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REVIEW

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Evaluation of Awareness and Knowledge Levels of Undergraduate (UGS) Dental Students About Radon

Diş Hekimliği Lisans Öğrencilerinin Radon Hakkındaki Farkındalık ve Bilgi Düzeylerinin Değerlendirilmesi

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ABSTRACT

INTRODUCTION: Radon gas, a significant natural source of ionizing radiation, is the leading cause of lung cancer in non-smokers. This highlights the need for radon protection measures and awareness among healthcare professionals. This study aimed to compare the awareness and knowledge levels of dental students at different stages of their undergraduate education regarding radon's health hazards.

MATERIAL and METHODS: 2nd- and 3rd-year dental students participated in the study. A 21-question survey assessed demographic data, general knowledge of radon, its health effects, and awareness and attitudes toward radon exposure. Data analysis was conducted using descriptive statistics, t-tests, and chi-square tests ($p<0.05$).

RESULTS: The two groups were homogeneously distributed. A significant difference in correct response rates was observed between the groups ($p<0.05$). 3rd-year students, who had received radon education, had a 55% correct response rate, compared to 11% among 2nd-year students, who had not yet received education ($p<0.05$). No significant gender-based difference was found in correct response rates ($p>0.05$).

CONCLUSION: Third-year students demonstrated higher radon knowledge and awareness levels than second-year students. Expanding radon education across all levels of dental programs through curriculum enhancements could improve awareness among future healthcare professionals.

Keywords: *Knowledge, Awareness, Radon, Radiation, Questionaire*

ÖZ

GİRİŞ: Doğal iyonizan radyasyon kaynaklarının en önemlisi olan radon gazı sigara içmeyen bireylerde akciğer kanserinin birincil etkeni olarak bilinmekte ve sağlık çalışanlarının radon hakkındaki farkındalıkları önem kazanmaktadır. Çalışmamızın amacı, diş hekimliği lisans eğitiminin farklı seviyelerindeki öğrencilerin radonun sağlık tehlikelerine ilişkin farkındalıklarını ve bilgi düzeylerini karşılaştırmalı olarak değerlendirmektir.

YÖNTEM ve GEREÇLER: Araştırmamızda, fakültemizde eğitim gören 2. sınıf ve 3. sınıf öğrencilerine hazırlanan anket formu uygulanarak demografik bilgiler, radona ilişkin genel bilgiler, sağlık üzerine olası etkileri ve radon maruziyeti hakkındaki farkındalık ve tutumlarının sorgulandığı 21 soru yöneltildi. Verilerin analizinde tanımlayıcı istatistikler, t testi ve ki-kare testi kullanılmıştır ($p<0,05$).

BULGULAR: 2 öğrenci grubunun homojen dağılım gösterdiği çalışmamızda; 2 grubun sorulara doğru yanıt verme oranları arasında istatistiksel olarak anlamlı bir fark bulundu ($p<0,05$). 3. sınıf öğrencilerinin doğru cevap oranının %55 olduğu, henüz radon eğitimi almamış 2. sınıf öğrencilerinin ise %11'lik oranla daha düşük başarı gösterdiği saptandı ($p<0.05$). Cinsiyetler arasında doğru yanıt oranı açısından istatistiksel olarak anlamlı bir fark bulunmadı ($p>0,05$).

SONUÇ: Diş hekimliği lisans programı kapsamında, temel radon eğitimi alan 3. sınıf öğrencileri ve henüz eğitim almamış 2. sınıf öğrencileri arasında bilgi düzeyleri ve farkındalık oranları açısından anlamlı fark saptanmıştır. Bu doğrultuda lisans eğitim programlarında yapılacak düzenlemeler sayesinde radon eğitimlerinin tüm öğrenim seviyelerini kapsayacak biçimde genişletilmesi, bireylerin farkındalıklarının artmasına katkı sağlayabilecektir.

Anahtar Kelimeler: *Bilgi, Farkındalık, Radon, Radyasyon, Anket çalışması*

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INTRODUCTION

From the past to present, radiation and its sources have been utilized in various aspects of daily life. Consequently, all living organisms on earth are continuously exposed to natural radiation originating from the air, water, and soil (external) and even in their own bodies (internal), as well as to the radiation of artificial radiation sources produced by humans every day.[1,2]

Radiation is divided into ionizing and non-ionizing radiation according to its interaction with matter.[1,2] Especially since ionizing radiation can have negative effects on human health, it is very important to examine the possible effects it may cause.[1,3] The main and the most important natural ionizing radiation source among natural radiation sources is radon gas.[3] Radon (222-Rn) is a byproduct of the radioactive decay chain of uranium (238-U) and radium (226-Ra) found in rocks, soil and water.[3-5] It is a colorless, odorless and tasteless gas classified as a noble gas in the periodic table.[3,6-8] It is estimated that radon gas provides up to 50% to 55% of the average annual dose from natural radiation sources.[4,9,10]

The general effects of radon on human health are caused by its radioactivity and the resulting risk of cancer development due to ionizing radiation.[3,4,8] The main factor causing health hazards from radon exposure is not the radon itself, but the radioactive decay products (218-Po and 214-Po) which are formed during its decay and can adhere to any surface.[3,5-8,11] The accumulation of these radioactive particles in the cells lining the airways every time inhaled can lead to DNA damage and, over time, lung cancer. [3,5-7] In 1988, the International Agency for Research on Cancer (IARC) classified radon gas and its decay products under the category of 'Group 1: Substances that are definitely carcinogenic to humans'.[3,12,13]

With the understanding of the adverse effects of radon gas on health, the number of studies on radon measurements for indoor environments such as residences and workplaces has increased day by day.[14] Many national and international studies have highlighted the association between indoor radon exposure and increased risk of lung cancer.[3,4,6,9,11,15,16] While radon gas is the most important primary cause of lung cancer in non-smokers, it ranks as the second most significant cause among smokers. [3,4,6,6,8,12,17] These striking findings increase the importance of informing the public about the health risks caused by radon gas and measures to protect against radon. The literature includes numerous studies investigating the level of awareness among individuals from diverse educational and social backgrounds regarding the health risks caused by radon gas. While some of these studies targeted the general population, others included healthcare workers who are expected to have a higher level of knowledge about the health hazards of radon.[4,5,7,9–11,13,15,17–26]

In a field such as dentistry, which is an integral part of the healthcare sector and involves frequent use of radiation sources, the knowledge and attitudes of undergraduate students regarding radiation hold significant importance. Dental students undergo undergraduate training on the use of radiation sources, and upon completing this educational process, they are expected to have a basic level of knowledge and awareness in terms of professional aspects and radiation protection practices.[27] However, there is no study in the literature investigating the level of knowledge of undergraduate dental students about radon and possible health hazards.

The aim of this study is to comparatively evaluate the awareness and knowledge levels of dental students at different levels of undergraduate dental education about the potential hazards of radon on general health.

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MATERIAL AND METHODS

Ethical Approval

This study was approved by Ege University Scientific Research and Publication Ethics Committee (EGEBAYEK, Approval No: 05/07-2456) and conducted in accordance with international ethical standards.

Study Group

The study included 2nd grade and 3rd grade students studying in the undergraduate program of Ege University Faculty of Dentistry. In this voluntary survey, students who refused to participate in the study were excluded. In determining the minimum sample size of the study, the sample size approach with an unknown population was used and as a result, the minimum sample size required for a certain level of statistical significance was determined as 200 participants.

Preparation of the Questionnaire Form

In order to prepare the questions, previous survey studies on similar topics in the literature were examined. [9,18, 28-31] A questionnaire form consisting of a total of 21 questions was created to measure the level of knowledge about radon gas, its properties and awareness of its potential risks on health. The form was completed by adapting some of the questions used in these studies and adding new questions to the study under the guidance of the reports/guidelines published in the literature about radon (Table 1).[3,12,32-38]

Table 1. Questionnaire form.

SECTION 1.	
1.Gender	Female ☐ Male ☐
2.Age	15-20 ☐ 21-25 ☐ 26-30 ☐ 30< ☐
3.Education level	2nd Grade ☐ 3rd Grade ☐
4.Smoking habit	Yes ☐ No ☐
SECTION 2.	
5. Have you ever heard of radon?	Yes ☐ No ☐
6. What is radon?	
Gas ☐ Solid ☐ Fluid ☐ Not sure ☐	
7. What are the characteristics of radon? (You can select multiple options.)	
Colorless ☐ Odorless ☐ Tasteless ☐ Not sure ☐	
8. What kind of material is radon?	
Natural ☐ Artificial ☐ Not sure ☐	
9. Is radon radioactive?	
Yes ☐ No ☐ Not sure ☐	
10. Where does radon come from? (You can select multiple options.)	
Air ☐	
Water ☐	
Soil/ Rock ☐	
Nuclear power plants ☐	
Food ☐	
Building materials ☐	
Not sure ☐	
11. In which environment is radon level higher?	
Indoor ☐ Outdoor ☐ Not sure ☐	
SECTION 3.	
12. Is radon harmful to human health?	Yes ☐ No ☐ Not sure ☐
13. Which health problems can radon cause? (You can select multiple options.)	
Lung cancer ☐	
Cardiovascular diseases ☐	
DNA damage ☐	
Dermatological diseases ☐	
Allergy ☐	
Neurological diseases ☐	
Other ☐	
Not sure ☐	
14. How does smoking change the effects of radon?	
Increases ☐ Decreases ☐ Does not effect ☐ Not sure ☐	
15. Can radon level be measured?	
Yes ☐ No ☐ Not sure ☐	
16. How do you think ventilation of indoor spaces in areas with high radon levels will affect radon exposure rates?	
Increases ☐ Decreases ☐ Does not effect ☐ Not sure ☐	
SECTION 4.	
17. If you have heard of radon before, what is your source? (You can select multiple options.)	
Internet ☐ School/Class ☐ TV ☐ Newspaper/Journal ☐ Radio ☐ Health Institution/Doctor ☐ Family/Friend ☐ Other ☐	
18. Do you have information about the precautions taken regarding Radon?	
Yes ☐ No ☐	
19. Do you think you have been exposed to radon?	
Yes ☐ No ☐ Not sure ☐	
20. Do you think the authorities are taking the necessary precautions regarding radon?	
Yes ☐ No ☐ Not sure ☐	
21. Are you worried about being exposed to radon?	
Yes ☐ No ☐ Not sure ☐	

In order to make a preliminary evaluation of the study, the questionnaire form was applied to 20 undergraduate dentistry students in the first stage and the final version of the form was formatted by rearranging it in line with the feedback received. The questionnaire form prepared after this process consisted of four sections in total. In the first section of the questionnaire, the demographic information of the participants as well as their smoking status (questions 1-4) were questioned. In the second section, after questioning whether the students had information about radon or not; there were a total of 7 questions (questions 5-11) aimed at determining the general level of knowledge about the basic characteristics of radon. In the third section, there were 5 questions (questions 12-16) measuring the level of knowledge about the possible effects of radon gas on health. In the last section of the questionnaire, a total of 5 more questions were involved to the questionnaire in order to examine the knowledge levels and attitudes of individuals towards radon gas exposure and measurements, as well as the sources of the participants' access to information about radon. Attention was paid to ensure that the questions aimed at measuring the knowledge level of the students included in the questionnaire (questions 17-21) had evidence-based correct answers (Table 1).

Data Collection

Prior to the study, three researchers (EŞ, İFK, BŞ) informed the students attending the 2nd grade and 3rd grade undergraduate programs of Ege University Faculty of Dentistry about the main purpose of the study and obtained their consent to participate. The students were reached in the classrooms where they received their education within the faculty, and the questionnaire forms were filled in face-to-face with the participants.

Statistical analyses

All statistical analyses of the data obtained from the questionnaire study were performed using IBM SPSS Statistics 20 software (SPSS Inc., Chicago, IL, USA).

The demographic data of the participants in the first section of the questionnaire form were analyzed using descriptive statistical methods. The t-test was used in the comparative analysis of the correct answer rates given to the questions measuring the knowledge levels of the participants (questions 6-16) in terms of the variables of the study (gender, education level, age, smoking). The Chi-squared test was used to calculate the distribution of the answers obtained from each question separately in terms of other survey questions. Statistical significance level was accepted as $p<0.05$.

RESULTS

A total of 332 (100%) dental students (185 female (55.7%) and 147 (44.3%) male) participated in this study. When the age distribution of the participants was analyzed, it was observed that the majority of the participants (98%) were between the ages of 18-25. Among the surveyed students, 149 (44.9%) were 2nd year students and 183 (55.1%) were 3rd grade students. It was found that 119 (35.8%) of the total students were smokers and 213 (64.2%) were non-smokers. Demographic data (gender, age, smoking, education level) of the participants are given in Table 2.

Table 2. Demographic characteristics of the participants.

Demographic Characteristics		n	%
Gender	**Female**	185	55,7
	Male	147	44,3
Age	**15-20**	109	32,8
	21-25	221	66,6
	26-30	1	0,3
	30<	1	0,3
Education Level	**2nd grade**	149	44,9
	3rd grade	183	55,1
Smoking Habit	**Yes**	119	35,8
	No	213	64,2
TOTAL		**332**	**100**

When a total of 3,652 answers given by the 332 dental students participating in the study to the questions with evidence-based definite correct answers (questions 6-16) were analyzed, it was determined that 1,385 (38%) of these answers were correct. When the rates of correct answers to the questions measuring knowledge levels were analyzed in terms of age and smoking parameters (Table 3) included in the study, no statistically significant difference was observed for both parameters ($p>0.05$). When the correct response rates to the questions measuring knowledge level were compared in terms of gender, it was observed that women (37%) were slightly more successful than men (33%), but no statistically significant difference was found between gender and correct response rates ($p>0.05$) (Table 4).

Table 3. Total numbers and percentages of correct answers given by participants to survey questions according to their smoking habits.

Question	Correct Answer		
	Yes	No	
	n (%)	n (%)	p value*
6. What is radon?	70(59)	108(51)	0,05<p
7. What are the characteristics of radon? (You can select multiple options.)	30(25)	73(34)	0,05<p
8. What kind of material is radon?	34(29)	62(29)	0,05<p
9. Is radon radioactive?	56(47)	95(45)	0,05<p
10. Where does radon come from? (You can select multiple options.)	23(19)	51(24)	0,05<p
11. In which environment is radon level higher?	41(34)	81(38)	0,05<p
12. Is radon harmful to human health?	70(59)	105(49)	0,05<p
13. Which health problems can radon cause? (You can select multiple options.)	26(22)	53(25)	0,05<p
14. How does smoking change the effects of radon?	53(45)	76(36)	0,05<p
15. Can radon level be measured?	59(50)	101(47)	0,05<p
16. How do you think ventilation of indoor spaces in areas with high radon levels will affect radon exposure rates?	45(38)	73(34)	0,05<p
TOTAL	119(100)	213(100)	

T-test*

Table 4. Total numbers and percentages of correct answers given by participants to survey questions by gender.

Question	Correct Answer		
	Female	Male	
	n (%)	n (%)	p value*
6. What is radon?	105(57)	73(50)	0,05<p
7. What are the characteristics of radon? (You can select multiple options.)	65(35)	38(26)	0,05<p
8. What kind of material is radon?	50(27)	46(31)	0,05<p
9. Is radon radioactive?	91(49)	60(41)	0,05<p
10. Where does radon come from? (You can select multiple options.)	53(29)	21(14)	0,05<p
11. In which environment is radon level higher?	70(38)	52(35)	0,05<p
12. Is radon harmful to human health?	103(56)	72(49)	0,05<p
13. Which health problems can radon cause? (You can select multiple options.)	44(24)	35(24)	0,05<p
14. How does smoking change the effects of radon?	72(39)	57(39)	0,05<p
15. Can radon level be measured?	92(50)	68(46)	0,05<p
16. How do you think ventilation of indoor spaces in areas with high radon levels will affect radon exposure rates?	69(37)	49(33)	0,05<p
TOTAL	185(100)	147(100)	

T-test*

Table 5. Total numbers and percentages of correct answers given to the survey questions by all participants and their education level.

Question	Correct Answer			p value*
	2nd grade	3rd grade	Total	
	n (%)	n (%)	n (%)	
6. What is radon?	23(15)	155(85)	178(54)	p<0,05
7. What are the characteristics of radon? (You can select multiple options.)	7(5)	96(52)	103(31)	p<0,05
8. What kind of material is radon?	12(8)	84(46)	96(29)	p<0,05
9. Is radon radioactive?	21(14)	130(71)	151(45)	p<0,05
10. Where does radon come from? (You can select multiple options.)	4(3)	70(38)	74(22)	p<0,05
11. In which environment is radon level higher?	21(14)	101(55)	122(37)	p<0,05
12. Is radon harmful to human health?	30(20)	145(79)	175(53)	p<0,05
13. Which health problems can radon cause? (You can select multiple options.)	5(3)	74(40)	79(24)	p<0,05
14. How does smoking change the effects of radon?	26(17)	103(56)	129(39)	p<0,05
15. Can radon level be measured?	30(20)	130(71)	160(48)	p<0,05
16. How do you think ventilation of indoor spaces in areas with high radon levels will affect radon exposure rates?	21(14)	97(53)	118(36)	p<0,05
TOTAL	**149(100)**	**183(100)**	**332(100)**	

T-test*

When the rates of correct answers to the questions measuring knowledge level at different educational levels were evaluated comparatively, it was found that the correct answer rate of 3rd grade students was statistically significantly higher than 2nd grade students ($p = 0.01$) (Table 5). Among all participants, 9 students (3%) who answered all the questions correctly were all 3rd grade students. It was also determined that 67% of these 9 students were female and 22% of them were smokers. It was seen that the question with the highest percentage of correct answers was question 6, "What is radon?" with 54%, and the question with the lowest percentage of correct answers was question 10, "Where does radon come from?" with 22% (Table 5).

The distribution of responses to the questions in the final section of the questionnaire, designed to assess participants' knowledge levels and attitudes regarding radon gas exposure and the associated preventive measures, is presented in Table 6. When the answers given to the questions in this section were evaluated comparatively according to different education levels; it was found that the answers given by the two study groups were similar. Regardless of the level of education, it was observed that the majority of the participants did not have information about the measurements about radon and were undecided about radon exposure and the measurements taken by the authorities regarding radon (Table 6). When the findings on the sources of access to information about radon were analyzed, it was determined that while 2nd grade students showed the internet (68%) as the primary source of information, 133 (59%) of 3rd grade students accessed information about radon through school/class (Figure 1).

Table 6. Total numbers and percentages of participants' answers to questions about radon exposure according to their level of education.

Question		2nd grade	3rd grade
		n (%)	n (%)
18. Do you have information about the precautions taken regarding Radon?	**Yes**	6(4)	38(21)
	No	143(96)	145(79)
19. Do you think you have been exposed to radon?	**Yes**	20(13)	94(51)
	No	8(5)	14(8)
	Not sure	121(81)	75(41)
20. Do you think the authorities are taking the necessary precautions regarding radon?	**Yes**	2(1)	15(8)
	No	27(18)	79(43)
	Not sure	120(81)	89(49)
21. Are you worried about being exposed to radon?	**Yes**	25(17)	91(50)
	No	13(9)	30(16)
	Not sure	111(74)	62(34)

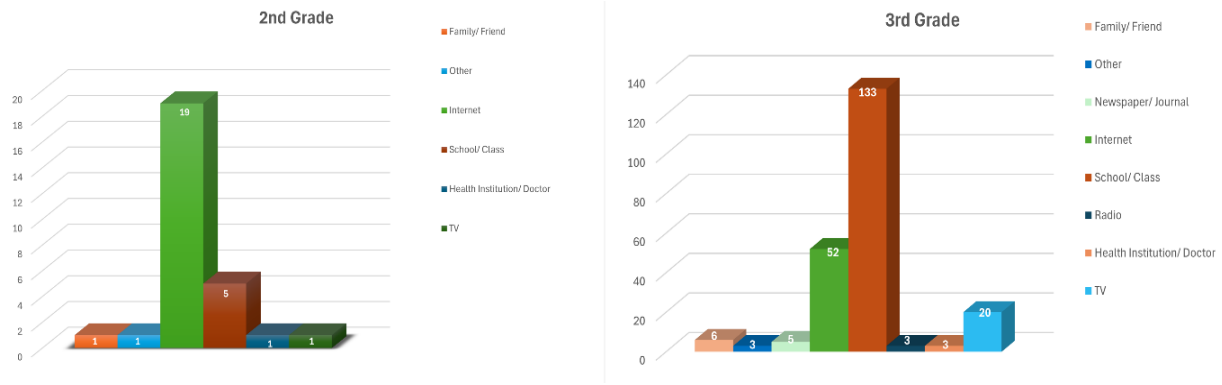

Figure 1. Distrubution of information sources about radon.

DISCUSSION

The use of radiation and its sources in dentistry and medical applications, particularly in the field of radiology, has become a routine aspect of daily practice. For this reason, it is critically important that healthcare workers, who are at high risk in terms of radiation exposure, have knowledge and awareness about radiation, its sources and protection methods. Radon gas, which has an important place among natural radiation sources, constitutes approximately 50%-55% of the average annual dose from natural radiation sources. Therefore, adverse effects of radon on human health are becoming more and more important day by day.[3,20,35,39]

In our study, aimed to comparatively evaluate the level of radon knowledge among dental students at various stages of undergraduate education, it was found that 98% of the participants were aged between 18 and 25 years. A review of similar studies assessing radon knowledge levels reveals a lack of consensus in the literature on this aspect. In some studies, it has been reported that the level of knowledge about radon increases with age, while in some other studies, the level of knowledge decreases as the participants get older.[40-42] In our study, no statistically significant difference was observed with respect to age ($p > 0.05$). We believe that the possible reason of this finding may be the homogeneity of the sample group, which comprised students of similar ages enrolled in the same undergraduate program.

A review of previous studies on radon knowledge levels reveals that, similar to the age parameter, there was also no consensus regarding the demographic factor of gender.[13,40,41] In the survey study conducted by Halpern et al., which targeted the general population, it was observed that the knowledge level of female participants was lower compared to male participants.[40] In more recent similar studies, the knowledge level about radon among the public were found to be higher in male individuals.[13,41] In our survey, in which the gender distribution of the participants was quite close to each other (56% female, 44% male), no statistically significant difference was observed between gender and radon knowledge levels. However, it was observed that the rate of correct answers of female participants (37%) was slightly higher than male participants (33%). When examining the findings regarding another parameter included in our study, "smoking status," no significant difference was found in radon knowledge levels between students who smoked and those who did not ($p > 0.05$). The differences in the number and profile of participants and educational levels in similar studies conducted on this subject prevented the formation of a common opinion in the literature and made us unable to compare some of our findings with the aforementioned studies.

In this study, although no significant difference was found between age and gender parameters and radon knowledge level, a significant difference was observed between "education level" and knowledge level about radon ($p<0.05$). In undergraduate dental education, basic education on radiation sources is given at the 3rd grade level. Our findings show that the knowledge level of 2nd grade dentistry students who have not yet been trained in this subject within their curriculum is lower than 3rd grade students who have received basic training on radiation sources. When examining similar studies where both the participant groups and the number of participants vary, it is evident that education level is positively correlated with radon knowledge levels.[9,40,42,43] This finding is further supported by studies involving healthcare professionals and students in healthcare-related fields, where the use of radiation sources is prevalent, demonstrating a similar positive correlation between education level and radon knowledge.[7,10,17,44] The findings of our study consistent with the existing literature. However, unlike other studies assessing radon knowledge levels, where participant groups and numbers exhibit significant variability, the relatively balanced and homogeneous distribution of participant groups in our study has facilitated a more robust and accurate analysis of the obtained results.

In our study, questions measuring the level of knowledge of dental students on two different basic

subjects, which are “general characteristics of radon” and “possible effects of radon on health and radon measurement”, were included. In the second section of the questionnaire, which focused on the "general characteristics of radon," the question "What is radon?" emerged as the most correctly answered question. However, a remarkable finding at this stage was that as the questions in this section became more detailed, the accuracy rates decreased. This trend was observed across both study groups with differing education levels included to the present study. In the third section of the questionnaire, the effects of radon on health were examined. Analyzing responses to the first question in this section, "Is radon harmful to human health?", 20% of 2nd-year students and 79% of 3rd-year students answered "yes." This finding suggests that education at the undergraduate level enhances knowledge about radon. However, similar to the finding obtained for the second part of the questionnaire, it was observed that the correct response rates decreased for both 2nd graders (3%) and 3rd graders (40%) as the questions about the level of knowledge were more detailed by asking which health problems radon causes. This remarkable finding is consistent with similar studies in the literature. Rafique et al. found that 80% of healthcare workers had heard of radon before, while only 30% had knowledge about radon and its hazards.[10] This finding observed in both studies raises concerns about the level of awareness of radon and its hazards in the healthcare field, where knowledge and attitudes about radon are very important, as in dentistry.

The final section of the questionnaire focused on participants' sources of information about radon, as well as their knowledge and attitudes toward radon gas exposure. When asked about their sources of information on radon and its effects, notable differences were observed between the two study groups. While the majority of 2nd-year students (68%) selected "Internet," over half of 3rd-year students (59%) chose "School/ Class." Among 3rd-year students—who had received basic education on radon—"Internet" was the second most common response after "School/Class". When the findings of similar studies conducted with the general population are reviewed, it was found that the highest rate of response to this question differed.[13,15] However, a distinguishing factor in these studies is the older average age of participants compared to our study. Another notable observation is that, consistent with our findings, younger individuals in these studies were more likely to select "Social Media/Internet" as a primary source of information, with this trend being evident across both genders.[13] The fact that younger individuals use the internet/social media more could be the possible reason for the answer given in favor of the “Internet” option as the age decreases both in our study and in similar studies in the past.

The sources from which the participants received information about radon and their awareness and attitudes towards radon gas exposure were another parameter questioned in our study. In this regard, only 13% of the 2nd grade students answered “Yes” to the question “Do you think you have been exposed to radon?”, while this rate was 51% among the 3rd grade students. It is noteworthy that the answers given by two different study groups to another question asked in the last section of the questionnaire as “Are you worried about being exposed to radon?” are similar. 17% of 2nd grade students and 50% of 3rd grade students stated that they were concerned about radon exposure. The fact that 3rd grade students have a higher rate of concern about radon exposure compared to 2nd grade students coincides with their higher level of knowledge about radon. However, it is noteworthy that only 51% of 3rd grade students think that they have been exposed to radon despite having received radon education. This finding raises doubts about the adequacy of the education on radiation sources and radon, although it has increased the knowledge level of the 3rd graders.

In the literature, there are many studies evaluating the level of knowledge and awareness of radon and its potential effects.[7,9,12,12,18,23,26,29,45,46] These studies mostly included individuals from different educational and social levels of the population. In the limited number of studies conducted on healthcare professionals, it is noteworthy that most of them belong to different groups such as nurses/physicians and healthcare staff.[7,10,17,44] Similar to our study, only two studies in the literature specifically evaluate the impact of radon gas on students pursuing education in healthcare-related fields.[7,10] However, no prior research has been identified that specifically targets dental students in undergraduate programs. In this regard, our study is the first to assess the knowledge levels of dental students about radon and its potential health hazards within the scope of a dental undergraduate curriculum.

CONCLUSION

In this study, we investigated the level of knowledge of dental students at different levels of undergraduate dental education about radon and its potential health hazards. As a consequence, a significant difference was found between 3rd year students who received basic education about radon and 2nd year students who had not yet received any education in terms of knowledge levels and awareness rates. However, the low overall accuracy rate (38%) in responses to the knowledge-based questions among all participants highlights the insufficient level of knowledge about radon, even among those who had received basic education. In light of these findings, incorporating curriculum revisions within dental undergraduate programs to expand radon-related education may contribute significantly to increasing

students' knowledge and awareness. Although our study is the first study to evaluate the knowledge levels about radon and possible health hazards in the dental field with all parameters, it includes only two different grades of students in the dentistry undergraduate program. Future studies with larger participant populations encompassing all levels of undergraduate education would provide a clearer understanding of the need for curriculum updates and allow for more accurate conclusions. This could ultimately facilitate more effective integration of radon-related education into dental training programs.

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Evaluation of the Elongation Amount in Prepared Molar Teeth With the Aid of an Intraoral Scanner

Prepare Edilmiş Molar Dişlerdeki Uzama Miktarının Dijital Sistem ile Değerlendirilmesi

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ABSTRACT

INTRODUCTION: To evaluate the amount of displacement of endodontically treated molar teeth after tooth preparation for crown restoration in short term.

MATERIAL and METHODS: Eighteen endodontically treated molar teeth were scanned using digital intra-oral scanner on the day of tooth preparation and a week later. The data of the first and last scans were compared to evaluate the possible tooth displacement with color maps. For each tooth, measurements from 5 different reference points were performed to qualitatively determine the amount of displacement. Statistical analysis was done with the Wilcoxon test. Statistical significance was set at p<0.05.

RESULTS: No difference was determined in the bucco-lingual and cervico-incisal directions, but there was a difference in the mesio-distal direction according to color maps. But the difference was not statistically significant (p>0.05)

CONCLUSION: According to the findings of this study the amount of mesio-distal displacement that observed in root canal-treated molars in adults found to be neither statistically nor clinically significant.

Keywords: *Color map, digital intra-oral scanner, tooth movement*

ÖZ

GİRİŞ: Bu çalışmanın amacı; kron restorasyonu için diş preperasyonu yapılmış endodontik tedavili azı dişlerinin, kısa sürede yer değiştirip değiştirmediğinin değerlendirilmesidir.

YÖNTEM ve GEREÇLER: Endodontik tedavi görmüş 18 azı dişi, dişin prepare edildiği gün ve bir hafta sonrası dijital ağız içi tarayıcı kullanılarak tarandı. Olası diş yer değiştirmesini renkli haritalarla değerlendirmek için ilk ve son taramaların verileri karşılaştırıldı. Yer değiştirme miktarının niteliksel olarak belirlenmesi amacıyla her diş için 5 farklı referans noktasından ölçümler yapıldı. İstatistiksel analiz Wilcoxon testi ile yapıldı. İstatistiksel anlamlılık p<0.05 olarak belirlendi.

BULGULAR: Renk haritalara göre bukko-lingual ve serviko-insizal yönlerde farklılık saptanmazken mesio-distal yönde farklılık tespit edildi. Ancak fark istatistiksel olarak anlamlı değildi (p>0,05)

SONUÇ: Bu çalışmanın bulgularına göre erişkinlerde kanal tedavili azı dişlerinde gözlenen mezio-distal yer değiştirme miktarının ne istatistiksel ne de klinik olarak anlamlı olmadığıdır.

Anahtar Kelimeler: *Renk haritası, dijital ağız içi tarayıcı, diş hareketi*

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INTRODUCTION

Restoration with a full crown is recommended for molar teeth with root canal treatment as these teeth are subjected to heavier occlusal forces compared with anterior teeth.[1,2] A crucial amount of hard tissue is lost during the removal of carious tissues and preparation of the access cavity. Brittleness of teeth increases as a result of moisture loss and change in the collagen microstructure of the dentin after removing pulp tissues.[1,2] Temporary crowns are preferred to prevent tooth sensitivity and tooth displacement. Sensitivity is not a problem for endodontically treated teeth and temporary restoration of these teeth may potentially lead to allergic reactions, plaque buildup, or gingival irritation.[3,4] Because of these reasons, temporary crown restorations may not be necessary for these teeth if contact losses in the prepared tooth do not result in possible occlusal, mesio-distal, or bucco-lingual tooth movement.[5] Tooth movement of prepared teeth even if in the short term may affect the fit of the final restoration or aesthetics.

In the light of the literature, scarce information existed regarding the amount of displacement of teeth for prosthetic purposes.[6] To the best of our knowledge, this is the first study aimed to digitally evaluate the three-dimensional (3D) displacement of the prepared endodontically treated teeth for crown restoration in short term.

The null hypothesis is ‘‘there is no difference in the position of endodontically treated before and one week after preparation’’

MATERIAL and METHODS

The present study was executed with the approval of Nuh Naci Yazgan University Scientific Research and Publication Ethics Committee Presidency, numbered 2022/8112. All patients were informed about the study and who were willing to participate signed an informed consent.

The required minimum sample size was determined using the G*Power v.3.1.9.4 program (Heinrich Heine, University of Duesseldorf, Duesseldorf) according to the data from Zhang et al.[6] The effect size calculated using the data of the mentioned study is 1,386. An alpha-type error of 0.05 and a beta power of 0.95 was specified, and each group's minimal estimated sample size was computed as 9 to determine the displacement of prepared teeth. A total of 18 samples were included to increase the statistical power of this study and consider potential sample loss. The study was carried out retrospectively with the data of the patients who applied to Aydın Adnan Menderes University Faculty of Dentistry, Prosthetic Dentistry clinic between 01.01.2020 and 01.01.2021. The data from the intraoral scanning of patients who underwent prosthetic treatment after root-canal treatment without temporary restoration due to patient-related reasons were used in the present study.

The following inclusion and exclusion criteria were considered in the selection of patients to be treated;

The inclusion criterias were as follows:

1) endodontically treated molars which are to be further treated with single crown,
2) first and the second molars which has approximal contacts and occlusal antagonists,
3) adults,
4) completion of prosthetic treatment no more than one week.

The exclusion criteria were as follows:

1) history of systemic and periodontal disease,
2) history of orthodontic treatment.

After tooth preparation, the impressions were taken by an intraoral scanner (Trios 3 Scanner, 3Shape, Copenhagen, Denmark). After one week, a second scan (final scan) was performed during the final appointment and recorded in the digital archive of the scanner system. After color map superimpositions, measurements were performed on initial and final intraoral scannings to determine whether the color difference was due to the displacement of the tooth in any direction.

Reference points were determined for linear measurements as; the central fossa, mesial and distal marginal ridges, and buccal and lingual cusp of the tooth located mesial to the prepared tooth. [7]

Linear measurements were as follows (Figure 3);

1- The distance between the palatal midpoint of the prepared tooth and the palatal surface of the reference tooth,
2- The distance between the buccal midpoint of the prepared tooth and the buccal surface of the reference tooth,
3- The distance between the mesial transverse ridge of the prepared tooth and distal transverse ridge of the reference tooth,
4- The distance between the midpoint of the central fossa of the prepared tooth and the midpoint of the central fossa of the reference tooth,
5- The distal transverse ridge of the prepared tooth and the mesial transverse ridge of the reference tooth .

The data of the initial and the final scans were compared, and possible tooth displacements were analyzed with three-dimensional color maps and lineer measurements.

Statistical Analysis

Statistical data analysis was performed using the IBM SPSS Statistics V25 (Armonk, NY: IBM Corp)

program. The normal distribution of the data was examined with the Shapiro-Wilk test. Descriptive statistics were presented as mean and standard deviation. Statistical analyzes were performed with the Wilcoxon Test. The significance level was 0.05 in all analyzes.

RESULTS

Eighteen teeth (six maxillary, twelve mandibular teeth) of twelve patients who met the inclusion criteria were included in the study.

The initial and the final scans were superimposed in 3D using Ortho Analyzer™ (3Shape, Copenhagen, Denmark) software. After registration, no color difference was observed in the bucco-lingual and cervico-incisal directions (Figure 1), but there was a difference in the mesio-distal direction (Figure 2). Measurements were made using the initial and the final scan to determine whether the color difference in the mesiodistal direction was due to any movement in the tooth. These measurements were by calculating the distance among reference points. The difference between the measured values was analyzed statistically. There is no statistically significant difference when five different data from the scale are evaluated over the initial and final screening data (Table 1).

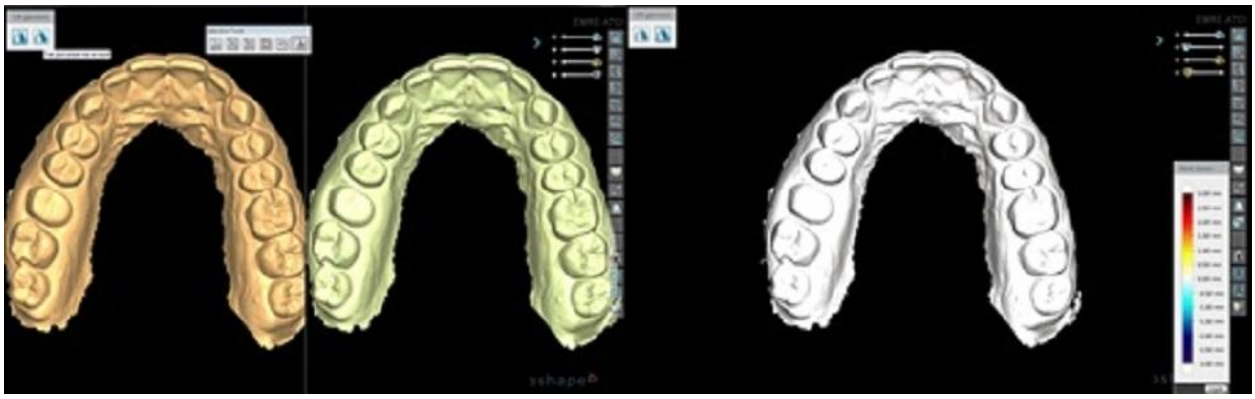

Figure 1. A 3D registration and colormap image of a sample.

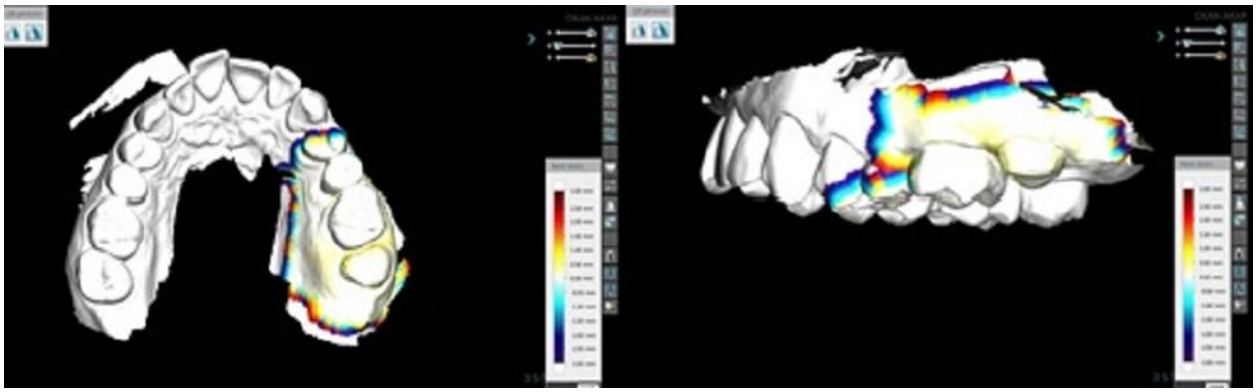

Figure 2. A 3D registration and colormap image of a sample.

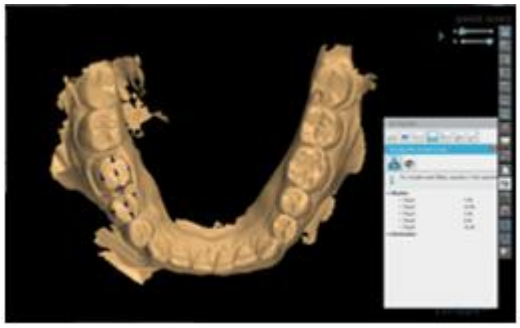

Figure 3. Measurements made by taking reference points in the mesio-distal direction

Table 1. Wilcoxon analysis results

Obtained from 1st and 2nd Scan Data	P
Between 1. Measurements	0,372
Between 2. Measurements	0,616
Between 3. Measurements	0,349
Between 4. Measurements	0,647
Between 5. Measurements	0,931

*p<0,05

DISCUSSION

There has been a general belief that permanent teeth without contact or antagonists over-erupt, rotate, or tip. Displacement of teeth is a complex issue to study as the relevant mechanisms affected and the slow development of the movement have not been fully understood.

Most of the literature examining displacement has investigated movements in periods of a long time after tooth loss or orthodontic treatment. [7,8] According to literature, there is only one study that investigates the tooth movement from a prosthodontic perspective.[6]

To the best of our knowledge, this is the first study in the literature that evaluate the amount of displacement of prepared teeth for crown restoration in short term.

Despite the rapid development in technologies, the delivery of a metal-ceramic restoration expected to take at least a week. The study was planned over a short term (1 week) to reflect typical clinical practice. The findings of this study is believed to be helpful to guide clinicians in terms of time and material planning.

In prosthodontic literature, tooth movement has been evaluated using panoramic radiographs[9], confocal laser scanning microscopy (CLSM) [10], dental casts[8-11], and the use of colormaps obtained by superimposition.[6] In this study color maps and superimposition technique was adopted from the study of Liu et al.[6]

Continuous eruption, hyper eruption, over-eruption, super-eruption, and supra-eruption terms have been used to describe continued tooth movement in the occlusal direction even during adulthood.[9] It has been shown that the dentoalveolar height increases throughout adulthood, and the teeth continue to move during this small but stable growth, and this movement has been shown for both opposite and non-opposite teeth.[9,12] There have been conflicting reports on the degree and severity of posterior tooth movements that occur when there are no opposing or neighboring teeth.[11,13,14] Craddock et al. found that 92% of non-opposite posterior teeth excessively erupted in study of 100 individuals over the age of 18, and prevelance of whom with missing teeth for more than five years of with more than 2 mm eruption was 27%.[13] The authors also reported that excessive movement of the maxillary teeth was significantly more than the mandibular teeth. Shugars et al. in their retrospective study with 111 adults, unopposed posterior teeth over a median period of 7 years revealed excessive eruption of >1 mm in only 1% of cases studied. [15] Altough the amount is not certain, the results in these studies which belong to long-term tooth movements have shown that there is an over eruption. While, in this present study short term tooth movements were examined.

Christou and Kiliaridis examined the changes in the position of maxillary molars without antagonists in adults.[7] The results of their 10-year evaluation demonstrated that displacement of unopposed teeth occurs in three dimensions, however in patients with healthy periodontal tissues, this is clinically insignificant. Also, healthy teeth are likely to show uniform vertical displacement over time due to the continued activity of the periodontal ligament.[7] However, irregular vertical movement of periodontally affected teeth is very likely due to the nature of the disease.[7] Another result was the significant palatal displacement of the molars, which did not have an antagonist. This can be attributed to the constant strength of the soft tissues adjacent to the tooth and the perioral muscle system, particularly the buccinator muscle, which is a significant environmental determinant of the tooth position.[16] Another factor for the compensation of teeth may be occlusal forces. They play an essential role in maintaining the transverse dimension of dental arches but there are no occlusal forces on teeth without antagonists.[17]

Compagnon and Woda examined the unrelated upper first molars in both healthy mouths and mouths with some periodontal pathologies.[18] Their study showed that most overeruption occurs in the first years following losing the opposing tooth.[18] They reportedthat the gingival margin remained at its original level during this occlusal tooth movement in healthy individuals. In these studies vertical tooth movement is frequently evaluated.[7,13,15,18] Since developments in digital technologies shorten the treatment time, the reason why vertical tooth movement was not observed in the present study may be that a shorter treatment time was determined compared to the treatment time in other studies.

Moreover, in the present study, unlike other studies, teeth that endodontically treated were evaluated.[7,13,15,18] Further studies are needed to investigate whether there is a difference between overeruption of vital and endodontically treated teeth.

A 12-year study conducted by Lindskog-Stokland et al. in women over 50 years of age showed that the risk of excessive eruption of unopposed molars increased significantly.[9] In contrast, the risk of molars facing a mesial edentulous space showed a low risk for mesial tipping as a result of tooth extraction was low. However, there was a significant interaction between overeruption and tipping; in both conditions, an increase in overeruption was associated with molar tipping. In the present study, Contrary to the results of this study, in the current study, mesial movement of the teeth was observed, although the working time was much shorter. The change that occurs during one week span may not be clinically important and may be compensated by the cement space.

Studies examining tooth movements are often

orthodontic, and only one study is in prosthodontics is performed by Liu et al. [6] They prepared molars to make post-core and reported that the most tooth movement is in the mesiodistal direction, followed by bucco-lingual and occluso-gingival. In our study, the most displacement was in the mesiodistal direction however, the displacement was not statistically significant. The absence of movement in the buccolingual direction may be attributed to the distribution of periodontal ligaments. Teeth generally exhibit a tendency for mesial migration, and to control this movement, the mesial ligaments are more densely organized.[19]

One of the limitations of this study was that this study is the small sample size. Another limitation may be the exclusion of teeth with decreased periodontal support, as those teeth may be more prone to diplacement. Future research may focus on the displacement of prepared teeth. taking into account the periodontal factors in larger sample.

In this study, mesialization was observed in endodontically treated and prepared teeth but it was not considered clinically significant. The study presents a scientific evidence for the determination to make a temporary restoration from the time of the preparation to the delivery of the crown restoration. Within the limitations of this study, temporary crowns may not be necessary in cases of allergies or in cases where occlusal force is not desired during recovery of endodontically treated teeth. Moreover, this will reduce both the chair time and the cost.

CONCLUSION

Within the limitations of this study;

The decision to place a temporary crown during the prosthetic process for an endodontically treated tooth should be made by the clinician after carefully evaluating the advantages and disadvantages of the procedure.

Only mesio-distal displacement was observed in endodontically treated molars after tooth preparation.

Mesiodistal tooth displacement was neither statistically nor clinically significant.

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Prevalence of Third Molar Tooth Agenesis and its Association with Hypodontia in Pediatric Population

Pediyatrik Popülasyonda Üçüncü Molar Diş Agenezisinin Prevalansı ve Hipodonti ile İlişkisi

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ABSTRACT

INTRODUCTION: This study aims to identify differences in third molar (M3) agenesis between genders and jaws and its association with other congenital tooth deficiencies.

MATERIAL and METHODS: The study included patients aged 11–13 years who visited the Dokuz Eylull University Pediatric Dentistry Clinic between December 1, 2022, and January 30, 2024, had no systemic diseases, and possessed panoramic radiographs of diagnostic quality. Congenital absence of M3 and other teeth were recorded. Data were analyzed using SPSS 24.0, and statistical evaluation was performed with the chi-square test. Significance was set at p<0.05.

RESULTS: A total of 630 patients, 325 (51.6%) females, were evaluated. Agenesis was observed in one or more M3 teeth in 136 (21.5%) patients, and 4.6% had agenesis in all M3 teeth. M3 agenesis prevalence was higher in the maxilla (11.0%) than in mandible (7.5%) (p<0.001). More females (11.9%) than males (9.6%) had one or more M3 teeth absent, but the difference was not statistically significant (p< 0.348). Hypodontia in other permanent teeth was detected in 31.3% of patients with four M3 agenesis (p<0.001).

CONCLUSION: Early detection of M3 and other tooth agenesis in children is crucial for planning future treatments for both dentists and patients.

Keywords: *Prevalence, Agenesis, Third molar, Hypodontia*

ÖZ

GİRİŞ: Bu çalışmanın amacı, üçüncü molar (M3) dişlerin agenezisinin cinsiyet ve çeneler arasındaki farklılıklarını saptamak ve diğer konjenital daimi diş eksiklikleri ile olan ilişkisini belirlemektir.

YÖNTEM ve GEREÇLER: Çalışmaya, 01.12.2022 ile 30.01.2024 tarihleri arasında, Dokuz Eylül Üniversitesi Çocuk Diş Hekimliği Kliniği'ne başvuran, herhangi bir sistemik hastalığı olmayan, uygun diagnostik kaliteye sahip panoramik radyografileri bulunan 11-13 yaş aralığındaki tüm hastalar dahil edildi. Panoramik radyografik görüntülerin incelenmesi sonrası, M3 dişlerin ve diğer dişlerin konjenital eksiklikleri kaydedildi. Verilerin analizinde SPSS 24.0 programı kullanıldı, ki-kare testiyle istatistiksel olarak değerlendirildi ve anlamlılık düzeyi p<0,05 olarak kabul edildi.

BULGULAR: 325'i (%51,6) kız olmak üzere toplamda 630 hastanın bulguları değerlendirildi. 136 (%21,5) hastanın bir veya daha fazla M3 dişinde agenezi gözlenirken, %4.6'sında tüm M3 dişlerinde agenezi olduğu saptandı. M3 diş agenezisi görülme prevalansı maksillada (%11,0) mandibulaya (%7,5) göre daha yüksek bulundu (p<0.001). Bir veya birden fazla M3 diş eksikliği kadınlarda (%11,9), erkeklere (%9,6) oranla daha yüksek gözlenmesine rağmen; fark istatistiksel olarak anlamlı bulunmadı (p<0.348). Dört adet M3 agenezisi kaydedilen hastaların %31,3'ünde diğer daimi dişlerinde de bir ya da daha fazla hipodonti tespit edildi, fark istatistiksel olarak anlamlı bulundu (p<0.001).

SONUÇ: Çocuklarda M3 diş agenezisi ve diğer konjenital diş agenezilerinin erken yaşta tespit edilmesi ileriye yönelik uygulanacak tedaviler açısından diş hekimleri ve hastalar için önem taşımaktadır.

Anahtar Kelimeler: *Prevalans, Agenezis, Üçüncü molar, Hipodonti*

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INTRODUCTION

The third molar (M3) teeth are the last molars to erupt in the oral cavity. [1] The eruption of these teeth typically begins during late adolescence (ages 14-23) and may continues into adulthood.[2] As the last permanent teeth to develop in the dentition, and due to their clinical implications in oral health and treatment planning, they have been a subject of extensive dental research.[1,2]

A comprehensive understanding of factors such as their positional variations, morphological characteristics, number, and developmental stages is crucial, as these elements can significantly influence diagnostic and therapeutic decision-making in dental practice.[2-3] Several studies have evaluated the development and calcification stages of M3 teeth in children at various ages.[4-6] Despite ethnic variations, it has been reported that crown calcification of the M3s generally initiates between the ages of 7-10 years, completed by 12-16 years.[5,7]

In studies examining congenital tooth agenesis across different populations, the prevalence of permanent tooth agenesis is typically reported with the exclusion of third molars (M3).[8] The reason for this exclusion is that the absence of M3 teeth is more commonly observed than the absence of other permanent teeth.[2] Furthermore , studies specifically focusing on M3 agenesis have shown that its prevalence varies significantly between populations, ranging from 1.9% to 40%.[1,2,7,9] In a meta-analysis conducted by Carter and Worthington[9], the global prevalence of M3 agenesis was reported to be an average of 22.6%.

There are studies that indicate a gender-based difference in M3 agenesis, as well as studies that report no such difference.[2,10-13] Alamoudi et al.[10] and Pamukcu et al.[13] have both reported that the likelihood of one or more M3 agenesis is higher in females compared to males.

Studies have indicated that genetic factors play a significant role in M3 agenesis.[14-17] Genome-wide association studies have identified several candidate genes, such as MSX1, PAX9, and AXIN2, that are involved in the development of various teeth, including the third molar.[14,15] Some researchers have reported that PAX9 gene mutations are implicated in cases of non-syndromic hypodontia and/or oligodontia, and that M3 agenesis is associated with these mutations.[16,17] Other studies suggest that mutations in the MSX1 gene, in particular, are associated with the agenesis of second premolars and third molars.[14,15] Additionally, a study on monozygotic and dizygotic twins has demonstrated that genetic factors play a significant role in M3 agenesis, with these factors strongly influencing the phenotype.[18]

While genetic predisposition plays a significant role, environmental factors such as nutrition, oral hygiene, and overall health have also been shown to influence tooth development. Additionally, craniofacial structure and tooth size have been linked to the presence or agenesis of third molars.[19]

Alamoudi et al.[10] suggested that individuals with agenesis of other permanent teeth have a higher likelihood of agenesis of all four third molars, and that the absence of other teeth may serve as an indicator for the absence of third molars. Garn et al.[20] reported that the presence of one or more M3 agenesis increases the likelihood of other permanent tooth agenesis by 13 times. Additionally, Endo et al.[21] demonstrated that as the severity of M3 agenesis increases, the frequency of hypodontia also rises.

This study aims to examine the relationship between M3 agenesis and congenital agenesis of other permanent teeth in pediatric patients, as well as the prevalence of M3 agenesis based on gender and jaw location. Additionally, by reviewing the current literature on M3 agenesis, the study seeks to contribute to the growing knowledge in pediatric dentistry and help develop effective management strategies for children affected by this condition.

MATERIAL AND METHODS

This study, designed as a retrospective cross-sectional study, included patients aged 11–13 years who visited the Dokuz Eylul University Pediatric Dentistry Clinic between December 1, 2022, and January 30, 2024, had no systemic diseases, and possessed panoramic radiographs of diagnostic quality. A total of 647 panoramic radiographs were obtained using a Planmeca Proone device, with an exposure setting of 64 kV/7mA and an exposure time of 8.9 seconds, following the manufacturer's standard protocols for pediatric imaging. Of these, 17 radiographs were excluded due to motion artifacts that impaired diagnostic quality, leaving 630 patient images available for analysis. Two pediatric dentists (GK, GB) performed repeated measurements on 25 panoramic radiographs, one week apart, which were not included in the study. This procedure standardized the methodological errors. Cohen’s Kappa scores were determined to be 0.95 and 0.85. In addition to age and gender, the congenital agenesis of permanent and M3 teeth was recorded in the patient files. Ethical approval for the study was obtained from the Dokuz Eylul University Non-Interventional Ethics Committee (Decision number: 2023/23-23).

Statistical Analysis

The statistical analysis of the data was performed using SPSS 24.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics, including percentage distribution, mean (±) values, and standard deviation, were calculated. The analysis of categorical variables was conducted using the Chi-square test and Fisher's exact test. Inter-observer agreement was assessed using

Cohen's Kappa analysis. A p-value of <0.05 was considered statistically significant.

RESULTS

The clinical and radiographic (panoramic) findings of 630 patients, including 325 females (51.6%) and 305 males (48.4%), with ages ranging from 11 to 13 years (mean age: 12.13 ± 0.78), were analyzed. Among the patients whose panoramic radiographs were examined, 78.5% had all M3 teeth present, while 21.6% (136 patients) exhibited agenesis of one or more M3 teeth. Agenesis of all M3 teeth was identified in 4.6% (29 patients) of the cases. The prevalence of agenesis in one or two M3 teeth was found to be 7.1%, while agenesis in three M3 teeth was observed in 2.7% of the patients (Table 1).

Table 1: Status of Third Molar Teeth in Patients

Third Molar(M3) Teeth	N (%)
Agenesis of a Single M3 Tooth	45 (%7,1)
Agenesis of Two M3 Teeth	45 (%7,1)
Agenesis of Three M3 Teeth	17 (% 2,7)
Agenesis of Four M3 Teeth	29 (% 4,6)
All M3 Teeth Present	494 (%78,5)
TOTAL	630 (%100)

* M3: Third molar

The most common M3 tooth agenesis was observed in the upper right M3 (15.1%), followed by the upper left M3 (13.2%), lower left M3 (10.2%), and lower right M3 (9.2%) (Table 2). The prevalence of M3 tooth agenesis in the maxilla was found to be higher than in the mandible, with the difference being statistically significant (p < 0.001) (Table 3).

Table 2: Agenesis of Third Molar (M3) Teeth in Patients

Agenesis of Third Molar (M3) Teeth	N (%)
Maxillary right M3 (18)	95 (%15,1)
Maxillary left M3 (28)	83 (%13,2)
Mandibular left M3 (38)	64 (%10,2)
Mandibular right M3 (48)	58 (%9,2)
Maxillary M3(18-28)	69 (%11)
Mandibular M3 (38-48)	47 (%7,5)
Upper right-lower right side (18-48)	35 (%5,6)
Upper left-lower left side (28-38)	40 (%6,3)
TOTAL	630 (%100)

* M3: Third molar

Table 3: Status of Third Molar (M3) Teeth in the Maxilla and Mandible

Third Molar (M3) Teeth	Present (N %)	Absent (N %)	P
Maxillary M3 (18-28)	561(%89,0)	69 (%11,0)	0.000*
Mandibular M3 (38-48)	583 (%92,5)	47 (%7,5)	

Chi-square test, *p<0.001

No statistically significant difference was found between gender and the prevalence of M3 tooth agenesis or congenital tooth agenesis (hypodontia) in other teeth. M3 tooth agenesis was slightly more common in females (11.9%) than in males (9.7%) (p = 0.348) (Table 4).

Table 4: Distribution of Third Molar Teeth (M3) by Gender and Prevalence of Hypodontia in Other Teeth

Gender	Female (N %)		Male (N %)		P
	Present	Absent	Present	Absent	
M3 Tooth Agenesis (One or More)	75(%11,9)	250(%39,6)	61(%9,7)	244(38,7)	0.348
Upper right M3 (18)	276 (%43,8)	49 (%7,8)	259 (%41,1)	46(%7,3)	0.999
Upper left M3 (28)	280 (%44,4)	45 (%7,1)	267 (%42,4)	38 (%6,0)	0.607
Lower left M3 (38)	293 (%46,5)	32 (%5,1)	273 (%43,3)	32 (%5,1)	0.789
Lower right M3 (48)	299 (%47,5)	26 (%4,1)	273 (%43,3)	32 (%5,1)	0.280
Maxillary M3 (18-28)	290 (%46,0)	35 (%5,6)	271 (%43,0)	34 (%5,4)	0.879
Mandibular M3 (38-48)	305 (%48,4)	20 (%3,2)	278 (%44,1)	27(%4,3)	0.198
Upper right- Lower right M3 (18-48)	310 (%49,2)	15 (%2,4)	285 (%45,2)	20 (%3,2)	0.288
Upper left- Lowe left M3 (28-38)	306 (%48,6)	19 (%3,0)	284 (%45,1)	21 (%3,3)	0.593
Agenesis of Four M3 Teeth	12 (%1,9)	313(%49,7)	17 (%2,7)	288 (%45,7)	0.260
Agenesis of Three M3 Teeth	10 (%1,6)	315 (%50)	7 (%1,1)	298 (%47,3)	0.545
Agenesis of Two M3 Teeth	24 (%3,8)	301(%47,8)	21 (%3,3)	284 (%45,1)	0.808
Agenesis of a Single M3 Tooth	29 (%4,6)	296(%47,0)	16 (%2,5)	289 (%45,9)	0.073
Hypodontia in Other Permanent Teeth	18 (% 2,9)	307(%48,7)	14(%2,2)	291(% 46,2)	0.588

Chi-square test, *p<0.001

In our study, hypodontia (one or more missing teeth) was detected in 5.1% (32) of the 630 patients. Among patients with agenesis of all four M3 teeth, 31.3% (10 patients) demonstrated hypodontia in one or more permanent teeth, and this difference was statistically significant (p<0.001). In the 10 patients with agenesis of all four M3 teeth, congenital agenesis was observed in a total of 20 teeth, including eight maxillary laterals, five mandibular second premolars, and seven maxillary second molars. No statistically significant difference was found between patients with agenesis of one, two, or three M3 teeth and the occurrence of hypodontia in permanent teeth (p=0.840, p=0.615, p=0.203, respectively) (Table 5).

Table 5: Presence of Tooth Agenesis (Hypodontia) in Patients with M3 Tooth Agenesis

	Hypodontia		P
	Present (N %)	Absent (N %)	
Agenesis of Four M3 Teeth	10 (%1,6)	19(%3,0)	0.000*
Agenesis of Three M3 Teeth	2 (%0,3)	15 (%2,4)	0.203
Agenesis of Two M3 Teeth	3(%0,5)	42(%6,7)	0.615
Agenesis of a Single M3 Tooth	2 (%0,3)	43 (%6,8)	0.840

Chi-square test, *p<0.001

DISCUSSION

In this study, panoramic radiographs of children aged 11–13 years, who had no systemic diseases, were examined, and the relationship between M3 tooth agenesis and hypodontia in other permanent teeth was assessed. It has been suggested that genetic, epigenetic, and environmental factors play a significant role in the development of permanent tooth agenesis, with these factors interacting with each other.[2,22] Among permanent teeth, agenesis is most commonly observed in M3 teeth (5.3%–56.0%).[9-15] The agenesis of these teeth can be associated with a syndrome, but it can also occur without any specific underlying cause.[2,9-15]

In our study, the prevalence of one or more M3 agenesis was found to be 21.5% (136 patients), while the prevalence of hypodontia in permanent teeth was 5.1% (32 patients). In a study by Karaca and Çapan[7], conducted on 1460 children within a similar age group, the prevalence of one or more M3 tooth agenesis was reported to be 35.6%. Atay et al.[12,] in their study of 1471 patients, found the prevalence of M3 tooth agenesis to be 10.3%, while the prevalence of hypodontia in other permanent teeth was 2.7%. These differences may be attributed to variations in sample size and the genetic diversity of the populations studied. Specifically, the broader population examined in the study by Karaca and Çapan[7] may have contributed to the higher prevalence of agenesis observed.

In a study conducted by Sujon et al.[23] on 5923 patients in Malaysia, the prevalence of M3 tooth agenesis was found to be 38.4%, while the prevalence of hypodontia in other permanent teeth was 3.1%. In our study, consistent with the findings of previous researchers, we detected hypodontia in other permanent teeth in 31.3% of patients with agenesis of all four M3 teeth, and this difference was statistically significant. This suggests that the early diagnosis of M3 agenesis in pediatric patients not only helps identify the absence of these teeth but also aids in the detection of potential agenesis in other permanent teeth. In clinical practice, it is crucial to conduct thorough radiographic and clinical evaluations to assess the absence of other teeth in children with M3 agenesis.

In patients with agenesis of all four M3 teeth, we found that the most commonly absent permanent teeth were the maxillary lateral incisors, followed by the maxillary second molars and mandibular second premolars. Similarly, previous studies have reported that maxillary lateral incisor agenesis is more frequently observed in patients with agenesis of all four M3 teeth.[1,24] Scheiwiller et al.[24] found that the prevalence of hypodontia in other permanent teeth was 2.5 times higher in individuals with agenesis of one or more M3 teeth compared to those without M3 agenesis.

In our study, although the prevalence of M3 tooth agenesis was higher in females (11.9%) compared to males (9.6%), no statistically significant difference was observed. This may suggest that gender differences in younger age groups might not yet be pronounced, or that the sample size was insufficient to detect such a difference. The literature includes studies reporting no gender differences in M3 agenesis,[2] a higher prevalence in females[9,10] or equal prevalence in both genders.[25]

In our study, the prevalence of one or more M3 tooth agenesis was found to be 21.5%, with agenesis observed in one or two teeth at rates of 7.1%, three teeth at 2.7%, and four teeth at 4.6% (1 = 2 > 4 > 3). In their meta-analysis, Carter and Worthington[9] reported that agenesis of one or two M3 teeth is more common, while the prevalence of agenesis in three or four teeth is lower. Atay et al.[12] found the prevalence of M3 agenesis in four teeth to be 4.3%, which is very similar to our finding of 4.6%. Endo et al.[21] indicated that the highest prevalence of M3 agenesis occurred in two teeth, while the lowest was in three teeth (2 > 1 > 4 > 3), whereas Sujon et al.[23]

reported the highest prevalence in one M3 tooth and the lowest in three M3 teeth (1 > 2 > 4 > 3). As in many studies [9, 14, 21, 23, 24], M3 agenesis in our study was most rarely observed in three teeth.

In our study, the prevalence of M3 agenesis was found to be higher in the maxilla than in the mandible. Similar findings have been reported in studies conducted both in our country [2,7,12,13] and internationally [9,23,24], where the rate of M3 agenesis is also higher in the maxilla compared to the mandible. Possible explanations for this include developmental differences between the maxilla and mandible, as well as genetic factors.

When examining M3 tooth agenesis on the right and left sides of the jaws, it was found that the highest prevalence occurred in the upper right jaw (15.1%), followed by the upper left jaw (13.2%), lower left jaw (10.2%), and lowest in the lower right jaw (9.2%). However, the difference was not statistically significant. Sujon et al.[23] reported no significant difference between the right and left sides of the jaws, with the highest frequency of M3 agenesis found in the upper right jaw and the lowest in the lower left jaw.

Since this study uses a retrospective and cross-sectional design, the data obtained only provide a snapshot of the population included. Therefore, the long-term effects of third molar (M3) agenesis or its impact on dental development in later years could not be assessed. Additionally, the role of genetic factors was not thoroughly examined in our study, as no genetic analysis was performed.

Future studies should involve broader age groups and diverse ethnic populations to explore how third molar (M3) agenesis varies with age and genetic factors. Additionally, the potential connections between M3 agenesis, temporomandibular joint disorders, occlusal issues, and jaw irregularities should be examined through more detailed clinical and genetic research. Genome-wide association studies could help identify genetic markers linked to M3 agenesis, providing a deeper understanding of this condition. Finally, longitudinal studies should investigate how M3 agenesis affects oral health in the long term.

CONCLUSION

In our study, hypodontia was detected in approximately one-third of patients with agenesis of all four M3 teeth. This finding suggests that M3 agenesis may not be limited to the third molars but could also be associated with the agenesis of other permanent teeth. Early diagnosis of M3 agenesis and associated hypodontia in pediatric dentistry is crucial for comprehensive oral care and treatment planning.

Early evaluations should be conducted in individuals with M3 agenesis to assess potential spaces that may require prosthetic, implant, or orthodontic interventions in the future. Furthermore, monitoring temporomandibular joint disorders and occlusal issues in these patients may help facilitate the implementation of preventive treatment strategies.

Finally, considering the potential genetic predisposition of M3 agenesis, it is important to examine family members, as this may facilitate the early diagnosis of similar deficiencies. Our study highlights that identifying the relationships between M3 agenesis and other permanent tooth agenesis can contribute to patient diagnosis and treatment, as well as improve oral health outcomes.

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Examination of the Effect of Periodontal Disease on Salivary Gas6 and MFG-E8 Proteins

Periodontal Hastalığın Tükürük Gas6 ve MFG-E8 Proteinleri Üzerindeki Etkisinin İncelenmesi

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ABSTRACT

INTRODUCTION: Periodontal disease is a chronic inflammatory process whose primary etiological factor is microbial dental plaque. MFG-E8 is known to play a role in the regulation of apoptotic pathways, angiogenesis, and the maintenance of tissue homeostasis. Gas-6 protein is reported to have effects on cell proliferation and adhesion, as well as the phagocytosis of apoptotic cells and platelet aggregation. The aim of this study is to elucidate the role of Gas6 and MFG-E8 molecules in the pathogenesis of periodontal disease.

MATERIAL and METHODS: The study included 20 healthy individuals and 20 patients with stage 3 grade B periodontitis who applied to clinic for dental treatment. Clinical periodontal parameters were recorded, and the levels of Gas6 and MFG-E8 in saliva samples were evaluated using ELISA kits.

RESULTS: Salivary MFG-E8 level in the periodontitis group was significantly lower than healthy participants (p: 0.021). Salivary MFG-E8 level showed a negative correlation with SCD among the clinical parameters (r: -0.082, $p < 0.05$). There was no significant difference in salivary Gas-6 levels between the control and periodontitis groups (p: 0.282).

CONCLUSION: The lower amount of salivary MFG-E8 in individuals with periodontal disease compared to healthy individuals suggests that MFG-E8 is an effective molecule for tissue homeostasis.

Keywords: *Periodontal disease, saliva, cytokine*

ÖZ

GİRİŞ: Periodontal hastalık primer etiyolojik faktörü mikrobiyal dental plak olan kronik inflamatuvar bir süreçtir. MFG-E8 apoptotik yolakların düzenlenmesi, anjiyogenez ve doku homeostazının sağlanmasında görev aldığı bilinmektedir. Gas-6 proteini ise hücre proliferasyonu ve adezyonunun yanı sıra apoptotik hücrelerin fagositozunda ve platelet agregasyonunda etkisi olduğu bildirilmiştir. Her iki molekülün çeşitli kronik sistemik hastalıklarla ilişkisi gösterilmiş olsa da periodontal hastalık ile ilgili sınırlı sayıda çalışma bulunmaktadır. Bu çalışmanın amacı Gas6 ve MFG-E8 moleküllerinin periodontal hastalık patogenezindeki yerinin aydınlatılmasıdır.

YÖNTEM ve GEREÇLER: Çalışmaya dişeti tedavisi amacıyla kliniğe başvuran sistemik ve periodontal olarak sağlıklı 20 kişi ve evre 3 derece B periodontitise sahip 20 hasta dahil edilmiştir. Klinik periodontal parametreler (SCD, SKİ, DÇ, KAS) kaydedilmiştir. Hastalardan elde edilen tükürük örneklerindeki Gas6 ve MFG-E8 seviyeleri ELISA kitleri ile değerlendirilmiştir.

BULGULAR: Klinik periodontal parametreler periodontitis grubunda sağlıklı gruba göre anlamlı seviyede yüksek bulunmuştur ($p: 0.001; p<0.05$). Periodontitis grubuna ait tükürük MFGE-8 seviyesi sağlıklı katılımcılara göre anlamlı düzeyde düşüktür (p: 0.021). Tükürük MFG-E8 seviyesi klinik parametrelerden SCD ile negatif korelasyon göstermektedir (r: -0.082 $p < 0.05$). Kontrol ve periodontitis gruplarına ait tükürük gas-6 seviyeleri arasında anlamlı bir fark bulunmamıştır (p: 0.282).

SONUÇ: Periodontitis bireylerdeki tükürük MFG-E8 miktarı sağlıklılara göre daha düşük bulunması MFG-E8'in doku homeostazı için etkili bir molekül olduğunu düşündürmektedir.

Anahtar Kelimeler: *Periodontal hastalık, tükürük, sitokin*

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INTRODUCTION

Periodontal disease is a chronic inflammatory condition initiated by a dysbiotic microbiota in susceptible individuals. The complex interaction between the host's inflammatory response and the dysbiotic microbiota leads to the progressive destruction of periodontal supporting structures, including the gingiva, cementum, periodontal ligament, and alveolar bone, ultimately resulting in tooth loss over time.[1] Upon activation of the host immune response, the inflammatory process is triggered, releasing various chemokines and cytokines (such as IL-1beta, TNF-alpha, and IL-17), which contribute to tissue destruction.[2] Simultaneously, certain anti-inflammatory mediators play a role in suppressing inflammation, aiming to restore tissue homeostasis.[3]

Milk fat globule-epidermal growth factor–8 (MFG-E8), also known as lactadherin, is produced in various organs and tissues, including macrophages, fibroblasts, dendritic and epithelial cells, as well as mammary glands.[4] Studies have shown that MFG-E8 plays a crucial role in multiple processes, such as enhancing apoptotic cell clearance, reducing neutrophil infiltration and tissue fibrosis, promoting angiogenesis, maintaining homeostasis, and mediating various anti-inflammatory responses.[5,6] In a study conducted by Abe et al. in 2014, MFG-E8 was reported to regulate osteoclast function by preventing their excessive resorptive activity.[5]

Growth arrest-specific gene 6 (Gas-6) is a 75-kDa molecule produced by various cell types, including immune cells, vascular cells, and endothelial cells.[7,8] In addition to its roles in cell proliferation and adhesion, platelet aggregation, and adipocyte development regulation, Gas-6 also influences the phagocytosis of apoptotic cells, similar to MFG-E8.[7] In human umbilical vein endothelial cells stimulated with lipopolysaccharides from Porphyromonas gingivalis, a key periodontal pathogen, Gas-6 has been reported to inhibit the release of inflammatory factors.[9]

Studies have demonstrated that MFG-E8 and Gas-6 play significant roles in biological systems. Although these molecules are known to be involved in the pathogenesis of chronic diseases such as obesity, diabetes, and atherosclerosis, no study has yet evaluated them together in individuals with periodontal disease.[10-15] Therefore, the aim of this study is to assess salivary MFG-E8 and Gas-6 protein levels in healthy individuals and those with stage 3 grade B periodontitis, thereby elucidating their role in the pathogenesis of periodontal disease.

MATERIAL and METHODS

The study group consisted of 20 patients who were systemically healthy, met the inclusion criteria, and were diagnosed with stage 3 grade B periodontitis (P) according to the 2017 World Workshop on Periodontology. These patients were selected from those who applied to the Periodontology Clinic of Istanbul Medipol University Faculty of Dentistry. The control (C) group included 20 systemically and periodontally healthy participants. The inclusion criteria were as follows: individuals aged between 18 and 65 years, without any systemic disease, having at least 20 natural permanent teeth in occlusion (excluding third molars), not using any orthodontic appliances, non-smokers, not having used antimicrobial and/or anti-inflammatory drugs in the last 3 months, not having undergone periodontal treatment in the last 6 months, and not having received surgical periodontal treatment in the last year.

The socio-demographic data and periodontal indices (PD, BOP, PI, CAL) of all participants in the study were recorded by a single researcher (M.Y.) using a William's periodontal probe at six sites per tooth.

Unstimulated saliva samples were collected from the patients in the morning. After comfortably seating the patients, they were instructed to rinse their mouths with distilled water and then spit into a plastic tube. The saliva samples were centrifuged at 2800 g for 10 minutes, transferred into Eppendorf tubes, and stored at -80°C until the day of the experiment.[16]

Biochemical Analysis

The levels of Gas-6 and MFG-E8 in the collected samples were determined using ELISA kits (human ELISA immunoassay, Shanghai Sunred Biological Technology, Shanghai, China) and analyzed according to the manufacturer's instructions. Colorimetric evaluation was performed using a microplate reader (Thermo Scientific, MA, USA) at 450 nm. The corresponding standard curve was used to calculate the concentrations. Each sample was analyzed in duplicate, and the average values of the results were used.

Statistical Analysis

Statistical calculations were performed using the GraphPad Prism 10 (Boston, MA) statistical software package. The Shapiro-Wilk test was used to assess data normality. For comparisons between groups, the Student's t-test was applied to normally distributed data, while the Mann-Whitney U test was used for non-normally distributed data. The Spearman correlation test was conducted to determine the relationship between salivary Gas-6 and MFG-E8 levels and clinical periodontal parameters. All tests were performed at a significance level of $\alpha = 0.05$.

RESULTS

An analysis of demographic and clinical data showed no significant differences between the groups in terms of age and gender ($p = 0.1012$ and $p = 0.956$, respectively).

However, periodontal parameters, including plaque index, probing pocket depth, bleeding on probing index, and clinical attachment level, were significantly higher in the periodontitis group compared to healthy participants ($p < 0.001$ for all) (Table 1).

Table 1. Demographic and clinical parameters of the control and periodontitis groups

	Control (C) n=20	Periodontitis (P) n=20	*p*
Age (year)	38.9 ± 5.6	41.7 ± 6.4	0.1012
Gender F/M	9/11	10/10	0.956
PI	0.49 ± 0.30	1.69 ± 0.31	<0.001*
PD (mm)	1.35 ± 0.16	3.04 ± 0.72	<0.001*
BOP (%)	7.55 ± 4.94	48.05 ± 16.43	<0.001*
CAL (mm)	1.21 ± 0.16	3.47 ± 0.66	<0.001*

PI, plaque index; PD, probing depth; BOP, bleeding on probing index; CAL, clinical attachment level.
*Statistically significant difference compared to the control group ($p < 0.05$).

The salivary MFG-E8 level in the periodontitis group was significantly lower compared to healthy participants ($p = 0.021$). However, there was no significant difference in salivary Gas-6 levels between the control and periodontitis groups ($p = 0.282$) (Figure 1).

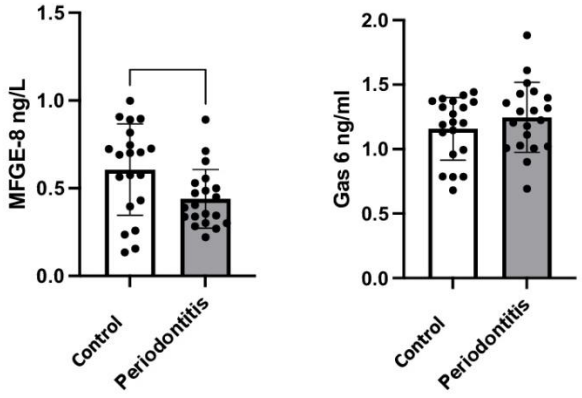

Figure 1: Salivary MFG-E8 and Gas-6 protein levels in healthy individuals and patients with stage 3 grade B periodontitis.

*Statistically significant difference compared to the control group ($p < 0.05$).

The salivary MFG-E8 level showed a weak but significant negative correlation with pocket depth ($r = -0.082$, $p < 0.05$). Additionally, a weak but significant positive correlation was observed between salivary Gas-6 and MFG-E8 levels ($r = 0.373$, $p < 0.05$) (Table 2).

Table 2. Correlation between clinical parameters and GAS-6, MFG-E8 proteins

	PI	BOP	PD	CAL	GAS-6
GAS-6	0.119	0.058	0.019	0.265	
MFGE-8	-0.216	0.114	-0.082*	-0.082	0.373*

(Spearman correlation coefficients, r) Spearman correlation test. Significance values of $p < 0.05$ are marked with (*).

DISCUSSION

Periodontal disease is the sixth most common disease worldwide, and its prevalence increases with age. As periodontal disease progresses, individuals may experience tooth loss, leading to both aesthetic and functional problems, ultimately reducing their quality of life. A comprehensive understanding of the disease pathogenesis and the elucidation of its unresolved mechanisms are crucial for early diagnosis and treatment.[1] For this reason, in our study, we evaluated the salivary levels of Gas-6 and MFG-E8 proteins, which are thought to play a role in the disease mechanism, in both healthy individuals and those with periodontal disease.

MFG-E8 is a peripheral membrane glycoprotein known to be involved in various processes, including apoptotic cell clearance, anti-inflammatory effects, and angiogenesis.[17] Recent studies have demonstrated that MFG-E8 plays a significant role in the development of autoimmune diseases such as systemic lupus erythematosus, age-related diseases, and inflammatory conditions.[17,18] However, there are only a limited number of studies investigating its role in periodontal disease, a chronic inflammatory condition. In a study conducted by Yavuz et al. in 2019, MFG-E8 and IL-1β levels in saliva and gingival crevicular fluid (GCF) were evaluated in healthy individuals, and those with gingivitis and chronic periodontitis. While salivary MFG-E8 levels did not show a significant difference among the groups, GCF MFG-E8 levels were found to be significantly higher in healthy individuals compared to those with gingivitis and chronic periodontitis. IL-1β, a known pro-inflammatory mediator, was found at lower levels in the serum and GCF samples of healthy participants compared to the other two groups.[19] In an animal study, experimental periodontitis was induced in MFG-E8-deficient mice, and greater bone loss was observed compared to the control group. The authors reported that osteoclasts are produced and regulated by MFG-E8.[5] When MFG-E8 levels were evaluated in gingival crevicular fluid (GCF) samples obtained from healthy individuals and patients with varying degrees of periodontal disease, higher levels were found in healthy individuals compared to those with periodontal disease. Furthermore, after periodontal treatment, an increase in MFG-E8 levels was observed in patients with periodontal disease.[20] In our study, the salivary MFG-E8 level was found to be significantly lower in the periodontitis (P) group compared to the control (C) group. Considering that MFG-E8 exhibits anti-inflammatory properties, its higher levels in the

saliva samples of healthy participants suggest that our findings are consistent with the literature. Additionally, the significant negative correlation between pocket depth and MFG-E8 levels further supports the notion that this molecule is secreted in greater amounts under healthy conditions (Table 2). The composition of saliva is influenced not only by the secretions of major and minor salivary glands but also by hormones, food residues, gingival crevicular fluid (GCF), and other sources.[21] Although our study did not evaluate MFG-E8 levels in GCF, previous studies have reported higher GCF MFG-E8 levels in healthy individuals compared to those with periodontal disease.[19,20] Given that saliva composition is also affected by GCF, our findings further support these previous studies. In light of our results, it is suggested that the potential role of MFG-E8 in periodontal disease is to mediate the transition to homeostasis by suppressing the inflammatory response.

Gas-6 belongs to the vitamin K-dependent protein family and is known to be involved in various pathophysiological processes, including thrombosis, phagocytosis of apoptotic cells, inhibition of inflammation, and vascular calcification.[7] In an animal study, the absence of Gas-6 was shown to cause increased production of inflammatory cytokines and reactive nitrogen species in mice. Additionally, it was reported that the increase in IL-6 production led to the induction of Th17 cells. With the rise in inflammatory burden, the oral microbiota transitioned towards dysbiosis, and the authors suggested that Gas-6 serves as a key immunological regulator in host-commensal interactions.[22] When the GAS6/AXL signaling pathway was evaluated in human periodontal ligament cells stimulated with P. gingivalis lipopolysaccharides, a decrease in Gas-6 and AXL levels was observed.[23] Moreover, when serum Gas-6 levels were assessed in 50 patients with type 2 diabetes, they were found to be lower compared to healthy individuals.[24] To the best of our knowledge, only one study in the literature has evaluated salivary Gas-6 levels in periodontitis patients. However, in that study, Gas-6 was not detected in the ELISA raw data of either the healthy or periodontitis salivary samples.[25] In our study, although Gas-6 was detectable in the salivary samples of the periodontitis group, it did not differ significantly from the levels in healthy individuals. However, its positive correlation with MFG-E8 suggests that this molecule may play a role alongside MFG-E8 in the suppression of inflammation.

Periodontal disease is a complex process involving various inflammatory pathways. Clarifying the missing aspects of its pathogenesis is essential for disease prevention and early diagnosis. Therefore, in our study, we investigated the MFG-E8 and Gas-6 proteins, which, to our knowledge, have not been previously evaluated together in salivary samples, in healthy individuals and patients with stage 3 grade B periodontitis. According to our results, the lower levels of MFG-E8 in the periodontitis group suggest that it may serve as a potential indicator of periodontal disease. However, to determine the possible role of MFG-E8 and Gas-6 in periodontal disease, further long-term studies with larger sample sizes, including serum and gingival crevicular fluid (GCF) samples, are needed.

CONCLUSION

In conclusion, research on the mechanism of periodontal disease has predominantly focused on pro-inflammatory molecules. However, considering the significant role of anti-inflammatory mediators in the disease process, increasing studies on these molecules may contribute to the identification of new therapeutic targets that could aid in periodontal treatment.

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Evaluation of Internet Search Data for Pediatric Dentistry in Turkey and the Relationship with Oral Health: A Google Trends Analysis

Türkiye'de Çocuk Diş Hekimliği ile İlgili İnternet Arama Verilerinin Değerlendirilmesi ve Ağız-Diş Sağlığı ile İlişkisi: Google Trends Analizi

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ABSTRACT

INTRODUCTION: The aim is to investigate the relationship between Google Trends (GT) data of search terms related to pediatric dentistry and the Gross National Product (GNP) of cities, as well as the current caries index values (dmft/DMFT) in Turkey for the year 2023.

MATERIAL and METHODS: As publicly available data was utilized in the study, ethical approval was not necessary. Search terms related to pedodontics ("pedodontics", "pedodontist", "primary tooth", "pediatric dentist", "toothpaste", "toothbrush", "fluoride varnish", and "teething") were examined for 36 provinces in Turkey through GT. The correlation between internet search habits with GNP from the Turkish Statistical Institute and dmft/DMFT data for the 5-12 age group obtained from the Turkey Oral Health Profile Research Report were statistically examined using the Spearman correlation test.

RESULTS: Search terms "pedodontics", and "teething" were found to be associated with GNP; and "pedodontist", and "primary tooth" were found to be related to dmft values ($p<0.05$). Furthermore, statistical differences were also found in dmft values between regions.

CONCLUSION: Google Trends is an effective tool for determining individuals' interest in pediatric dentistry, and these data can be associated with the oral health status of the population.

Keywords: *Internet data, pediatric dentistry, preventive dentistry, primary teeth*

ÖZ

GİRİŞ: Türkiye'de 2023 yılına ait çocuk diş hekimliği ile ilgili terimlerin Google Trends (GT) verileri ile (süt dişi, çocuk diş hekimi, pedodonti, pedodontist, çocuk diş macunu, çocuk diş fırçası, diş çıkarma, florürlü vernik), şehirlerin gayrisafi yurtiçi hasıla miktarları (GSYH) ve güncel çürük indeksi değerleri (dmft/DMFT) arasındaki ilişkisini incelemektir.

YÖNTEM ve GEREÇLER: Çalışmada kamuya açık veriler kullanıldığı için etik kurul onayı gerekmemektedir. GT üzerinden pedodonti ile ilgili, "pedodonti", "pedodontist", "süt dişi", "çocuk diş hekimi", "çocuk diş macunu", "çocuk diş fırçası", "florürlü vernik" ve "diş çıkarma" arama terimleri, Türkiye genelinde 36 il için incelenmiştir. İnternet arama alışkanlıkları, Türkiye İstatistik Kurumu'ndan alınan GSYH ve Türkiye Ağız Diş Sağlığı Profili Araştırma Raporu'ndan elde edilen 5-12 yaş grubuna ait dmft/DMFT verileri ile istatistiksel olarak Spearman korelasyon testi kullanılarak ilişkilendirilmiştir.

BULGULAR: Çalışmamızda, çocuk diş hekimliği ile ilgili "pedodonti" ve "diş çıkarma" arama terimlerinin GSYH; "pedodontist" ve "süt dişi" arama terimlerinin ise dmft değerleri ile ilişkili olduğu bulunmuştur ($p<0,05$). Ayrıca bölgeler arası dmft değerleri arasında da istatistiksel farklar saptanmıştır.

SONUÇ: Bireylerin çocuk diş hekimliğine ilgilerini saptamada Google Trends etkin bir araçtır ve bu veriler toplumun ağız diş sağlığı durumu ile ilişkilendirilebilir.

Anahtar Kelimeler: *Çocuk diş hekimliği, internet verileri, koruyucu diş tedavileri, süt dişi*

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INTRODUCTION

Dental caries is one of the most commonly observed oral health problems in children.[1] Although the development of dental caries is primarily dependent on host factors, microorganisms, diet and time, many environmental factors also influence its development.[2] One such environmental factor is the socioeconomic status of the patient. There is a direct and very strong causal relationship between the increased prevalence of dental caries and lower socioeconomic status.[3]

Pediatric dentistry provides comprehensive preventive and therapeutic oral health services to children from birth to adolescence. Pediatric dentists specialize in jaw and tooth development, the application of caries-preventive treatments in primary and permanent dentition, restorative and endodontic procedures, and the management of dental trauma.[4] In preventing dental caries, pediatric dentists serve as the first-line healthcare providers, with the principal aim of preventing dental caries formation.[4] Caries risk assessment, topical fluoride applications, fissure sealants, diet regulation, oral hygiene education, and regular dental check-ups are among the preventive dentistry approaches. Avoiding cariogenic foods and maintaining good oral hygiene can prevent the development of dental caries. Using a toothbrush and toothpaste appropriate for the child's age, under parental supervision can help achieve good oral care.[5]

Untreated and undiagnosed dental caries in children causes pain, difficulty chewing, loss of appetite and weight loss.[3] Restorative treatment is possible for cavitated caries lesions, while deeper cavitation may affect the pulp, requiring endodontic treatment. If endodontic treatment is not possible, the tooth is extracted.[1] Indices have been developed to assess an individual's lifetime caries experience, of which the DMF score is the most widely used. The DMF score is the sum of the number of decayed (d), missing due to caries (m) and filled (f) teeth (t). The "dmft" value indicates caries experience in the primary dentition and ranges from 0 to 20, while the "DMFT" value indicates caries experience in the permanent dentition and ranges from 0 to 32.[6] The "DMFT" value indicates caries experience in the permanent dentition and ranges from 0 to 32.

Among the resources parents use to obtain more information when their children have an oral or dental health problem is the internet. The internet is not only a source of health information for people who have certain symptoms and wish to educate themselves before consulting a doctor, but also for those who want to learn more about treatment options.[7] [8] Google is the most widely used keyword-based search engine on the internet, offering an analytical service called “Google Trends” (GT) since 2004 to study population behaviors. GT, which is freely accessible, analyzes part of the roughly three billion daily Google searches and provides geographic and temporal models of search volumes for specified terms.[9] The popularity of searched terms is assessed regionally with a score between 0 and 100.[10] However, Google Trends filters out certain types of searches, such as those conducted by very few people. Because Google Trends only shows data for popular terms, low volume searches will appear as "0"[10].

GT data are used in many studies related to healthcare. Health research can be divided into three categories: causal inference, descriptive studies, and monitoring.[9] Examples include studies on dermatological problems,[8] sleep-related breathing disorders,[11] rheumatic diseases,[12] and cardiovascular diseases,[13] in which GT data derived from terms in these medical fields are examined. Within dentistry, the number of studies evaluating GT data is limited but includes terms such as “oral diseases,”[14] “toothache,”[15] “silver diamine fluoride,”[16] “early childhood caries,”[17] “dental trauma,”[18] and “toothpaste.”[19]

Oral health is also associated with socioeconomic status.[20] In public health studies, annual Gross Domestic Product (GDP) is utilized to assess socioeconomic levels in national populations.[21] There are also studies investigating the correlation between GT data and socioeconomic status indicators such as GDP.[22]

No studies have been found in the literature evaluating the GT data of selected terms related to pediatric dentistry in relation to caries indices (dmft/DMFT) and GDP. Yet, by identifying the public’s interest in pediatric dentistry through these data, necessary public health measures can be implemented. This study aims to analyze, in Turkey for the year 2023, GT data for selected pediatric dentistry terms (“primary tooth,” “pediatric dentist,” “pedodontics,” “pedodontist,” “children’s toothpaste,” “children’s toothbrush,” “teething,” “fluoride varnish”), along with the GDP values of cities and current caries index values (dmft/DMFT). Our hypothesis is that internet search data related to pediatric dentistry in Turkey yield results that are associated with the country’s socioeconomic status and oral health.

MATERIAL and METHODS

As this study used publicly available data, ethical committee approval was not required. Internet data obtained from Google Trends for the search terms “pedodontics,” “pedodontist,” “primary tooth,” “pediatric dentist,” “children’s toothpaste,” “children’s toothbrush,” “fluoride varnish,” and “teething” were examined across Turkey. The keywords were selected from terms that provided sufficient data on Google Trends. Data for the period from January 2023 to 2024 was accessed on 16 February 2024. As an example, Figure 1 shows the frequency of searches and the

provincial distribution within Turkey in the last 12 months for the term "pedodontics". Among the provinces used in this study, 36 provinces with sufficient GT data were selected, while those with insufficient data were excluded. In the analysis, GT automatically evaluates provinces capable of scoring between 1 and 100 for the searched term; those scoring 0—indicating low search volume—were excluded from the study due to insufficient data. The provinces were then grouped according to the Statistical Regional Units Classification (NUTS 2 in Turkish: İBBS). The data were correlated with the Gross Domestic Product (GDP, in annual US dollars) for 2021 from the Turkish Statistical Institute.[23] Additionally, provincial-level dmft/DMFT data for 2018 from the Turkey Oral and Dental Health Profile Research Report were used. This report examined the data for ages 5 and 12, which cover the primary and mixed dentitions.[24]

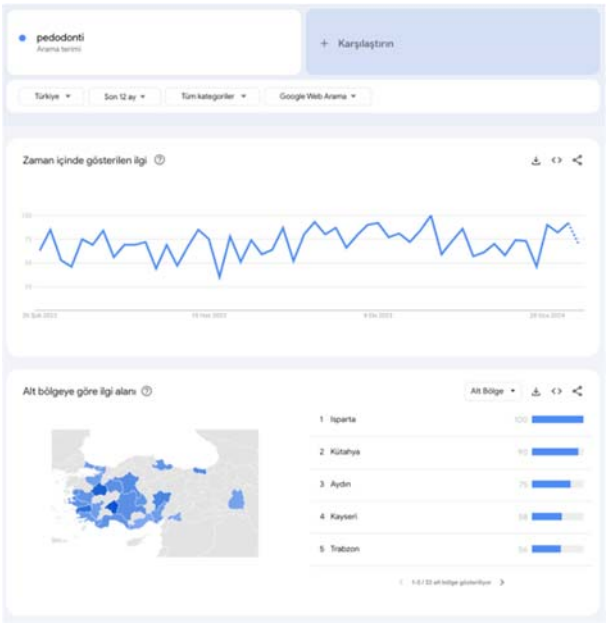

Figure 1. Search results for the term "pedodontics" in Turkey over the past 12 months

Statistical Analysis

A statistical analysis was conducted to examine the relationship between Google Trends search terms, population data, and the dmft/DMFT status in the 36 included provinces. Descriptive statistics (count, percentage, mean, standard deviation, median, minimum, maximum) were calculated. The Shapiro-Wilk test was employed to verify the normality assumption. The Spearman correlation test was used to measure the association between continuous variables that did not follow a normal distribution. Analyses were performed using IBM SPSS (Version 25, IBM Corp., USA).

RESULTS

The descriptive statistics of the search data obtained from Google Trends are shown in Table 1.

When the Google Trends data were grouped by regions in accordance with the Statistical Regional Units Classification (NUTS/İBBS), the following provinces were included:

- Mediterranean Region: Adana, Antalya, Hatay, Isparta, Kahramanmaraş, and Mersin
- Northeastern Anatolia Region: Van, Malatya, Elazığ
- Eastern Black Sea Region: Ordu, Trabzon
- Western Marmara Region: Çanakkale, Kırklareli, Tekirdağ
- Central Anatolia Region: Sivas, Kayseri, Aksaray
- Aegean Region: Aydın, Denizli, İzmir, Kütahya, Manisa
- Southeastern Anatolia Region: Şanlıurfa, Mardin, Gaziantep, Diyarbakır
- East Marmara Region: Bursa, Balıkesir, Eskişehir, Kocaeli
- West Anatolia Region: Konya, Ankara
- Northeast Anatolia Region: Erzurum

Table 1. Distribution of 12-month Google Trends data

	Minimum	Maximum	Mean	Standard Deviation	Median
GDP per Capita (USD, 2022 - TurkStat)	3274,77	18269,32	9055,18	3503,28	8467,42
5-year-old dmft	2,78	5,47	3,69	0,68	3,49
12-year-old DMFT	1,07	4	1,66	0,64	1,4
Pedodontics (12 Months)	22	100	39,14	17,61	34,5
Pedodontist (12 Months)	28	100	66,33	36,23	71
Primary Tooth (12 Months)	61	100	83,55	13,17	85
Pediatric Dentist (12 Months)	34	100	61	31,78	42
Children's Toothpaste (12 Months)	85	100	95	7,07	97,5
Children's Toothbrush (12 Months)	86	100	92,33	6,47	91
Teething (12 Months)	42	100	63,82	13,07	62

Istanbul is regarded as a region by itself in the NUTS classification and is included in the study in this manner.

The Spearman correlation test was applied to investigate the relationships among GDP, 5-year-old dmft, and 12-year-old DMFT. Statistically significant correlations were found between GDP and the search terms “pedodontics” and “teething” (Table 2). Analyses revealed a statistically significant, negative, moderate correlation between per capita GDP (in US dollars) and “pedodontics,” with a correlation coefficient of −0.523 ($p < 0.05$). There was a statistically significant, negative, moderate correlation of −0.390 between per capita GDP (in US dollars) and “teething” ($p < 0.05$).

Significant relationships were found between the 5-year-old dmft score and the search terms “pedodontist” and “primary tooth” (Table 2). A correlation coefficient of 1.000 was calculated between the 5-year-old dmft score and “pedodontist,” indicating a statistically significant, perfectly positive relationship ($p < 0.05$). A correlation coefficient of 0.630 was calculated between the 5-year-old dmft score and “primary tooth,” indicating a statistically significant, moderately positive relationship ($p < 0.05$). The distribution of these correlations is shown in Figure 2.

Table 2. Relationships between GDP, 5-year-old dmft, and 12-year-old DMFT

	2022 GDP per Capita (USD - TurkStat)		5-year-old dmft		12-year-old DMFT	
	r	p	r	p	r	p
Pedodontics	-0,523	0,013*	0,078	0,731	0,160	0,476
Pedodontist	0,271	0,825	1,000	0,000*	0,500	0,667
Primary Tooth	0,457	0,157	0,630	0,038*	0,528	0,095
Pediatric Dentist	-0,790	0,111	0,800	0,104	0,400	0,505
Children’s Toothpaste	0,383	0,617	-0,632	0,368	-0,949	0,051
Children’s Toothbrush	0,498	0,314	-0,179	0,734	-0,299	0,565
Teething	-0,390	0,023*	0,073	0,682	0,077	0,667

*$p < 0.05$, r = Spearman correlation coefficient.

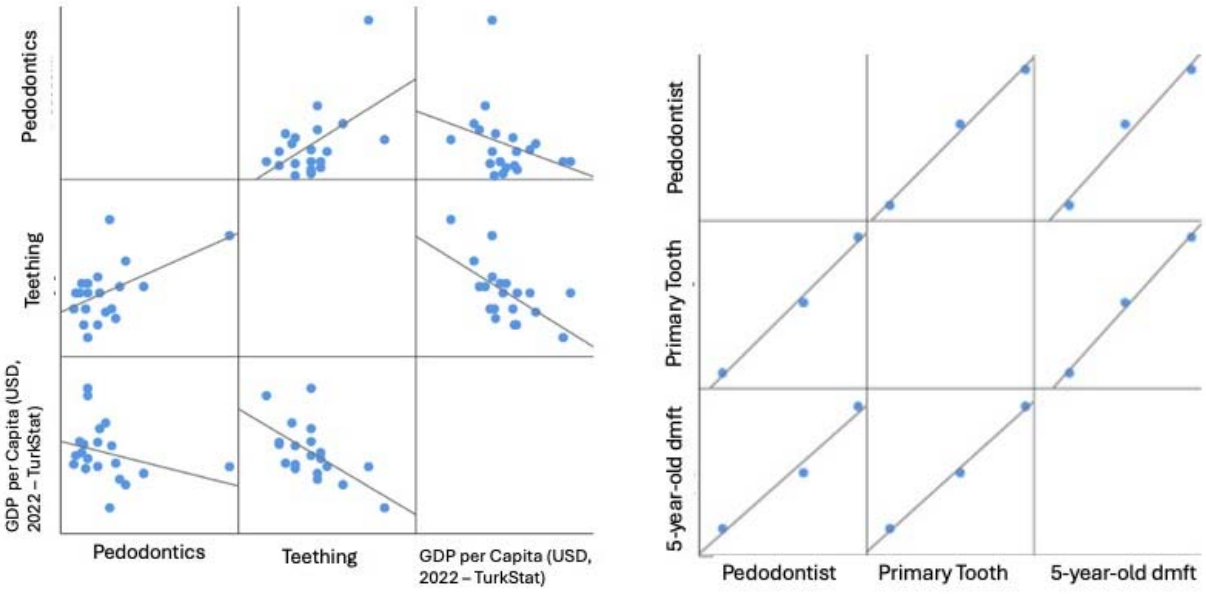

Figure 2. Scatter plot illustrating the relationships among GDP and 5-year-old dmft

Table 3. Distribution and comparison of relevant variables by region

		n	Min.	Max.	Mean	S.D.	Median	Test Statistic	p
Pedodontics	Mediterranean	6	23,00	67,00	38,00	19,85	31,00	6,753$^{\beta}$	0,344
	Eastern Anatolia	3	40,00	40,00	40,00	-	40,00		
	Aegean	6	26,00	100,00	45,67	29,01	32,00		
	Southeastern Anatolia	4	22,00	22,00	22,00	-	22,00		
	Central Anatolia	6	34,00	43,00	39,00	3,92	39,50		
	Black Sea	3	45,00	48,00	46,50	2,12	46,50		
	Marmara	9	25,00	41,00	31,00	6,93	29,00		
Pedodontist	Aegean	6	28,00	28,00	28,00	-	28,00	2,000$^{\beta}$	0,368
	Central Anatolia	6	100,00	100,00	100,00	-	100,00		
	Marmara	9	71,00	71,00	71,00	-	71,00		
Primary Tooth	Mediterranean	6	69,00	85,00	77,00	8,00	77,00	7,930$^{\beta}$	0,094
	Aegean	6	73,00	73,00	73,00	-	73,00		
	Southeastern Anatolia	4	61,00	77,00	69,00	11,31	69,00		
	Central Anatolia	6	95,00	100,00	97,50	3,54	97,50		
	Marmara	9	87,00	100,00	94,00	6,56	95,00		
Pediatric Dentist	Mediterranean	6	91,00	91,00	91,00	-	91,00	0,800$^{\beta}$	0,849
	Aegean	6	38,00	38,00	38,00	-	38,00		
	Central Anatolia	6	42,00	42,00	42,00	-	42,00		
	Marmara	9	34,00	100,00	67,00	46,67	67,00		
Children's Toothpaste	Aegean	6	100,00	100,00	100,00	-	100,00	2,667$^{\beta}$	0,264
	Central Anatolia	6	100,00	100,00	100,00	-	100,00		
	Marmara	9	85,00	95,00	90,00	7,07	90,00		
Children's Toothbrush	Mediterranean	6	86,00	86,00	86,00	-	86,00	2,525$^{\beta}$	0,471
	Aegean	6	100,00	100,00	100,00	-	100,00		
	Central Anatolia	6	93,00	93,00	93,00	-	93,00		
	Marmara	9	86,00	100,00	91,67	7,37	89,00		
Teething	Mediterranean	6	42,00	60,00	52,40	6,80	55,00	3,017$^{\alpha}$	0,050
	Eastern Anatolia	3	79,00	83,00	81,00	2,83	81,00		
	Aegean	6	50,00	78,00	62,67	8,98	62,50		
	Southeastern Anatolia	4	55,00	100,00	77,00	18,74	76,50		
	Central Anatolia	6	52,00	65,00	57,40	5,73	54,00		
	Black Sea	3	62,00	77,00	69,67	7,51	70,00		
	Marmara	9	44,00	82,00	62,89	13,60	60,00		
GDP per Capita (USD)	Mediterranean	6	7057,90	11494,75	8578,57	1737,50	7887,88	6,888$^{\alpha}$	p<0.001 *
	Eastern Anatolia	3	3274,77	6179,20	4956,57	1505,67	5415,73		
	Aegean	6	7590,80	13201,19	10023,89	2018,25	9831,82		
	Southeastern Anatolia	4	3886,87	8724,75	5788,42	2204,13	5271,03		
	Central Anatolia	6	5646,21	13919,12	8654,12	2835,98	8291,10		
	Black Sea	3	5078,02	6849,73	6033,24	893,97	6171,98		
	Marmara	9	9047,00	18269,32	12819,91	3343,80	11591,26		
5-year-old dmft	Mediterranean	6	3,42	3,42	3,42	0,00	3,42	25,595$^{\beta}$	p<0.001 *
	Eastern Anatolia	3	4,18	5,47	4,61	0,74	4,18		
	Aegean	6	2,78	2,78	2,78	0,00	2,78		
	Southeastern Anatolia	4	3,49	3,49	3,49	0,00	3,49		
	Central Anatolia	6	3,59	4,69	4,19	0,49	4,36		
	Black Sea	3	2,97	4,69	3,54	0,99	2,97		
	Marmara	9	3,15	4,35	3,96	0,48	4,35		
12-year-old DMFT	Mediterranean	6	1,40	1,40	1,40	0,00	1,40	29,640$^{\beta}$	p<0.001 *
	Eastern Anatolia	3	1,96	2,17	2,03	0,12	1,96		
	Aegean	6	1,29	1,29	1,29	0,00	1,29		
	Southeastern Anatolia	4	1,07	1,07	1,07	0,00	1,07		
	Central Anatolia	6	1,35	1,96	1,59	0,23	1,63		
	Black Sea	3	1,36	4,00	3,12	1,52	4,00		
	Marmara	9	1,66	1,82	1,80	0,05	1,82		

* ($p<0,05$) and α:Kruskal-Wallis test β: ANOVA test

ANOVA and Kruskal-Wallis tests were applied to compare these variables by region. The analyses revealed statistically significant differences among regions in per capita GDP (in US dollars), 5-year-old dmft, and 12-year-old DMFT ($p < 0.05$) (Table 3). According to Bonferroni tests for GDP, there were statistically

significant differences between the Marmara region and the Eastern and Southeastern Anatolia regions ($p = 0.001$ and $p = 0.006$). Per capita income in the Marmara region is higher than in the Eastern and Southeastern Anatolia regions. According to Bonferroni tests for the 5-year-old dmft, there were statistically significant differences between the Aegean region and the Eastern Anatolia, Central Anatolia, and Marmara regions ($p = 0.012$, $p = 0.001$, and $p = 0.003$). The 5-year-old dmft value in Eastern Anatolia, Central Anatolia, and the Marmara region is higher than in the Aegean region. For the 12-year-old DMFT, Bonferroni tests revealed statistically significant differences between the Aegean region and the Eastern Anatolia and Marmara regions, and between the Southeastern Anatolia region and the Eastern Anatolia, Black Sea, and Marmara regions ($p = 0.012$, $p = 0.012$, $p = 0.003$, $p = 0.030$, and $p = 0.003$). The DMFT values in Eastern Anatolia and the Marmara region are higher than in the Aegean region, while the DMFT values in Eastern Anatolia, the Black Sea, and the Marmara region are higher than in the Southeastern Anatolia region.No statistically significant differences were observed among regions for "teething," "pedodontics," "pedodontist," "primary tooth," "pediatric dentist," "children's toothpaste," or "children's toothbrush" ($p > 0.05$).

DISCUSSION

In our study, it was found that the search terms "pedodontics" and "teething" are related to GDP, and the search terms "pedodontist" and "primary tooth" are related to dmft values. Consequently, our hypothesis for these terms is accepted within their respective categories.

Google Trends is widely used in health-related studies. Researchers employ these online data to analyze public interest and behavior and to evaluate seasonal variations in diseases and their symptoms.[25] Since search engines are a common source of health information for individuals seeking additional details about symptoms or treatment options, this database grows ever more important as a tool to examine large datasets and produce significant insights in health research.

In our study, a negative correlation was found between GDP and searches for "pedodontics" and "teething." As the gross domestic product in Turkey decreases, the increase in "pedodontics" search trends in lower-income cities may reflect the population's difficulty accessing pediatric dentists.[26] This may imply that people rely on internet searches to compensate for this deficiency. Moreover, in particular, the habit of regular dental checkups for monitoring physiological development may be lacking in lower-income communities.[27] This may help explain the negative correlation between "teething" and GDP. These findings provide valuable hints about how economic factors can affect access to pediatric dental care. The data obtained shed light on identifying areas where access to dental care is inadequate, allowing for future targeted interventions.

In our study, as the dmft values for the 5-year-old group increased, there was a positive correlation showing increased online searches for the term "primary tooth." Considering that the dmft values solely indicate decayed, missing, and filled primary teeth, it is expected that parents' inclination to seek information on primary teeth would rise as their child's oral and dental health problems intensify.

Dental caries in primary teeth cause pain, chewing difficulty, loss of appetite, and weight loss. Especially when untreated deep caries affect the pulp, symptoms such as abscess, swelling, and night pain occur.[28] As caries and the symptoms it causes become more severe in younger patients, the need for dental treatment also increases. Parents may search the internet for suitable pediatric dentists who can treat their children's dental problems. We found that, accordingly, as the 5-year-old dmft value increases, searches for "pedodontist" likewise increased.

The dmft/DMFT values obtained from the Turkey Oral and Dental Health Profile Research Report appear as a secondary finding in our study. According to the 2022 Address-Based Population Registration System of the Turkish Statistical Institute, Şanlıurfa has the highest percentage of child population, at 44.9%. Şırnak follows at 41.4%, and Ağrı at 39.3%.[23] The high dmft/DMFT values of 5-year-olds and 12-year-olds in Eastern Anatolia can be explained by the substantial number of children in these areas and the resulting socioeconomic impact, such that not every child may receive adequate oral and dental health care.

Studies that use Google Trends often look at how the data for certain terms relate to economic indicators, population density, oral and dental health problems, and seasonal changes.[17 19] In this study, Google Trends data for seven pediatric dentistry terms were examined in relation to economic income (GDP) and children's caries experience (dmft/DMFT).

A systematic review by Nuti et al. emphasized the potential of Google Trends to provide meaningful insights into population behavior and connections between health and healthcare services, due to the free and simple access it provides to large sets of population search data. However, it was noted that Google Trends must become more transparent for it to be used as a reliable research tool, which would bolster the credibility of the results generated and their overall applicability to health research. Furthermore, researchers must clearly state their rationale and document their experiments to ensure reproducible findings.[9]

Although digital analyses of health interests and trends via Google Trends exist in various fields, there is a gap in knowledge regarding the correlation of these data specifically with pediatric dentistry-related terms. Our study contributes to the literature in this regard. Moreover, in this study, real-time data are collected anonymously and periodically, and the format of this data presentation helps reduce reporting bias.[29] However, such studies cannot replace traditional epidemiological methods, because this method only analyzes the behavior of unknown, remote Google users. It is impossible to identify the social and demographic characteristics of the users performing the searches. It is also uncertain whether all searches are conducted exclusively by affected individuals or whether these queries might be repeated by the same person using different electronic media. Another limitation of our study is that the data were collected from a single search engine. Other search engines such as Yahoo, Yandex, and Bing were not included. Therefore, focusing on data from people who use Google as their primary search engine raises a risk of selection bias, although this risk is minimized by the fact that Google accounts for more than two-thirds of all internet searches.

An additional limitation is that out of Turkey's 81 provinces, only 36 had sufficient data to be included in the study. This indicates that there is little interest in pediatric dentistry on the internet in the excluded provinces. Furthermore, the most recent dmft data available for Turkey were from 2018, which is another limitation. Having a larger sample and more current dmft/DMFT values would enable more accurate and effective use of similar analytical studies.

CONCLUSION

According to the findings of this study, the pediatric dentistry-related search terms "pedodontics" and "teething" are associated with GDP, while "pedodontist" and "primary tooth" are associated with dmft values. Furthermore, significant differences are observed among regions in their dmft values. In light of these findings, it can be said that Google Trends is an effective and useful tool for analyzing Turkish individuals' interest in pediatric dentistry. However, more data from additional provinces are needed in order to make inferences on a national scale. These data can aid in understanding the relationship between children's oral and dental health and socioeconomic status in the country. They also facilitate identifying areas with insufficient dental health services so that preventive measures may be taken. Consequently, more analyses and reporting of up-to-date internet data are necessary to improve pediatric oral and dental health in society.

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Investigation of Salivary miRNA-155 Levels in Patients with Periodontitis and Plaque-Induced Gingivitis: A Cross-Sectional Study

Periodontitis ve Plak Kaynaklı Diş Eti İltihabı Olan Hastalarda Tükürük miRNA-155 Düzeylerinin Araştırılması: Kesitsel Çalışma

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ABSTRACT

INTRODUCTION: Periodontal diseases are characterized by the progressive inflammation of periodontal tissues, leading to functional impairment and substantial economic burdens. The utilization of biomarkers in early diagnosis and prognosis is a promising approach for predicting disease progression and optimizing treatment strategies. This study aims to evaluate the potential use of miRNA-155 as a biomarker for the early diagnosis of periodontitis and gingivitis.

MATERIAL and METHODS: This study involved seventytwo systemically healthy non-smoker individuals. Based on periodontal characteristics participants were categorized into three equal study groups: periodontal health, gingivitis, and Stage III periodontitis (n = 24). Saliva samples collected from all participants and miRNA expression analysis was performed utilizing the miRCURY LNA SYBR Green PCR Kit. The data were statistically analyzed using SPSS software.

RESULTS: miRNA-155 expression levels demonstrated statistically significant differences between the periodontal healthy, gingivitis and periodontitis groups. A decrease in miRNA-155 expression was observed in the gingivitis group compared to healthy individuals, while a marked increase in miRNA-155 expression levels was detected in the periodontitis group.

CONCLUSION: The findings of this study suggest that miRNA-155 is actively involved in the inflammatory modulation responsible for the development of periodontitis and may potentially serve as a diagnostic biomarker for the disease.

Keywords: *Periodontal diseases, periodontitis, gingivitis, miRNA-155, biomarker*

ÖZ

GİRİŞ: Periodontal hastalıklar, periodontal dokuların ilerleyici inflamasyonu sonucu fonksiyon kaybı ve ekonomik yük oluşturan hastalıklardır. Biyobelirteçlerin erken teşhis ve prognozda kullanımı, hastalığın seyrinin öngörülebilmesi ve tedavi stratejilerinin optimize edilmesi açısından potansiyel bir araç olarak önem arz etmektedir. Çalışmamızın amacı miRNA-155'in periodontitis ve gingivitisin erken tanısında biyobelirteç olarak kullanım potansiyelini değerlendirmektir.

YÖNTEM ve GEREÇLER: Bu çalışmaya sistemik olarak sağlıklı sigara içmeyen yetmişiki gönüllü katıldı. Katılımcılar periodontal karakterlerine göre üç eşit çalışma grubuna ayrıldı: periodontal sağlıklı, gingivitis ve Evre III periodontitis (n = 24). Tüm katılımcılardan toplanan tükürük örneklerinde miRNA-155 seviyeleri miRCURY LNA SYBR Green PCR Kit kullanılarak analiz edildi. Veriler istatistiksel olarak SPSS software ile değerlendirildi.

BULGULAR: miRNA-155 ekspresyon seviyeleri, gruplar arasında istatistiksel olarak anlamlı farklılıklar gösterdi. Sağlıklı bireylere kıyasla gingivitis grubunda miRNA-155 ekspresyonunda azalma gözlemlenirken, periodontitis grubunda bu seviyelerde belirgin bir artış tespit edildi.

TARTIŞMA ve SONUÇ: Bu çalışmanın bulguları, miRNA-155'in periodontitisin gelişiminden sorumlu inflamatuar modülasyonda aktif olarak yer aldığını ve potansiyel olarak hastalık için bir tanı biyobelirteci olarak kullanılabileceğini düşündürmektedir.

Anahtar Kelimeler: *Periodontal hastalıklar, periodontitis, gingivitis, miRNA-155, biyobelirteç*

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INTRODUCTION

Periodontal diseases (PD) are chronic inflammatory disorders affecting gingiva and supporting tissues. Conditions such as periodontitis and plaque-induced gingivitis are particularly prevalent within populations, posing a significant economic burden on global healthcare systems.[1]

Gingivitis is an inflammatory condition confined to the soft tissues above the marginal bone, characterized by signs such as bleeding on probing, swelling, and redness in the interdental papillae. Weakened host response, along with risk factors, increased levels of inflammatory mediators, and pathogenic bacteria, can facilitate the progression of gingivitis to periodontitis.[2]

In periodontitis, the inflammation spreads to the deeper periodontal tissues, resulting in alveolar bone resorption and loss of connective tissue attachment. The pathogenesis of the disease is intricately linked to the host immune response, wherein nuclear factor-kappa B (NF-Kb) activation plays a pivotal role in facilitating bone loss by modulating osteoblastic activity.[3]

MicroRNAs (miRNAs) are nearly 19-22 nucleotides long, single-stranded RNAs, and have a vital function in regulating gene expression after transcription. They exhibit regulatory effects on both the innate and acquired immune systems.[4] Secreted miRNAs are identifiable in a range of body fluids, including spinal fluid and blood serum, along with gingival crevicular fluid (GCF) and saliva.[5] Circulating miRNAs, which can remain stable in human biofluids, are regarded as promising indicators for diagnosing and predicting the course of diseases. Additionally, miRNA-based therapies are considered to hold significant potential for the treatment of various diseases.[6]

MiRNAs have been shown to exhibit distinct profiles in diseased tissues associated with various pathological conditions, including PD. These differential miRNA profiles offer significant diagnostic potential as biomarkers or prognostic indicators.[7,8]

MiRNAs regulate gene expression by facilitating mRNA degradation or preventing its translation thereby controlling the differentiation, and survival of osteoblasts. In this capacity, they play a critical role in osteogenesis, spanning processes from the formation of bones during embryonic stages to the preservation of adult bone tissue.[9,10] Osteoclastogenesis, is also regulated by miRNAs through the direct modulation of osteoclast activity, signaling cascades, or inhibitory feedback mechanisms.[11]

MiRNA-155 can be defined as a multifunctional microRNA derived from the BIC gene located on chromosome 21, which is crucial in regulating immune responses or inflammation.[12] It is present in hematopoietic progenitor and stem cells, in hematopoietic cells, such as B cells, T cells, monocytes, or granulocytes.[13] This miRNA regulates the $CD4^+$ T cells differentiation, particularly influencing the development of helper T cells and regulatory T cells (Tregs). Additionally, it is crucial for the proper differentiation of B cells and the production of antibodies.[14] MiRNA-155, which participates in multiple biological reactions, including hematopoiesis, inflammation, or immunity, plays a pro-inflammatory role by deactivating anti-inflammatory cytokines.[15] In vitro studies have demonstrated that activated NF-κB enhances the expression of miRNA-155, subsequently activating downstream the genes related to pro-inflammatory cytokine.[11]

MiRNA-155 has been demonstrated to promote macrophage pyroptosis during the early infection phase of P. gingivalis, a bacterium frequently associated with PD. Its inhibition has been demonstrated to reduce pyroptosis rates in P. gingivalis-stimulated macrophages, thereby enhancing their phagocytic ability to eliminate the bacteria.[16]

MiRNA-155 expression increases rapidly in response to infections and injuries, triggered by inflammatory stimuli and hypoxia. In contrast, anti-inflammatory cytokines and negative regulators suppress miRNA-155 expression, thereby terminating the immune response.[8]

It has also been identified to display both pro-inflammatory and anti-inflammatory characteristics. Its dysregulated expression is associated with chronic inflammatory diseases, highlighting its role as a key modulator of inflammatory mechanisms.[17] Zheng et al.[10] demonstrated that miRNA-155 negatively impacts bone regeneration and reduces bone mass. This finding underscores the potential therapeutic significance of miRNA-155 inhibitors in promoting bone regeneration under inflammatory conditions.[10] Additionally, miRNA-155 has been shown to function as a negative regulator by suppressing osteogenic differentiation triggered by bone morphogenetic protein 9 located in mesenchymal cells.[18]

Numerous studies suggest that miRNAs hold significant potential as effective biomarkers and therapeutic targets in the identification of diseases, prognosis, and trerapy of various diseases.[5, 9, 12, 15] MiRNA-155, the focus of this study, is recognized for its pivotal role in inflammatory and immune response processes. Our study aims to investigate the potential of miRNA-155 as an indicator for early diagnosis of pathological conditions such as periodontitis and plaque-induced gingivitis, as well as its viability as a treatment target.

MATERIAL AND METHODS

This research adhered to the Helsinki Declaration and received approval from the S.D.U Medical Ethics Board

(05.11.2024. No: 38). Written and Verbal consent was acquired from all participants before the procedures. A statistical power analysis was carried out via GPower version 3.1 to determine the required sample size (Heinrich-Heine-University, Germany). With an effect size of 0.25 and a power level of 90%, the total sample size was calculated. The study was performed with a total of 72 volunteers, consisting of 24 participants in each group.

A total of 72 systemically healthy, non-smoking individuals were included. Eligibility criteria mandated that participants should not have systemic diseases, be on current medications, or have crowns, veneers, or restorations, and must possess at least 20 teeth in their mouths. Exclusion factors encompassed the presence of systemic diseases, active medication usage, pregnancy, menstrual periods, periodontal therapy within the last six months, or the use of antibiotics or anti-inflammatory medications, either locally or systemically, in the previous two weeks.

Participants with PD were categorized into three groups according to their periodontal status: periodontitis (Group P), gingivitis (Group G) and healthy periodontium (Group H) with 24 individuals in each group. The definitions of gingivitis and periodontitis were established according to the revised 2017 Classification of Periodontal and Peri-Implant Diseases and Conditions by the World Workshop on Periodontology.

Participants in Group H exhibited a periodontium in a healthy state, characterized by the absence of clinical attachment loss (CAL), probing depths (PD) of 3 mm or less, and bleeding on probing (BOP) scores lower than 10% at all examined sites. Group G consisted of individuals diagnosed with gingivitis, showing no CAL and alveolar bone loss on radiographic images, PD less than 3 mm, and BOP levels of 10% or higher at all sites. Group P included individuals diagnosed with Stage III, Grade B periodontitis, with at least two non-adjacent sites exhibiting PDs of 6 mm or greater and CAL of 5 mm or greater, along with radiographic analysis demonstrated a bone loss ranging from 15–35% or extending to the middle third of the root or beyond.

Panoramic radiographs were utilized to assess the loss of alveolar bone. Clinical periodontal parameters, including CAL, PD, and plaque index (PI), were evaluated at six sites per tooth using a periodontal probe. The PI was assessed following the Silness and Löe plaque index criteria.

Unstimulated saliva samples were collected for the study. Participants were warned not to eat, drink or chew gum at least one hour before collecting the samples. Saliva samples were obtained between 9:00 AM and 11:00 AM under similar room conditions. Unstimulated saliva was collected using plastic containers and then transferred to centrifuge tubes via sterile syringes.

To enhance the accuracy of analysis and reduce turbidity, the saliva samples were vortexed at 23 °C for 10 minutes. The supernatants were carefully obtained and stored at -80°C until using miRNA analysis.

After thawing, the saliva samples were centrifuged +4ºC for 20 minutes at 11.000 g and miRNAs were extracted from the supernatant utilizing the miRNeasy Serum/Plasma Kit (Cat. No./ID: 217184, Qiagen, Germany) following the manufacturer's guidelines. The NanoDrop 2000 spectrophotometer was employed to determine the purity and concentration of the extracted miRNAs (Thermo Scientific, Waltham, MA, USA).

cDNA synthesis was carried out using the miRCURY LNA RT Kit (Cat. No./ID: 339340, Qiagen, Germany). The isolated miRNA samples underwent reverse transcription during the cDNA synthesis process. The concentration of transcribed miRNAs was quantified using the Qubit 3.0 Fluorometer (Thermo Scientific) following the standard protocol of the Qubit miRNA Assay Kit. After concentration measurements, appropriate dilutions were prepared as needed.

Following the quantification of sample concentrations, the expression levels of microRNA-155 (Cat. No./ID: 205986-1, Qiagen, Germany) were determined using the miRCURY LNA SYBR Green PCR Kit (Cat. No./ID: 339346-1, Qiagen, USA) on a Rotor-Gene Q real-time PCR system (Rotor-Gene Q, Qiagen). The housekeeping gene RNU6 (lot: 20800469-1, Qiagen Germany) was utilized as an internal control for normalization.

Statistical analyses were performed via SPSS software, version 26.0. The normality was assessed using the Kolmogorov-Smirnov test, and the homogeneity was evaluated with Levene's test. Differences in PI, gingival index, and PD among the study groups were analyzed using one-way analysis of variance (ANOVA) followed by post-hoc Tukey tests. The levels of miRNA-155 among the study groups were analyzed using the Kruskal-Wallis test. Statistical significance was arranged at $p < 0.05$ with a 95% confidence interval.

RESULTS

In this research, saliva specimens from 72 patients with periodontitis, gingivitis, and healthy periodontal conditions were collected and analyzed, with no laboratory losses occurring during the process. The age and gender distribution percentages and mean values of the patient and control groups are demonstrated in Table 1.

Table 2 provides the periodontal parameters for the study groups. The values for the PI, PD in mm, CAL in mm, and BOP (%) were markedly higher in Group P than in both healthy and Group G ($p<0.001$). In the gingivitis group, periodontal parameters were markedly higher in comparison to those observed in the healthy group ($p<0.001$).

Table 1. The age and gender distribution percentages and mean values

	Periodontitis (n=24)	Healthy (n=24)	Gingivitis (n=24)
Gender, n (%)			
Male	10 (40.0%)	5 (20.0%)	9 (36.0%)
Female	15 (60.0%)	20 (80.0%)	16 (64.0%)
Age			
Mean (SD)	43.9 (11.71)	25.9 (6.03)	27.8 (6.80)

Table 2. The periodontal parameters for the study groups

Periodontal Parameters	Healthy (n=24)	Gingivitis (n=24)	Periodontitis (n=24)	P value
PI	0.56 ±0.03[a]	1.07±0.04[b]	1.93±0.04[b]	<0.001*
BOP (%)	2.02±0.1[a]	49.76±4.3[b]	52.40±14.3[b]	<0.001*
CAL	0.00±0.001[a]	0.45±0.002[a]	5.2±0.032[b]	<0.001*
PPD	1.92±0.02[a]	2.75±0.04[a]	3.76±0.05[b]	<0.001*

PI: Plaque Index, BOP: Bleeding on Probing, CAL: Clinical Attachment Level, PPD: Probing Pocket Depth.
[a,b,c] For the Kruskal-Wallis test, groups with a different superscript letter were statistically significant
* means statistical difference

Salivary miRNA-155 expression levels in the gingivitis patient group showed a statistically marginally significant decrease compared to the healthy group (Table 3, Figure 1). In contrast, the periodontitis group exhibited significantly higher expression levels compared to the healthy group (Table 3, Figure 1).

When all groups were analyzed collectively, a significant statistical difference was observed in miRNA-155 salivary expression levels (Table 3, Figure 1). MiRNA levels in the periodontitis group were notably elevated than those in the gingivitis and healthy groups ($p<0.05$).

Table 3. miRNA-155 expression levels

ΔCT	Periodontitis (n=24)	Gingivitis (n=24)	Healthy (n=24)	P-value
Mean (SD)	-2.1 (2.85)[a]	-3.7 (1.48)[b]	-2.9 (1.62)[c]	**0.0245***

ΔCT : Delta cycle threshold
[a,b,c] For the Kruskal-Wallis test, groups with a different superscript letter were statistically significant
* means statistical difference

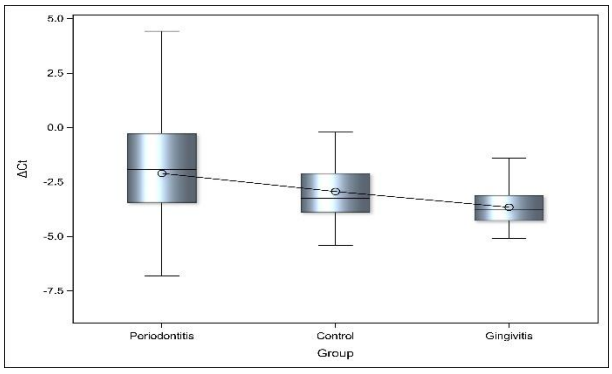

Figure 1.

In our study, sensitivity, and specificity calculations for various ΔCT threshold values in predicting disease status were performed, and the optimal threshold value for ΔCT was determined along with its corresponding sensitivity and specificity values. Additionally, an empirical ROC curve was generated using a non-parametric method with SAS software. For gingivitis, an AUC value of 0.61 was obtained with a 95% confidence interval (CI) of 0.4610–0.7774 and a $p<0.001$ (Table 4, Figure 2). For periodontitis, an AUC value of 0.63 was calculated with a 95% CI of 0.4701–0.7923 and a $p<0.001$ (Table 5, Figure 3). Both curves and their corresponding AUC values indicate that ΔCT has predictive capacity in distinguishing diseased individuals from healthy individuals.

Table 4. ROC Analysis of miRNA-155 ΔCT or Gingivitis

	Estimate	95% Confidence Limits	
PPV	0.6500	0.4409	0.8590
NPV	0.6000	0.4246	0.7753
Sensitivity	0.5200	0.3241	0.7158
Specificity	0.7200	0.5439	0.8960
AUC	0.6192	0.4610	0.7774
	cutoff	**prob**	**Youden**
deltaCT	-3.78	0.5374	0.24
	Somers' D	**Gamma**	**Tau-a**
	0.2384	0.2392	0.1216
True Positive	**True Negative**	**False Positive**	**False Negative**
13	18	7	12

PPV: Positive Predictive Value, NPV: Negative Predictive Value, AUC: Area Under the Curve

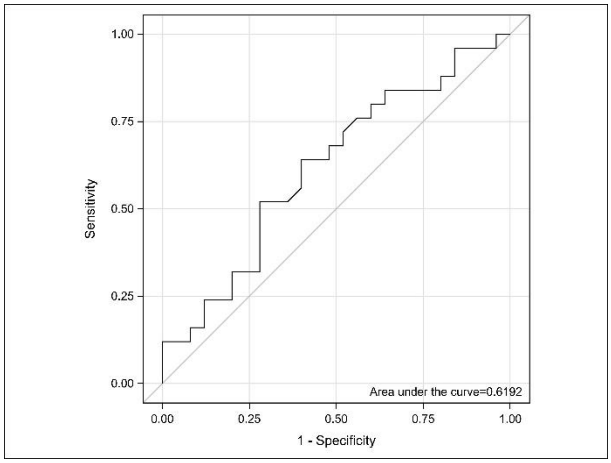

Figure 2.

Table 5. ROC Analysis miRNA-155 ΔCT for Periodontitis

	Estimate	95% Confidence Limits	
PPV	0.7222	0.5153	0.9291
NPV	0.6250	0.4572	0.7927
Sensitivity	0.5200	0.3241	0.7158
Specificity	0.8000	0.6432	0.9568
AUC	0.6312	0.4701	0.7923
	cutoff	**prob**	**Youden**
deltaCT	-1.91	0.52501	0.32
	Somers' D	**Gamma**	**Tau-a**
	0.2624	0.2628	0.1339
True Positive	**True Negative**	**False Positive**	**False Negative**
13	20	5	12

PPV: Positive Predictive Value, NPV: Negative Predictive Value, AUC: Area Under the Curve

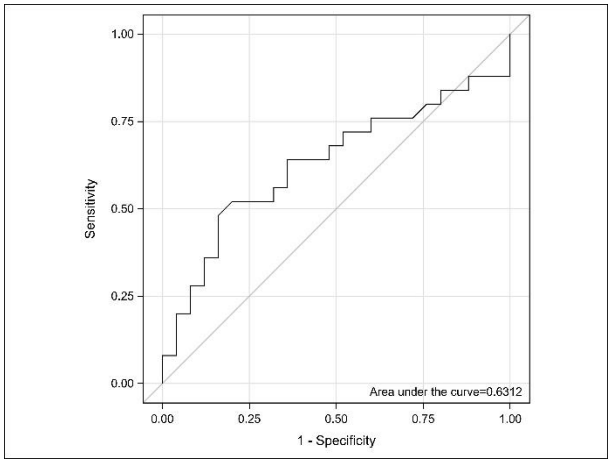

Figure 3.

DISCUSSION

Saliva is increasingly recognized as a valuable biofluid and source of biomarkers for the diagnosis of various dental and systemic conditions. The utilization of miRNAs in the non-invasive diagnosis and prognosis of periodontal diseases is emerging as a promising approach.[19]

In the periodontium, miRNAs serve critical regulatory functions in growth, maintaining periodontal balance, and disruption of periodontal tissue cohesion associated with the pathogenesis of PD. [3]

Infections with various pathogens induce the temporally regulated expression of specific microRNA subsets. Among these, miRNA-155 plays a pivotal role in modulating host cellular reactions to bacterial challenges and in regulating adaptive immunity, serving as a central regulator of T-cell responses.[7,20]

MiRNA-155 is regulated via toll-like receptors (TLRs) in inflammatory diseases, with all TLR signaling pathways converging on the activation of NF-κB, manages the expression of genes that are involved in producing cytokine related to inflammation. [21,22] TLRs are responsible for mediating innate immune responses through signaling pathways to ensure effective host defense against pathogenic infections.[23,24]

In our study, we observed that miRNA-155 expression is elevated during periodontitis and further increases as gingivitis progresses to periodontitis. Mogharehabed et al.'s study[25] found that miRNA-155 levels in tissue and blood samples from individuals with chronic periodontitis support our findings. They reported that miRNA-155 expression levels were significantly elevated in the patients with chronic periodontitis compared to the control group. Additionally, they stated a positive correlation between miRNA-155 levels and clinical parameters. In another study focused on gingival tissue samples, a five-fold increase in miRNA-155 expression was detected in the patient group than the control group.[11]

Al-Rawi et al.[26] reported that miRNA-155 was highly expressed in PD patients' saliva and that these expressions were observed to be positively correlated with the PD severity. They concluded that miRNA-155 might be crucial in the development and progression of PD.

In our study, we observed that patients in the gingivitis group had lower levels of miRNA-155 compared to the healthy control group. Given that gingivitis is a reversible PD and has not been thoroughly investigated in terms of miRNA expression levels, it is noteworthy that miRNA-155 levels were similar to those in the healthy group. It has been reported that miRNA-155 gene expression is increased in individuals with PD than in the control group and that it is significantly increased in the early-stage periodontitis group than in gingivitis group. [27]

MiRNAs are differentially expressed in cells induced by TLRs, which function as membrane-bound initiators

and trigger the inflammatory cascade.[28] Xie et al.[29] observed that, similar to our findings in gingivitis patients, Hsa-miR-155 expression in inflamed tissues was significantly lower compared to that in healthy control tissues. They suggested that this miRNA might be important in the pathogenesis of periodontal inflammation by regulating or interacting with TLR-associated pathways. It has been recorded that an anti-inflammatory cytokine IL-10 reduces the inflammatory response following pathogen invasion and protects the host from excessive inflammation, inhibits miRNA-155 expression in response to TLR4 stimulation. [30]

The detection of low levels of miRNA-155 in the gingivitis group may be attributed to the fact that this disease represents an earlier and reversible inflammatory process. Since gingivitis is not characterized by the more advanced inflammatory responses seen in chronic periodontitis, the suppressed expression of miRNA-155 may be associated with the milder course of the disease and the absence of tissue destruction. This suggests that miRNA-155 may be essential in the control and regulation of severe inflammation.

Additionally, miRNA-155 participates in inflammatory processes and the pathogenesis and molecular management of periodontal inflammation through its targets, such as suppressors of cytokine signaling and fibroblast growth factors.[31] The conflicting results between gingivitis and periodontitis can be attributed to dissimilarities in the characterization of cell types and histology of tissues examined, considering that gingival tissue includes various cell types, including fibroblasts or epithelial cells, adding significant complexity to the regulatory process.

Our research represents the pioneering study in literature to examine salivary miRNA-155 expression levels in individuals with both gingivitis and periodontitis. This comparison enhances the understanding of the role of miRNA-155 in periodontal inflammation and aids in assessing its potential as a biomarker for PD. Our findings indicate that miRNA-155 is associated with increased inflammation, with salivary levels being the lowest in gingivitis and the highest in periodontitis. These results suggest that miRNA-155 could be a biomarker correlated with the severity of inflammation and potentially a therapeutic target for PD.

A limitation of our study is the inability to determine expression levels post-treatment. However, we believe that this preliminary study will shed light on changes in miRNA-155 levels in a larger sample group and verify post-treatment changes by comparing them with miRNA levels in GCF or serum.

CONCLUSION

The role of miRNA-155 in PD is analyzed by comparing the miRNA-155 expression levels in the saliva of individuals with gingivitis and periodontitis. Our findings indicate that miRNA-155 is closely associated with periodontal inflammation and that its expression changes in parallel with the severity of inflammation. Notably, the significant difference in miRNA expression levels between gingivitis and periodontitis underscores the potential of this molecule as a biomarker for inflammation

The fact that miRNA-155, known to be closely related to physiological and pathological processes, can be detected in the saliva of individuals with PD through a non-invasive method, suggests that this molecule could be an important biomarker for early diagnosis as well as a potential therapeutic target. Future research is expected to contribute more robust evidence on the role of miRNA-155 in the early diagnosis and treatment strategies of PD, thereby making significant contributions to clinical applications in this field..

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Environmental Sustainability Related to the Materials and Procedures in Endodontics: A Critical Review

Endodontide Kullanılan Materyaller ve Prosedürlerle İlgili Çevresel Sürdürülebilirlik: Eleştirel Bir İnceleme

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ABSTRACT

The aim of this study is to identify strategies for protecting the environment in dental practices, including the materials used in these treatments, and to determine how simple measures can contribute to green dentistry. Articles published between 1996 and 2024 in PubMed, Scopus, Google Scholar, and Web of Science were reviewed. A total of 36 non-duplicate English-language articles containing the keywords 'green dentistry,' 'eco-friendly dentistry,' and 'sustainable dentistry' were included, and studies conducted in this field were analyzed. Green dentistry promotes the use of eco-friendly materials and technologies, such as digital impressions, lasers, restorative materials and irrigation solutions to minimise waste generation and energy consumption. It is easy to transform current dentistry into green dentistry by adopting simple measures and small changes. Dental practices can contribute to sustainability by implementing waste segregation, recycling and using renewable energy sources. Embracing green dentistry principles reduces environmental pollution, enhances patient health and ensures long-term sustainability. More incentives should be introduced for the adoption of green dentistry principles. Furthermore, access to these principles should be made easier and inexpensive.

Keywords: *Eco-friendly dentistry, green dentistry, dental materials, dental procedures, endodontology, sustainable dentistry*

ÖZ

Bu çalışmada amaç diş hekimliği uygulamaları ve bu tedavilerde kullanılan malzemelere kadar çevreyi korumaya yönelik stratejilerin tespit edilmesi ve alınacak basit önlemlerle yeşil diş hekimliğine ne gibi katkılar sağlanabileceğinin belirlenmesidir. 1996-2024 yılları arasında Pub Med, Scopus, Google Scholar ve Web of Science'ta yayımlanan makaleler tarandı. "Yeşil diş hekimliği", "çevre dostu diş hekimliği" ve "sürdürülebilir diş hekimliği" anahtar kelimelerini içeren İngilizce olan ve dublike olmayan toplam 36 makale dahil edildi ve bu alanda yapılan çalışmalar incelendi. Yeşil diş hekimliği, atık üretimini ve enerji tüketimini en aza indirmek için dijital ölçü yöntemleri, lazerler, restoratif materyaller ve irrigasyon solusyonları gibi çevre dostu materyallerin ve teknolojilerin kullanımını teşvik etmektedir. Basit önlemler ve küçük değişikliklerle mevcut diş hekimliğini yeşil diş hekimliğine dönüştürmek kolaydır. Diş hekimliği muayenehaneleri atık ayrıştırma, geri dönüşüm ve yenilenebilir enerji kaynakları kullanarak sürdürülebilirliğe katkıda bulunabilir. Yeşil diş hekimliği ilkelerinin benimsenmesi çevre kirliliğini azaltır, hasta sağlığını iyileştirir ve uzun vadeli sürdürülebilirlik sağlar. Yeşil diş hekimliği ilkelerinin benimsenmesi için daha fazla teşvik sağlanmalıdır. Ayrıca, bu prensiplere erişim daha kolay ve ucuz hale getirilmelidir.

Anahtar Kelimeler: *Çevre dostu diş hekimliği, yeşil diş hekimliği, dental malzemeler, dental prosedürler, endodontoloji, sürdürülebilir diş hekimliği*

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INTRODUCTION

Synchronicity and balance between humans and nature are greatly challenged by the consequences of rapid economic growth that has been triggered by scientific and technological innovations. In 2012, UNESCO stated that sustainability is a paradigm for creating a future in which environmental, social and economic considerations are balanced in the pursuit of development and improved quality of life.[1]

Sustainable development is defined as 'development that meets the needs of today without compromising the ability of future generations to meet their own needs'.[1] Furthermore, the collaborative efforts of countries are essential to protect this earth, which is humanity's home.[2] Therefore, the following possible strategies for global environmental sustainability have been proposed: reducing waste through the implementation of strategies to reduce, reuse and recycle waste materials; reducing toxicity by using non-toxic or less harmful materials and chemicals; conserving resources by minimising the consumption of water, energy and other resources; and implementing responsible waste management while preventing or minimising pollution.

In today's world, the concept of sustainability is gaining importance across various industries, including dentistry. Dental practices, like other healthcare facilities, can significantly impact the environment through their operations. Thus, there's a growing emphasis on adopting sustainable practices in dental offices, which is commonly referred to as 'green dentistry'. Green dentistry includes the concept of 'Reduce, Reuse, Recycle and Rethink'.[3] 'Reduce' is one of the easiest principles to implement. By reducing the number of resources used, the amount of waste produced can be reduced, protecting the environment. A few measures that can be implemented are reducing electricity and water consumption and preventing paper waste. 'Reuse' refers to extending the life of materials being used. Reusing products prevents waste generation and reduces the amount of energy used for producing new materials. Biodegradable disposable instruments and sterilisable stainless-steel instruments can be used to implement this principle. Waste generated in dentistry consists of materials that can be 'recycled' with simple separation techniques. Some of these recyclable materials include aluminium, paper, steel and plastic. 'Rethinking' every treatment step, clinic operation and clinical layout in the dental office can be an important step towards sustainability and environmental protection. This can be achieved with the following strategies: avoiding heavy chemicals to prevent water pollution during sterilisation, using digital methods instead of paper for storing patient data to prevent paper waste, choosing renewable energy sources to power the clinic and choosing conventional radiography instead of digital radiography to prevent water and soil pollution.[3]

By following the principle of 'Reduce, Reuse, Recycle and Rethink', sustainability can be naturally achieved. Sustainability brings about a healthier society, less environmental pollution and healthier use of existing resources. Integration of dentistry innovations in daily practice promotes the efficient use of time and resources, reduces supply costs, curbs waste generation and prevents environmental pollution. Thus, patients benefit from higher quality treatments at lower costs.

The increase in carbon footprint is an important factor in global warming and impacts the environment. In recent years, the carbon footprint of dental clinics has significantly increased. Therefore, using sustainable materials and devices in dentistry is crucial. Furthermore, waste reduction and separation should be emphasised to ensure a sustainable future.[4] A typical dental clinic uses several disposable materials and chemicals daily. Although these disposable materials are useful for maintaining sterility, they should be avoided to limit waste generation. Green dentistry practices often encourage the use of sterilisable materials.[5] From treatments to office supplies, there are numerous easily accessible and affordable ways to help dentists and endodontists be more environmentally conscious.[6]

MATERIAL AND METHODS

This scoping review followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). A comprehensive search was conducted across four electronic databases, namely Google Scholar, PubMed, Scopus and Web of Science, using a research query detailed in Figure 1. The terms 'green dentistry', 'eco-friendly dentistry' and 'sustainable dentistry' were searched independently, and 1,332 articles were identified. The search was last conducted on August 18th, 2024, and included papers published between 1996 and 2024. All identified records were screened in two sequential stages. Initially, two independent reviewers scrutinised titles and abstracts to eliminate studies beyond the review scope. Non-English, duplicate and inaccessible full text articles were excluded. The remaining articles were further reviewed under the headings of dental lasers, natural irrigation solutions and medicaments, root canal filling materials, dental filling materials and dental impressions. The individual articles identified under these five headings were scrutinised and articles relevant to the topic but not identified during the literature search were included in the study. Finally, 36 articles were

included in the study. The included articles were categorised according to the areas of expertise (Table 1) and topics (Table 2).

RESULTS

The 36 included studies were categorised according to dentistry sub-branches, and their suitability was examined (Table 1). The studies were also sub-divided into five thematic headings: dental lasers (n = 4), natural intermediate session medications and irrigation solutions (n = 12), root canal filling materials (n = 4), dental filling materials (n = 6) and separation of impression materials (n = 10) (Table 2). These data will allow readers to focus on specific points according to their general areas of interest and expertise, while data related to thematic headings have been examined in detail.

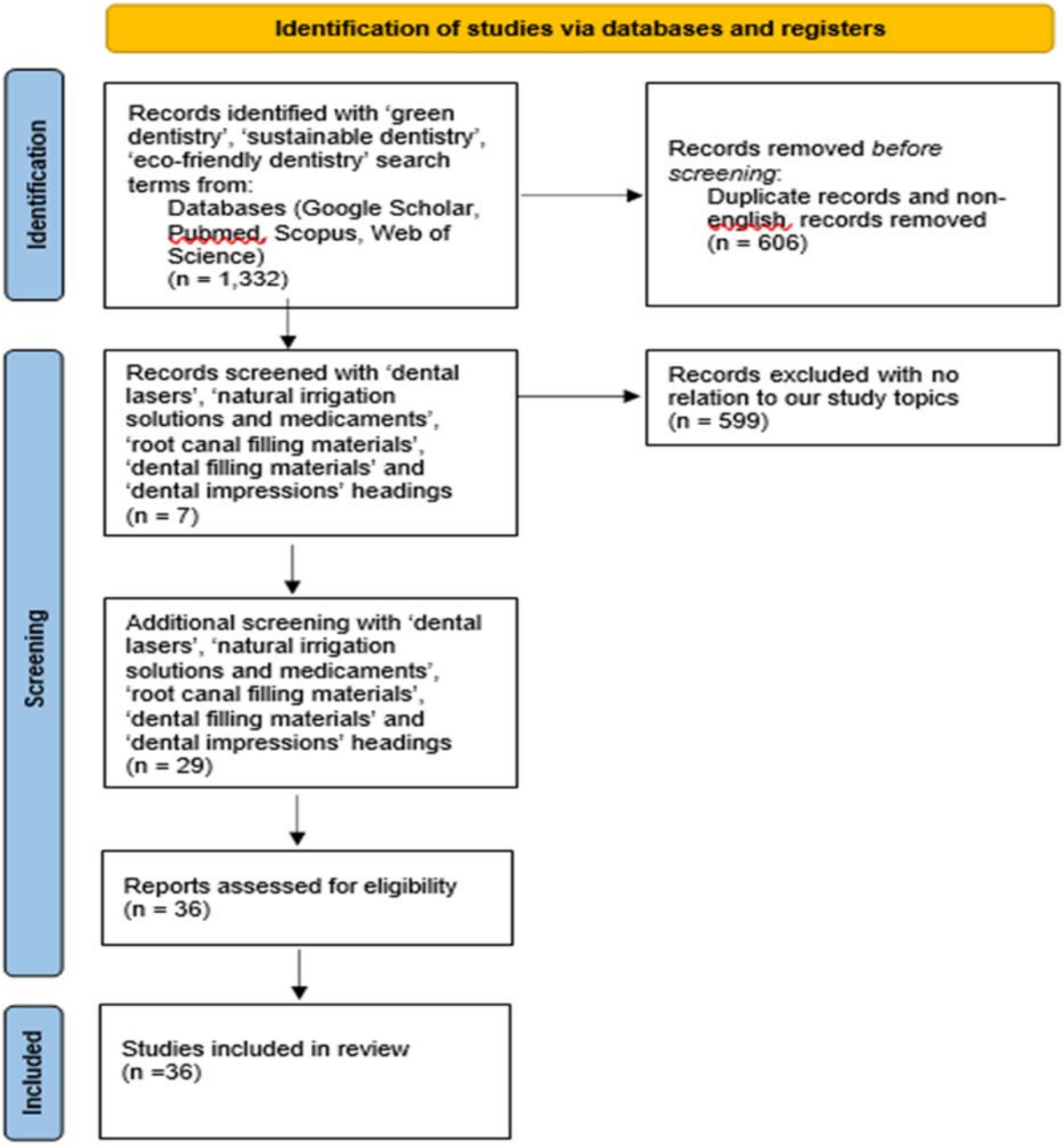

Figure 1. Flow diagram of the literature search and included studies.

Table 1. The included studies according to the sub-branches of dentistry.

Studies	*Endodontics*	Restorative	Prosthetic Dentistry	Periodontology	Radiology	Orthodontics	Oral and Maxillofacial Surgery	General Dentistry
Gupta & Brizuela, 2023								+
Duane & Steinbach 2023								+
Raoof et al. 2023	+							
Ruchi Gupta et al. 2022	+	+			+			+
Kaval et al. 2022	+							+
Wanicharat et al.2022	+							
Martin et al. 2021		+						+
Bota et al. 2021	+							+
Mittal et al 2020								+
Pallavi et al. 2020 (noinfo)								
Tekin&Demirkaya 2020	+							
Dobrzański et al 2020	+	+	+	+				+
Khanna&Dhaimade, 2019								+
Alikhasi et al. 2018a			+					
Alikhasi et al. 2018b			+					
Nedelcu et al 2018			+					
Ahlholm et al., 2018			+					
Rathakrishnan&Priyadarhini 2017								+
Chopra&Raju, 2017								+
Al-Haddad& Che Ab Aziz, 2016	+							
Srinivasan&Chitra 2015		+			+			+
Joda & Brägger 2015			+					
Lee et al 2015			+					
Rupa et al. 2015		+			+			+
Costa et al. 2014				+				
Flügge et al. 2013						+		
Silva et al. 2013	+							
Thopegowda et al 2013			+					
Kumar, 2012		+			+			+
Passi& Bhalla 2012								
Schembri et al. 2010	+	+						
Matsunaga et al. 2010	+							
Murray et al. 2008	+							
Bramante et al. 2008	+				+		+	
Oncag et al. 2006	+							
Wynn, 2005				+	+		+	
Estrela et al. 2004	+							
Ozbek&Sanin, 2004								+
Batchu et al. 2004		+						
Hepşen et al. 1996	+							

Table 2. The included studies according to the dental applications.

Studies	*Dental Lasers*	*Natural Medicaments and Irrigation Solutions*	*Root canal filling materials-*	*Dental filling materials*	*Dental impressions*
Raoof et al. 2023		+			
Kaval et al. 2022		+			
Gupta&Brizuela, 2023					+
Juman et al, 2022					+
Wanicharat et al.2022		+			
Martin et al 2021				+	
Bota et al. 2021		+			
Tekin&Demirkaya 2020		+			
Dobrzański et al 2020				+	
Mittal et al, 2020					+
Pallavi et al. 2020	+				
Khanna&Dhaimade, 2019	+			+	
Alikhasi et al. 2018a					+
Alikhasi et al. 2018b					+
Nedelcu et al 2018					+
Ahlholm et al., 2018					+
Rathakrishnan&Priyadarhini 2017				+	
Chopra&Raju, 2017	+				
Al-Haddad& Che Ab Aziz, 2016			+		
Lee et al 2015					+
Rupa et al. 2015				+	
Joda & Brägger 2015					+
Costa EM et al. 2014		+			
Flügge et al. 2013					+
Silva et al. 2013		+			
Kumar 2012	+				
Schembri et al. 2010			+		
Matsunaga et al. 2010			+		
Murray et al. 2008		+			
Bramante et al. 2008			+		
Oncag et al. 2006		+			
Wynn RL, 2005		+			
Estrela C et al. 2004		+			
Ozbek&Sanin, 2004				+	
Batchu et al.2004				+	
Hepşen et al. 1996		+			

Dental lasers

Lasers play a crucial role in various dental procedures, offering several benefits in the field of oral health. Lasers are used to remove tooth decay and prepare the surrounding enamel for a replacement filling.[7] Additionally, soft tissue lasers are utilised to reshape gums and eliminate bacteria during root canal procedures during the treatment of gum disease.[3] Furthermore, lasers expedite office teeth whitening processes by serving as a

heat source and activating a peroxide bleaching solution on the tooth surface.[8] Lasers have also been used in conducting biopsies and removing oral cavity lesions. They enable the extraction of small tissue samples for cancer screening and assist in alleviating the discomfort associated with canker sores.[9]

The adoption of lasers in dentistry is associated with several advantages and aligns with the concept of sustainable dentistry. Lasers have replaced traditional drills and the self-sterilising nature of the active laser tip eliminates the need for autoclaving and the associated sterilisation costs. Longevity is another feature of lasers. The inserted fibre ends, when used appropriately, can last for an extended period. The use of lasers to reduce intraoperatively bleeding can save time and minimise the need for materials to staunch the bleeding. Furthermore, the diminished pain experienced during cavity preparation is associated with reduced anaesthesia consumption. Finally, the absence of scalpel use negates the generation of hazardous medical waste, aligning with environmentally conscious practices in healthcare. A single laser device encompasses multiple dental applications, eliminating the necessity for numerous individual devices. Furthermore, the extended lifespan of laser devices contributes to its cost-effectiveness.

Natural irrigation solutions and medicaments

Effective irrigation is an important procedure to disinfect the root canal in endodontic treatments. Traditional irrigation methods, such as sodium hypochlorite, Ethylenediaminetetraacetic acid and chlorhexidine, have been used for a long time. Although these solutions are effective disinfectants, they are associated with the risks of cytotoxicity, allergic reactions and environmental concerns. These limitations and patients' growing environmental concerns and sensitivities there is an increasing need and desire for sustainable and natural solutions. Natural irrigation solutions have emerged as an alternative to address these needs.[10]

Natural irrigation solutions offer promising benefits in endodontic practice. Natural irrigation solutions utilise the therapeutic properties of plants and organic compounds to achieve effective disinfection. These solutions offer biocompatibility, reduced toxicity and potential synergistic effects with conventional treatment methods.[10]

Bouea macrophylla kernel extract

Bouea macrophylla kernel extract is used as an intracanal medicament between root canal treatment appointments. It disrupts the fungal and bacterial cell membranes and inhibits root canal biofilm formation. Its exhibits antimicrobial effects against *Enterococcus faecalis, Streptococcus gordonii* and *Candida albicans*.[11]

Vinegar

Consisting mainly of acetic acid, vinegar has natural antimicrobial properties that make it effective against bacteria within the root canal. Furthermore, its acidic structure facilitates the dissolution of organic tissue and ensures thorough cleaning of the root canal system. Unlike some traditional irrigation solutions, vinegar is biocompatible and rarely causes adverse reactions, making it a safer option.[10]

Vinegar can eliminate the smear layer, which consists of organic and inorganic components that block the dentinal tubule entrances. Furthermore, it exhibits a bactericidal effect against microorganisms frequently associated with endodontic infections, such as *Staphylococcus aureus* and *Enterococcus faecalis*. The high malic acid content in vinegar also contributes to the repair process in the periapical region.[12]

Although vinegar offers several advantages, it also has its disadvantages. Its acidic nature may cause tissue irritation if not diluted properly and long-term exposure could impact dental materials. Furthermore, the patient's acceptance of vinegar irrigation may vary due to its taste and smell, requiring communication and education regarding its benefits and safety.[10]

Propolis

Propolis is a sticky resinous mixture produced by the *Apis mellifera* bees from materials collected from different plants to protect the honeycomb structure.[10] Propolis exhibits potent antimicrobial and anti-inflammatory properties. Its inclusion in irrigation protocols has demonstrated a reduction in bacterial load and promotion of tissue healing, making it a valuable adjunct in endodontic therapy.[13] Propolis has demonstrated good in vitro antibacterial activity against *E. faecalis* in root canals and has been suggested as an alternative intracanal medicament.[14]

Chitosan

Chitosan, a derivative of chitin found in the exoskeletons of crustaceans, has garnered attention for its versatile properties across various industries. It has been included in research studies in dentistry due to its biocompatibility, adhesive capability, lack of toxicological activity and genotoxic effect.[15] Thus, chitosan is a promising irrigation solution in endodontics. In 2013, Silva et al. used scanning electron microscopy (SEM) to evaluate the effectiveness of the final irrigation agents used after root canal instrumentation in removing the smear layer. SEM analysis demonstrated that 0.2% chitosan solution could remove the smear layer and similar results were obtained only with high concentration solutions such as 15% ethylenediaminetetraacetic acid (EDTA) and 10% acetic acid.[16]

Chitosan is a hydrophilic biopolymer prepared by the alkaline deacetylation of chitin. It exhibits high biocompatibility, biodegradability, antimicrobial and anti-inflammatory activities. Furthermore, it positively affects wound-healing, hemostasis and tissue regeneration. A study examining the anti-inflammatory activity of chitosan revealed that at a concentration of 50 μg/mL, it lowered the expression levels of IL-1β, IL-6 and TNF-α.[17]

Morinda Citrifolia

Morinda citrifolia (Rubiaceae), known as noni, is indigenous to Southeast Asia and the Pacific and has a longstanding history of medical use.[10] The combination of antimicrobial, anti-inflammatory and tissue healing properties make the *Morinda citrifolia* juice (CMJ) a versatile solution for the complexities of endodontic infections and inflammation and a promising alternative irrigation solution.

Murray et al. (2008) compared the effectiveness of CMJ, sodium hypochlorite (NaOCl) and chlorhexidine solutions in removing the smear layer from root canal walls and their antimicrobial properties. The growth of *E. faecalis* was inhibited by CMJ at a concentration of 6%. Furthermore, 6% CMJ, 6% NaOCl and 17% EDTA were required to effectively remove the smear layer during the final irrigation.[18]

Aloe vera

Aloe vera gel (*Aloe barbadensis* Miller), renowned for its anti-inflammatory and wound-healing properties, is a viable irrigation solution in endodontics. Its soothing effect on periapical tissues and ability to enhance dentin remineralisation make it a viable option for clinicians seeking natural alternatives.[10] Aloe vera demonstrates antimicrobial activity against various species such as *Streptococcus pyogenes, S. aureus, E. faecalis* and *Candida albicans*.[19]

Triphala

Triphala, composed of three medicinal herbs (*Emblica officinalis* [Amalaki], *Terminalia bellerica* [Bibhitaki] and *Terminalia chebula* [Haritaki]), is revered in Ayurveda for its therapeutic properties.[10] Rich in antioxidants and bioactive compounds, Triphala exhibits antimicrobial, anti-inflammatory and wound-healing properties, making it a promising alternative for endodontic irrigation. Its multifaceted mechanism of action ensures thorough cleansing while promoting tissue healing and addressing the dual challenges of infection control and tissue preservation in endodontic therapy.

Herbal extracts

Herbal extracts such as neem, tea tree oil and thyme have demonstrated antimicrobial activity against endodontic pathogens. Their natural origin and broad-spectrum efficacy make them promising candidates for irrigation solutions, particularly against antibiotic-resistant strains.[20]

Essential oils

Essential oils such as clove, eucalyptus and cinnamon possess potent antibacterial and anti-inflammatory properties. Thus, incorporating these oils into irrigation solutions can enhance microbial control and promote periapical healing, offering a holistic approach to endodontic therapy.[21]

Root canal filling materials

Using more biocompatible materials in dentistry is crucial for the health of patients, dentists and the environment. To ensure that the health of patients, dentists and the environment is not threatened by the dental materials used, we should aim to improve the clinical practices of dentistry, the maintenance of the products and the use of dental materials. Thus, the mineral trioxide aggregate (MTA) and its bioceramic properties have been modified.

The MTA is composed of Portland cement[22], which contains primarily aluminium and trace amounts of arsenic, lead and chromium elements. Studies have demonstrated that the Portland cement generates negative effects.[23-27] Thus, second generation materials such as pure tricalcium silicate cement have been developed. Additionally, bioceramic-based materials have been introduced. Bioceramic root canal sealers, composed of second-generation materials, do not allow the leakage of these trace elements and aluminium into the surrounding tissues.[22] They have become very popular recently, and contain a dental material that continues to be developed and modified. Bioceramic root canal sealers are highly biocompatible materials that do not irritate the periapical tissue, making them popular. Furthermore, they allow the formation of tooth and bone-like tissue via a series of chemical reactions during the hardening process. The other theories for tooth formation include the diffusion of second-generation materials into dentin tubules, infiltration of the area with collagen fibres released due to dentin contact and hydroxyapatite formation due to absorption of moisture from the dentin.[28] Furthermore, the antimicrobial activity gained by bioceramic root canal sealers due to calcium ion release increases the success rate of endodontic treatments by eliminating the possibility of intraradicular infection.[28]

Dental filling materials

Although dentists are careful during treatments, waste material can be released into the environment. The most important of these are the chemicals released from the frequently used amalgam fillings. Dental amalgam is preferred over other fillings because it is inexpensive,

durable and easy to use. However, mercury is the most abundant metal in amalgam fillings, which contributes to the high worldwide mercury consumption. Mercury can bioaccumulate in the environment, plants, animals and humans, producing a toxic effect. Mercury is a neurotoxic and teratogenic heavy metal. Due to reactions at the site of accumulation, mercury can turn into methylmercury, which can also accumulate in the food chain.[29] Dentistry accounts for approximately 6% of the global mercury consumption and 14% of the mercury waste. Excess mercury in waterways can cause various health complications in humans and severely affect the local ecosystem.[30] Apart from this, dentistry contributes to cotton, plastic, paper and other 'disposable' waste.[31] Using sustainable resources reduces the burden on dentistry and produces less waste. The adoption of green dentistry offers numerous benefits, both for dental practitioners and the environment. Some of these benefits are as follows: reduced treatment costs due to reduction in resource consumption and waste generation; enhanced reputation of the dental practice via its commitment to sustainability, which can attract environmentally conscious patients; and reduced exposure of patients and physicians to harmful chemicals due to the use of eco-technology. Green dentistry can promote and contribute to the conservation of natural resources and ecosystems by minimising the harmful effects on the environment and ensuring better oral and general health.

Recently, researchers have focused on the polluting effect of amalgam.[3,9,32-34] Several measures have been proposed to eliminate or reduce this polluting effect. The most important target of these measures is dental aspiration units. Dental suction units evacuate numerous products that are generated during dental treatment, including restoration by-products and milling waste. The improper disposal of mercury, especially during the removal of amalgam fillings, can harm the environment. In dental clinics, low-cost amalgam separators should be used to recycle mercury and prevent the mercury residue from entering water sources and therefore the environment. Several ISO 11,143-certified amalgam separators are capable of significantly reducing amalgam particles and by-products in the wastewater of dental clinics [29]. Amalgam separators are inexpensive, easily available and very easy to maintain.[29]

Dental separators are designed to capture waste. However, they are not universally used due to the lack of equipment, legal obligations and updated regulations. Oxidising agents used to disinfect the dental unit after dental treatments also reportedly increase mercury release.[29] The mercury level in dental clinics is much higher than acceptable due to difficulties in controlling mercury release, insufficient equipment support, inadequate ventilation systems and wrong practices such as mixing amalgam by hand instead of using amalgam capsules.[29]

Dental impressions

Dental impressions are moulds or copies of a patient's teeth and oral tissue that are used by dentists to create accurate dental restorations such as crowns, bridges, dentures and orthodontic devices. Traditional and digital impression techniques differ in terms of their features and applications. Traditional impressions involve the use of impression materials, such as alginate, polyvinyl siloxane or polyether, to capture a detailed replica of the patient's teeth and surrounding tissue.[35] Dental waxes are not required after being shaped by heat and used in the patient's mouth. Moreover, 80–90% of the wax can be collected and purified by removing sticky impurities using simple techniques. Thus, the wax can be effectively reused and recycled several times without any deterioration in its properties.[36]

Traditional impression materials become unusable after they have been used in the patient's mouth and thus generate waste. To prevent this waste generation, digital measurement methods can be employed, which is beneficial for the patient, dentist and environment. Digital impressions serve as virtual models of the patient's mouth structure, eliminating the need for traditional impression materials that negatively affect the environment. This in turn preserves the energy resources used in the production of traditional impression materials. Digital impressions offer numerous advantages over traditional methods, including greater efficiency, better accuracy, improved patient comfort, reduced time consumption, remote collaboration and less environmental impact.[37,38] Furthermore, digital impressions can be easily shared electronically between dental laboratories or specialists, enabling remote collaboration and communication for treatment planning and fabrication of dental restorations.[37]

Digital impressions have demonstrated environmental benefits such as reduction in material waste, energy efficiency, long-term sustainability, elimination of disposable trays, conservation of natural resources, reduction in water use, reduction in carbon emissions, reduction in hazardous waste and promotion of green practices.[39] Digital impressions eliminate the need for traditional impression materials, which are often single-use and contribute to waste generation. By replacing these materials with digital scanning technology, the amount of disposable waste generated during dental procedures is significantly reduced.[38]

Digital impression technology is continuously evolving and becoming more sustainable over time. With advancements in materials, equipment and software, digital impressions could become more environmentally friendly and contribute to long-term sustainability in dental practice.[40]

Digital impressions contribute to the conservation of natural resources by reducing the demand for raw materials used in traditional impression materials, trays

and packaging. By minimising the extraction and processing of these resources, digital impressions support the sustainable practices in dental care.[41] Furthermore, digital impressions eliminate the need for increased water consumption associated with rinsing trays and cleaning traditional impression materials. Thus, it contributes to water conservation efforts.[40,42]

Digital impressions can reduce carbon emissions associated with the transportation and shipping of traditional impressions to dental laboratories. Thus, it helps decrease the carbon footprint of dental practices and contributes to environmental sustainability.[41]

Traditional impression materials often contain hazardous chemicals, such as mercury in dental amalgam or polymethyl methacrylate in acrylic resins, which can pose risks to human health and the environment if not disposed of properly. Digital impressions eliminate the need for these hazardous materials, resulting in a reduction in hazardous waste generation.[41]

Technological advancements in obtaining digital impressions are intraoral scanning, computer-aided design/computer-aided manufacturing (CAD/CAM) integration and cloud-based solutions. Modern intraoral scanners capture detailed digital impressions of patients' teeth and oral structures with high accuracy and precision. These scanners eliminate the need for messy impression materials, offering a more comfortable experience for patients while producing digital models that can be stored electronically.[37] Digital impressions seamlessly integrate with CAD/CAM systems, allowing for the efficient fabrication of dental restorations such as crowns, bridges and veneers. This integration streamlines the production process, which reduces waste generation and enhances the precision of dental restorations.[43] Several digital impression systems offer cloud-based storage solutions for securely storing and sharing digital models. This eliminates the need for physical storage space and facilitates the collaboration between dental professionals, contributing to a more sustainable and interconnected dental community.[44]

RESULTS

In this comprehensive review, we identified 36 studies that contribute to our understanding of environmentally sustainable oral health. The analysis highlights five dentistry themes: dental lasers, natural root canal medicaments and irrigation solutions, root canal filling materials, dental filling materials, and dental impressions. The 36 studies were also categorised according to the sub-branches of dentistry such as endodontics, restorative, prosthetics, periodontics, orthodontics, oral and maxillofacial radiology and general dentistry. This contributed to the creation of a road map for dental practices to achieve a more sustainable world.

The analysis revealed that attention should be paid to the separation, recycling and disposal of waste.[45] Reusable tools and equipment should be used instead of disposable ones.[46] By switching to the use of digital radiography, the amount of waste lead foil and chemicals, such as fixatives and developers, which can cause serious soil and water pollution, can be reduced.[47] One can switch to sustainable and renewable energy sources, such as solar energy, to power the dental offices.[48] Recycling reduces the amount of waste thrown into landfills while also limiting resource consumption.[45] Green dentistry promotes the use of biodegradable and non-toxic cleaning products as well as environmentally friendly dental materials to minimise chemical exposure and environmental pollution.[49,50] Green dentistry also promotes the adoption of digital technology, such as digital radiography, electronic health records and digital impressions, to reduce the use of paper and chemical processing associated with traditional film-based radiography and record-keeping.[51] By embracing digital impressions, dental practices demonstrate their commitment to sustainability and contribute to a greener future for dental healthcare. Adopting digital technology aligns with the growing trend of green dentistry, which emphasises environmentally friendly practices in dental care. The importance of sustainability in dentistry has not been fully understood until recent years, leading to a lack of sufficient research on the topic. This limitation may have constrained our review.

CONCLUSIONS

In conclusion, sustainability in dental practice, via the adoption of green dentistry principles, is essential for mitigating the environmental impact, promoting patient health and ensuring long-term viability. By incorporating sustainable practices into dental operations, practitioners can contribute to a healthier planet while maintaining high-quality oral healthcare services. As the global community increasingly prioritises environmental stewardship, green dentistry will play a vital role in shaping the future of the dental industry.

Conflict of interest

The authors have no competing interests to declare that are relevant to the content of this article.

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Evaluation of Mechanical, Biocompatibility and Cytotoxicity of Different Monolithic Hybrid and Zirconia-Added Ceramics

Farklı Monolitik Hibrit ve Zirkonya Katkılı Seramiklerin Mekanik, Biyouyumluluk ve Sitotoksitite Değerlendirmesi

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ABSTRACT

Today advances in CAD/CAM technology have enabled the production of indirect monolithic restoration materials and increased their use in prosthodontics. CAD/CAM-formed materials that can be used monolithically include composites, feldspathic glass ceramics, leucite crystals glass ceramics, glass ceramics reinforced with lithium disilicate crystals, lithium disilicate ceramics doped with zirconia, hybrid ceramics, and zirconia. The mechanical and physical properties of restorative materials must be biocompatible with the oral environment and free of toxic substances that may cause harmful local effects or systemic reactions. Some of the expected properties of dental materials include aesthetics, ease of use, long clinical lifespan, durability, and biocompatibility. Cytotoxic substances can cause harmful tissue reactions ranging from postoperative sensitivity to irreversible pulp damage in both the short and long term. These materials should be tested in vivo or in vitro before use. This article aims to present the results of the mechanical and biological studies of monolithic hybrid and zirconia-doped ceramic materials and the biocompatibility and cytotoxicity values obtained in the materials.

Keywords: *Prosthodontics, hybrid ceramic, glass ceramic, biocompatibility, cytotoxicity*

ÖZ

Günümüz CAD/CAM teknolojisinde indirekt monolitik restorasyon materyallerinin üretimi arttırılmış ve protetik diş hekimliğinde kullanımı sağlanmıştır. Monolitik olarak kullanılan CAD/CAM ile şekillendirilen materyaller; kompozit, feldspatik cam seramik, lösit kristal cam seramikler ve lityum disilikat kristalleri ile güçlendirilen cam seramikler, zirkonya katkılı lityum disilikat seramik, hibrit seramik ve zirkonya gelmektedir. Restoratif materyallerin mekanik ve fiziksel özellikleri, ağız ortamında biyouyumlu olmalı, zararlı lokal etkilere veya sistemik reaksiyona neden olabilecek toksik maddeler içermemelidir. Dental materyallerin sahip olması beklenen bazı özellikleri; estetik, kullanımı kolay, klinik ömrü uzun, dayanıklı ve biyouyumlu olmasıdır. Sitotoksik maddeler, postoperatif hassasiyetten geri dönüşümsüz pulpa hasarına kadar uzanan kısa ve uzun vadeli zararlı doku reaksiyonlarına neden olabilir. Bu nedenle dental materyallerin kullanımından önce in vivo veya in vitro olarak test edilmesi gerekmektedir. Bu makalenin amacı, monolitik hibrit ve zirkonya katkılı seramik materyallerine uygulanan mekanik ve biyolojik özellik çalışmalarının sonuçlarına ait bulguların ve materyallerden elde edilen biyouyumluluk ve sitotoksititeye ait değerlerinin incelenerek sunulmasıdır.

Anahtar Kelimeler: *Protez, hibrit seramik, cam seramik, biyouyumluluk, sitotoksitite*

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INTRODUCTION

Due to increasing expectations of dentists and patients in restorative dentistry, ceramic materials are seen as an alternative to traditional restorative materials due to their aesthetic, mechanical, and biological properties.[1] High-quality materials have been produced and developed with the rapid development of Computer Aided Design-Computer Aided Manufacturing (CAD/CAM) technology.

With developments in CAD/CAM technology, monolithic restorations have become possible in dentistry.[2,3] CAD/CAM-shaped materials that can be used monolithically: Glass ceramics, zirconia-doped lithium disilicate ceramics, hybrid ceramics, and zirconia.[4] Newly developed hybrid and zirconia-doped ceramics are also among monolithic materials shaped with CAD/CAM.

Many metal, all-ceramic, or polymer materials have been used in dentistry. It is necessary to test the mechanical performance of materials in randomized controlled clinical trials. Therefore, preclinical testing helps to evaluate materials physically and mechanically and to determine the indications for clinical use (Table 1).

Table 1. Comparison of the mechanical and biological properties of the materials tested in this study.

HYBRID CERAMIC MATERIALS	CONTENT	MANUFACTURER
Paradigm Mz100 (PM)	85% Zirconia-silica ceramic, bis-GMA, TEDGMA	3M ESPE, Minnesota, USA
Lava Ultimate (LU)	Bis-GMA, Bis-EMA, UDMA, TEGDMA 80% ZrO□/SiO□ clusters SiO□ (20 nm) and ZrO□ (4-11 nm)	3M ESPE, Minnesota, USA
Vita Enamic (VE)	86% Feldspathic ceramic network, UDMA, TEDGMA	Vita Zahnfabrik, Bad Säckingen, Germany
Cerasmart, (CS)	71% Silica and barium, 2,2-Bis propane, UDMA, DMA	GC Dental, Tokyo, Japan
Shofu Block (SB)	61% Silica powder, zirconium silicate, and micro-clustered silica components	Shofu Dental, Ratingen, Germany
Katana Avencia (KA)	Fillers containing colloidal silica and aluminum oxide, UDMA	Kuraray Noritake, Kurashiki, Japan
Grandio Block (GB)	Bis-GMA, TEGDMA, Barium boron alumino silicate glass (0.1-2.5 µm), silica (20-60 nm)	Voco Dental, Cuxhaven, Germany
ZIRCONIA-REINFORCED LITHIUM SILICATE MATERIALS	**CONTENT**	**MANUFACTURER**
Vita Suprinity (VS)	8–12% Zirconia, 56–64% Silicon Dioxide, 15–21% Lithium Oxide	Vita Zahnfabrik, Bad Säckingen, Germany
Celtra Duo (CD)	%58 Silicon Dioxide, %5 Phosphorus Pentoxide, %1.9 Alumina, %18.5 Lithium Oxide , %10 Zirconium Dioxide	Dentsply Sirona, Erlangen, Germany

Ceramics and resin-containing composites constitute two main groups of dental prosthetic materials.[5,6] Dental ceramics are inorganic materials with a crystalline phase and/or glass matrix composition.[6] Ceramic materials have been widely used in dentistry due to their high tissue compatibility, durability, abrasion resistance, low plaque accumulation, color stability, and aesthetics.[7,8] Ceramic materials have high bending strength and elastic modulus. However, due to this property, dental ceramics do not absorb the incoming load and are less flexible and more brittle.[9]

Lithium silicate-reinforced glassceramics have been produced to develop a higher strength and fracture resistance material. This system has a much higher crystal content than leucite glass ceramics to strengthen substrate ceramic. Lithium disilicate crystals are used in 70% of material content.[10]

Zirconia-reinforced Lithium Silicate glass ceramics (ZLS) were obtained by enriching glass ceramics with approximately 10 wt% zirconia. This newly developed ceramic material, which has a homogeneous microstructure and small particle size, shows superior mechanical resistance to other glass-ceramic materials. The fracture resistance of these ceramics containing 8-12% ZrO_2 is 210 MPa after milling and increases to 420 MPa after crystallization.[11]

New alternative materials have been introduced to market that combine the favorable properties of ceramics

and composites and are shaped by CAD/CAM. In 2013, ADA defined ceramics as 'pressed, fired, polished or milled materials containing many inorganic refractories such as porcelain, glass, ceramic and/or glass-ceramic'. These newly developed materials are categorized as ceramic-like materials because they contain more than 50% by weight of inorganic content and a small amount of organic phase.[12]

Resin composites are a polymer matrix reinforced with inorganic fillers (ceramic, vitreous ceramic, or glass), organic, or composite. Composite materials cause minimal abrasion to opposing tooth and are easy to handle.

Advantages of newly developed monolithic hybrid ceramic materials include less abrasion of opposing tooth tissue, less preparation, ease of repair with similar resin composites, and chemical compatibility with adhesive resin cement. It also has the same anisotropy as dentin.[13] Hybrid ceramic materials are much more durable, less brittle, and less porous than ceramics. This new generation of polymer-containing ceramics shows better bending and lower fracture resistance due to their elastic modulus being close to dentin.[14] These materials have been named under various names: Resin nanoceramics, hybrid ceramics, resin-matrix ceramics, and double-meshed materials.[12] Using hybrid ceramics in prosthodontics has increased gradually.

Mechanical and Biological Properties of Hybrid Ceramic Materials

Hybrid ceramic materials and Zirconia-reinforced Lithium Silicate glass ceramic (ZLS) materials are frequently used in prosthodontics (Table 2).

Table 2. Summary of studies included in this review.

Arthur Furtado et al. (2019).[25]	-IPS e.max CAD (IEX) -Vita Suprinity (VS) -Cerasmart (CS) -Vita Enamic (VE)	To evaluate the fracture strength of one lithium disilicate, one zirconia-doped lithium silicate, and two hybrid ceramic materials.	IPS e.max CAD (4100 N, IEX) and Vita Suprinity (3659 N, VS) materials have significantly higher fracture toughness values compared to Vita Enamic (2003 N, VE) and Cerasmart (1562 N, CS) materials.
Frank A. Spitznagel et al. (2021).[26]	-3Y-TZP -4Y-TZP -5Y-TZP -Vita Enamic (VE)	To evaluate the thermo-mechanical fatigue behavior and failure modes of three different zirconia and one hybrid ceramic material.	All tested materials showed higher failure loads (>1750 N) than normal physiological occlusal loads in the posterior region (200-900 N) and can be recommended for posterior clinical use.
N. Juntavee et al. (2020).[33]	-IPS e.max CAD (IEX) -Vita Suprinity (VS) -Y-TZP	To evaluate the influence of different tempering processes on the flexural strength of one zirconia-reinforced lithium silicate glass ceramic, one lithium disilicate ceramic and one monolithic zirconia materials.	Y-TZP indicated significantly higher flexural strength upon slow tempering (1,183.98 ± 204.26 MPa) than Vita Suprinity (VS, slow tempering: 267.15 ± 32.71 MPa) and, IPS e.max Cad (IEX, slow tempering: 392.09 ± 37.91 MPa)
T. Srichumpong et al. (2019).[34]	-IPS e.max CAD (IEX) -IPS Empress CAD (IES) -Vita Suprinity (VS) -Celtra Duo (CD)	To evaluate the fracture strength of one lithium disilicate, two zirconia-reinforced lithium silicate, and one leucite-reinforced glass-ceramic materials.	The fracture toughness of IPS e.max CAD (2.64 MPa, IEX) was the highest, and IPS Empress CAD (1.09 MPa, IES) had the lowest fracture toughness.
J.B. Monteiro et al. (2018).[35]	-Vita Suprinity (VS) -Celtra Duo (CD)	To evaluate the effect of ceramic thickness on the fatigue failure load of two zirconia-reinforced lithium silicate ceramic materials.	The ceramic thickness influenced the fatigue failure load for both zirconia-reinforced lithium silicate ceramic materials: Vita Suprinity (VS, 716 N up to 1119 N) and Celtra Duo (CD, 404 N up to 1126 N).

The Microstructure of first hybrid ceramic shaped by CAD/CAM (Paradigm Mz100, PM, 3M ESPE, Minnesota, USA) consists of 85% weight of zirconia-silica ceramic particles. Polymer matrix contains bisphenol A glycidyl methacrylate (bisGMA), triethylene glycol dimethacrylate (TEDGMA), and an initiator system.[12,15,16] This material is used in inlay, onlay, crown, and veneer restorations.[17]

Hybrid ceramic called “resin nanoceramic” by manufacturer (Lava Ultimate, LU, 3M ESPE, Minnesota, USA) consists of 80% of the weight of nanoceramic particles in a resin matrix.[12,17] This material has a modulus of elasticity equivalent to dentin and is less brittle than glass ceramics. Since they are flexible, they resist chipping and cracking during grinding.[17] Thanks to their low elastic modulus, they absorb masticatory forces

better. Indications for this material are inlay, onlay, and veneer restorations.[17,18]

In the production of one of new hybrid ceramic materials currently used in prosthodontics (Vita Enamic, VE, Vita Zahnfabrik, Bad Säckingen, Germany), a pre-sintered porous feldspar ceramic is first produced. Resin is then infiltrated into this porous ceramic network by capillary action. By applying polymerization with heat, polymer forms polymer network that enables the formation of a polymer-infiltrated ceramic mesh.[19] Feldspathic ceramic network constitutes 86% of its weight. Thanks to this double network structure, crack propagation is stopped. Polymer network contains UDMA (Urethane Dimethacrylate) and TEGDMA.[12,17] The advantages of this material are low brittleness, the ability to be milled in thin areas without cracks/fractures, higher modulus of elasticity compared to conventional ceramics, the ability to mill restorations with diamond burs, and less milling time. It is used in the crown, inlay, onlay, and veneer restorations and is contraindicated in bridges and parafunctional cases.[17]

Another hybrid ceramic used (Cerasmart, CS, GC Dental, Tokyo, Japan) consists of 71% filler particles by weight and is called nano ceramic by manufacturer. Filler particles contain silica and barium, and resin matrix contains 2,2-Bis propane, UDMA, and DMA (dimethacrylate).[20] Indications are inlay, onlay, veneer, crown, and implant-supported crown restorations.

The microstructure of one of new generation hybrid ceramic restorative materials (Shofu Block, SB, Shofu Dental, Bad Ratingen, Germany) contains silica powder, zirconium silicate, and micro-clustered silica, with inorganic component constituting more than 61% by weight.[12,20] The advantages of this material are high-stress absorption due to its high elasticity and flexural strength. The flexural strength of material is more than 190 MPa. In the system of this material, two-layer blocks are available for anterior restorations, it has good light transmission and fluorescence properties, as well as easy and sustainable polishing. Due to its tooth-like light transmission and good mechanical properties, it is used in anterior and posterior restorations, implant-supported restorations, inlay, onlay, and veneer restorations.

Currently used hybrid ceramic material (Katana Avencia, KA, Kuraray Noritake, Kurashiki, Japan) is produced by compressing nano-sized fillers in a block and then impregnating with a resin monomer, polymerized by heat. Main components are fillers containing colloidal silica and aluminum oxide, polymerized resins, methacrylate monomers (urethane dimethacrylate copolymers and other methacrylate monomers), and pigments. It is used to prepare inlay, onlay, veneer, and full crown restorations.[21]

Hybrid ceramic material (Grandio Block, GB, Voco Dental, Cuxhaven, Germany), new to market, has a polymerization shrinkage of 1.57% due to its 87% nanofiller content. In this way, nanoparticles act as a network within matrix, increasing abrasion and tensile strength. Surface finishing processes are faster than other CAD/CAM materials. It does not require baking during restoration construction phase. Milling, matching, and polishing processes are more accessible. Intraoral adaptations, additions, and repairs can be applied with light polymerized restorative materials. Cementation with adhesive cement is recommended.[22]

Nowadays, using zirconia-reinforced lithium silicate glass ceramics in prosthodontics has gradually increased.

Mechanical and Biological Properties of Zirconia-Reinforced Lithium Silicate Glass Ceramic Materials

Hybrid ceramics are frequently used in prosthodontics and Zirconia-reinforced Lithium Silicate glass-ceramics (ZLS) (Table 2).

One of these materials, Vita Suprinity (VS, Vita Zahnfabrik, Bad Sackingen, Germany), is fully crystalline and in pre-crystallized form. Due to the homogeneous distribution of crystals of approximately 0.5μm in size, even fully crystallized form can be easily milled and polished. There are varieties with different degrees of translucency, including High Translucent (HT) and Translucent (T). Anterior and posterior crowns, implant crowns, veneers, inlay, and onlay restorations can be produced with these blocks.[23]

Zirconia-reinforced Lithium Silicate glass ceramic ZLS (Celtra Duo, CD, Dentsply Sirona, Erlangen, Germany) is obtained by adding 10% ZrO_2 to lithium silicate. It has properties similar to natural tooth enamel as its lithium silicate crystals correspond to the wavelength range of natural daylight, which is responsible for opalescence. This provides a significant advantage, especially for inlay and onlay restorations produced chairside.[23]

The mechanical properties of hybrid ceramics were investigated by Abdallah Awada[24] and Arthur Furtado[25], Frank A. Spitznagel[26].

Abdallah Awada et al.[24] investigated the mechanical flexural strength of four different hybrid ceramic materials (Vita Enamic, VE, Lava Ultimate, LU, Cerasmart, CS, and Paradigm MZ100 Block, PM), one feldspathic ceramic (Vitablock Mark II, VM2, Vita Zahnfabrik, Bad Säckingen, Germany) and one one leucite-reinforced glass ceramic (IPS Empress Cad, IES, Ivoclar Vivadent, Liechtenstein, Germany). Cerasmart (219 MPa, CS) and Lava Ultimate (178 MPa, LU) exhibited higher mechanical flexural strength than the other materials. As a result, it was found that newly developed hybrid ceramics exhibited high mechanical bending strength and modulus of resistance values.

Arthur Furtado et al.[25] investigated the fracture toughness of one lithium disilicate (IPS e.max CAD, IEX, Ivoclar Vivadent, Liechtenstein, Germany), one zirconia doped lithium silicate (Vita Suprinity, VS), and two hybrid ceramic (Cerasmart, CS, Vita Enamic, VE) materials. As a result, IPS e.max CAD (4100 N, IEX) and Vita Suprinity (3659 N, VS) materials were found to have significantly higher fracture toughness values compared to Vita Enamic (2003 N, VE) and Cerasmart (1562 N, CS) materials.

Frank A. Spitznagel et al.[26] investigated the thermo-mechanical fatigue behavior of three monolithic zirconia (3Y-TZP, 4Y-TZP, 5Y-TZP, Dentsply Sirona, Erlangen, Germany) and one hybrid ceramic (Vita Enamic, VE) materials. All tested materials showed failure loads (200-900 N) higher than normal physiological occlusal loads (>1750 N) in posterior region and were considered suitable for clinical use.

Biological Properties of Hybrid Ceramic Materials

The biological properties of hybrid ceramics were analyzed by Soho. A. Hassan[27], Numan Aydin[28], MA Bottino[29], Kyoung K. Him[30], and Miriam Zaccaro Scelzan[31] (Table 3).

Table 3. Summary of studies included in this review.

AUTHORS (Year)	MATERIALS	OBJECTIVE	CONCLUSION
Soho. A. Hassan et al. (2022).[27]	-Brilliant Crios (BC) -Cerasmart (CS) -Vita Enamic (VE)	To investigate the biocompatibility of three different hybrid ceramic materials.	Brilliant Crios (278.1 CFU/ml, BC) showed the highest value, followed by Cerasmart (105.1 CFU/ml, CS) and Vita Enamic (102 CFU/ml, VE).
Numan Aydin et al. (2020).[28]	-Brilliant Crios (BC) -Cerasmart (CS) -Vita Enamic (VE) -Celtra Duo (CD) -Grandio Block (GB)	To investigate the cytotoxic effect of four different hybrid and zirconia-reinforced lithium silicate ceramic materials on human gingival keratinocyte cells.	Vita Enamic (102%, VE) provided the highest cell viability; Brilliant Crios (71.3%, BC) and Celtra Duo (73.5%, CD) exhibited minimal cell viability.
MA Bottino et al. (2019).[29]	-Vita Enamic (VE) -Y-TZP	To investigate the biofilm formation and cell viability of one hybrid and one Yttrium-stabilized Tetragonal Zirconia ceramic materials.	Vita Enamic (95.06%, VE) and Y-TZP (90.53%) exhibited similar biofilm formation.
Kyoung K. Him et al. (2017).[30]	-Vita Enamic (VE) -Lava Ultimate (LU) -VitaBlock Mark II (VM2) -Wieland-Reflex (WF)	To investigate the effect of surface treatment of two different hybrids, one leucite-reinforced glass and one nano-leucite-reinforced glass ceramic material, on biofilm formation.	Surface treatment promoted significantly more biofilm formation in Lava Ultimate (216.5, LU), Vita Enamic (168, VE), and Wieland Reflex (183.5, WF), while Vitablock Mark II (92.5, VM2) did not affect biofilm formation.
Miriam Zaccaro Scelzan et al. (2018).[31]	-Vita Enamic (VE) -Lava Ultimate (LU) -Vita AC-12 (VA12) -InSync (ISC)	To investigate the cytotoxicity of two different hybrids and two different glass ceramic materials.	Vita Enamic (VE) and Lava Ultimate (LU) materials showed better biocompatibility than Vita AC-12 (VA12) and InSync (ISC) materials at the 24-hour extraction time points.
De Luca Pedro et al. (2018).[38]	-Vita Suprinity (VS) -Y-TZP	To investigate the biocompatibility of two different zirconia-reinforced lithium silicate ceramic materials.	Only crystallized Vita Suprinity (4.00 cells/cm², VS) showed significantly higher proliferation compared to Y-TZP (2.5 cells/cm²).
Mohamed Mahmoud Abdalla et al. (2021).[39]	-Vitablocks TriLuxe Forte (VTF) -IPS e.max Press (IEP) -Vita Suprinity (VS)	To investigate the effect of polishing on surface roughness and biofilm formation on one feldspathic ceramic, one lithium disilicate glass-ceramic and one zirconia-doped lithium silicate ceramic materials.	The polished samples of Vita Suprinity (VE, 9.24%) had a significantly lower percentage of biofilm coating than Vitablocks TriLuxe Forte (68.27%, VTF) and IPS e.max Press (30.83%, IEP).
Rizo-Gorrita et al. (2018).[40]	-Y-TZP -Celtra Duo (CD)	To investigate the biofilm formation of one Y-TZP and one zirconia-reinforced lithium silicate ceramic materials.	Y-TZP (68.90 ± 49.02 cells/cm²) exhibited better cellular proliferation than Celtra Duo (CD, 34.55±17.52 cells/cm²).

Soho A. Hassan et al.[27] examined surface roughness, biofilm formation, cytotoxicity, and genotoxicity of three different hybrid ceramic materials (Brilliant Crios, BC, Cerasmart, CS, and Vita Enamic, VE). They performed an MTT test for cytotoxicity evaluation. It was reported that materials showed different values in terms of cytotoxicity. Brilliant Crios (278.1 CFU/ml, BC) showed the highest value, followed by Cerasmart (105.1 CFU/ml, CS) and Vita Enamic (102 CFU/ml, VE). Therefore, Vita Enamic was considered the most biocompatible material among tested materials.

Numan Aydın et al.[28] aimed to investigate the cytotoxic effect of four different hybrid (Brilliant Crios, BC, Cerasmart, CS, Vita Enamic, VE, Grandio Blocks, GB, and Zirconia reinforced lithium silicate containing (Celtra Duo, CD) ceramics on human gingival keratinocyte cells in vitro and incubated prepared samples for 1, 3 and 7 days. The cell viability of samples was analyzed by MTT assay. As a result, materials showed 100% cell viability at the end of the first day. On day 3, cell viability decreased, but no significant difference was found. Vita Enamic showed 100% cell viability at all time points. Brilliant Crios (71.3%, BC) and Celtra Duo (73.5%, CD) showed a statistically significant difference in cell viability on day 7. Among materials, Vita Enamic (102%, VE) provided the highest cell viability, while Brilliant Crios (71.3%, BC) and Celtra Duo (73.5%, CD) exhibited minimal cell viability.

Bottino et al.[29] aimed to investigate the biofilm formation of one hybrid ceramic (Vita Enamic, VE) and one Yttrium-stabilized Tetragonal Zirconia Polycrystalline (Y-TZP) material and found that Vita Enamic (95.06%, VE) and Y-TZP (90.53%) exhibited similar biofilm formation. Both Vita Enamic and Y-TZP are recommended materials for indirect dental restorations and were found to be non-cytotoxic.

Kyoung K. Him et al.[30] aimed to investigate the effect of surface treatment of two different hybrid ceramic materials (Vita Enamic, VE and Lava Ultimate, LU), one leucite-reinforced glass ceramic (VitaBlock Mark II, VM2) and one nano-leucite-reinforced glass ceramic (Wieland Reflex, WF, Wieland Dental, Pforzheim, Germany) on biofilm formation. There were two groups in total; the first group was surface-treated with disks of different sizes, while the second group did not receive any surface treatment. Results showed that surface treatment promoted significantly more biofilm formation (Lava Ultimate = 216.5, LU, Vita Enamic = 168, VE, and Wieland Reflex = 183.5, WF), while Vitablock Mark II (92.5, VM2) did not affect biofilm formation. As a result of surface treatment, the highest biofilm formation was found in Lava Ultimate (LU).

Miriam Zaccaro Scelza et al.[31] compared the cytotoxicity of two different hybrids (Vita Enamic, VE and Lava Ultimate, LU) and two different glass ceramic (Vita AC-12, VA12, Vita Zahnfabrik, Bad Säckingen, Germany and InSync, ISC, Jensen Dental, North Haven, USA) materials. Samples of each material were prepared by incubation for 1, 7, and 40 days. Human gingival fibroblasts were exposed to these samples, and cell viability was assessed by mitochondrial activity (XTT) assay. In XTT test, Vita Enamic (VE) and Lava Ultimate (LU) materials showed better biocompatibility than Vita AC-12 (VA12) and InSync (ISC) materials at 24-hour extraction time points, and the clinical use of these restorative materials was evaluated positively.

Mechanical properties of zirconia-reinforced lithium silicate glass-ceramics have been studied by C. Liu[32], N. Juntavee[33], T. Srichumpong[34], J.B. Monteiro[35], R. Ottoni[36], and Fernando Zarone[37].

N. Juntavee et al.[33] evaluated the effect of thermal tempering procedures on the mechanical flexural strength of a Yttrium-stabilized Tetragonal Zirconia Polycrystalline (Y-TZP), a zirconia-reinforced lithium silicate glass ceramic (Vita Suprinity, VS) and a lithium disilicate ceramic (IPS e.max Cad, IE) material. As a result of the study, it was found that while slow thermal tempering of monolithic Y-TZP (slow tempering: 1,183.98 ± 204.26 MPa, normal tempering: 1,084.43 ± 204.79 MPa, fast tempering: 777.19 ± 99.77 MPa) increased the mechanical flexural strength, the strengthening of Vita Suprinity (VS) (slow tempering: 267.15 ± 32.71 MPa, normal tempering: 218.43 ± 38. 46 MPa, fast tempering: 252.67 ± 37.58 MPa) and IPS e.max Cad (slow tempering: 392.09 ± 37.91 MPa, normal tempering: 378.88 ± 55.38, fast tempering: 390.94 ± 25.34 MPa) cannot be achieved by tempering process; therefore, slow, normal, or fast tempering procedures can be applied.

T. Srichumpong et al.[34] investigated the fracture toughness of one lithium disilicate ceramic (IPS e.max Cad, IEX), one leucite-reinforced glass-ceramic (IPS Empress Cad, IES), and two zirconia reinforced lithium silicate glass ceramic (Vita Suprinity, VS and Celtra Duo, CD) materials. As a result, the fracture toughness of IPS e.max CAD (2.64 MPa, IEX) was significantly higher than other materials, and IPS Empress CAD (1.09 MPa, IES) had the lowest fracture toughness. Based on the data obtained, tested restorative dental materials were found to be suitable for clinical use.

J.B. Monteiro et al.[35] evaluated the fatigue strength of two zirconia-reinforced lithium silicate glass ceramic materials (Vita Suprinity, VS and Celtra Duo, CD) at different thicknesses. Vita Suprinity (1 mm: 716.5 ± 95.5 N, 1.5 mm: 907.5 ± 34.5 N, 2 mm: 959.5 ± 81.8 N, 2.5 mm: 1119.6 ± 241.7 N, VS) and Celtra Duo (1 mm: 404.0 ± 43.3 N, 1.5 mm: 628.1 ± 79.6 N, 2 mm: 764.5 ± 43.9 N, 2.5 mm: 1126.8 ± 80.2 N, CD) exhibited higher fatigue strength compared to CD. In conclusion, it was found that different microstructures of zirconia-

reinforced lithium silicate glass ceramics can affect the fatigue behavior of restorations.

Biological Properties of Zirconia-Reinforced Lithium Silicate Glass Ceramic Materials

The biological properties of zirconia-reinforced lithium silicate glass ceramics were investigated by P.G. De Luca[38], Numan Aydın[28], Mohamed Mahmoud Abdalla[39], and M. Rizo-Gorrita[40] (Table 3).

De Luca Pedro et al.[38] evaluated the biocompatibility of zirconia-containing lithium silicate (Vita Suprinity, VS) polished at different stages with human gingival fibroblasts in vitro, and the results were tested using cell proliferation and viability of Yttrium-stabilized Tetragonal Zirconia Polycrystalline (Y-TZP). Polishing the surface of Vita Suprinity before crystallization was found to promote cell proliferation. Only crystallized Vita Suprinity (4.00 cells/cm², VS) showed significantly higher proliferation compared to Y-TZP (2.5 cells/cm²).

Mohamed Mahmoud Abdalla et al.[39] investigated the effect of polishing on surface roughness and biofilm formation on feldspathic ceramic (Vitablocks TriLuxe Forte, VTF, Vita Zahnfabrik, Bad Sackingen, Germany), lithium disilicate glass-ceramic (IPS e.max Press, IEP), and zirconia doped lithium silicate (Vita Suprinity, VS) ceramic blocks. They found that for Vitablocks TriLuxe Forte (roughened: 81.55%, polished: 68.27%, VTF), IPS e.max Press (roughened: 68.27%, polished: 30.83%, IEP), and Vita Suprinity (roughened: 31.25%, polished: 9.24%, VS), the mean percentage of living bacteria and biofilm coverage of substrate was significantly higher for roughened ceramic blocks than for polished blocks. The polished samples of Vita Suprinity (9.24%) were reported to have a considerably lower percentage of biofilm coating than the other groups.

In their study, Rizo-Gorrita et al.[40] evaluated morphology, biofilm formation, and fibroblast viability using MTT assay of human gingival fibroblasts in contact with Yttria-stabilized Tetragonal Zirconia Polycrystal (Y-TZP, Vita YZ® T) and lithium silicate reinforced with zirconium (Celtra Duo, CD) treated with two different finishing techniques, either polishing or glazing. The study results revealed that Y-TZP (68.90 ± 49.02 cells/cm²) exhibited better cellular proliferation than Celtra Duo (34.55 ± 17.52 cells/cm²).

Restorative materials' mechanical and physical properties must be biocompatible in both hard and soft oral environments. These restorative materials should not contain toxic substances that can cause harmful local effects or systemic reactions. Cytotoxic substances can lead to short- and long-term adverse tissue reactions, ranging from postoperative sensitivity to irreversible pulp damage. Therefore, these materials must be tested before use in vivo or in vitro.

Biocompatibility is condition that a material in direct or indirect contact with living tissues has inert (non-reactive) properties that do not cause local or systemic toxicity, allergic reaction, and mutagenic or carcinogenic effects, thus can create an appropriate biological response in applied area. Non-biocompatible materials develop adverse tissue reactions, considered 'toxicity'.[41,42]

The components released from the material's structure and their effects at cellular level allow us to evaluate biocompatibility. For a material to be considered biocompatible, there must be compatibility between the host, material, and the function of material. Biological response can change over time depending on the interaction among these three factors. Therefore, biocompatibility is a dynamic process.[43]

Variation in biological response is related to whether material is in direct contact with blood, saliva, gingival crevicular fluid, or the distance between the pulp and enamel-dentin thickness.[42,44] Potential side effects a dental material might cause in the body are monitored before and after it is released to market. Before being released, it is evaluated for local and systemic side effects. Local side effects may include mucosal and pulpal toxicity, while systemic side effects may include allergic, mutagenic, estrogenic, and toxic reactions. Materials that are evaluated and deemed biocompatible regarding local and systemic side effects continue to be assessed for long-term side effects even after being introduced to market.[45]

Some expected characteristics of dental materials include aesthetic, biocompatible, easy to use, durable, and extended clinical lifespan. The biocompatibility of materials depends on several factors, such as surface properties, the structure and amount of monomers released from material, the chemical and physical properties of its components, the type and location of tissues that will contact material, and the duration of exposure. As a result of contact between dental materials and intraoral tissues, such as enamel, dentin, pulp, gingiva, tongue, cheeks, and lips, cytotoxic, genotoxic, allergic, or inflammatory reactions can develop.

In determining biocompatibility, a test method that is simple, standardized, and provides quick results should be preferred.[42] Sequentially, in vitro (primary) tests, animal experiments (secondary tests), and clinical trials in humans (usage tests) are conducted.[43,46,47]

CONCLUSION

Data on mechanical and biological studies of hybrid and zirconia-doped lithium silicate ceramic materials are presented below.

1. In the mechanical bending strength studies, Cerasmart (CS) and Lava Ultimate (LU), hybrid ceramic materials, and in the other study, YTZP, lithium disilicate ceramic materials were found to have higher bending strength.

2. Fracture toughness values of IPS e.max CAD (IEX) were higher than hybrid ceramic materials, and IPS e.max CAD (IEX) was higher than glass and zirconia-doped lithium silicate materials in the other study.
3. In fatigue failure load studies, YTZP and hybrid ceramic Vita Enamic (VE) showed similar results, while in the other study, Celtra Duo (CD) showed higher fatigue failure load values than Vita Suprinity (VS).
4. In biocompatibility studies, the Brilliont Crios (BC) material was compared with hybrid ceramic materials. It showed better biocompatibility than Vita Enamic (VE) and Cerasmart (CS), while in another study, Vita Enamic (VE) was compared with different ceramic materials and showed higher biocompatibility than Cerasmart (CS) Grandio Block (GB), Brilliont Crios (BC) and Celtra Duo (CD). Vita Enamic (VE) and Lava Ultimate (LU) was compared with glass ceramic materials and showed better biocompatibility values than Vita AC-12 (VA12) and InSync (ISC). In another study, Vita Suprinity (VS) material was compared with YTZP, and a higher biocompatibility value was determined than YTZP. Another biocompatibility study reported better biocompatibility values for YTZP material than Celtra Duo (CD) zirconia-doped lithium silicate ceramic material.
5. In biofilm formation studies, Vita Enamic (VE) and YTZP showed similar biofilm formation values. In contrast, Lava Ultimate (LU) showed higher biofilm formation values than Vita Enamic (VE), VitaBlock Mark II (VM2), and Wieland-Reflex (WF) when compared to hybrid and glass ceramic materials. In another study, Vitablock Triluxe Forte (VTF) showed higher biofilm formation than IPS e.max Press (IEP) glass and Vita Suprinity (VS) zirconia doped lithium silicate ceramic materials.

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Diagnosis and Evidence-Based Treatment of Stage IV Periodontitis: Contemporary Clinical Treatment Guideline from the Framework of Updated Disease Classification

Evre IV Periodontitisin Tanısı ve Kanıta Dayalı Tedavisi: Yenilenen Periodontal Hastalık Sınıflandırması Çerçevesinden Güncel Klinik Tedavi Rehberi

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ABSTRACT

Periodontal diseases are chronic, non-communicable inflammatory diseases that occur due to interactions between microbial dental plaque and host response. In the field of periodontology, efforts have been made for many years to classify periodontal diseases and determine treatment approaches for these conditions. In particular, in the management of Stage IV periodontitis, where confounding factors prevail, data obtained from treatment guidelines are of great importance in determining the sequencing and timing of treatments that clinicians will apply. The aim of this review is to present scientific evidence and findings through clinical guidelines prepared for the treatment of periodontitis, especially for the treatment approach of Stage IV periodontitis patients, in the light of current literature.

Keywords: *Periodontal disease, periodontitis, diagnosis, treatment*

ÖZ

Periodontal hastalıklar mikrobiyal dental plak ve konak yanıtı arasındaki etkileşimlere bağlı olarak oluşan kronik ve bulaşıcı olmayan enflamatuvar hastalıklardır. Periodontoloji alanında uzun yıllardır periodontal hastalıkların sınıflandırılması ve bu periodontal hastalıkların tedavi yaklaşımını belirlemeye yönelik rehberler geliştirilmekte ve güncellenmektedir. Özellikle karıştırıcı faktörlerin hakim olduğu evre IV periodontitisin yönetiminde klinisyenlerin uygulayacakları tedavilerin sıralama ve zamanlaması konusunda tedavi rehberlerinden elde edilen veriler büyük önem arz etmektedir. Bu derlemenin amacı; güncel literatür ışığında periodontitisin tedavisi ve özellikle evre IV periodontitis hastalarının tedavi yaklaşımı için hazırlanan klinik rehberler üzerinden, bilimsel kanıt ve bulguların aktarılmasıdır.

Anahtar Kelimeler: *Periodontal hastalık, periodontitis, tanı, tedavi*

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INTRODUCTION

Periodontitis is recognized as one of the most prevalent chronic inflammatory non-communicable diseases in the population, characterized by the dysregulation of the host immune-inflammatory response due to the accumulation and dysbiosis of the microbial dental plaque biofilm at the gingival margin.[1–3] Beyond inducing inflammation and destruction in the periodontal tissues, periodontal diseases have the potential to exert detrimental effects on distant organs and tissues. To date, periodontal diseases have been associated with more than 50 systemic conditions,[4] including diabetes,[5] atherosclerotic cardiovascular disease,[6] and adverse pregnancy outcomes such as low birth weight and preterm birth.[7] Consequently, the treatment of existing periodontal disease has been proposed as an adjunctive therapeutic strategy in the management of certain systemic conditions.[8]

In the 2017 workshop, periodontal diseases were reclassified in accordance with the latest literature, replacing the previously used terms such as "Chronic Periodontitis" and "Aggressive Periodontitis"[9] with a staging and grading system for periodontitis.[10] This classification system remains in use in contemporary clinical practice. According to the classification, the presence of radiographically detectable marginal bone loss is a prerequisite for a preliminary diagnosis of periodontitis. Additionally, the clinical level of attachment loss is assessed. Patients exhibiting interdental attachment loss in at least two non-adjacent teeth, or buccal or oral attachment loss of ≥3 mm with probing pocket depths of ≥3 mm in at least two teeth, are given a preliminary diagnosis of periodontitis. Subsequently, for individuals with a preliminary diagnosis of periodontitis, it is necessary to investigate whether the observed clinical attachment loss is attributable to alternative etiologies, including traumatic gingival recession, endo-periodontal lesions, vertical root fractures, caries, restorations, or local factors associated with impacted third molars. If a patient with a preliminary diagnosis of periodontitis exhibits probing pocket depths of ≥4 mm in at least one site during periodontal examination, a definitive diagnosis of periodontitis is established. The staging and grading of periodontitis are determined based on comprehensive oral radiographic evaluation, periodontal records, and the history of tooth loss.[11]

The grading system provides insight into the biological characteristics of periodontitis, including its progression rate, anticipated response to treatment, and systemic health implications, while staging reflects the severity, complexity, and extent of the disease. The staging framework is broadly outlined as follows:

- Stage I: Patients with clinical attachment loss of 1–2 mm, bone loss confined to the coronal third of the root in at least one of two adjacent teeth, probing pocket depth of ≤4 mm, and no tooth loss due to periodontitis.
- Stage II: Patients with clinical attachment loss of 3–4 mm, bone loss extending to the coronal third of the root in at least one of two adjacent teeth, probing pocket depths of 4–5 mm, and no periodontitis-related tooth loss.
- Stage III: Patients with clinical attachment loss of ≥5 mm, bone loss extending to the middle third or beyond in more than two adjacent teeth, or periodontitis-related tooth loss of ≤4 teeth. Additionally, criteria from Stage II must be met, with probing pocket depths of ≥6 mm, vertical bone loss of ≥3 mm, or the presence of Class II or Class III furcation defects.

The distinction between Stage IV periodontitis and Stage III lies in the following criteria:

1. A reduction in the number of occluding teeth to fewer than 20 due to periodontitis-related tooth loss.
2. Presence of masticatory dysfunction.
3. Class II or more severe tooth mobility.
4. Severe alveolar bone defects characterized by bone loss extending beyond the middle third of the root (Figure 1).
5. Occlusal irregularities.[10,11]

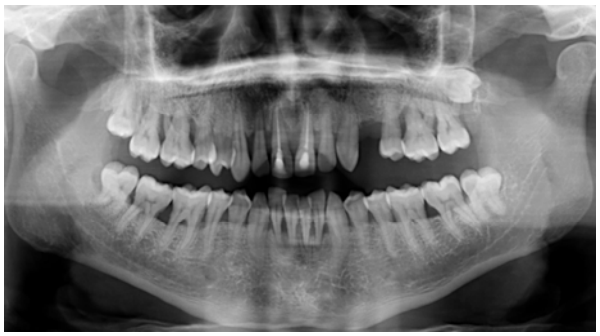

Figure 1: Panoramic radiographic view of a patient diagnosed with stage IV periodontitis.

These distinguishing features inherent to Stage IV periodontitis contribute to the increased complexity of treatment, often necessitating a multidisciplinary approach. In 2020, the European Federation of Periodontology published a clinical practice guideline outlining treatment strategies for Stage I-III periodontitis.[12] Subsequently, in 2022, a clinical treatment guideline was introduced specifically for Stage IV periodontitis. This guideline aimed to provide guidance on multidisciplinary treatment approaches, enhance the overall quality of periodontal therapy, reduce periodontitis-related tooth loss, and consequently improve systemic health and quality of life.[13]

- *Clinical diagnosis of Stage IV periodontitis*

The differential diagnosis between Stage IV and Stage III periodontitis is primarily based on radiographic evidence of bone loss extending beyond the middle third of the root. The complexity of Stage IV periodontitis treatment arises from the presence of one or more of the following factors: tooth hypermobility associated with reduced periodontal attachment, secondary occlusal trauma, tooth migration and diastema formation due to severe attachment loss, periodontal-related loss of five or more teeth, posterior support loss, and "fan-shaped" (i.e., flared anterior teeth due to loss of periodontal support) anterior dentition divergence (Figure 2). These features collectively contribute to the loss of masticatory function and necessitate complex rehabilitative treatment.

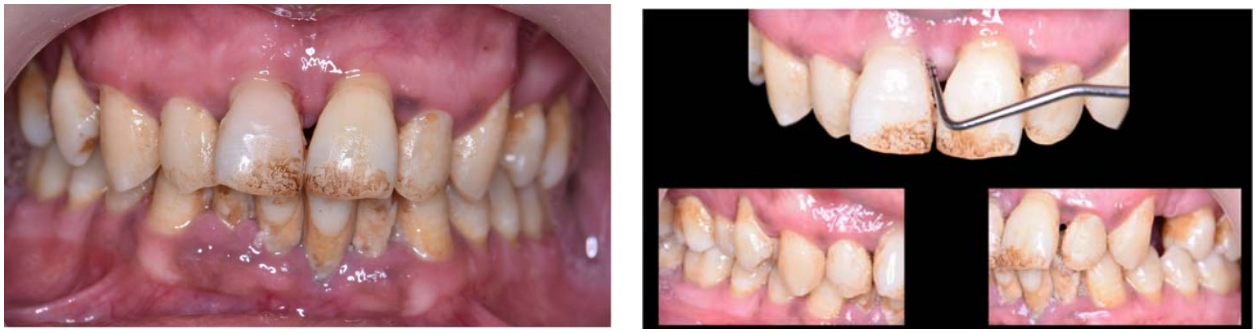

Figure 2: Intraoral photographs of a patient diagnosed with Stage IV periodontitis prior to treatment.

Notably, some of these clinical manifestations such as malocclusion or dental caries can also be observed in patients with Stage I or II periodontitis, making an accurate differential diagnosis of Stage IV periodontitis of critical clinical importance.[13]

- *Definition of Clinical Case Types in Stage IV Periodontitis and the Importance of Individualized Approaches*

The concept of personalized medicine has gained significant importance in modern medicine and dentistry.[14] Personalized periodontology is an innovative approach that considers genetic predispositions, environmental influences, lifestyle factors, and individual behavioral differences. Thus, personalized periodontology can be defined as the integration of clinical decision-making and treatment strategies with the stratification of patients into distinct subgroups.[15] The influence of this patient-centered approach is also evident in contemporary classifications and treatment guidelines for periodontal diseases.

Within this framework, the clinical treatment guidelines for Stage IV periodontitis categorize patients into four distinct clinical case types:

- **Case type 1**: Patients presenting with tooth mobility due to secondary occlusal trauma, which can be managed without the need for tooth extraction.
- **Case type 2**: Patients exhibiting pathological tooth migration characterized by extrusion, tipping, and diastema formation, who are suitable candidates for orthodontic correction.
- **Case type 3**: Partially edentulous patients who can undergo prosthetic rehabilitation without requiring full-arch bridge restoration.
- **Case type 4**: Partially edentulous patients requiring full-arch bridge rehabilitation, who necessitate either tooth-supported or implant-supported treatment.

These case type classifications can coexist within the same patient. For instance, while the maxilla may correspond to Case type 4, the mandible of the same patient may align with Case type 2. Therefore, the treatment guidelines recommend that, prior to formulating a treatment plan for patients with Stage IV periodontitis, a comprehensive assessment should be conducted for each individual tooth. This evaluation should consider the number and distribution of remaining natural teeth, the residual alveolar bone support, periodontal sustainability, and the restorability of the dentition.[13]

- *Sequencing of Periodontitis Treatment*

In the treatment guidelines for Stage I-III periodontitis, periodontal therapy is structured into sequential stages.[4] These stages are outlined as follows:

- *Step 1:* Control of supragingival dental biofilm, oral hygiene education, and patient motivation, implementation of adjunctive therapies to reduce gingival inflammation, professional plaque removal, including supragingival plaque and calculus debridement, and management of risk factors (e.g., metabolic control of diabetes, smoking cessation).
- *Step 2:* Subgingival instrumentation, use of adjunctive physical or chemical agents, application of host modulation therapies (local or systemic), administration

of local subgingival antimicrobials, and systemic antimicrobial therapy when indicated. Following the second stage, a reassessment of the periodontal tissues is recommended to evaluate individual treatment response (periodontal re-evaluation). If the clinical treatment objectives—defined as the absence of periodontal pockets deeper than 4 mm with bleeding on probing or the absence of deep periodontal pockets ≥6 mm—are not achieved, progression to the third stage of treatment is advised. If the treatment objectives are met, patients should be transitioned into what was historically referred to as "periodontal maintenance therapy",[16,17] now termed "supportive periodontal therapy",[18] ensuring continued monitoring and care.

- *Step 3:* In cases where treatment objectives are not achieved, additional therapeutic interventions, either alone or in combination, are recommended. These may include re-instrumentation (repeat mechanical debridement), periodontal flap surgery, and either resective or regenerative surgical approaches.
- *Supportive Periodontal Therapy:* A personalized follow-up program should be established based on the patient's periodontal condition to maintain periodontal stability. The guidelines emphasize the necessity of appropriate diagnostic and treatment planning based on the patient's needs identified during follow-up visits. Additionally, oral hygiene maintenance and patient motivation should be reassessed as integral components of this phase.[12] Supportive periodontal therapy represents a key aspect of the contemporary patient-centered treatment philosophy, requiring lifelong, personalized strategies for periodontitis patients. In Stage IV periodontitis, this phase is even more pronounced, evolving from merely the final phase of therapy into a fundamental component of periodontal disease management.[12,13]

Periodontal health was redefined during the 2017 workshop. It is possible to achieve and maintain periodontal health not only in an intact periodontium but also in a reduced periodontium. While the clinical goal in gingivitis patients is to establish health in an intact periodontium, the primary objective of non-surgical periodontal therapy in periodontitis patients is to achieve health in a reduced periodontium, as the attachment loss observed in periodontitis is irreversible (Figure 3).[19] Individuals diagnosed with periodontitis remain classified as periodontitis patients for life, with an increased risk of disease recurrence. At this point, the importance of supportive periodontal therapy in maintaining periodontal stability becomes evident.[20,21] Researchers advocate for a lifelong, personalized approach to supportive periodontal therapy. Additionally, numerous clinical studies have demonstrated that supportive periodontal therapy sessions conducted at 3- to 6-month intervals significantly reduce periodontitis-related tooth loss.[22]

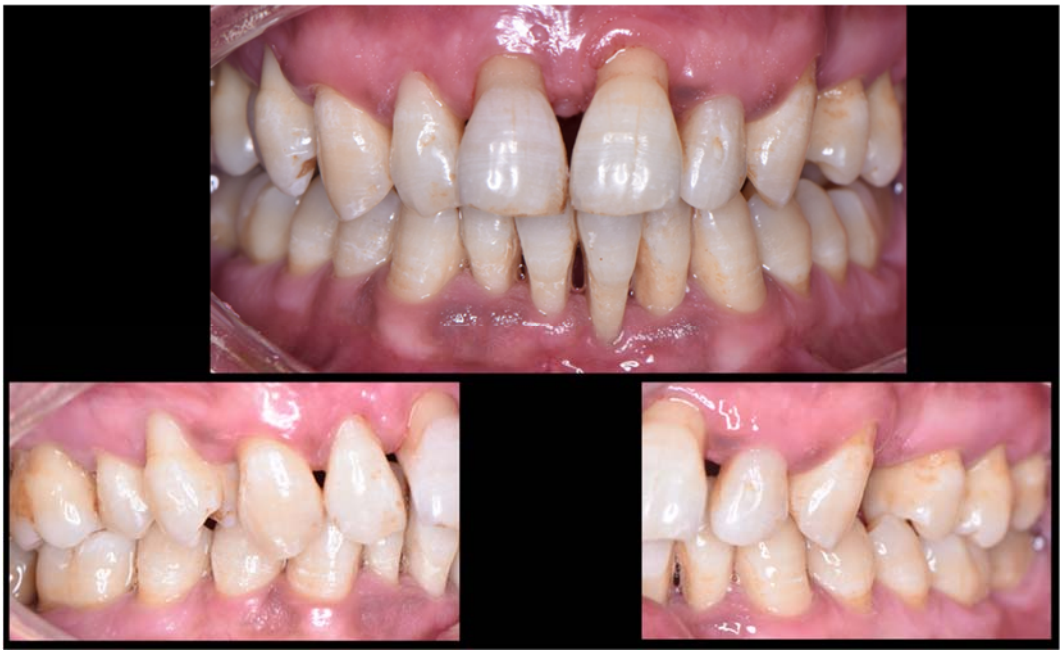

Figure 3: Intraoral view of a patient diagnosed with Stage IV periodontitis at the 6-month follow-up after non-surgical periodontal treatment.

Beyond the structured treatment stages outlined in contemporary guidelines, adjunctive therapeutic approaches, such as local and systemic drug applications, have been extensively investigated. Among these, local

or systemic antimicrobial agents and host modulation therapies are the most commonly employed interventions.[23–25] While antimicrobial therapy primarily targets periodontal pathogens within the periodontal pockets, specific approaches—such as sub-antimicrobial dose doxycycline—have been reported to modulate the host response effectively.[26] The clinical practice guideline for Stage I-III periodontitis restricts the use of systemic antimicrobials to young patients diagnosed with generalized Stage III periodontitis and reports low levels of evidence for local antimicrobial applications.[12]

Host modulation therapy has emerged as a strategy aimed at controlling the host response that drives periodontal destruction.[27] Although no definitive recommendations for host modulation therapy are provided in the Stage I-III treatment guidelines, recent systematic reviews have reported promising outcomes regarding the use of omega-3 fatty acids, low-dose aspirin, and probiotics.[28,29] However, further studies are required before these approaches can be routinely integrated into clinical practice.

- *Stage IV Periodontitis Treatment and Critical Timing*

In the treatment of Stage IV periodontitis, the therapeutic stages applied in Stage I-III cases serve as the foundation, with surgical and non-surgical periodontal interventions tailored to the specific needs of each case. While the overall treatment approach does not fundamentally differ from that of Stage I-III periodontitis, it is more complex due to the necessity of restoring masticatory function through the replacement of missing teeth and ensuring adequate stabilization for highly mobile teeth subjected to traumatic occlusal forces.[13]

The comprehensive management of these cases, following the elimination of the periodontal inflammatory process through non-surgical and/or surgical approaches, often requires orthodontic treatment to correct pathological tooth migration, as well as the rehabilitation of lost teeth using removable prostheses, tooth-supported fixed prostheses, and/or dental implants.[30] In summary, a significant aspect of Stage IV periodontitis treatment involves addressing masticatory dysfunction, which is more frequently observed in these patients compared to those with other stages of periodontitis.[31]

In patients with Stage IV periodontitis, the initial step includes establishing a comprehensive diagnosis and clinical evaluation, clearly informing the patient about their periodontal condition, and formulating an individualized treatment strategy. It is critical to emphasize to the patient that there is a significant risk of tooth loss if timely treatment is not initiated. Additional orthodontic, restorative, and prosthetic interventions tailored to the severity of Stage IV periodontitis and the patient's specific needs should be integrated into the treatment plan, either during active periodontal therapy or in subsequent phases.[13]

According to the Stage IV periodontitis treatment guidelines published in 2022, additional treatment options for these cases include:

- Temporary control of occlusal trauma
- Orthodontic treatment
- Rehabilitation of edentulous spaces
- Rehabilitation of unilateral or bilateral free-end edentulous areas
- Tooth-supported full-arch fixed prosthetic restorations
- Tooth-supported full-arch removable prosthetic restorations
- Implant-supported full-arch fixed prosthetic restorations
- Implant-supported full-arch removable prosthetic restorations[13]

Beyond functional impairments, Stage IV periodontitis also negatively impacts dental aesthetics.[32,33] The current clinical treatment guidelines for Stage IV periodontitis emphasize the significance of a multidisciplinary approach. Successful rehabilitation of both function and aesthetics is achievable through a comprehensive strategy incorporating periodontal therapy, orthodontics, and prosthetic dentistry.[34,35] For instance, when evaluating a tooth intended to serve as a fixed prosthetic abutment, it is necessary to assess not only the condition of the residual periodontium but also the mechanical strength of the tooth as a prosthetic abutment. However, this does not imply that teeth with reduced periodontal support cannot function as prosthetic abutments. Literature reports confirm the feasibility of using such teeth for prosthetic support, with their suitability being significantly influenced by the design of the prosthesis (fixed vs. removable).[31]

Additionally, orthodontic tooth movement following periodontal therapy may yield clinical benefits such as reduced probing pocket depth and gains in clinical attachment levels,[32] thereby enhancing the potential for periodontally affected teeth to serve as prosthetic abutments. Achieving long-term success necessitates meticulous treatment planning and a thorough evaluation of biomechanical factors.[34] In these complex cases, the management of occlusal discrepancies and tooth loss through fixed or removable prosthetic rehabilitation plays a crucial role.[35] In conclusion, prosthetic planning should be carried out with a careful evaluation of both periodontal and prosthetic factors, ensuring that the patient's expectations and preferences are taken into account.

CONCLUSION

Periodontal diseases represent a significant public health concern and impose a substantial economic

burden. In the treatment of periodontal diseases, patient-centered approaches are gaining increasing prominence. Current literature provides robust scientific evidence highlighting the interconnection between oral and systemic health and underscores the critical role of oral health in overall well-being. Although clinical expertise remains central in individualized patient assessments, treatment guidelines serve as essential resources that provide a structured framework for clinicians. In the management of Stage IV periodontitis, interdisciplinary collaboration and a multidisciplinary approach play a pivotal role in achieving clinical success.

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Is Non-Surgical Treatment Sufficient for Stage IV Periodontitis ? Report of Three Cases

Evre IV Periodontitis İçin Cerrahisiz Tedavi Yeter Mi ? Üç Olgu Sunumu

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ABSTRACT

Periodontal diseases are chronic inflammatory conditions that begin and progress as a result of the interactions between bacteria in the microbial dental plaque and the host's immune system, with the course being influenced by factors such as environmental risk factors, genetics, and systemic conditions. Chronic infection caused by plaque bacteria leads to tissue destruction via immune response, and the severity of destruction increases if left untreated. Patients diagnosed with Stage IV periodontitis characterized by periodontal pocket formation and clinical attachment loss, and classified as Grade C, which exhibits a high rate of progression not proportional to the amount of biofilm, leads aesthetic concerns, masticatory dysfunction, secondary occlusal trauma, and severe bone defects. Rehabilitation of these cases is challenging for clinicians and requires complex treatment procedures. The present report presents the clinical periodontal findings before and after non-surgical periodontal treatment of three patients diagnosed with Stage IV Grade C periodontitis.

Keywords: *Nonsurgical Periodontal Treatment, Periodontitis, Stage IV*

ÖZ

Periodontal hastalıklar, mikrobiyal dental plak bakterileri ile konağın immün sistemi arasındaki etkileşimler sonucu başlayan ve ilerleyen, çevresel risk faktörleri, genetik ve sistemik durumlar gibi etiyopatolojik faktörlerin varlığında seyri değişebilen kronik iltihabi hastalıklardır. Plak bakterileri tarafından oluşturulan kronik enfeksiyona verilen bu immün yanıt sonucunda doku yıkımı ortaya çıkar ve tedavi edilmezse zamanla ilerler. Periodontal cep oluşumu ve klinik ataşman kaybı ile karakterize olan periodontitisin en ileri aşaması olan Evre IV ve yıkım miktarının mevcut biyofilm ile orantılı olmadığı yüksek ilerleme hızına sahip Derece C tanısı almış periodontitis hastalarında estetik sorunlar, çiğneme disfonksiyonu, sekonder oklüzal travma ve şiddetli kret defektleri görülmektedir. Klinisyenleri teşhis ve tedavi sırasında oldukça zorlayan bu olguların rehabilitasyonunda karmaşık tedavi işlemlerine ihtiyaç duyulmaktadır. Bu raporda, kliniğimize tedavi için başvuran, ağız bakımı yetersiz ve çok fazla miktarda supragingival ve subgingival diş taşlarına sahip Evre IV, Derece C periodontitis teşhisi konulmuş üç hastanın tedavi öncesi ve cerrahisiz periodontal tedavi sonrası klinik periodontal bulguları sunulmaktadır.

Anahtar Kelimeler: *Cerrahisiz Periodontal Tedavi, Evre IV, Periodontitis*

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INTRODUCTION

Periodontitis is a chronic inflammatory disease characterized by relatively short episodes of exacerbation, accompanied by signs and symptoms such as gingival recession, drifting, hypermobility, and tooth loss. These are followed by some natural repair processes and prolonged intervening periods of remission.[1] In periodontal inflammation, signalling pathways of the innate and acquired immune responses, which occur due to the pathogenicity of microbial dental plaque bacteria, take place through mediators and cytokines secreted from the resident cells of periodontium or from those cells migrated in response to bacterial stimulation. Unless gingivitis is treated and the inflammatory reaction is controlled, matrix metalloproteinases (MMPs) are upregulated with the stimulation by interleukin-1 beta (IL-1β) and tumour necrotizing factor-alpha (TNF-α), extracellular matrix destruction increases, bone loss initiates, and the condition evolves into periodontitis.[2]

The current classification for periodontal diseases and conditions was developed by the American Academy of Periodontology and the European Federation of Periodontology during the 2017 World Workshop.[3] This classification of periodontitis is based on a staging and grading system derived from the unique characteristics of each case, considering the data obtained. Staging indicates the severity of the disease and the complexity of the required treatment (Stage I,II,III,IV) while grading reveals the rate of disease progression, prognosis, assessed additional biological features, and existing risk factors (Grade A,B,C).[4]

In the clinical practice guidelines published by the European Federation of Periodontology in 2020, treatment protocols for Stages I-III periodontitis are discussed. A significant distinction in the treatment of periodontitis Stages III and IV lies in the requirement for Stage IV patients to maintain or re-establish a functional dentition and the necessity for a rigorous supportive care program prior to, throughout, and following the rehabilitation phase of care.[5] Non-surgical periodontal treatment aims to disrupt the microbial dental biofilm by means of supragingival and subgingival instrumentation, remove deposits on the tooth surfaces, and provide motivation and instruction for optimal home care. Successful outcomes of non-surgical periodontal treatment are reduction of pocket depths and elimination of clinical signs of inflammation.[6] Clinical outcomes of non-surgical periodontal treatment are evaluated by conventional parameters such as probing depth (PD), clinical attachment level (CAL), and bleeding on probing (BOP). Sites with PD ≥ 5 mm and presence of BOP after active periodontal therapy are termed as residual pockets.[7]

The present report demonstrates that significant success can be achieved through comprehensive non-surgical periodontal treatment followed by a rigorous supportive periodontal therapy phase in patients diagnosed with Stage IV Grade C periodontitis.

CASES

A 25-year-old male patient presented with complaints of heavy calculus build-up, tooth mobility, and gingival bleeding. The patient was systemically healthy and a non-smoker (Figure 1a,b,c,d).

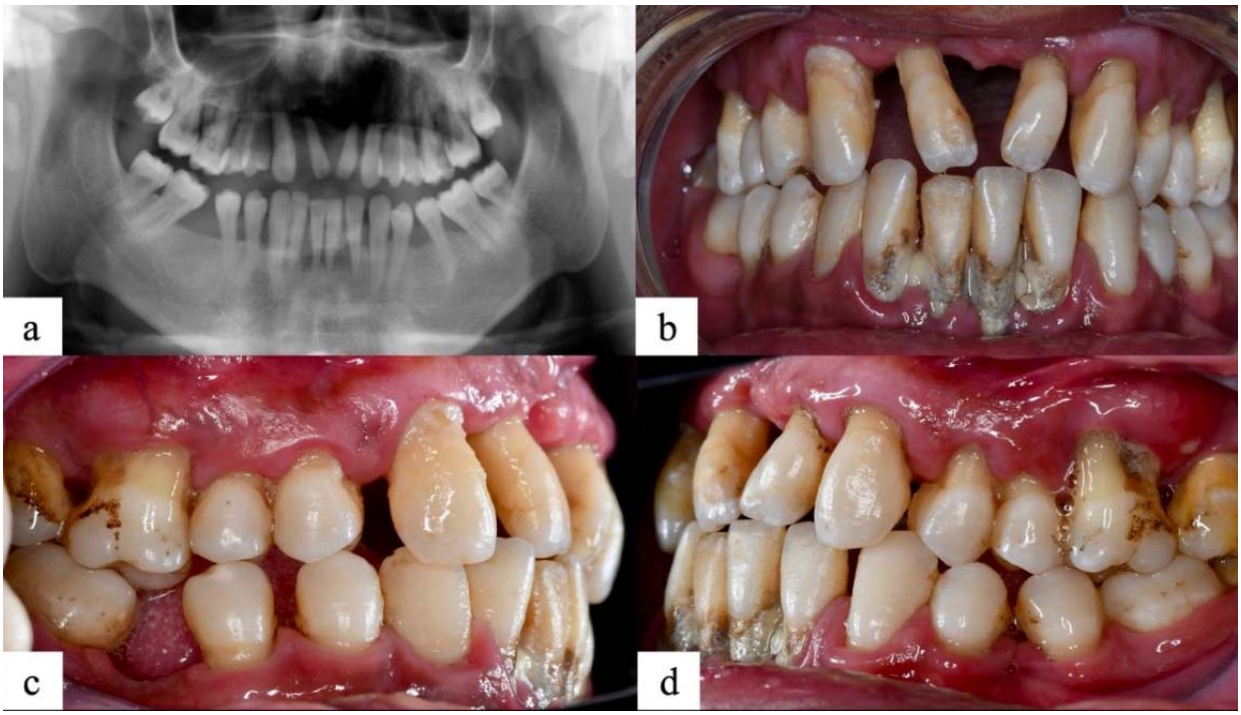

Figure 1. Case 1 baseline

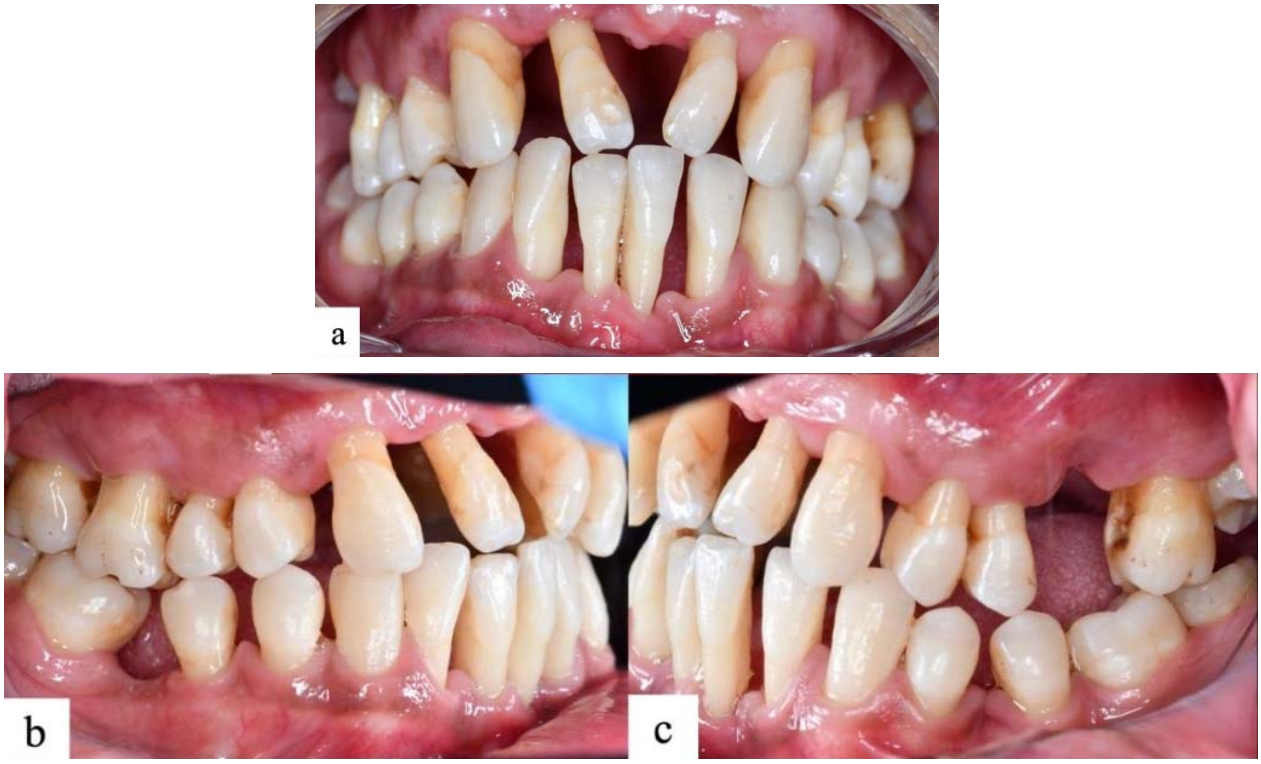

Figure 2. Case 1 third month control

Another systemically healthy male patient, who was 43 years old was seeking treatment due to tooth mobility, gingival bleeding, and difficulty in chewing. This patient was a smoker, smoking 10 cigarettes daily (Figure 3 a,b,c,d). The third patient was 52 years old and male presenting with heavy calculus build-up, tooth mobility, gingival bleeding, and pus discharge on the upper left central incisor tooth. The patient was systemically healthy and smoking 20 cigarettes/day (Figure 5 a,b,c,d).

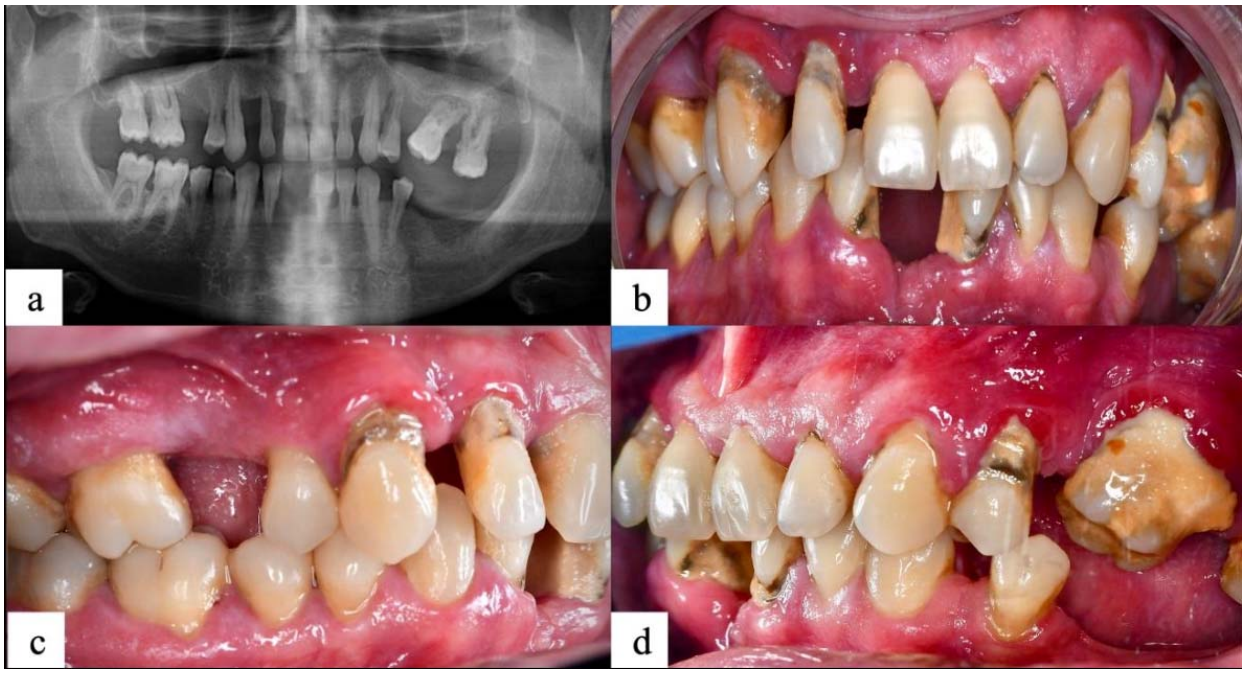

Figure 3. Case 2 baseline

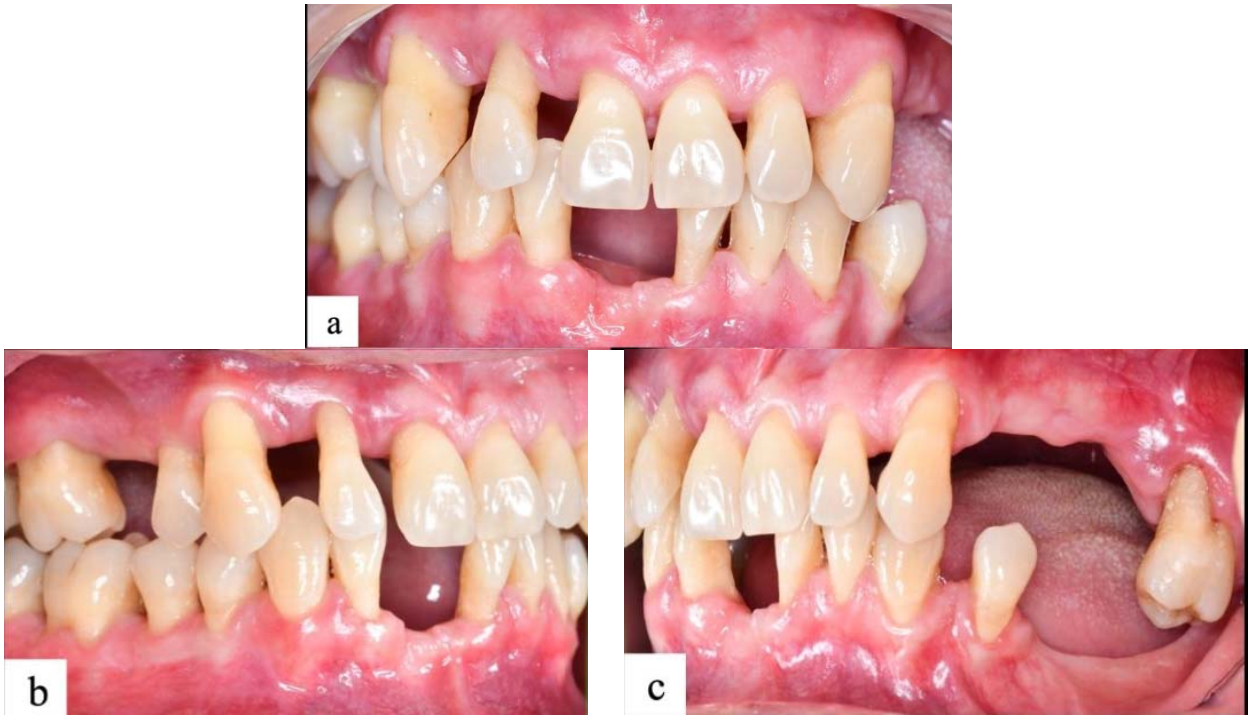

Figure 4. Case 2 third month control

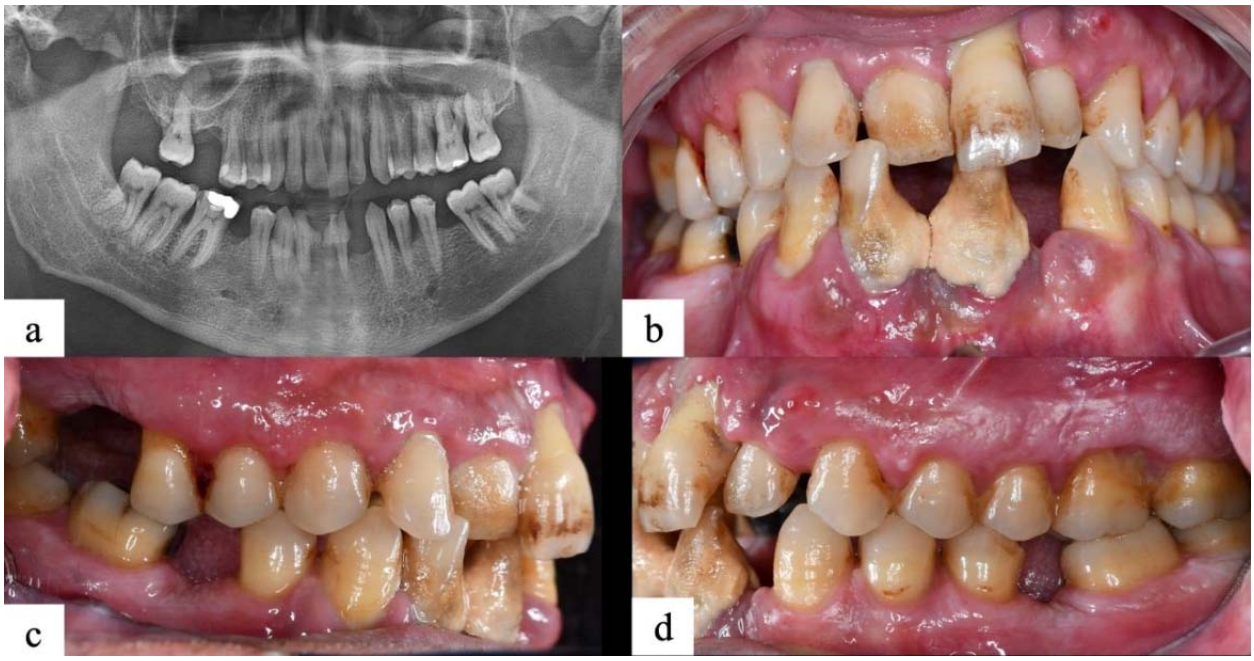

Figure 5. Case 3 baseline

All three cases were diagnosed to have Stage IV periodontitis due to attachment loss exceeding 5 mm, mobility exceeding grade 2 (Miller Mobility Classification, 1993), more than 5 teeth lost due to periodontal reasons (cases 2 and 3), and the ratio of bone loss/age in the area with the deepest bone destruction being greater than 1. Moreover, these two cases had Grade C periodontitis due to smoking habits of 10 or more cigarettes/day. Following non-surgical periodontal treatment, PD, CAL measurements at six sites/tooth, and whole-mouth bleeding scores were recorded using a Williams probe at baseline and at the 3-month follow-up visits. Dichotomous (+/-) plaque index (PI) and BOP scores were recorded at six sites/tooth at baseline and at the 3-month follow-up visits (Table 1,2).

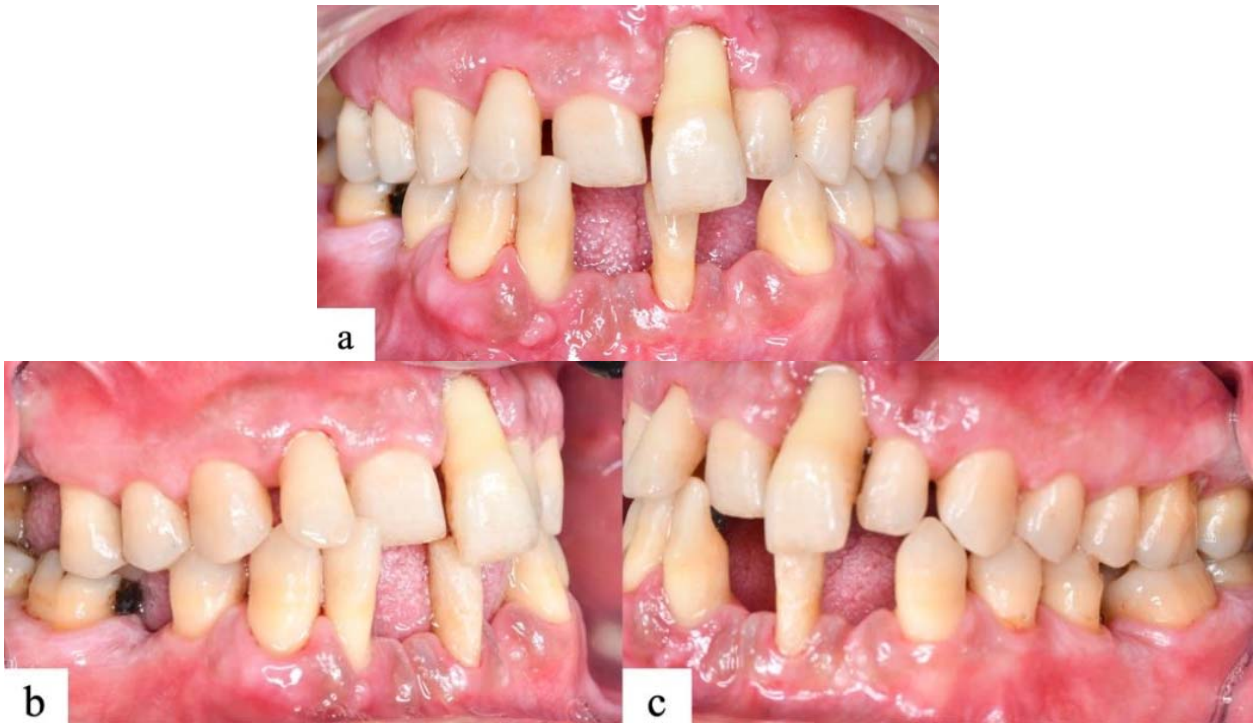

Figure 6. Case 3 third month control

Table 1. Probing depth (PD) measurements at baseline and three months after completion of non-surgical periodontal treatment.

	PD (mm) n (%)					
	Baseline			3-Month Control		
	0-3 mm	4-6 mm	7 mm	0-3 mm	4-6 mm	7 mm
Case 1	12 (8.5)	57 (41.5)	69 (50)	71(51.5)	60 (43.5)	7 (5)
Case 2	45 (37.5)	59 (49)	16 (13)	96 (80)	21(17.5)	3 (2.5)
Case 3	29 (23)	76 (60)	21(17)	69 (54.5)	50 (40)	7 (5.5)

Table 2. Full-mouth bleeding on probing (BOP), plaque index (PI), and clinical attachment level (CAL) measurements at baseline and three months after completion of non-surgical periodontal treatment.

	BOP (%)		PI (%)		CAL median (mm)	
	Baseline	3-Month Control	Baseline	3-Month Control	Baseline	3-Month Control
Case 1	95	8	85.7	7.2	7.12	5.49
Case 2	93	4	88.1	5.7	5.21	3.35
Case 3	86	6	86.3	6.8	5.49	3.62

Patients signed informed consent forms and non-surgical periodontal treatment initiated in the first session (baseline). Supragingival cleaning was performed using ultrasonic scalers, and motivation and instruction for optimal oral hygiene including efficient and regular tooth brushing, interdental cleaning techniques was provided in detail. In the subsequent sessions, root surface planing was performed using Gracey curettes (Hu-Friedy Mfg., Chicago, IL, USA). At each follow-up appointment, plaque control was assessed, and motivational reinforcement for oral hygiene was provided as required. No antimicrobial agents were used during the treatment

of the cases. The second patient received occlusal adjustment due to the presence of secondary occlusal trauma in the upper right canine tooth. After the removal of all supragingival and subgingival deposits, planing of root surfaces, and ensuring the patients' compliance with oral hygiene, they were placed in a supportive periodontal therapy program. At the three-month follow-up control, all three patients exhibited proper clinical periodontal outcomes (Table 2) with continuing high quality home care and there was no need for any further periodontal treatment.

DISCUSSION

The clinical signs and symptoms of periodontal diseases include changes in the colour, stiffness, and volume of the gingiva; gingival bleeding; formation of periodontal pockets; tooth hypermobility; loss of attachment and alveolar bone; and eventually tooth loss. Non-surgical periodontal treatment (NPT) involves oral hygiene instruction (OHI), scaling and root planing (SRP) using ultrasonic instruments and curettes, and the application of antimicrobial agents if necessary.[8] The response of soft tissues to NPT reflects the effectiveness of the treatment. It has been reported that various follow-up intervals ranging from two weeks to six months are used to evaluate the clinical outcomes after NPT. Healing of the junctional epithelium occurs within two weeks following NPT, yet the granulation tissue remains immature and is not replaced by collagen fibers.[9] It is recommended to frequently assess motivation and adherence to self-performed supragingival plaque removal and risk factor control in patients with Stage IV periodontitis to optimise the outcomes of treatment.[10] Oral hygiene of the patients were checked regularly 2, 4, and 8 weeks after completion of the SRP. The clinical periodontal measurements were recorded and intraoral photographs were obtained at baseline and also at the 3-month follow-up visits. The three cases presented in this report were meticulously monitored for effective plaque control at each session throughout the active periodontal therapy.

During nonsurgical periodontal treatment for patients with Stage 4 Grade C periodontitis, multidisciplinary treatment approaches should be implemented simultaneously. These may include addressing secondary occlusal trauma causing excessive mobility, planning prosthetic treatment to restore lost aesthetics and function, resolving endodontic issues, and correcting inappropriate restorations.[10] In the treatment planning of Stage 4 Grade C periodontitis cases, retaining natural teeth that suffer from attachment loss should be considered as the primary goal. Firstly, the option of tooth retention needs to be evaluated, and alternatives should be justified for the specific case ideally basing on factors such as individual tooth prognosis, technical feasibility, patient expectations, and preferences, and cost-benefit assessments.

The re-evaluation visit should be scheduled 6-8 weeks after completion of NSP and PD, CAL, BOP, PI measurements should be recorded for the entire dentition. Based on this data, a decision is made whether to initiate the supportive periodontal therapy phase. Supportive periodontal treatment plays a critical role in achieving long-term success particularly in the treatment of Stage III and IV periodontitis.

CONCLUSION

In this report, three patients with Stage IV, Grade C periodontitis received non-surgical periodontal treatment solely including mechanical interventions with close follow-up of home care and good patient-doctor co-operation. Thus, the present report emphasises the importance and power of meticulous conventional mechanical non-surgical periodontal therapy. All three cases of Stage IV, Grade C periodontitis presented proper clinical outcomes without using any adjunctive chemicals and there was no requirement for any surgical periodontal intervention.

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Childhood Intraosseous Myofibroma: A Case Report and Review of the Literature

Çocukluk Çağı İntraosseöz Myofibroma: Bir Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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ABSTRACT

Myofibroma, a rare benign tumor, frequently occurs in the head and neck regions, particularly the tongue, gingivae, maxillary, and mandible, often involving the bone. This tumor comprises highly proliferative spindle cells, including fibroblasts and myoblasts, and often presents with lytic radiographic areas and painless masses. Treatment varies from conservative management to radical resection, depending on patient age, tumor location, and severity. This report details a rare case of mandibular myofibroma with bony involvement in a 6-year-old girl, highlighting its diagnosis and treatment. The patient presented with a painless, smooth red mass in the right lower jaw, impairing chewing and causing bleeding. Clinical and radiological evaluations revealed a fixed mass between the right primary canine and permanent first molar, with radiolucent features on panoramic radiography. An excisional biopsy under general anesthesia was performed, leading to the removal of the lesion and the first molar. Histopathological examination identified spindle cells with myofibroblastic differentiation, and immunohistochemical staining showed a high proliferative rate of Ki67. Follow-up over two years showed no recurrence, and soft tissue healing was satisfactory. This case emphasizes the importance of conservative management and thorough follow-up in treating pediatric myofibroma with bony involvement, avoiding radical procedures where possible.

Keywords: *Myofibroma, Oral Pathology, Mandibular Neoplasms*

ÖZ

Nadir görülen benign bir tümör olan myofibroma sıklıkla baş ve boyun bölgelerinde, özellikle dil, gingiva, maksilla ve mandibulada görülür. Mandibular kemik tutulumu olan myofibroma çocuklarda nadir görülmektedir. Bu tümör, fibroblastlar ve myoblastlar dahil olmak üzere yüksek oranda proliferatif iğsi hücrelerden oluşur ve genellikle litik radyografik alanlar ve ağrısız kitlelerle kendini gösterir. Tedavi hastanın yaşı, tümörün yeri ve şiddetine bağlı olarak konservatif tedaviden radikal rezeksiyona kadar değişir. Bu raporda, 6 yaşında bir kız çocuğunda kemik tutulumu ile seyreden nadir bir mandibular myofibroma olgusunun tanı ve tedavisi anlatılmaktadır. Hastamızda sağ alt çenede ağrısız, düzgün yüzeyli, kırmızı renkli, çiğnemeyi bozan ve kanamaya neden olan bir kitle saptandı. Klinik ve radyolojik değerlendirmelerde sağ süt kanin ile daimi birinci büyük azı dişi arasında panoramik radyografide radyolusent özellikler gösteren bir kitle tespit edildi. Genel anestezi altında eksizyonel biyopsi yapılarak lezyon ve birinci molar diş çıkarıldı. Histopatolojik incelemede myofibroblastik farklılaşma gösteren iğsi hücreler tespit edildi ve immünohistokimyasal boyamada yüksek Ki67 proliferatif oranı görüldü. İki yıl boyunca yapılan takiplerde nüks görülmedi ve yumuşak doku iyileşmesi iyi sonuç verdi. Bu vaka, kemik tutulumu olan pediatrik myofibroma tedavisinde mümkün olduğunca radikal prosedürlerden kaçınarak konservatif yönetimin ve kapsamlı takibin önemini vurgulamaktadır.

Anahtar Kelimeler: *Myofibroma, Oral Patoloji, Mandibular Neoplazmlar*

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INTRODUCTION

Myofibroma is a rare condition that is classified according to the body region where it is diagnosed[1-3]. Benign tumour myofibroma is often diagnosed in the head and neck region, followed by the tongue, gingivae, maxillary and mandible[1-4]. This benign tumour, which is defined as multicentric myofibromatosis, has highly proliferative spindle cells, including fibroblasts and myoblasts[5-7].

This tumour has similar appearances among many clinical situations, such as lytic areas on radiography and gingival changes, including a painless mass, when cortical plate perforation occurs[8]. Thus, determining a differential diagnosis is rather difficult[5].

The histological characteristics of Myofibroma are defined by a polylobulated spindle cell proliferation arranged in a biphasic pattern. Immunohistochemical staining reveals that the tumour cells express alpha-smooth muscle actin (α-SMA), while they are typically negative for myogenin, desmin, CD34, S-100 protein, and beta-catenin[9]. However, the immunohistochemical analysis of Ki-67-positive cells in a range of tumour types has been demonstrated to be an effective method for evaluating tumour growth potential[10].

Treatment options are quite extensive, such as conservative management, curettage or radically resective surgery[1-6,11]. The age of patients, localization and involvement of the tumour, and life-threatening conditions are the determining factors for its management[12].

This report describes the diagnosis and treatment of a rare case of myofibroma in a 6-year-old girl on the posterior mandibular region. Attention has been focused on similar histopathological features of this tumour with many oral pathologies and a high proliferative rate (< 15%) of Ki-67 marker, as in this present case, has rarely been reported in literature.

CASE PRESENTATION

A 6-year-old female was referred to Oral and Maxillofacial Surgery Department of the University with a 1-month history of a painless smooth mass with a red colour in the right lower jaw area. The patient's parents had complained of the patient's inability to chew and bleeding of the expanding swelling. The patient had no history of trauma in the recent past, and her routine laboratory tests were normal.

Clinical and radiological evaluation

Clinical evaluation revealed a fixed palpable mass with a height of 2–3 mm from the occlusal level between the right primary canine and permanent first molar and without any associated cervical lymphadenopathy. The clinical appearance of this lesion was a soft tissue lesion resembling a peripheral giant cell granuloma. Panoramic radiography showed a radiolucent lesion with impacted premolars (Figure 1). In addition, cone beam computed tomography was performed to peruse the size and border of this lesion (Figure 2).

Based on the clinical and radiological findings, incisional biopsy under local anaesthesia was planned but due to the patient being uncooperative, the biopsy that was planned for diagnostic purposes could not be performed. Excisional biopsy under general anaesthesia was performed, after the family signed an informed consent agreement.

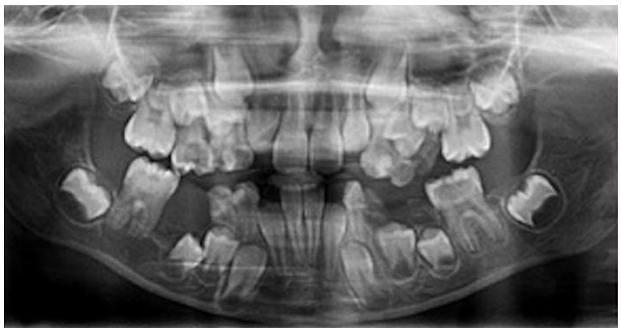

Figure 1: The lenght and size of the lesion on panoramic radiography

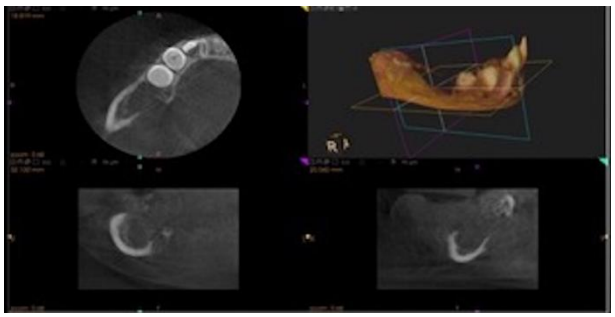

Figure 2: CBCT analysis of the lesion. Lingual plate perforation and extansion of the tumor were observed.

Dental treatment

Primarily, the mucoperiosteal flap was elevated from the mandibular right canine to the first molar. A burr or cutting device was not used, and the lesion was completely excised from the bone margin without difficulty. The mandibular first molar with root resorption and mobilization was extracted to avoid second dental approach. The crown of the impacted tooth related to the lesion were preserved when the surgical area was curetted. Primary closure of the surgical area was performed with 4/0 Monocyrl. The surgically removed curettage material was sent for histopathologic examination and the patient was scheduled for frequent routine follow-ups.

Histological evaluation

The tissue samples were stained with haematoxylin and eosin. Spindle cells with well-rounded, small nuclei and evidence of myofibroblastic differentiation were observed. Those cells were examined in nodular fasciitis and follicular dendritic tumours. However, they present positive CD21 staining, which is an exception for myofibroma. Morphological findings were compatible with myofibroblastic tumours, while a typical biphasic image was not seen. Additionally, there was a potential for recurrence because of the high proliferative activity of spindle cells (Figure 3). An immunohistochemical analysis including staining for alpha-smooth muscle actin (α-SMA), caldesmon, pHH3, Ki67 and desmin was implemented. The tumour cell staining was negative for desmin and caldesmon, but it was positive for α-SMA, which exhibited a pale colour staining. Furthermore, pHH3 was observed in ten large magnification areas in three cells. A high proliferative rate (< 15%) of Ki67 was identified in the tumour cells (Table 1).

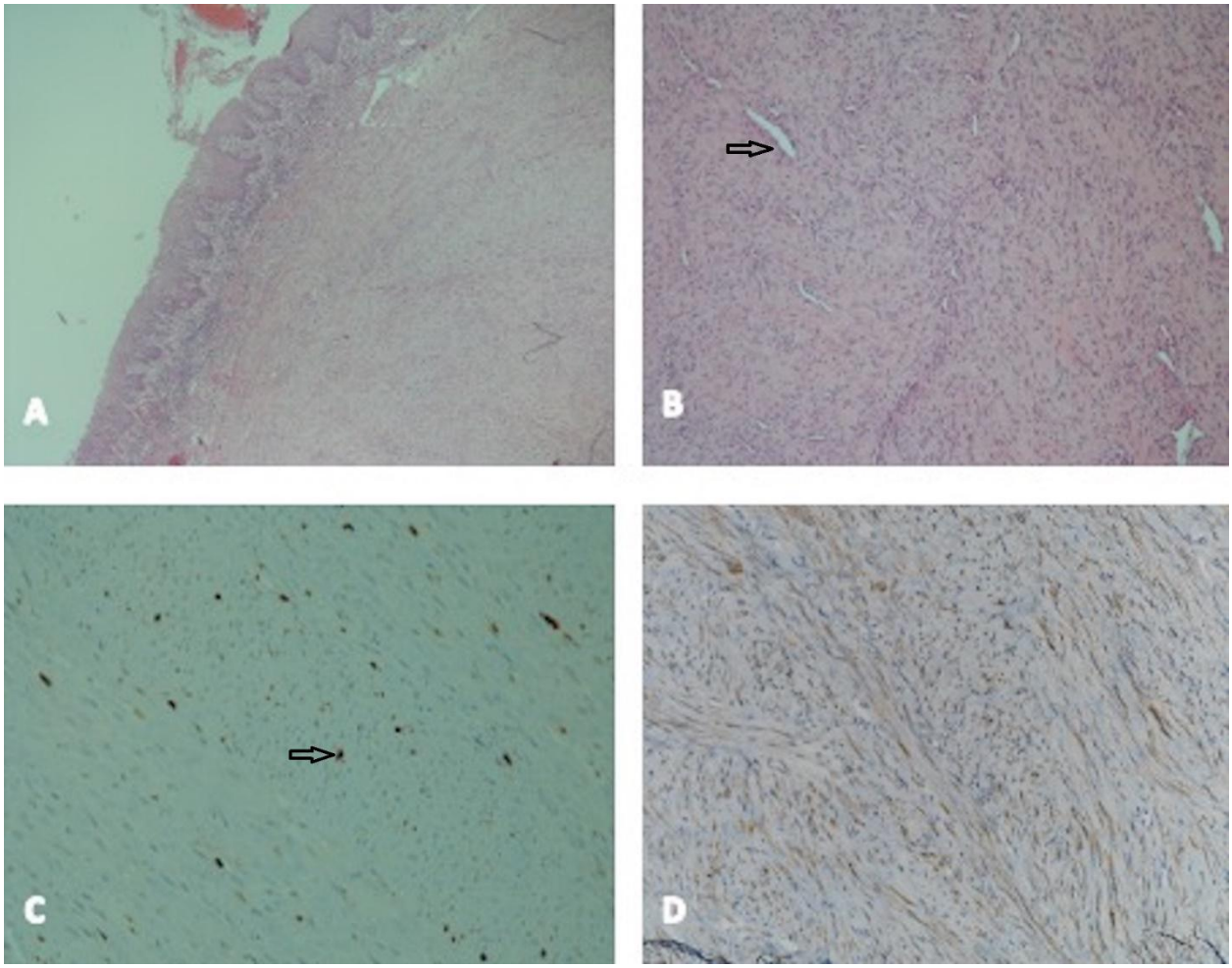

Figure 3 a) Submucosal nodulary lesion (Haematoxylin- eosin, x4). **b)** High power view of the lesion. Note the loosely arranged plump spindled myofibroblastic cells and slit-like vasculary spaces (Haematoxylin-eosin, x10). **c)** Ki-67 proliferation index increased up to %15 in some areas. **d)** Myofibroblastic cells faintly staining with smooth muscle actin (SMA,x10).

Table 1: Immunohistochemical examination after excision

Biomarkers	(+) / (-)
α-SMA	+
Caldesmon	-
PHH3	+
Ki67	+
Desmin	-

RESULTS

Radiologic and clinical examination was performed for 2 years, with a period of every 6 months in the first year and then once a year in the second year. During the follow-up sessions, the lesion showed no signs of recurrence (Figure 4). In addition, soft tissue healing and the permanent teeth, which erupted after the tumour pressure was removed, were indicated clinically (Figure 5).

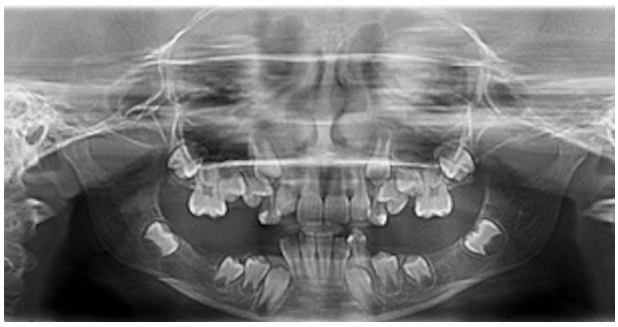

Figure 4: A first year, the bone healing and lack of pressure on the mandibular premolars were observed.

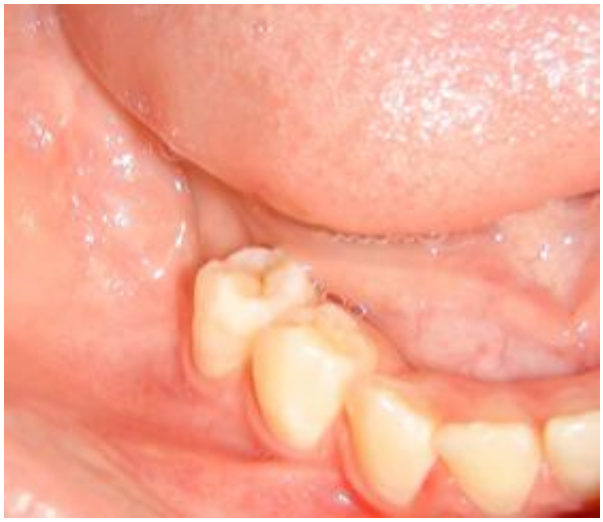

Figure 5: After 2 years, the soft tissue healing and eruption of the mandibular premolars were observed.

DISCUSSION

Myofibroma is a solitary benign tumour that is aggressive and can develop into a rapidly growing mass or an asymptomatic, painless intraosseous mass[2,13]. Myofibroma typically occurs during the first decade of life and is more common in males than in females[5]. Some authors suggest that genetic inheritance with an autosomal dominant or recessive trait could contribute to the formation of this tumour. But the aetiology of this tumour is still unknown[13].

In cases where the jaws are affected, myofibroma manifests as a painless, destructive osteolytic lesion with well-defined borders and slow growth. The clinical signs and symptoms observed are largely contingent upon the specific anatomical site affected, exhibiting considerable variability[14].

Myofibroma represents a rare occurrence within the oral cavity and exhibits morphological similarity with other malignant or benign mesenchymal lesions. This situation can present a challenge in making an accurate diagnosis[15].

Odontogenic lesions such as dentigerous cyst, eosinophilic granuloma, ameloblastoma or nodular fasciitis could have a differential diagnosis of myofibroma clinically[1]. To prevent subsequent deformity and eventual destruction of anatomic structures in children and adolescents, it is essential to ensure an accurate diagnosis and to perform the appropriate surgical intervention. A meticulous histological and immunohistochemical evaluation can prevent erroneous diagnoses and unnecessary radical surgery[16].

Histopathologically, proliferative spindle cells and an aggressive pattern of lesion growth are affected in the differential diagnosis, including inflammatory myofibroblastic tumour, myofibrosarcoma, leiomyoma, neurofibroma, schwannoma, fibrosarcoma, leiomyosarcoma, rabdomyosarcoma, haemangiopericytoma or desmoplastic fibroma[1,3]. In order to differentiate myofibroma from neural and smooth muscle tumours, a panel of antibodies for the detection of desmin, h-caldesmon, s-100, and α-SMA antigens has been proposed[14]. α-SMA is a protein that is commonly used to determine myofibroblastic formation[1-3,5,11,18,19]. The ACTA2 gene codes this protein on 10q22-q24. It is a main factor of contraction. Desmin is a muscle protein that regulates sarcomere structure. It is considered to transmit information of the α-SMA protein. However, caldesmon is a protein that inhibits ATPase activity in smooth muscles[20,21]. In a differential diagnosis, neural tumours, including neurofibroma, neurofibromatosis and schwannoma, are negative for desmin and actin staining. In addition, leiomyoma is a benign smooth muscle tumour that was referred to as a fibroid, and it is positive for desmin, caldesmon and α-SMA staining. Therefore, this tumour could be difficult to distinguish from myofibroma, and it is important that it be assessed clinically as radiologic or oral findings[3,21].

pHH3 is a marker for mitotic activity in early prophase. Staining shows that it is non-specific for neutrophils, macrophages and mast cells. Additionally, Ki67 is a marker that identifies proliferative cells within a tumour. This protein is used to determine an aggressive potential and whether metastasis could result in this tumour. These biomarkers should be considered rather than those of inflammatory myofibroblastic tumour (IMT)[20]. In addition, staining for immunohistochemical

analyses of IMT and alanine aminotransferase (ALT) plays an important role. This enzyme affects the nervous system in 50% of positive IMT cases[20]. However, there is no positive staining for the anaplastic lymphoma kinase (ALK) biomarker in myofibroma.

In the present case, the tumour cells showed negative staining for desmin and caldesmon; however, α-SMA was stained positively with a pale colour. Furthermore, pHH3 was observed in ten large magnification areas in three cells. Ki67 was identified a high proliferative rate (< %15) in the tumour cells.

The number of well-documented cases with long-term follow-up is limited, as is the experience with myofibroma. This situation makes it challenging to determine the best treatment. As is acknowledged, the defining characteristics of myofibroma are well-defined borders, a benign nature, and low recurrence rates. Consequently, conservative surgery with enucleation and/or curettage represents the optimal treatment option[17]. Actually,the patient's age is an effective factor for total or partial radical resection as an en block excision or conservative treatment option[12]. Enucleation or curettage was mostly recognised as the best treatment option[13]. However, Hajeri et al.[2] demonstrated myofibroblastoma in a 3-year-old boy, and after the tumour excision was performed, they preferred to perform reconstruction surgery with a vascularized osteocutaneous fibula flap. In the present case, a minimally invasive approach was preferred in order to prevent the development of long-term complications in a paediatric patient. We performed excisional biopsy, as described by Souza et al.[18], and curettage was carefully executed to protect second permanent molar that were related to the lesion. Clinical and radiographical examination was performed during 2 years of follow-up, leading to no evidence of recurrence.

CONCLUSION

Myofibroma with mandibular bone involvement is rare in children. Conservative management affected the life quality of the patient in this case. We consider that treatment options can be organized to avoid radical resection, although tooth extraction, especially tooth mobility, and bone destruction are decisive factors. Immunohistochemical staining is required to accurate diagnose of myofibroma and identify the nature of tumour cells. Also, follow-up of patients can be preventive to aggressive treatment options even if there is recurrence of myofibroma.

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