (*Me* = 3), 2.75 ±2.49 (*Me* = 3) and 2.41 ±2.41 (*Me* = 2), respectively, before the intervention, and 3.86 ±2.59 (*Me* = 3), 2.75 ±2.68 (*Me* = 2) and 2.48 ±2.09 (*Me* = 2.5) after the intervention, without statistically significant differences ($p = 1.000$, $p = 1.000$ and $p = 0.700$, respectively) (Fig. 1).

The range of painless jaw abduction changed by an average of –1.2 ±6.8 mm (*Me* = 0 mm) as compared to the pre-intervention value. This change was not statistically significant ($p = 0.220$). The maximum mouth opening changed statistically significantly ($p < 0.05$) by an average of –2.2 ±5.8 mm (*Me* = –1 mm) (Fig. 2).

No adverse events were observed at the recipient sites (TMJs). Some patients reported transient pain and bruising at the donor sites (elbow bends), which did not differ from typical symptoms after venous blood collection from this area.

## Discussion

A single administration of I-PRF to TMJ statistically significantly reduced articular pain at a 2-week follow-up by –0.5 to –1.2 VAS points, depending on the assessment method. Between 39% and 48% of Wilkes II–V patients reported the alleviation of pain after a single intervention, and the non-respondents experienced no change in pain intensity or experienced worsening pain (5–14% of the patients). The deterioration did not exceed 2 VAS points. Regardless of the measurement method, the range of jaw mobility slightly decreased at a 2-week follow-up.

The sources of potential bias were: (1) a small sample size; (2) the lack of control group; (3) a short follow-up period; (4) the open-label design; and (5) subjective pain measures. The small study sample was due to recruitment limitations, which was open for 6 months, and included patients eligible for the study and willing to participate in it. All other limitations resulted from the pilot nature of the study. Moreover, the study included patients with general diseases, which could have increased the heterogeneity of the results.

Differences in the assessment of the intensity of the spontaneous pain and the assessment of the pain provoked by a physical examination were up to 10 VAS points at the same visit. The average differences between these variables were 2.36 (*SE* (standard error) = 0.48; $p < 0.05$) and 3.07 (*SE* = 0.38; $p < 0.05$) VAS points before and after the intervention, respectively, with the provoked pain lower each time. Although the pain associated with performing daily activities is of primary importance to the patient, it can be assumed that the assessment after a specific physical examination protocol may be more repeatable.

The individual consideration of treatment effectiveness allows us to note that despite the satisfactory difference in averages, the number of non-respondent TMJs is significant

and cannot be underestimated. Our own experience and that of other researchers indicate that many patients respond to injection therapy only after a series of administrations, and the initial lack of effect does not mean failure.[20,21,24,25] In our material, a slight increase in pain (up to 2 VAS points) was observed in some patients. It is believed that initially, intra-articular intervention causes the mechanical irritation of the tissues, which results in inflammation.[26] This theory is also supported by a slight, statistically significant decrease in the range of jaw mobility in the study group. Intra-articular injections generally increase the range of jaw abduction, but initially, it may be slightly limited.[27]

The equal average values of muscle pain and headache observed in the study sample during the 1st and 2nd medical interviews are coincidental. The intensity of both types of pain in individual patients changed slightly, increasing and decreasing. However, in both domains, the sums of the VAS scores before and after the intervention turned out to be equal and gave equal means.

In the current state of knowledge, there is a solid theoretical basis for using subsequent generations of centrifuged blood products.[24,28–30] Injectable PRF seems to have a more favorable composition than its predecessors, plasma rich in growth factors (PRGF) and PRP.[24,28–30] Primary research on the intra-articular administration of I-PRF into TMJ is summarized in a review and presents promising results.[14] These encourage future clinical trials on I-PRF. Larger samples, control groups and longer follow-up periods will be crucial to determine the long-term safety and efficacy of the treatment in question.

Another task is to search for the most effective protocol for administering I-PRF. The number of administrations, the time interval between them, and the appropriateness of preceding the first or each administration with arthrocentesis require clarification. This study proposed the least invasive protocol, i.e., the injection of an I-PRF amount smaller than the volume of the articular cavity, without additional burdensome co-interventions, such as administering an anesthetic or rinsing the joint. The study showed that 86–95% of patients experienced improvement or no deterioration, which justifies the search for a more extensive protocol. First of all, using a series of injections is worth considering.

# Conclusions

A single injection of I-PRF into the articular cavity of TMJ brings statistically significant joint pain relief, regardless of the method of its examination. These results and the lack of reported complications provide rational grounds to consider the administration of I-PRF intra-articularly in patients with TMJ pain. A single injection of I-PRF into TMJ revealed no statistically significant effect on muscle pain, headache and neck pain.

## Trial registration

The study protocol was registered in the ClinicalTrials.gov database: NCT05883982.

## Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee at the Świętokrzyska Chamber of Physicians, Kielce, Poland (1/2022-VIII). Informed consent to treatment and to participate in the study was obtained from each patient before enrollment in the study.

## Data availability

The datasets supporting the findings of the current study are available from the corresponding author on reasonable request.

## Consent for publication

Not applicable.

## Use of AI and AI-assisted technologies

Not applicable.


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