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Review Article

Comparative Effects of Fixed and Clear Aligner Therapy on Oral Microbiome Dynamics

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ABSTRACT

This review aimed to conduct a comprehensive review of the literature and statistically synthesize the data discovered about the effect of thermoplastic clear aligners and fixed orthodontic equipment on oral flora and salivary markers. The current systematic review followed the PRISMA criteria and the Cochrane Handbook. Five electronic databases were searched to find relevant articles. There were a total of 5345 articles on this topic. Due to the removal of duplicates, 4636 articles were included in the initial screening. Seven studies satisfied the requirements for qualifying. Of the four studies that were categorized as having a low risk of bias, two were considered to have a moderate risk of bias, and just one was considered to have a high risk of bias. The systematic review included each of them. Patients with permanent appliances had greater overall changes in their oral microbiota than patients with detachable equipment. Although the results of the fixed orthodontic appliances group differed in previous research, neither the salivary flow rate nor the salivary buffering capacity changed significantly for clear aligners. However, other salivary characteristics changed for the fixed orthodontic groups.

Keywords: Orthodontic appliance, Oral microbiota, Salivary parameters, Clear aligner

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Introduction

Malocclusion is generally thought to negatively impact people's social, psychological, and physical well-being [1, 2]. Adult patients are mostly motivated to improve their looks because they want orthodontic treatment to improve their quality of life, psychological well-being, dental function, and attractiveness. Both fixed and detachable orthodontic equipment are available nowadays. The main components of stable devices—brackets, bands, ligatures, and orthodontic wires—can impair the tongue's or cheeks' natural ability to clean themselves. They can also create different areas where plaque accumulates, which can interfere with oral hygiene practices and result in the development of white spot lesions, caries, gingival inflammation, and/or periodontal diseases [3]. Furthermore, brackets may result in various discomforts, functional limitations, and an unappealing look. More people are choosing tooth-colored brackets, lingual brackets, and/or invisible aligners over traditional ones as the demand for aesthetic dentistry has grown over the past few decades [4]. However, the use of portable orthodontic equipment can provide adequate oral hygiene measures that allow them to be readily removed for cleaning, reducing the likelihood of these negative dental and periodontal issues as well as increasing their aesthetic presentation [5].

It is very advised to have a periodontal diagnosis before orthodontic treatment and to provide guidance on maintaining proper oral hygiene [6]. While mutant streptococci are primarily important in caries stimulation, the taxonomic makeup of the microbiome is the crucial key to periodontitis [7, 8]. S. mutans is seen in early carious lesions and is a potent acid generator [9]. Salivary flow rate, antibacterial activity, microbe aggregation, and clearance from the oral cavity are some of the physiologic elements that help prevent dental cavities [10]. Saliva's pH varies from 6.2 to 7.6, with 6.7 being the average [11]. Research indicates that a pathologically reduced salivary flow rate is considered a risk factor for the development of dental cavities [12].

The oral microbiome is impacted by conventional orthodontic equipment, according to several research studies [13, 14].

Even though different research has examined the oral environment from various angles and with different protocols—for instance, evaluating oral microorganisms during the active orthodontic phase with clear aligners—fixed appliances have additionally assessed nonmicrobial salivary parameters. The supporting literature, however, is lacking in systematic reviews and meta-analyses that include all of these elements in a single research.

Hence, the goal of the present review is to consistently evaluate the literature and statistically summarize the found evidence evaluating the impact of thermoplastic clear aligners as well as fixed orthodontic appliances on oral microbiota and salivary parameters.

Materials and Methods

Search strategy and data sources

The review was registered with registration number FIRP/2020/66/252, and ethical approval has been obtained from the institutional review board IRP of Riyadh Elm (IRB) committee of Riyadh Elm University FIRP/2020/66/252/247.

Focused question

In orthodontic conventional fixed appliances and clear therapeutic aligners was there a systematic change in oral microbial type and/or concentrations of salivary parameters among non-grower patients?

Data source

This systematic review was done according to PRISMA guidelines [15] and the Cochrane Handbook [16]. A search was conducted in PubMed, Google Scholar, The Cochrane Library, Saudi digital library, And Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS).

The following keywords were used "((salivary parameter) OR (oral microbiota)) AND (periodontopathic bacteria)) OR (cariogenic bacteria)) AND (fixed orthodontic appliances)) OR (clear aligner)." The search was limited to the last five years from 2015 until 24/6/2020.

Duplicates were removed and articles were screened initially by title and abstract.

Studies were done during the retentive phase for orthodontic patients; articles measured oral health by PI, GI, and PSR only, and the study was done for growing patients, and articles uncorrelated to the aim of the present organized review were excluded. The collected articles were individually strictly applied to clear inclusion and exclusion criteria as shown in **Table 1**. The procedure of article choosing is shown in **Figure 1**.

Articles were screened using the Problem, Intervention, Comparator, and Outcome (PICO) approach. Population/Problem was defined as non-grower patients' orthodontic treatment needs. The intervention was defined as orthodontic treatment during the active phase. Comparators are defined as two types of orthodontic appliances (Fixed appliances and clear aligners). The outcome was defined as oral microflora and salivary parameters.

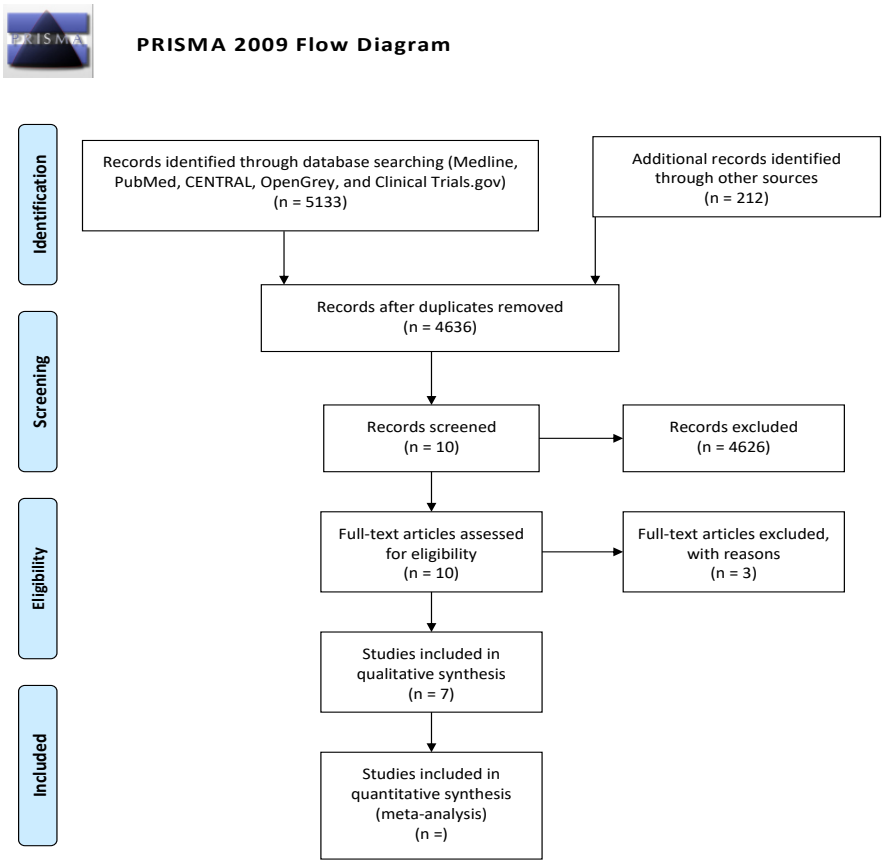

Figure 1. PRISMA chart shows the selection process of the articles

Table 1. Eligibility criteria

Criteria	Inclusion criteria	Exclusion criteria
Language	English language	Any other language
Population/Age group	Non-growers (18 years old patients or older) of both genders	Grower (patients younger than 18 years old)
Publication date	Articles from 2015 up to 2020	Studies published before 2015
Type of study	In human, randomized and non-randomized clinical trials -Retrospective and/or prospective cohort studies	-Animal studies -Low quality of evidence -Case reports, review studies, as well as cross-sectional studies (questionnaires-based). -Unsupported opinion of expert or replies to the author/editor. Books'/ conferences' abstract.
Intervention	Studies are done during the active phase of orthodontic treatment	Studies are done during the retentive phase among patients with retainer
Subjects	-Medically fit patient. -Patient with good oral hygiene.	-Medically compromised patients and patients with medication that causes side effects in the oral cavity environment -Patient with active periodontal disease. -Patient with poor oral hygiene.

Treatment protocol/ comparison	-Conventional fixed orthodontic appliances -clear therapeutic appliances	-Functional appliances. -Orthognathic surgical involvement.
Study duration	Studies were done for 1 month or more	Studies were done for less than 1 month.
Outcome	Studies evaluate the change in oral microflora and salivary parameters	Studies that evaluate candida only

Quality synthesis

One particular reviewer (First Author) assessed the methodological quality of the studies after the final assessment of the full text (n = 10) independently. Accordingly, 7 final articles were individually applied for qualitative and quantitative assessments. Quality assessment of the 7 final articles was appraised for risk of bias using a well-formulated quality assessment tool [15, 16]. Sampling bias was appraised by assessing and evaluating the sample selection, performance, detection of outcome assessors, attrition, and reporting. The overall assessment provided ranges from low to moderate risk of bias for the 7 articles; the main methodological points of these studies are summarized in **(Table 2)**.

Table 2. Risk of bias assessment

Bias Type	**Selection**		**Performance**	**Detection**	**Attrition**	**Reporting**	**Overall assessment**
Bias	**Random sequence generation**	**Allocation concealment**	**Blinding of participants and personnel**	**Blinding outcome assessment**	**Incomplete resulted data**	**Selective reporting**	
Levrini *et al*. [5]	Low	Unclear	Low	Unclear	Low	Low	Low
Guo *et al*. [17]	Low	Unclear	Low	Unclear	Low	Low	Low
Marda *et al*. [18]	Low	Unclear	Low	Unclear	Low	Low	Low
Alshahrani *et al*. [19]	Unclear	Unclear	Low	Unclear	Low	Low	Moderate
Al-Melh *et al*. [20]	Unclear	Unclear	Low	Unclear	Low	High	High
Mummolo *et al*. [14]	High	Unclear	Low	Low	Low	Low	Moderate
Mummolo *et al*. [21]	Unclear	Unclear	Low	Low	Low	Low	Low

Criteria for judging the risk of bias in the risk of bias assessment tool–reproduced from the Cochrane tool [16]. Criteria of judgment following low, high, or unclear risk were judged based on the following: 1- random succession creation: election bias (prejudiced allocation to interventions) because of insufficient formation of a randomized succession; 2- allotment hiding: election bias (biased allotment to interventions) as a result of insufficient hiding of allotments before the assignment; 3-blinding of participants and employees: function bias because of knowledge of the allotted interventions by participants and employees within the research; 4- blinding of result evaluation: recognition of bias as a result of knowledge of the allotted interventions by result assessors; 5- defected result data: attrition bias because of amount, nature, or handling of defected result data; and 6- elective reporting: reporting bias as a result of selective result reporting.

Results and Discussion

4636 in all were associated with this subject. Initial screening resulted in the exclusion of 4626 people. Ten studies were examined for qualifying requirements. Three of them were left out of the qualitative synthesis, while seven were included **(Table 3).**

Table 3. Summary of excluded studies

Reference	**Reason for exclusion**
Turssi *et al*. [22]	Full-text article can't be found
Zogakis *et al.* [23]	Mean age of 15.8 ± 4.4 years
Jing *et al.* [24]	Patients aged between 14 and 20 years

Overall, the bias risk for intended studies ranged from weak to high **(Table 2)**.

Oral microbiota

Six studies assessed orthodontic patients' oral microbiome during the active phase. **Table 4** provides a summary of their findings.

Table 4. Summary of changing the oral microbiota during orthodontic treatment

Reference	N	Type of study	Type of orthodontic appliance	Measures	Method/test	Duration	Results
Levrini *et al.* [5]	77	Prospective study	Invisalign Fixed Appliance	Total biofilm mass and periodontal pathogens	Real-time polymerase chain reaction (PCR)	3 months	- In contrast to the fixed orthodontic treatment group, which only had one patient with *A. actinomycetemcomitans*, the Invisalign treatment group had no periodontal pathogenic bacteria. - Bacterial condensation was more prevalent in the fixed orthodontic treatment group.
Marda *et al.* [18]	18	Prospective study	Fixed Orthodontic Appliances	Oral microbial flora changes	Using gauze, the plaque was removed from the teeth's surface. - API-20A (BioMerieux, SA) for anaerobic bacteria and Rapid ID32 STREP galleries for biochemical and enzymatic tests for streptococci. - To ensure that the microorganisms are recognized: automaton phoenix.	3 months	According to the present investigation, there is a rise in cariogenic bacteria, including *Lactobacillus*, *Streptococcus mitis*, and *Streptococcus sobrinus*.
Guo *et al.* [17]	10	Prospective study	Clear aligners	Subgingival Plaque Plaque index (PI) and gingival bleeding index (GBI) evaluations	DNA was taken from plaque specimens and analyzed by 16S rRNA gene sequencing	3 months	A notable change in microbial structure over the first three months of clear aligner therapy (CAT) and a decrease in microbial diversity. - During the first three months of treatment, clear aligners modify the subgingival microbiota in nonpathogenic ways, according to this study.
Mummolo *et al.* [14]	80	Prospective controlled study	Clear aligners (CA) Multibrackets Appliance (MB)	*S. mutans* and Lactobacilli count	Bacteria CRT	6 months	The MB group saw a gradual rise in S. mutans and Lactobacilli colonies, with 37.5% of patients exhibiting a hazardous value at t2, whereas only 8% of participants in the clear aligners group did so.
Mummolo *et al.* [21]	90	Prospective study	Clear aligners (CA) removable positions (RP)	*S. mutans* and Lactobacilli count in saliva	CRT® bacteria (Ivoclar vivadent clinical, schaan, liechtenstein)	6 months	After six months, the number of patients in the CA group with CFU/ml >105 increased considerably, but there was no statistically significant correlation. Patients who used RP equipment showed

			Multibracket s fixed orthodontic appliance (MB)				the same pattern. It improved gradually over time in the MB group, showing a statistically significant difference between the start and three and six months. At three and six months, the differences between the groups were statistically significant.
Al-Melh M. *et al.* [20]	80	Cross-sectional study	Patients with orthodontic brackets and healthy controls without brackets	Streptococci and a *Lactobacillus* species were diagnosed and assessed	Polymerase chain reaction (PCR) and real-time quantitative PCR	Involved patients with fixed orthodontic appliance s for at least 12 months	Compared to control subjects, orthodontic patients using brackets for a year have greater levels of *S. mutans* and *S. salivarius*.

Salivary parameters

Salivary parameters for orthodontic patients during the active period were assessed in two trials. **Table 5** provides a summary of their findings.

Table 5. Summary of salivary parameters assessment during orthodontic treatment

Reference	n	Type of Study	Type of orthodontic appliance	measures	Method/test	Duration	Results
Alshahrani *et al.* [19]	60	Prospective study	Fixed orthodontic treatment	Salivary parameter change: Glucose, total proteins, amylase, and calcium levels in the saliva samples. Salivary PH Flowrate	Enzyme-linked immunosorbent assay (ELISA)	Before and 2 months after treatment	- Two months after starting therapy, salivary pH and flow rate dropped while glucose and amylase levels sharply rose. - After starting therapy, there were notable decreases in the three indices of salivary buffering capacity, total protein concentration, and calcium levels. - After starting therapy, the proportion of patients in the high buffering category significantly decreased, whereas the number of patients with low and medium buffering capacity increased.
Mummolo *et al.* [14]	80	Prospective study	Clear aligners Fixed orthodontic appliance (multibrackets appliance)	Salivary flow Buffering power	CRT buffer system	6 months	No significant changes in salivary flow nor salivary buffering during orthodontic treatment for both groups

Six of the seven studies that made up this review focused on the oral microbiota, while the other two examined how salivary parameters changed as a result of orthodontic treatment. Additionally, there was one cross-sectional research study, although most of the investigations were prospective.

According to Levrini *et al*. [5], Mummolo *et al*. [21], Guo *et al*. [17], Marda *et al*. [18], Mummolo *et al*. [14], and Al-Melh *et al*. [20], there were alterations in the oral microbiota in orthodontic conventional fixed appliances and clear aligners. Levrini *et al*. [5] conducted prospective research with 77 individuals divided into three groups: the control group, the group using fixed orthodontic equipment, and the group using Invisalign. According to the authors, the clear aligner treatment group had no periodontal pathogenic bacteria, while the fixed orthodontic treatment group had greater levels of germs, and only one patient had A. actinomycetemcomitans. Mummolo *et al*. [14] conducted another prospective controlled trial, which included 80 subjects. Clear aligners (CA) were applied to 40 individuals, while fixed multi brackets (MB) were applied to another 40. The results indicated that S. mutans and Lactobacilli colonies were increasing in the MB group, with 37.5% of individuals showing a dangerous value at 6 months, whereas only 8% of people in the clear aligners group exhibited a risky value at 6 months. Furthermore, Marda *et al*. [18] reported in another prospective study that included 18 individuals, which demonstrated a rise in cariogenic bacteria like Streptococcus mitis, Streptococcus sobrinus, and Lactobacillus with permanent orthodontic equipment. During the first three months of treatment, clear aligners generate nonpathogenic alterations in the subgingival microbiota, according to different prospective research studies with ten patients conducted by Guo *et al*. [17]. According to a future research study by Mummolo *et al*. [21], which involved 90 patients split into three groups of 30 each: removable positioners (RP), fixed multi-brackets group (MB) appliance, and removable clear aligners (CA), only about 10% of CA patients and 13.3% of RP patients achieved microbial colonization after six months of therapy. This is in contrast to MB patients, for whom approximately 40% and 20% of cases are extremely susceptible to developing caries after three months. According to cross-sectional research published by Al-Melh *et al*. [20], which included 40 orthodontic bracket patients and 40 healthy controls without brackets, orthodontic patients who had brackets for a year had greater levels of *S. mutans* and *S. salivarius* than the control group.

Two prospective studies reported on the assessment of salivary parameters for orthodontic patients. Alshahrani *et al*. [19] undertook one of them, which involved 60 participants with fixed orthodontic equipment exclusively, to evaluate the changes in required salivary parameters in patients receiving fixed orthodontic therapy. The measurements were taken both before and two months following therapy. Salivary flow rate, pH, buffering capacity, and levels of amylase, total protein, and glucose are some examples of these metrics.

Up until two milliliters of unstimulated saliva were collected, the rate of salivary flow was recorded. Salivary pH was measured using a little portable pH meter. Shortly after the samples were collected, a small pH meter was utilized to measure buffering capacity. Meanwhile, the enzyme-linked immunosorbent assay (ELISA) was used to measure the amounts of calcium, amylase, glucose, and total proteins in the saliva samples. Two months after starting therapy, salivary pH and flow rate dropped, while glucose and amylase levels sharply rose. When the Wilcoxon matched pairs t-test was used to evaluate the levels of calcium, salivary buffering capacity, and total protein concentration before and after treatment started, all three parameters significantly decreased ($P < 0.001$).

The buffering capacity and the total salivary protein content were substantially associated after orthodontic treatment started ($r = 0.34$; $P < 0.05$).

Additionally, there were noteworthy correlations ($P < 0.05$) seen between salivary calcium and total protein levels, and also between salivary glucose and amylase levels.

After starting therapy, there was an increase in the number of patients with low and medium buffering capacity, but a substantial fall in the proportion of patients in the high buffering group.

Mummolo *et al*. [14] did the other investigation in 2020. Two groups of 40 participants each—orthodontic patients using transparent aligners and orthodontic patients using multibracket orthodontic appliances—were compared in this study. The salivary parameters included in this study are salivary flow and buffering power. Measurements were taken before orthodontic treatment, three months later, and six months later. According to the authors, neither the salivary buffering nor the salivary flow changed significantly for either group throughout orthodontic treatment. This contradicts the data presented in earlier articles.

Conclusion

In conclusion, compared to patients with detachable equipment, individuals with fixed appliances had more overall alterations in their oral flora. While glucose and amylase levels dramatically rose in the saliva of the fixed orthodontic instruments group, salivary pH, total protein concentration, and calcium level significantly decreased. Salivary flow rate and salivary buffering capacity did not significantly alter for transparent

aligners; however, earlier research showed that the fixed orthodontic appliances group's findings varied.

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Conflict of Interest: None

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