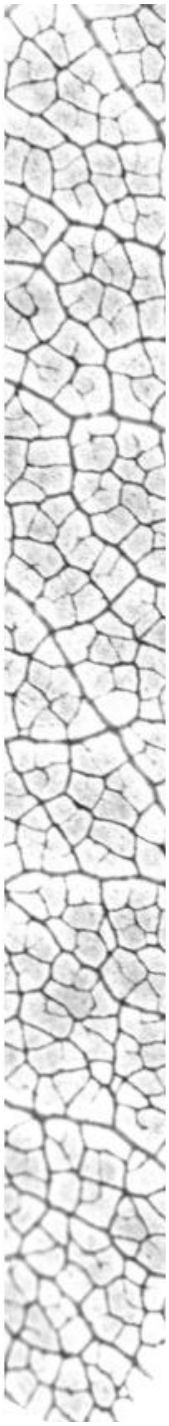

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Evaluate the levels changes of periodontal pathogens in children with malocclusion during orthodontic treatments: a systematic review and meta-analysis

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Abstract

Aim: the aim of the present systematic review and meta-analysis was evaluate the levels changes of periodontal pathogens in children during orthodontic treatments.
Method: From the electronic databases, PubMed, Cochrane Library, Embase, ISI have been used to perform a systematic literature until September 2020. Therefore, a software program (Endnote X8) has been utilized for managing the electronic titles. Searches were performed with mesh terms. Odds ratio between before and one or three months after treatment with 95% confidence interval (CI), Mantel-Haenszel method were calculated. Random effects were used to deal with potential heterogeneity and I^2 showed heterogeneity. The Meta analysis and forest plots have been evaluated with the use of a software program available in the market (i.e., Comprehensive Meta-Analysis Stata V16).
Result: A total of 46 potentially relevant titles and abstracts were found during the electronic and manual search. Finally, a total of three publications fulfilled the inclusion criteria required for this systematic review. Odds ratio of P.gingivalis was (OR, -0.58 95% CI -1.34, 0.18. P= 0.14) and
Odds ratio of T. forsythensis was (OR, -1.44 95% CI -2.16, 0.73. P= 0.00), also odds ratio of P. intermedia was (OR, -1.09 95% CI -2.09, -0.10. P= 0.03).
Conclusion: The present systematic review and met analysis showed the levels of periodontal pathogens in children during orthodontic treatments was increased after orthodontic treatments vs before orthodontic treatments. Only no change in P.gingivalis was observed.

Keywords: periodontal pathogens, children, orthodontic treatments

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INTRODUCTION

One of the three most common diseases in the oral and maxillofacial regions is malocclusion with periodontal disease and dental caries (Mummolo, et al. 2020, Golden, & White Jr, et al. 2015). Malocclusion is a misalignment or incorrect relation between the teeth of the two dental arches when they approach each other as the jaws close (Zou, et al. 2018). also impair the oral health and function and have a significant effect on the craniofacial development (Cha, Zhang, & Zhao, 2020). One of the most important methods used in orthodontic treatment are fixed orthodontic appliances that have been considered for their convenience and efficiency (Ehsani, et al. 2015. Abed Al Jawad,et al. 2012). But it is possible that this method leads to majority of complications at the same time (gingival inflammation, swelling, bleeding, hyperplasia and even slight attachment loss (AL) (Alajmi, Shaban, & Al-Azemi, 2020, Rosa, et al. 2020). Bacterial plaque accumulation, colonization and reproduction are also observed around fixed orthodontic appliances (Mummolo, et al. 2020). Studies have shown that aging is directly related to the rate of periodontitis, but it is inadequate to determine that orthodontic treatment of the juvenile period is related to the occurrence of periodontitis after middle age (Behr, et

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Table 1. PICO OR PECO strategy

PICO OR PECO strategy	Description
P	Population/ Patient: children during orthodontic treatments
E	Exposure/ Intervention: orthodontic treatments
C	Comparison: before and after orthodontic treatment
O	Outcome: oral microecological changes

al.2014, Ren, et al. 2020). Evaluation of clinical and microbial effects of orthodontic treatment with fixed orthodontic appliances is of great importance, especially in children, in order to provide theoretical foundations for the treatment of periodontal disease. Recent studies have focused more on clinical parameters based on PCR technology rather than the association between fixed orthodontic appliances and periodontal disease. There are some related subgingival periodontopathogens reported in previous studies, such as Porphyromonas gingivalis (P.gingivalis), Fusobacterium nucleatum (F. nucleatum), Prevotella intermedia (P. intermedia) and Tannerella forsythensis (T. forsythensis), which have been suggested to possess close relationships with the development of chronic periodontitis (Liu, et al. 2014- Tefiku, et al. 2020. Pan, et al. 2017. Guo,et al. 2016. Rafiei, et al. 2017). On the other hand, the simultaneous diagnosis of pathogenic bacteria and specific clinical indexes are important (Guo, et al. 2016). Therefore, a study that examines the effect of fixed orthodontic appliances on periodontal tissue and oral microecological changes and a general result that can be effective in clarifying current concerns is needed. Hence the aim of the present systematic review and meta-analysis was evaluate the levels changes of periodontal pathogens in children during orthodontic treatments.

METHOD

Search strategy

From the electronic databases, PubMed, Cochrane Library, Embase, ISI have been used to perform a systematic literature until September 2020. Therefore, a software program (Endnote X8) has been utilized for managing the electronic titles. Searches were performed with mesh terms:

("Malocclusion"[Mesh] OR "Malocclusion, Angle Class III"[Mesh] OR "Malocclusion, Angle Class II"[Mesh] OR "Malocclusion, Angle Class I"[Mesh]) AND "Orthodontic Brackets"[Mesh]) OR ("Orthodontic Appliances, Fixed"[Mesh] OR "Orthodontic Appliances"[Mesh] OR "Orthodontic Anchorage Procedures"[Mesh])) OR "Index of Orthodontic Treatment Need"[Mesh]) AND ("Periodontal Index"[Mesh] OR "Periodontal Diseases"[Mesh])) AND "GPI0100" [Supplementary Concept]) AND "Porphyromonas gingivalis"[Mesh]) OR "Fusobacterium nucleatum"[Mesh]) OR "Prevotella intermedia"[Mesh]) OR "Tannerella forsythia"[Mesh]) OR "Bacteria"[Mesh]) AND "Periodontium"[Mesh]) AND ("Child"[Mesh] OR "Adult Children"[Mesh] OR "Only Child"[Mesh]).

This systematic review has been conducted on the basis of the key consideration of the PRISMA Statement–Preferred Reporting Items for the Systematic Review and Meta-analysis (Liberati, et al. 2009), and PICO or PECO strategy (**Table 1**).

Selection criteria

Inclusion criteria

1. Randomized controlled trials studies, controlled clinical trials, and prospective and retrospective cohort studies.
2. Age ranging from 8 to 18 years old
3. Orthodontic treatments
4. Microbial changes at different time points of treatment (before, during and after treatment)
5. in English

Exclusion criteria

1. In vitro studies, case studies, case reports and reviews.
2. Adults

Data Extraction and method of analysis

The data have been extracted from the research included with regard to the study, years, study design, sample size, mean/ range of age, microbial analysis method, pathogens. The quality of the studies included was assessed using the Methodological index for non-randomized studies (MINORS). In this index the items 1–12 represent: 1, a clearly stated aim; 2, inclusion of consecutive patients; 3, prospective collection of data; 4, endpoints appropriate to the aim of the study; 5, unbiased assessment of the study endpoint; 6, follow-up period appropriate to the aim of the study; 7, loss to follow-up less than 5%; 8, prospective calculation of the study size; 9, an adequate control group; 10, contemporary groups; 11, baseline equivalence of groups; and 12, adequate statistical analysis. The item scored 0 means not mentioned, 1 means reported but inadequate, and 2 means reported and adequate. The total score is 24 for cohort study and clinical controlled trial, 16 for self-controlled study. For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included. Moreover, odds ratio between before and one or three months after treatment with 95% confidence interval (CI), Mantel-Haenszel method were calculated. Random effects were used to deal with potential heterogeneity and I^2 showed heterogeneity. The Meta analysis and forest plots have been evaluated with the use of a software program

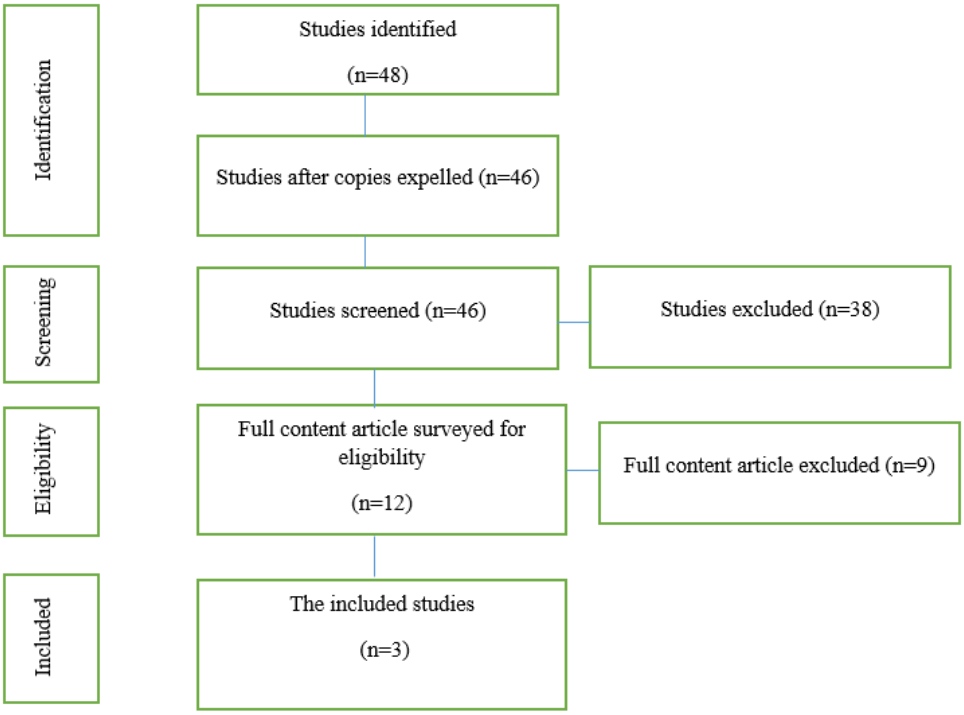

Fig. 1. Study Attrition

Table 2. Studies selected for systematic review and meta-analysis

Study. Years	design	Number of Patient	mean/ range of age (years)	Microbial analysis method	pathogens	Total score
Martha et al. 2016 (19)	Controlled Clinical Trials	25	14.4±2.45	PCR	P.gingivalis, F. nucleatum, P. intermedia and T. forsythensis	17
Guo et al. 2016 (15)	Controlled Clinical Trials	62	8–15	PCR	P.gingivalis, F. nucleatum, P. intermedia and T. forsythensis	12
Kim et al. 2012 (20)	Self-controlled study	30	16.7±6.5 y	PCR	P.gingivalis, F. nucleatum, P. intermedia and T. forsythensis	18

available in the market (i.e., Comprehensive Meta-Analysis Stata V16).

RESULTS

According to the research design, 46 potentially important research abstracts and titles have been discovered in our electronic searches. At the first phase of the study selection, 38 research have been with regard to the topics and abstracts. Therefore, we fully assessed the complete full-text papers of the rest 12 studies in the second stage so that we excluded 9 publications due to the lack of the defined inclusion criteria. Then, three papers remained in agreement with our inclusion criteria required (**Fig. 1**). **Table 2** reports the individual studies in this meta-analysis.

Sample size

Therefore, three studies (non-randomized controlled trial) have been included. The Number of Patients a total was 107. The mean of age was 14.58 years (**Table 2**). In all studies used PCR.

P.gingivalis

Odds ratio was (OR, -0.58 95% CI -1.34, 0.18. P= 0.14) among 3 studies and heterogeneity found (I^2 = -695.23%; P =0.88). This result showed there was no statistically significant difference between after and before orthodontic treatments in children and did not significantly change (p=0.14). There was no statistically significant difference between studies (p=0.88) (**Fig. 2**).

T. forsythensis

Odds ratio was (OR, -1.44 95% CI -2.16, 0.73. P= 0.00) among 3 studies and heterogeneity found (I^2 = -47.02%; P =0.51). This result showed there was statistically significant difference between after and before orthodontic treatments in children and significant increase (p=0.14). There was no statistically significant difference between studies (p=0.51) (**Fig. 3**).

P. intermedia

Odds ratio was (OR, -1.09 95% CI -2.09, -0.10. P= 0.03) among 3 studies and heterogeneity found (I^2 = -1.24%; P =0.37). This result showed there was statistically significant difference between after and before orthodontic treatments in children and significant

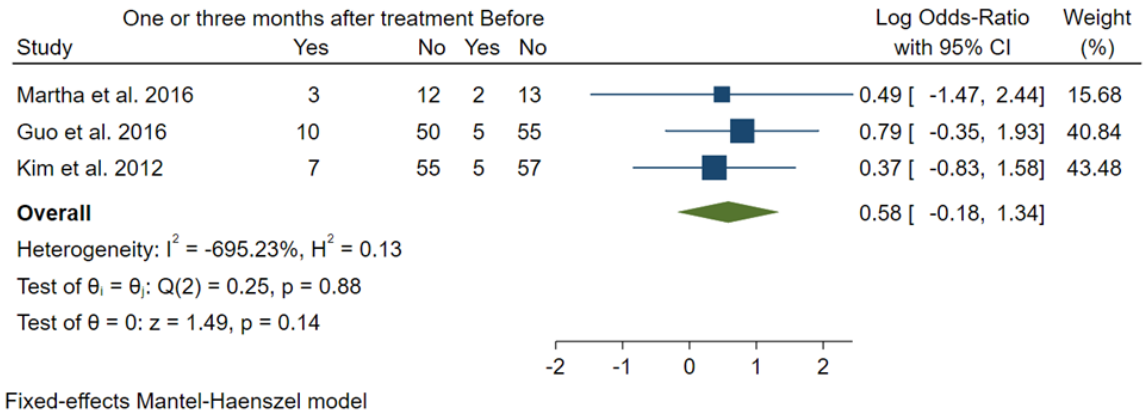

Fig. 2. P.gingivalis changes in children during orthodontic treatments

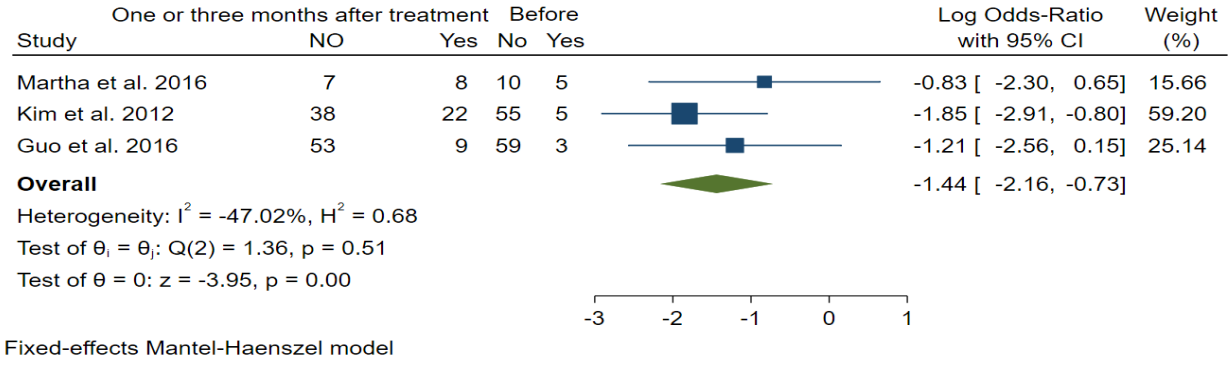

Fig. 3. Forsythensis changes in children during orthodontic treatments

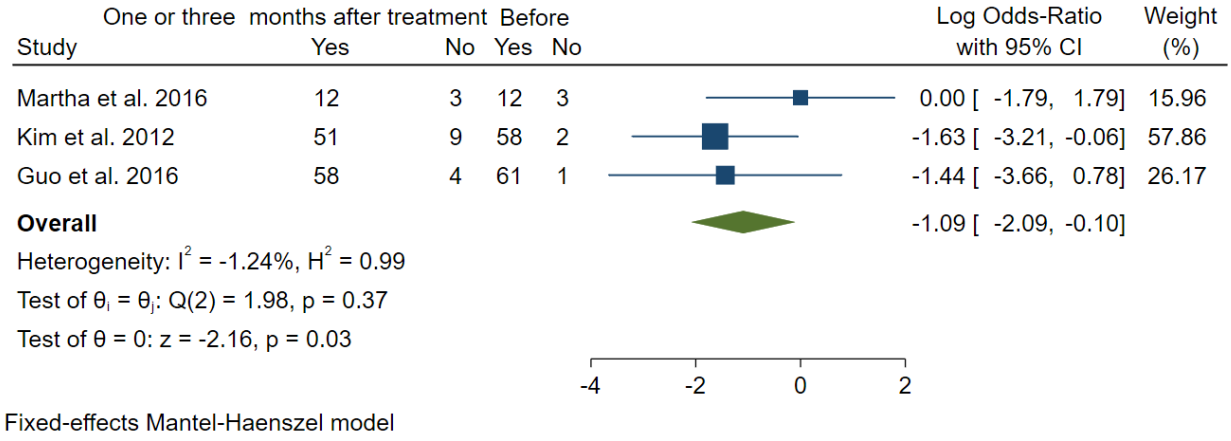

Fig. 4. P. intermedia changes in children during orthodontic treatments

increase (p=0.14). There was no statistically significant difference between studies (p=0.51) (**Fig. 4**).

Bias assessment

According to MINORS, All studies had a moderate to low risk of bias (**Table 2**).

DISCUSSION

Under normal circumstances, most periodontal plaque microorganisms can be maintained relatively stable due to the semi-enclosed structure of gingival sulcus, but not the same with the placement of fixed orthodontic appliance (Takahashi, & Nyvad, 2011). In all studies that included in present systematic review and met analysis, detection rates of four different pathogens (P.gingivalis, F. nucleatum, P. intermedia, T. forsythensis) were gradually increased from baseline to one month and lately three months after treatment. Upward trends were also showed in children, significantly higher at the time point of the third month

after treatment than that at baseline, whereas it was stable in 46 adults. In addition, the percentage of pathogens in the overall samples increased with time especially at the time point of the third month after treatment, gradual upward trends were found both in adults and children (Potârnichie, et al. 2013). However with the extension of treatment time, orthodontic appliance placement will change the survival condition of sub gingival microorganisms and promote the propagation of the periodontal pathogen, which in turn create favorable conditions for the onset of periodontal diseases Thus it could be illustrated out that fixed orthodontic appliance might have significant different influence in microecological environment for children. Under the stimulation of orthodontic appliance and due to plaque accumulation, children' sub gingival pathogens proliferation was more obvious than that in adults (Rodrigues, Silveira, & Rego, 2020).

In present systematic review and meta-analysis result showed before and after orthodontic treatments in children, P.gingivalis had no significant change ($P = 0.14$). T. forsythensis was significantly increased ($P \leq 0.01$). This result indicated that the risk of periodontal infection increased during orthodontic treatment. The change in P. intermedia was a significant increase ($P \leq 0.01$). In Kim et al. (Kim, et al. 2012) study, the frequency of T.forsythia, C.rectus, and P.nigrescens significantly increased after placement of orthodontic appliances. For the other species, the frequency tended to increase but no statistically significant difference was noted. Also the placement of orthodontic appliances affects the sub gingival microbial composition even during the early period of orthodontic treatment, increasing the prevalence of periodontopathogens, especially in the molar region. Mártha et al. (Mártha, et al. 2016) assess the prevalence and occurrence of eleven periodontopathogens in sub gingival biofilm of banded and bonded molars during the first period of fixed orthodontic treatment. Result showed orthodontic tubes and bands influence the accumulation and composition of sub gingival microbiota. Guo et al. (Guo, et al. 2016), investigate levels changes of periodontal pathogens in malocclusion patients before, during and after orthodontic treatments. The detection rates of P.gingivalis, F. nucleatum, P. intermedia and T. forsythensis increased from baseline to the third month without significant difference, and then returned to pretreatment levels 12 month after applying fixed orthodontic appliances. Also Periodontal and microbiological statuses of malocclusion patients may be influenced by fixed orthodontic appliances in both adults and children, more significant in children than in adults. Some microbiological indexes have synchronous trend with the clinical indexes. Long-term efficacy of fixed orthodontic appliances for malocclusion should be confirmed by future researches. A recent systematic review and meta-analysis by Guo et al (Guo, et al.2017) showed Following orthodontic appliance placement, the frequencies of P.gingivalis showed no significant change ($P = 0.97$ and $P = 0.77$), whereas the frequency of T. forsythensis significantly increased ($P < 0.01$) during short-term observation (0–3 months). The frequency of P. intermedia showed a tooth-specific difference, as it presented no significant difference ($P = 0.25$) at the site of the first molar but was significantly increased ($P = 0.01$) at the incisor. The results of Guo et al (Guo, et al.2017) study are similar to the results of the present study, with the difference that in Guo et al (Guo, et al.2017) study, all age groups are considered, but in the present study, only children were examined. From other observed, it can be seen that levels changes of periodontal pathogens are more common in children than in adults.

CONCLUSION

The present systematic review and met analysis showed the levels of periodontal pathogens in children during orthodontic treatments was increased after orthodontic treatments vs before orthodontic treatments. Only no change in P.gingivalis was observed. One of the limitations of the present study is the lack of high quality RCT studies, as well observation times of the included studies were relatively short. Only one study examining Consequences of orthodontic treatment in malocclusion children was found, that results are not complete for review. In the future, randomized clinical trial studies with higher sample sizes and class of malocclusion will be proposed.

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