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Systematic Review

Changes in the pH and the Flow Rate of Saliva During Orthodontic Treatment with Fixed Orthodontic Appliances: A Systematic Review

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Main Points
- The aim of the study was to evaluate changes in salivary flow and pH in different periods of orthodontic treatment with fixed appliances.
- Most studies have stated that stimulated salivary flow rate and pH tend to increase.
- According to the data, unstimulated salivary flow rate changes, while unstimulated saliva pH decreases.

ABSTRACT

This systematic review aimed to assess salivary flow and pH changes at various stages of orthodontic treatment with fixed appliances. A comprehensive searches in electronic databases, including Medline, ResearchGate, Web of Science, SAGE Journals, Cochrane Oral Health Group's Trials Register, and ScienceDirect, without any publication date restrictions until January 2022 was conducted. The Pre-ferred Reporting Items for Reporting Systematic Reviews and Meta Analyses (PRISMA 2020 version) protocol was adopted and the risk of bias assessments were performed using the Cochrane ROBINS-I tool for non-randomized studies. Out of 4902 articles, 25 were fully evaluated, and seven studies that met the inclusion criteria were included in the review. The results showed that orthodontic treatment with fixed orthodontic appliances increased the stimulated salivary flow rate during various stages of treatment. However, the unstimulated salivary flow rate showed different changes. Furthermore, stimulated salivary pH increased, whereas unstimulated salivary pH significantly decreased, depending on the specific period of orthodontic treatment. Overall, fixed orthodontic appliances have an impact on salivary flow rate and pH during different stages of treatment. Nevertheless, the current literature is insufficient to draw definitive conclusions. More well-designedrandomized studies with larger sample sizes are necessary to confirm these findings.

Keywords: Saliva, fixed orthodontic treatment, fixed orthodontic appliances, dental brackets

INTRODUCTION

Orthodontic treatment effectively improves people's quality of life by restoring regular and stable occlusion, optimal chewing function, and dentofacial aesthetics.[1] However, the use of fixed orthodontic devices can have adverse effects on soft tissues, teeth, and saliva.[2] Nowadays, ensuring good oral hygiene with fixed orthodontic appliances remains a significant challenge, as the areas around brackets are difficult to clean and prolonged plaque retention, which may cause white enamel spot lesions and gingivitis.[3,4] Saliva typically consist of water (99%), and organic and non-organic elements (1%).[5] During orthodontic treatment, plaque stagnation can lead to changes in the qualitative and quantitative indicators of saliva. The concentration of cariogenic bacteria, such as *Streptococcus mutans* and *Lactobacillus*, may increase due to the increased plaque retention, which promotes the development of active tooth decay.[6,7] Changes in the quality of saliva are often observed in its pH, buffer capacity and the viscosity of saliva.[8] Saliva pH, as a qualitative indicator of saliva, is particularly important for oral and dental health. The optimal saliva pH in healthy individuals typically ranges from 6.7 to 7.3.[9] However, in some

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cases, orthodontic treatment can lead to a decrease in salivary pH with changes in oral microbes.[10] A decreased saliva pH can increase the risk of demineralization of dental hard tissues and inflammation of the gums.[11]

During orthodontic treatment with fixed orthodontic devices, the quantitative indicator of saliva, i.e., which is the amount of saliva excreted, also undergoes changes. The statistical mean of average unstimulated saliva output is typically between 0.25-0.35 mL/min, while the non-pathological mean volume of stimulated saliva output ranges from 1-3 mL/min.[12] A decrease in saliva secretion, can lead to dry mouth, known as xerostomia. Decreased salivation may be associated with tooth decay, demineralization of dental hard tissues, and gingival inflammation. Fiyaz et al.[13] found that the saliva flow of selected patients with tooth decay was almost twice that of the control group, without caries.

However, some patients may experience an increase in saliva output during orthodontic treatment, and hypersalivation is diagnosed when saliva levels rise above the reference range.[14] Meanwhile, increased but non-pathological salivation can have benefits, such as improving mouth cleansing and enhancing the antimicrobial properties of saliva, leading to better anti-caries resistance. The study suggests that hypersalivation during orthodontic treatment may be associated with increased patient sensitivity due to the presence of fixed orthodontic devices.[11] Therefore, understanding how the qualitative and quantitative parameters of excreted saliva may change during the duration of orthodontic treatment is crucial. Numerous studies with diverse patient samples have explored the relationship between the use of fixed orthodontic appliances and alterations in salivary parameters, yielding different conclusions.[2,11,15-19] The primary objective of this systematic review was to assess the methodological quality, analyse and summarize the currently available information on changes in salivary flow and pH in different periods of orthodontic treatment with fixed appliances. The null hypothesis tested was that there would be no significant difference between baseline and during orthodontic treatment regarding these salivary parameters.

METHODS

Protocol and Registration

A systematic review was conducted in line with the PRISMA 2020 version statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), as illustrated in Figure 1. The protocol was registered with PROSPERO (registration number CRD42022300434).

Eligibility Criteria

According to the Participants Intervention Comparison Outcome Study design schema (PICOS), the study included prospective trials (S) on patients undergoing orthodontic treatment (P) with fixed orthodontic appliances (I). In these studies, changes in quantitative and qualitative indices of saliva were observed at different times of treatment (C). The outcome of this systematic review included changes in salivary flow and pH at different time points during long-term orthodontic treatment (O).

The criteria for the study inclusion were full-text studies, clinical studies with humans, patients treated with fixed orthodontic appliances, and stimulated and unstimulated saliva samples collected before orthodontic treatment, and at different time points during orthodontic treatment. Additionally, the studies needed to present the exact mean values of salivary flow rate and pH were presented in the studies. Exclusion criteria were all case reports, case series, systematic reviews, and animal and *in vitro* studies. Furthermore, studies comparing saliva parameters between different orthodontic appliances or studies involving patients treated with orthodontic removable appliances were also excluded. The number of sample sizes was not a criterion for exclusion.

Search Strategy

The systematic search was conducted in six electronic databases, which included Medline, ResearchGate, Web of Science, SAGE Journals, Cochrane Oral Health Group's Trials Register, and ScienceDirect. The databases were searched using the specified keywords both separately and in different combinations. The search strategy used for PubMed was as follows: (saliva OR salivary) AND (fixed orthodontic appliances OR fixed orthodontic treatment OR orthodontic braces OR orthodontic brackets OR dental braces OR dental brackets OR brackets OR braces). This search strategy was appropriately adapted for ResearchGate, SAGE Journals, Web of Science, Cochrane Oral Health, and ScienceDirect electronic databases. The selection of studies was carried out independently by two investigators. Any discrepancies between the investigators were resolved through discussion. It's important to note that the librarian was not consulted during this process.

Study Selection

Before beginning the search in the selected databases, the search strategy was discussed and developed by two analyzers, and thereafter the study selection was carried out by two researchers. Search filters were applied to refine the results and duplicates entries were removed. Initially, the titles and abstracts of the identified studies were analyzed. Following this initial screening, complete articles were selected for a more comprehensive review and analysis, based on the predefined eligibility criteria. If the articles met the inclusion criteria for the review, the entire content of those articles was read to make the final decision regarding their suitability for inclusion in the systematic review.

Data Extraction

The characteristics and data of the included studies that met the eligibility criteria were extracted by two reviewers. Two independent reviewers performed data extraction using spreadsheets (Microsoft Excel Version 16.49, Redmond, WA, USA). The following variables were recorded for each reviewed article: author, country, year of publication, type of study,

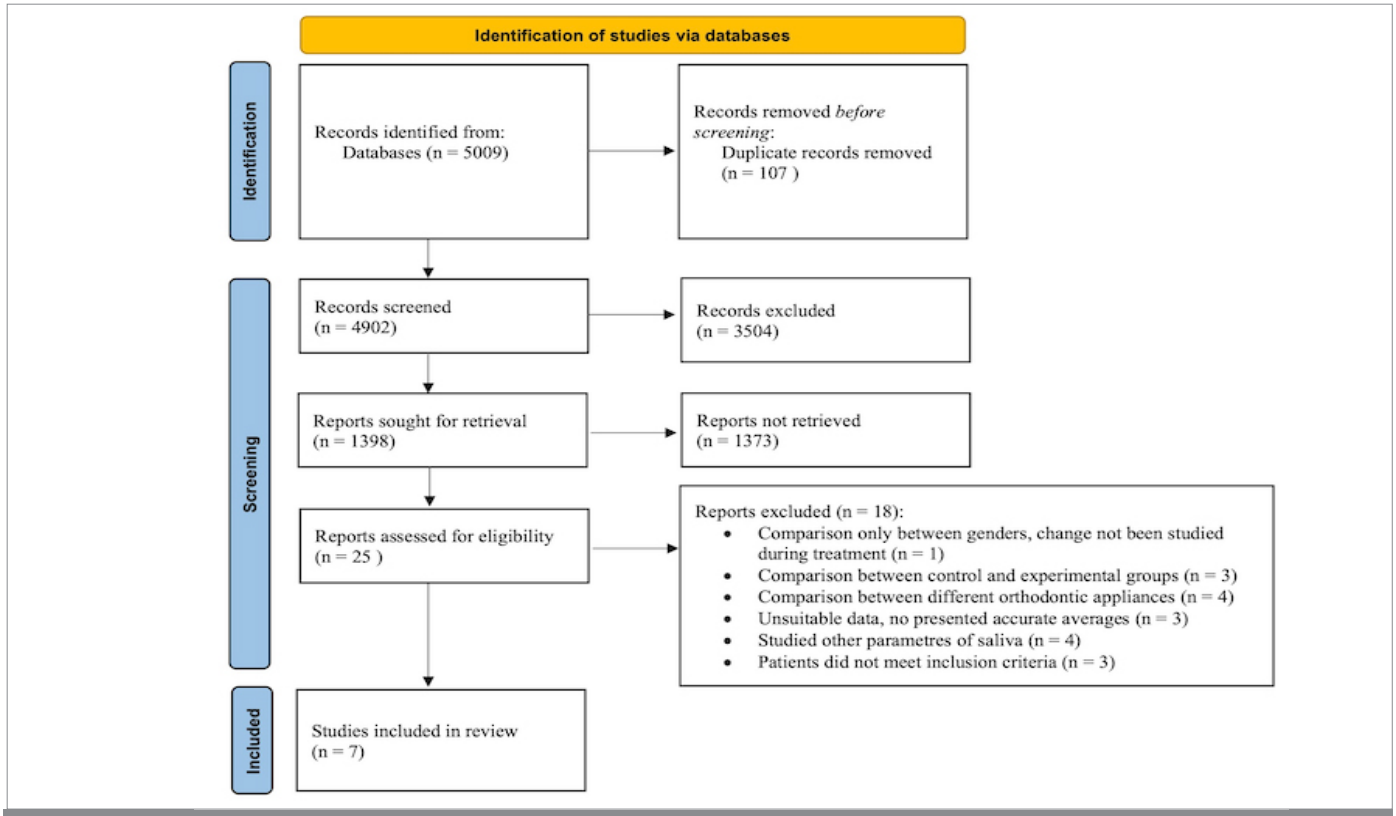

Figure 1. Identification of studies via databases

characteristics of study participants such as sample size, sex, age, intervention type (fixed orthodontic appliances), type of saliva samples, evaluation methods (methods of saliva measurements and timing on evaluation), and treatment outcomes (changes in salivary flow rate and pH in different time points). To assess the agreement between the two reviewers' data extraction, Kappa statistics were utilized after the initial selection of articles.

RESULTS

Study Characteristics

The characteristics of the included studies are summarized in Table 1.

Participants in the included studies consisted of a total of 242 patients treated with fixed orthodontic appliances. The sample sizes of the studies varied, ranging from 21 to 60 patients. Additionally, the age of the participants in the studies ranged from 10 to 34 years, with male patients being 84 and female 98. in the study conducted by Alshahrani et al.[11], the gender of 60 patients was not separated or specified in the data.

Intervention: Most studies did not indicate which bracket systems were used; only two studies identified Edgewise braces[2,19] and one study utilized self-ligating braces.[17] In all studies, the most popular method of saliva collection was the spitting method into a sterile tube. The samples were collected at different times of the day between 8 am and 3.30 pm.[2,15-19] However, one study did not specify the exact time of day for sample collection.[11] Out of the included studies, four studies, collected, unstimulated saliva samples,[2,11,15,16] while the other three studies used stimulated saliva obtained through paraffin wax or orthodontic elastic bands.[17-19]

Quality Assessment

To assess the quality of studies, the ROBINS-I tool for non-randomized studies was used, and the data are summarized in Table 2.[20] The risk of bias within the non-randomized studies from the two trials was evaluated to have an overall moderate bias due to certain discrepancies in confounding and measurement of outcome domains.[2,17] Three additional non-randomized studies[11,15,19] were found to have an overall serious risk of bias. The other two studies[16,18] were determined to present a critical risk of bias. The most problematic domains associated with bias were the lack of blinding, inadequate assessment of confounding factors, and imprecise outcome measurements.

Study Selection

The protocol for this systematic review followed the guidelines presented in the PRISMA 2020 version statement (Figure 1). For reference management, Mendeley Desktop 1.19.8 software (Mendeley Ltd, London, UK) was used. The electronic database search initially identified 5009 records. After duplicate removal, 4902 records remained, which were then screened for relevance. Screening of titles and abstracts resulted in the exclusion of 3504 studies. Additionally, 1373 full-text reports were not accessible among the 25 full-text articles we assessed for eligibility, 18 studies were subsequently excluded.[3,6,8,10,12,21-43] Finally, 7 studies

Table 1. Summary of the characteristics of included studies

	Authors	Study design	The study sample: Patients (M/F); Age Range/Mean (years)	Types of saliva samples	Intervention: Types of orthodontic appliances	Methods of measurements and timing of evaluation	Eligible outcome
1	Alshahrani et al.,[11] Saudi Arabia	PCT	60 (-); 18-30 /21.7	Unstimulated	Fixed orthodontic appliances (bracket system not specified)	Spitting method (into a 2 mL gradu-ated tube) pH digital meter. The saliva samples were collected between 8 and 11 am. Follow-up: before and 2 months.	Variations in saliva flow rate and pH at different stages of orthodontic treatment
2	Arab et al.,[15] Iran	PCT	30 (6/24); 12-18/-	Unstimulated	Fixed orthodontic appliances: *Straight wire 0.022-inch bracket slot system (AO, Sheboygan, WI, USA)	Spitting method (into a sterile test tube for 10 min.). pH meter strips. The saliva samples were collected between 10 and 12 am. Follow-up: before treatment: 6, weeks.	Variations in saliva flow rate and pH at different stages of orthodontic treatment
3	Altaee et al.[16] Iraq	PCT	34 (15/19); 16-32/23.60±5.46	Unstimulated	Fixed orthodontic appliances (bracket system not specified)	Spitting method (into a clean graduated glass tube for 10 min.) pH test paper. The saliva samples were collected between 1-3.30 pm. Follow-up: before and 1 month	Variations in saliva flow rate and pH at different stages of orthodontic treatment
4	Kouvelis et al.,[17] Greece	PCT	30 (17/13); 12-18/ 13.97±2.07	Stimulated (by a paraffin pellet)	Fixed orthodontic appli-ances (self-ligating metallic labial bracket system + InnovationR and Sentalloy 0.014-inch wire)	Spitting method (made by using sterile urine boxes). pH indicator strips. The saliva samples were collected between 9 and 12 am. Follow-up: before, 4 and 12 weeks.	Variations in saliva flow rate and pH at different stages of orthodontic treatment
5	Sanchez and Honores[18] Peru	PCT	44 (23/21); 10-34/17.27	Stimulated (by Orthodontic elastic bands)	Fixed orthodontic appliances (bracket system not specified).	Spitting method (in glass test 10 mL tubes for 5 min.) The saliva samples were collected between 9am and 12 pm. Follow-up: before and 1 month.	Variations in saliva flow rate at different stages of orthodontic treatment
6	Peros et al.,[19] Croatia	PCT	23 (9/14); 12-17/14.04±1.52	Stimulated (by paraffin wax)	Fixed orthodontic appliances: *Labial bracket system with metal wire ligatures (Forestadent, Pforzheim, Germany). *Archwires: started with 0.012-inch NiTi, followed with 0.016-inch NiTi after 6 weeks and 0.016-inch x 0.022-inch NiTi for the next 6 weeks	Spitting method (into a sterile plastic graduated cup for 10 min.) pH digital meter. Follow-up: before, 6, 12, and 18 weeks	Variations in saliva flow rate and pH at different stages of orthodontic treatment

The PCT, prospective controlled clinical trial; M, males; F, females.

were included in a systematic review.[2,11,15-19] An overview of the search results and the screening process is summarized in the study flow chart (Figure 1).

Results of Individual Studies

The results of the seven included studies are summarized and presented in Table 3. Figure 2 demonstrates changes in the stimulated and unstimulated salivary flow rate during orthodontic treatment periods, while Figure 3 demonstrates changes in the stimulated and unstimulated salivary pH.

Unstimulated Salivary Flow Rate

Three of the included studies analyzed the unstimulated salivary flow rate.[11,15,16] Due to the observed different in age groups and the fact that saliva production decreases with age, the results of unstimulated salivary flow rate were separated into two groups.

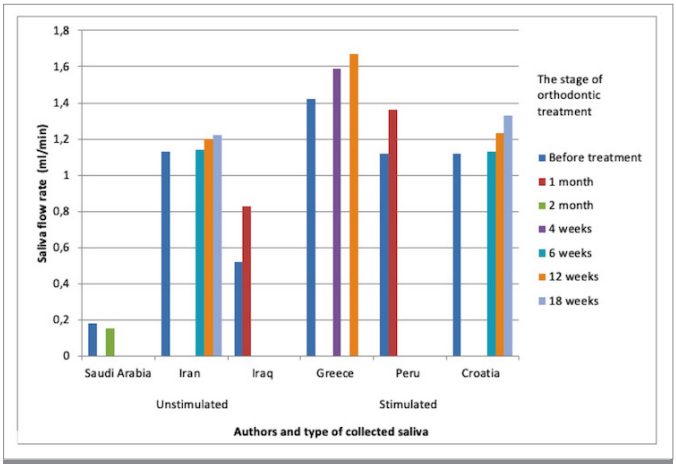

Figure 2. Changes in the salivary flow rate

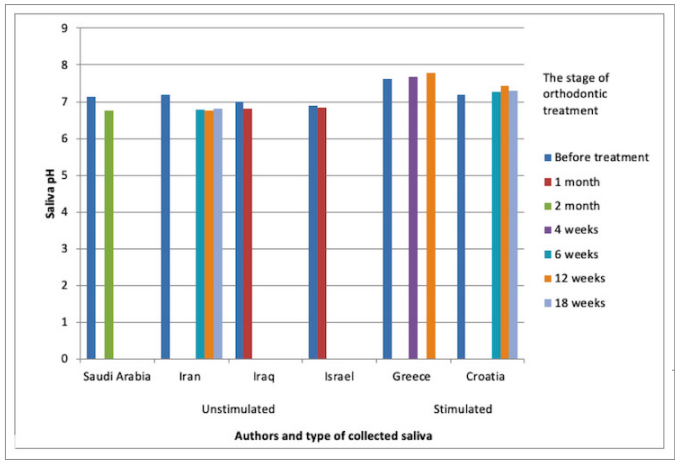

Figure 3. Changes in the salivary pH

Table 2. Risk of bias of the included studies

Studies	Confounding	Selection bias	Classification of interventions	Intended interventions	Missing data	Measurement of outcomes	Reported result	Overall
Peros et al.[19]	Low	Low	Low	Low	Low	Serious (no method error, not blinded assessor	Low	Serious
Altaee et al.[16]	Critical (difference in age, sex between groups, pH in total before treatment)	Moderate	Low	Moderate (treatment details partially provided)	Low	Serious (no method error, not blinded assessor)	Moderate	Critical
Sánchez at al.[18]	Critical (difference in age and sex between groups)	Moderate	Low	Moderate (treatment details partially provided)	Low	Serious (no method error, not blinded assessor)	Low	Critical
Arab et al.[15]	Serious (difference in sex between groups)	Moderate	Low	Low	Low	Serious (no method error, not blinded assessor)	Low	Serious
Zogakis et al.[2]	Moderate	Low	Low	Low	Low	Moderate (not blinded assess)	Low	Moderate
Alshahrani et al.[11]	Serious (difference in age, unknown difference in sex)	Moderate	Low	Moderate (treatment details partially provided)	Low	Serious (no method error, not blinded assessor)	Low	Serious
Kouvelis et al.[17]	Moderate	Low	Low	Low	Low	Moderate (not blinded assessor)	Low	Moderate

Table 3. A summary of the results of the included studies (salivary flow rate and pH measurements)

	Authors	Stage of orthodontic treatment	The type of collected saliva	Saliva flow rate (mL/min)	Saliva pH	Conclusions
1	Alshahrani et al.[11], Saudi Arabia	Before treatment 2 months of treatment	Unstimulated	0.18 0.15	7.14±0.29 6.75±0.29	Statistically significant reductions in salivary flow and pH
2	Arab et al.[15], Iran	Before treatment 6 weeks of treatment Twelve weeks of treatment 18 weeks of treatment	Unstimulated	1.13±0.42 1.14±0.25 1.20±0.33 1.22±0.42	7.18±0.35 6.78±0.23 6.76±0.28 6.81±0.31	The salivary flow increased but did not change significantly, while the saliva pH significantly decreased during orthodontic treatment
3	Altaee et al.[16], Iraq	Before treatment 1 month of treatment	Unstimulated	0.52 0.83	7.01±0.53 6.8±0.63	A statistically significant increase in the salivary flow rate. Significant decrease in the salivary pH
4	Kouvelis et al.[17], Greece	Before treatment 4 weeks of treatment Twelve weeks of treatment	Stimulated	1.42 1.59 1.67	7.63 7.67 7.78	A statistically significant increase in the salivary flow rate. However, the salivary pH did not change significantly
5	Sanchez et al.[18], Peru	Before treatment 1 month of treatment	Stimulated	1.12 1.36	Not studied	A statistically significant increase in salivary flow. Salivary pH not studied
6	Peros et al.[19], Croatia	Before treatment 6 weeks of treatment Twelve weeks of treatment 18 weeks of treatment	Stimulated	1.12 1.13 1.23 1.33	7.18 7.27 7.42 7.30	A significant increase in salivary flow rate and pH was found
7	Zogakis et al.[2], Israel	Before treatment 4-6 weeks of treatment	Unstimulated	Not studied	6.9 6.83	No statistically significant reduction in salivary pH

The first age group included participants aged 16-32 years.[11,16] Alshahrani et al.[11] reported that the unstimulated salivary flow rate was significantly higher one week before orthodontic treatment than after 2 months of orthodontic treatment ($p<0.05$). According to the results, the mean unstimulated saliva flow rate before treatment was 184.57±53.41 µL/min, compared to 149.12±50.57 µL/min of flow rate after 2 months of treatment.[11] In contrast, Altaee et al.[16] stated that the unstimulated saliva flow rate of participants increased significantly during the 1-month orthodontic treatment period, from 0.52±0.1 mL/min to 0.83±0.16 mL/min ($p<0.05$). The second age group included participants aged 12-18 years.[15] Arab et al.[15] analyzed younger patients before orthodontic treatment and at 6, 12, 18 weeks of orthodontic treatment with fixed appliances and revealed that the unstimulated salivary flow rate increased significantly after every 6 weeks of treatment ($p<0.05$). In detail, the salivary flow rate before starting fixed orthodontic treatment (1.13±0.42 mL/min) had a significantly lower mean than after 18 weeks of treatment (1.22±0.42 mL/min).[15] Evaluating the unstimulated salivary flow rate of these three studies, a general conclusion cannot be drawn due to the different results observed between the studies.

Stimulated Salivary Flow Rate

Three studies evaluated the status of stimulated salivary flow rate parameters.[17-19] In the study by Sánchez and Honores[18] the average stimulated salivary flow rate changed significantly from 1.12 mL/min to 1.36 mL/min after a month of bracket placement. However, these results should be interpreted with caution due to the wide range of age groups involved (10-34 years). Nonetheless, similar results were reported by researchers in two other studies over time.[17,19] Kouvelis et al.[17] showed a significantly greater stimulated salivary flow rate after 12 weeks (1.67 mL/min) of treatment compared to before treatment (1.42 mL/min). Peros et al.[19] also showed a significant increase in stimulated salivary flow rate with values increasing from 1.12 mL/min before treatment to 1.33 mL/min after 18 weeks of treatment. Regarding changes between the genders, it was noticeable that the stimulated salivary flow rate of females increased by 0.22 from baseline to 1 month (from 1.16 mL/min to 1.38 mL/min), while that of men increased by 0.25 (from 1.06 mL/min to 1.31 mL/min) during the same period of treatment.[18] Concerning the status of stimulated salivary flow rate, the results of the studies showed a significant increase during different periods of long-term orthodontic treatment.

Unstimulated Salivary pH

Four of the included studies analyzed the unstimulated salivary pH in different periods of treatment with fixed orthodontic appliances.[2,11,15,16] Evaluating the records of patients who underwent such treatment revealed that unstimulated salivary pH significantly decreased after various periods of orthodontic

treatment.[11,15,16] Alshahrani et al.[11] reported a decrease in salivary pH by 0.39±0.29 during a 2- month period ($p<0.05$), while Altaee et al.[16] showed a decrease in pH by 0.21±0.13 during a 1-month period ($p<0.05$). The findings from the study by Arab et al.[15] also showed a significant reduction in unstimulated salivary pH from 7.18±0.35 to 6.76±0.28 during a 12-week period; however, from 12 to 18 weeks, salivary pH increased to 6.8±0.3.[15] In the study conducted by Zogakis et al.[2], the reduction in unstimulated salivary pH was 0.07, but it was not significant compared to the values before and 4-6 weeks of orthodontic treatment ($p>0.05$). Regarding the status of unstimulated salivary pH , the results of three studies revealed a significant decrease during different periods of orthodontic treatment, while in one study, the decrease in salivary pH was not significant.

Stimulated Salivary pH

Two authors investigated stimulated salivary pH.[17,19] Kouvelis et al.[17] and Peros et al.[19] published results of stimulated salivary pH. Kouvelis et al.[17] studied stimulated salivary pH at different time points: before treatment - 7.63, 4 weeks of treatment - 7.67, and 12 weeks of treatment - 7.78. The salivary pH of stimulated saliva increased by 0.15 during the 12-week period, but the difference was not statistically significant ($p>0.05$).[17] On the other hand, Peros et al.[19] reported that the measurements of stimulated salivary pH increased significantly compared the initial examination (7.18) during the 12-week period of treatment (7.42). However, there was a reduction of stimulated salivary pH by 0.12 during the 12- to 18-week period.

DISCUSSION

Salivary Flow Rate

No single conclusion was reached when evaluating the unstimulated salivary flow rate.[11,15,16] Other authors have also obtained variable results. Li et al.[33] found an increase in the non-stimulated salivary flow rate during the first month, followed by a return to the norm after 3 months. Three other authors[10,21,34] presented one month and half-year results of unstimulated salivary flow, where a significant increase was observed; however, in one study, the authors did not provide accurate measurements of salivary flow, and results were presented in the ranges (<3.5 mL, 3.5-5 mL., >5 mL).[21] Considering an even longer treatment period, such as one year, Alessandri Bonetti et al.[8] found an increased salivary flow rate, but these results were not statistically significant. Different results may have been obtained because most study groups were not divided into smaller age groups, and adults were not separated from children. It is known that children's saliva secretion is more intensive compared to adults and decreases over time.[35,36] Another important factor that may affect the results is the evaluation of salivation over a long period of time,since orthodontic treatment itself takes an average of about 19.9 months.[37] Therefore, it is essential to evaluate the salivary flow rate over a long period, and the results may change over time due to adaptive processes happening in the human body.

Some authors compared changes between genders. Females' unstimulated salivary flow rate increased during 1 month of treatment by 0.13 (from 0.51 mL/min to 0.64 mL/min), while men's salivary flow rate increased by 0.2 (from 0.51 mL/min to 0.71 mL/min) during the same period of treatment. Thus, the unstimulated salivary flow rate was greater in males than females as shown in a study by Altaee et al.[16] However, Alessandri Bonetti et al.[8] found no significant difference between the sexes over a period of one year.

Concerning stimulated salivary flow rate, as observed in the results of the present systematic review, all authors reported an increase in stimulated salivary flow rate at different treatment periods compared to baseline, even between different age groups.[17-19] Similar findings were found by other authors: Lara-Carillo et al.[12] found an increased stimulated salivary flow rate in patients after 1 month of orthodontic treatment. Increased rates were also found in patients treated with fixed orthodontic appliances one and three months later.[38,39] In one study, a significant increase in the stimulated salivary flow rate was also established even six months after the placement of fixed orthodontic appliances.[21] This confirms the statement that bonded brackets create a mechanical stimulus to receptors in the brain, promoting increased salivary secretion.

Comparing changes between genders, an increased stimulated salivary flow rate was obtained with a greater change in males compared to females, where the initial flow rate was higher in the female group.[18] These results may be inaccurate due to the inclusion of various age groups (10-34 years). Lara-Carillo et al.[12] also compared results between genders and found increased stimulated saliva flow in both gender groups, but with a higher initial flow rate in the male group. On the other hand, Kado et al.[40] evaluated stimulated salivary flow between genders of pre-orthodontic patients and found a significantly higher flow rate in males than in females. These results were explained by the smaller size of salivary glands in females compared to males the influence of hormonal patterns.[12]

Salivary pH

A reduction in unstimulated salivary pH during orthodontic treatment was found in all included studies that evaluated the pH of unstimulated saliva.[11,15,16] These results are consistent with those reported by Kanaya et al.[39], who found a decreased pH associated with an increased number of acidogenic bacteria, such as *Streptococcus mutans*, *Lactobacilli*.[39] When the pH decreases sharply and reaches the critical value (pH 5.5), the balance between demineralization and remineralization is pushed toward mineral loss and demineralization. Jurela et al.[10] also found a decrease in salivary pH of patients treated with braces and associated this decrease with an increased plaque index. This may be explained by the fact that plaque buildup is a mass of bacteria that produce acid and results in reduction in salivary pH.

Comparing the results of stimulated salivary pH, an increase in pH was observed during the 12-week period.[2,17,19] Lara-

Carillo et al.[12] also showed an increase in pH after one month of orthodontic treatment, while Maret et al.[6] demonstrated that 6 months with orthodontic appliances increased salivary pH. Specifically, Maret et al[6]. compared the salivary pH of children with fixed orthodontic appliances (pH=7.49) to a control group of children (pH=7.37) without orthodontic treatment, showing a statistically significant difference in pH levels. These results agree with the study by Ivanovic et al.[30], where the pH of saliva statistically significantly increased 12 weeks after wearing fixed braces compared to the control group of respondents who were not treated orthodontically. A higher pH value indicates higher basicity. However, it is essential to note that fixed appliances remain in the mouth for an extended period, and oral prophylaxis measures, such as oral hygiene practices, diet advice, and topical fluoride application, should be considered to maintain oral health.

Moreover, certain unexplored variables can significantly influence the oral environment. The utilization of probiotics, parabiotics, postbiotics, and natural compounds has demonstrated the ability to modify clinical and microbiological parameters in periodontal patients, a which may also have an impact during orthodontic treatment. All these variables should be considered in future clinical trials.[41,42]

Study Limitations

This systematic literature review analyzed the currently available information on changes in salivary flow and pH during orthodontic treatment with fixed orthodontic appliances. The quality of the included studies was mainly medium, which means that the results of these studies should be interpreted with caution. Some studies provided limited details of their methods, making quality assessment difficult. The main limitations of the included studies were; blinding, assessment of confounding factors, non-homogeneous study designs, and small sample sizes. Additionally, in some studies, children and adults were not separated into different groups, and the evaluation of salivary parameters was not consistently performed at the same time as orthodontic treatment. Some studies had short follow-up periods, limiting the ability to assess long-term outcomes. The accuracy of saliva parameters might have been influenced by the different collection times of saliva, emphasizing the importance of standardized saliva collection protocols in future research. To gain a more comprehensive understanding of the long-term effects, future research should consider following the participants for extended evaluation periods. The limited number of studies evaluating the same procedures, outcomes, and evaluation periods precluded the performance of meta-analyses. Due to resource limitations, full texts of non-English-language articles identified during the searches were not retrieved, potentially resulting in the omission of relevant evidence. It is important to note that this study was not funded, and the authors declare that there are no conflicts of interest.

CONCLUSION

Orthodontic treatment with fixed orthodontic appliances increases the salivary flow rate during various periods of orthodontic treatment. However, the changes in salivary pH differ depending on whether the saliva is stimulated or unstimulated. Stimulated salivary pH tends to increase during orthodontic treatment, while unstimulated salivary pH tends to decrease. Although the published results are promising, they are not sufficient to confirm final changes in quantitative and qualitative indices of saliva during orthodontic treatment with fixed appliances. Further well-conducted multicenter randomized studies with a large sample are needed to confirm this statement to establish more robust evidence.

Ethics

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - R.J., A.Ž.; Design - R.J., A.Ž.; Supervision - R.J., A.Ž.; Data Collection and/or Processing - R.J., A.Ž.; Analysis and/or Interpretation - R.J., A.Ž.; Writing - R.J., A.Ž.; Critical Review - R.J., A.Ž.

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