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Is there a safe dental plaque index to prevent periodontal diseases related to plaque? A systematic review and meta-analysis.

Existe um índice de placa ideal para prevenir as doenças periodontais relacionadas à placa? Revisão sistemática e metanálise.

¿Existe un índice de placa dental seguro para prevenir la enfermedad periodontal relacionada con la placa? Revisión Sistemática y metanálisis.

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Abstract
Periodontitis is a chronic multifactorial inflammatory disease associated with a dysbiotic biofilm and characterized by progressive destruction of the tooth-supporting apparatus. This systematic review aimed to establish the quantitative association between dental plaque index and plaque-induced periodontal outcomes, as well as, clinical plaque index (PI) cut-off points. MEDLINE electronic searches were performed with at least two outcomes (healthy, G or P). 124 articles met the eligibility criteria and were included in meta-analysis. Healthy (H) group had a PI three times lower than G group (ROM 3.21; 95% CI 2.35-4.39) and P group (ROM 3.34; 95% CI 2.97-3.76); P group had 32% higher PI than G group (ROM 1.32; 95% CI 1.15-1.50). The meta-analyses of different PI (Silness and Löe, PI-SL; and percentage of faces, PI-%), PI-SL H group (MRAW 0.52) differed from G group (MRAW 1.58) and P group (MRAW 1.83) although it was not possible to distinguish the G group (95% CI 1.28-1.89) from the P group (95% CI 1.67-1.98). This was also observed in the PI-% (MRAW 22% H, MRAW 68% G and P group). PI was able to distinguish periodontal health individuals from whom with periodontal conditions associated with plaque. This systematic review proposes the following PI values cutoff points: H group lower than 0.7 (PI-SL), 30% (PI-%); G group 0.7 to 1.6 (PI-SL) or 31% to 60% (PI-%); and P group up to 1.6 (PI-SL) or 60% (PI-%). The results have clinical application on health promotion and disease prevention through population-based interventions.
Keywords: Dental plaque index; Gingivitis; Chronic periodontitis; Systematic review; Health promotion.

Resumo
Periodontite é uma doença inflamatória crônica multifatorial, associada ao biofilme disbiótico e caracterizada pela destruição progressiva da estrutura de suporte dental. O objetivo dessa revisão sistemática foi estabelecer a associação quantitativa entre o índice de placa e os diferentes desfechos periodontais associados à placa, assim como estabelecer os pontos de corte do índice de placa (IP). Foram realizadas buscas eletrônicas no Medline com pelo menos dois desfechos periodontais (saudável - H, gengivite - G e periodontite - P). 124 estudos foram incluídos. O grupo H apresentou um IP três vezes menor que o G (ROM 3.21; IC95% 2.35-4.39) e o grupo P (ROM 3.34; IC95% 2.97-

3.76). P teve um IP 32 % maior que o grupo G (ROM 1.32; IC95 %: 1.15-1.50). Nas meta-análises dos diferentes IP (Silness & Löe, PI-SL e porcentagem de faces, PI-%), o grupo IP-SL H (MRAW=0.52) diferenciou-se dos grupos G (MRAW=1.58) e P (MRAW=1.83), porém não foi possível distinguir os grupos G (IC95% 1.28-1.89) e P (IC95% 1.67-1.98). O mesmo foi observado no IP-% (grupo H MRAW=22%, MRAW=68% grupos G e P). O IP foi capaz de distinguir os desfechos sem doença e com doença periodontal associada a placa, propondo os seguintes pontos de corte: IP grupo H inferior a 0,7 ou 30 %; grupo G entre 0,7 e 1,6 ou 31% e 60%; e grupo P maior que 1,6 ou 60%. Esses resultados permitem a aplicação clínica na promoção da saúde e prevenção da doença periodontal através de intervenções de base populacional.
Palavras-chave: Índice de placa dentária; Gengivite; Periodontite crônica; Revisão sistemática; Promoção da saúde.

Resumen
Periodontitis es una enfermedad inflamatoria crónica multifactorial asociada a biopelícula disbiótica y caracterizada por la destrucción progresiva de las estructuras de soporte dental. Esta revisión sistemática tuvo como objetivo establecer la asociación cuantitativa entre el índice de placa y los resultados periodontales inducidos por la placa, así como los puntos de corte del índice de placa (IP). Se realizaron búsquedas electrónicas en MEDLINE, con al menos dos resultados (salud – H, gingivitis – G o periodontitis –P group). 124 se incluyeron en la metanálisis. El grupo H tuvo un IP tres veces menor que G (ROM 3.21; IC95% 2.35-4.39) y grupo P (ROM 3.34; IC95% 2.97-3.76). P tuvo un IP 32 % más alto que G (ROM 1.32; IC95 %: 1.15-1.50). Em las metanálisis de diferentes IP (Silness y Löe, PI-SL; y porcentaje de rostros, PI-%), grupo IP-SL H (MRAW=0.52) diferían del G (MRAW=1.58) y grupo P (MRAW=1.83) aunque no fue posible distinguir G (IC95% 1.28-1.89) del grupo P (IC95% 1.67-1.98). El mismo observó en el IP-% (grupo H MRAW=22%, MRAW=68% grupos G y P). IP pudo distinguir a los individuos con buena salud periodontal de los que tenían condiciones periodontales. Esta revisión sistemática propone los siguientes puntos de corte: grupo H inferior a 0,7 (PI-SL), 30 % (PI-%); grupo G 0,7 a 1,6 (PI-SL) o 31% a 60% (PI-%); y grupo P hasta 1,6 (PI-SL) o 60% (PI-%). Los resultados tienen aplicación clínica en la promoción de la salud y la prevención de enfermedades a través de intervenciones basadas en la población.
Palabras clave: Índice de placa dental; Gingivitis; Periodontitis crónica; Revisión sistemática; Promoción de la salud.

1. Introduction

Periodontal diseases and caries are highly prevalent worldwide. Both, cause tooth loss, are preventable and remains a major public health problem. Although both diseases are multifactorial, the dental biofilm is a major biological determinant common to the development of the two diseases. Thus, prevention and management of caries and periodontal diseases is based on biofilm removal through self-performed dental plaque control (van der Weijden & Hioe, 2005). Periodontitis is characterized by microbial-associated, host-mediated inflammation that results in loss of periodontal attachment. The bacterial biofilm initiates gingival inflammation; however, periodontitis initiation and progression depend on dysbiotic ecological changes (Tonetti *et al.*, 2018). Gingivitis is an inflammatory condition, site-specific and caused due to the accumulation of dental biofilm. It is characterized by edema and gingival redness, without loss of attachment. When compared to periodontitis, plaque-induced gingivitis is completely reversible once the dental biofilm is removed and adequate hygiene measures are implemented (Trombelli *et al.*, 2018).

Plaque quantification indices are frequently used to measure oral hygiene and there are several techniques to assess the amount of dental biofilm. The Visible Plaque Index (PI-%) was proposed by Ainamo and Bay (1975) to assess the quality of oral hygiene through clinical observation of the presence of biofilm on dental surfaces by means of simple categorical definitions (presence or absence of plaque). The measurement of the state of oral hygiene by Silness and Löe (1964) (PI-SL) is given a score from 0-3 according presence both soft debris and mineralized deposits.

Careful diagnosis, elimination of the causes and reduction of modifiable risk factors are paramount for successful prevention and treatment of periodontitis, periodontal evaluation, treatment and maintenance therapy should analyze the following: (a) presence of dental biofilm; (b) presence of periodontal destruction; (c) clinical history (anamnesis); and (d) presence of systemic conditions (modifying factors of periodontal disease) (Kwon *et al.*, 2021).

Given the lack of a quantitative investigation focused on dental plaque index (PI) and periodontal diseases, this systematic review aims to establish the relationship between the amount of dental biofilm (represented and clinically measured

through plaque index), and the periodontal condition (healthy, gingivitis and periodontitis) in adult individuals without interference from other periodontal disease modifying factors.

2. Methodology

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA 2020 Statement) guidelines for conducting a meta-analysis were followed and the study was registered in the PROSPERO database under protocol code CRD42020180333.

The current review addresses clearly a focused question by using the participant, exposure, comparison, and outcomes (PECO) criteria (Richardson *et al.*, 1995). The guiding question was "Is there a quantitative relationship between dental plaque index and periodontal condition in adults?" The exposure was PI, comparator were, another periodontal parameter; outcomes were periodontal health (H), gingivitis (G) and periodontitis (P).

Studies were identified from Medline database, searched from May 2020 to May 2021, using standardized methodological filters. Search strategies were mainly constructed based on the primary objective with two domains (i.e. periodontitis OR gingivitis), AND ('dental plaque' OR 'plaque index' OR 'oral hygiene index' OR 'plaque score'). A filter was used to include only adult studies. No restrictions were made on language or design of the study. Only studies after 1999 Consensus Classification of Periodontal Diseases were included.

Titles, abstracts, and full text were independently analyzed for eligibility by two review authors (C.L.A. and L.R.V.S.), and in case of disagreement between them, a third reviewer was consulted to make the final decision (C.G.A).

Eligibility Criteria

Studies were selected based on the PECO question including periodontal disease, gingivitis, oral hygiene, oral health and oral effects. The exclusion criteria applied in the full-text analysis were studies including under 18 years old, smokers, and other comorbidities, studies without at least two groups data (healthy, gingivitis or periodontitis) and two different index. The severity of gingival inflammation (represented and measured clinically by the gingival index, GI, and bleeding on probing, BOP) and the amount of periodontal breakdown (represented by probing of depth, PD and clinical attachment level, CAL); will be also evaluated, considering that they are the benchmark diagnostic parameters of periodontal disease.

Studies about periodontal diseases unrelated to dental biofilm (rapid progression periodontitis, acute periodontitis, juvenile periodontitis, necrotizing periodontitis and drug-induced gingival hyperplasia) and studies with conditions that could interfere with plaque index (dental implants, orthodontic appliance, dental prosthesis and root caries), were also excluded.

Data Extraction

To summarize the main findings, the following data were extracted from the included articles: authors and year, country, study design, characteristics of the sample (size, age, sex, statistical unit, examiner and study group); evaluation method (from periodontitis, gingivitis and healthy diagnosis; PI and GI technique), and results (periodontitis group, gingivitis group and control group for PI, GI, BOP, PD and CAL).

The data showed as median, interquartile range or minimum and maximum; were transformed to mean and standard deviation following the recommendations of Wan *et al.* (2014) and Hozo *et al.* (2005). It was used the average of the deviations from each outcome, in case of standard deviation non-availability. In longitudinal studies, only baseline data was collected.

Risk of Bias Assessment

Predefined templates based on the Cochrane approach were used to assess the risk of bias in the included studies. The bias was assessed using ROBINS-E (Risk Of Bias In Non-randomized Studies of Exposures) for observational studies, whereas ROBINS-I (Risk Of Bias In Non-randomized Studies of Interventions) for intervention studies; which considers seven domains for one overall bias.

The assessment tools were piloted and tested, and the risk of bias of the first 3 included studies was assessed by 2 independent researchers (C.L.A. and L.R.V.S) to ensure consistency and quality. One researcher (C.L.A.) evaluated the risk of bias of the other studies. Discrepancies in the assessment were resolved by a third researcher (C.G.A).

Data Analysis

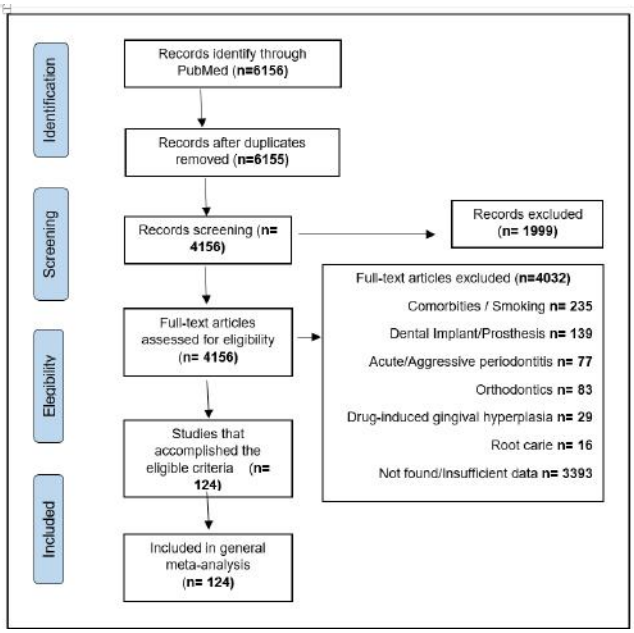
The meta-analysis were performed using RStudio software (meta package version 4.9-6) and evaluated according to the effect of the random model, to better distribute the weight between the studies and adjust to the normal sample distribution (Borenstein *et al.*, 2010). Meta-regression subgroup analysis was performed to explore a potential source of heterogeneity in the general meta-analysis model.

The meta-analysis to assess the relationship between PI and outcome was performed based on the ratio of means between the two different outcomes. For PI evaluation with more than five studies, a meta-analysis was also performed, using means and standard deviations for each outcome; in order to assess the possible relationship between periodontal condition and different types of PI. Similarly, for other periodontal parameters, were used the values of means and standard deviations for each outcome.

3. Results

The initial search retrieved 6,156 articles. After screening titles and abstracts, 4,156 were selected for further assessment. After full-text examination, 124 articles fulfilled the inclusion criteria and were included in the systematic review and quantitative/qualitative synthesis (Figure 1), representing a total of 6,157 individuals.

Figure 1. Flow diagram selection process for studies included in this systematic review and meta-analysis.



Source: The Authors.

Of the 124 studies included (table 1), 81 were cross-sectional, 39 interventional and 4 longitudinal. The studies have been conducted in 22 different countries, with the majority conducted in Turkey (n=48). Most studies aimed to periodontal diagnose (73%) mainly related to salivary and gingival crevicular fluid biomarkers, 25% (n=31) periodontal treatment effects and 2% (n=2) periodontal diseases prevention. Sample size ranged from 11 to 227. The age of individuals in the studies ranged from 18 to 75 years. The most used measures of periodontal disease were PD (n = 110), CAL (n = 97), BOP (n = 62), and Löe and Silness gingival index (1963) (GI-LS) (n = 67). The most used plaque indexes PI-SL (n= 77), PI-% (n= 25), and Quigley-Hein (1962) (Türkoğlu *et al.*,2009 ; Türkoğlu *et al.*,2010*;* Türkoğlu *et al.*,2011*;* Becerik *et al.*,2011*;* Eren *et al.*,2016).

One study used the simplified oral hygiene index of Greene and Vermillion (1964) (Surna *et al.*, 2009), two studies were Quigley-Hein modified by Turesky *et al* (1970) (Teles *et al.*, 2012; Becerik *et al.*,*2017*) and 14 studies did not describe the plaque index method (Özmeriç *et al.*, 2000; Mariggio *et al.*,2001; Pinho *et al.*,2009*;* Chen *et al.*, 2010*;* Qi *et al.*, 2013*;* Deepika & Saxena, 2013*;* Banu *et al.*, 2015*;* Roberts *et al.*, 2015*;* Muthu *et al.*, 2015*;* To *et al.*, 2015*;* Ishizuka *et al.*, 2017*;* Mahajani *et al.*, 2017; Balci Yuce *et al.*, 2018; Laddha *et al.*, 2018). Half of the studies carried out a full mouth analysis for PI evaluation, 29 evaluated only some teeth (index teeth) and 33 did not present information on the number of teeth analyzed. Only six studies used the site, not the patient, as the unit of analysis (To *et al.*, 2015*;* Ishizuka *et al.*, 2017*;* Vinayak & VandanaIndian, 2007*;* Fujita *et al.*, 2012*;* Khongkhunthian *et al.*, 2014*;* Chen *et al.*, 2016). Most studies (n = 111) had a low or moderate risk of bias; 13 studies were serious or critical risk of bias (Türkoğlu *et al.*,2011*;* Pinho *et al.*,2009*;* Laddha *et al.*, 2018; Vinayak & VandanaIndian, 2007*;* Buduneli *et al.*, 2006; Tamaki *et al.*, 2009; Konopka *et al.*, 2012; Akpinar *et al.*, 2013; Gokhale *et al.*, 2013; Gokhale *et al.*, 2014; Jaradat *et al.*, 2013; Özdemir *et al.*, 2016; Gamel *et al.*, 2017). 108 studies described data collection through a calibrated examiner or a periodontist, 16 studies there was no information about the examiner (Surna *et al.*, 2009; Özmeriç *et al.*, 2000; Mariggio *et al.*,2001*;* Roberts *et al.*, 2015*;* Fujita *et al.*, 2012; Tamaki *et al.*, 2009; Kerdvongbundit *et al.*, 2003; Airila-Mansson *et al.*, 2005; Pejcic *et al.*, 2012; Swaminathan *et al.*, 2013; Wang *et al.*, 2013; Özcan *et al.*, 2015; Haytural *et al.*, 2015; Cifcibasi *et al.*, 2015; Lihala *et al.*, 2019; Gharbi *et al.*, 2019).

The comparison between P group also have a significant higher PI than H group (ROM 3.34; 95% CI 2.97-3.76; p<0.0001), as shown in figure 2. The combined estimates of the association between PI and the groups H and G are presented in figure 3 (ROM 3.21; 95% CI 2.35-4.39; p=0). High heterogeneity was found on both meta-analysis, so the random model was used. For the periodontitis outcome, G group had 32% higher PI than P group (ROM 1.32; 95% CI 1.15-1.50; p<0.01) (Türkoğlu *et al.*,2009 ; Türkoğlu *et al.*,2010*;* Becerik *et al.*,2011*;* Surna *et al.*, 2009; Becerik *et al.*, 2017*;* Khongkhunthian *et al.*, 2014*;* Gokhale *et al.*, 2013; Özcan *et al.*, 2015; Lihala *et al.*, 2019; Zheng *et al.*, 2006; Ay *et al.*, 2012; Pereira *et al.*, 2013; Papathanasiou *et al.*, 2014; Keles *et al.*, 2014; Khongkhunthian *et al.*, 2013; Kurşunlu *et al.*, 2015; Hendek *et al.*, 2015; Köseoğlu *et al.*, 2015; Atabay *et al.*, 2017; Öztürk *et al.*, 2016; Martinez *et al.*, 2017; Wei *et al.*, 2004; Tezel *et al.*, 2005; Emingil G *et al.*, 2006; İlgenli *et al.*, 2006; Ertugrul *et al.*, 2013a; Yang *et al.*, 2018; Nimcharoen *et al.*, 2019; Taşdemir *et al.*, 2020; Ertugrul *et al.*, 2013b).

The analysis revealed significant heterogeneity across studies. According to the adjusted meta-regression analysis, periodontal condition explained 71% (p <0.001) of the global heterogeneity. Despite that, the remaining heterogeneity could not be explained by the explored covariates (study design, objective and number of teeth evaluated), therefore the model has not been able to reduce heterogeneity or fully explain it.

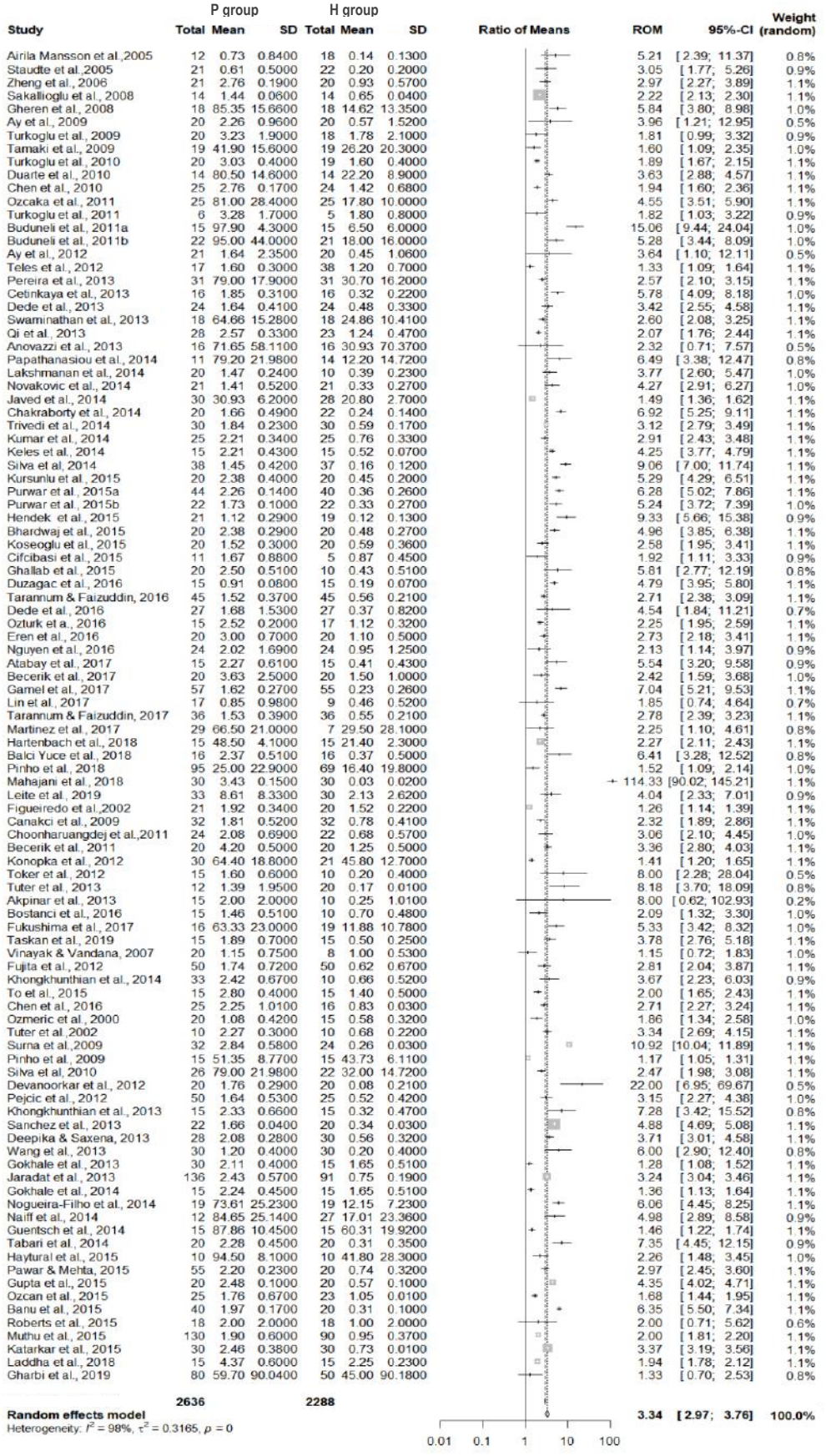
Regarding the number of teeth in PI evaluation, half of the studies used full-mouth analysis, 29 partial examination (index teeth) and for 33 studies the type of examination were not available. Some studies (n=16) presented both types of teeth examination (full-mouth and parcial) and were included in meta-analysis the PI data of all groups presented (H, G and/or P). The result for the random effect model (ROM 0.97; 95% CI 0.87-1.08) showed that even with combined studies (p=0.56) and by groups (p = 0.24), there are no significantly difference between the two types of examination.

Table 1. Overview of the studies included in the systematic review (n=124).

Autor, Year	Objective/ Study Design	Data Collection	Diagnose Criteria	Autor, Year	Objective/ Study Design	Data Collection	Diagnose Criteria
Airila-Mansson et al.,2005	D/L	FM	PD	Kursunlu et al., 2015	D/C	FM/ST	PD/GI/RAL/CAL/AL
Akalin et al., 2005	D/C	ST	1999 Classification	Kurtis et al., 2005	D/C	ST	PD
Akpinar et al., 2013	T/I	ST	PD/GI/CAL	Laddha et al., 2018	D/C	NI	NI
Anovazzi et al., 2013	T/I	FM/ST	PD/GI/CAL	Lakshmanan et al., 2014	D/C	FM/ST	1999 Classification
Atabay et al., 2017	D/C	FM/ST	PD/GI/CAL/AL	Leite et al., 2019	T/I	FM/ST	OH/GI/PD/CAL
Ay et al., 2009	D/C	FM/ST	PD/CAL/RAL	Lihala et al., 2019	T/I	NI	GI/CAL
Ay et al., 2012	D/C	FM/ST	1999 Classification	Lin et al., 2017	D/C	FM/ST	PD/CAL
Balci Yuce et al., 2018	D/C	FM/ST	1999 Classification	Mahajani et al., 2018	T/I	FM/ST	PD/GI/RAL/CAL
Baltacıoğlu et al., 2014a	D/C	ST	OH/GI/PD/CAL/AL	Mariggio et al.,2001	D/C	ST	NI
Baltacıoğlu et al., 2014b	D/C	FM/ST	OH/GI/PD/CAL/AL	Martinez et al., 2017	D/I	FM/ST	GI/AL/CAL
Banu et al., 2015	D/C	NI	1999 Classification	Muthu et al., 2015	T/I	NI	PD/GI/RAL/CAL
Becerik et al., 2011	D/C	FM/ST	PD/GI/CAL	Naiff et al., 2014	D/C	NI	PD/GI/RAL/CAL
Becerik et al., 2017	D/C	ST	PD/GI/CAL	Nguyen et al., 2016	D/C	FM/ST	OH/GI/PD/CAL
Bhardwaj et al., 2015	T/I	FM/ST	1999 Classification	Nimcharoen et al., 2019	T/I	FM/ST	PD/GI/RAL/CAL
Bostanci et al., 2014	T/I	ST	PD/GI/CAL	Nogueira-Filho et al.,	D/C	NI	PD/GI/CAL
Bostanci et al., 2016	T/I	ST	PD/GI/AL	Novakovic et al., 2014	T/I	FM/ST	PD/GI/AL
Buduneli et al., 2006	D/I	FM/ST	1999 Classification	Özcaka et al., 2011	D/C	FM/ST	PD/CAL/AL
Buduneli et al., 2011a	D/C	FM/ST	PD/GI/CAL/AL	Özcan et al., 2015	D/C	NI	PD, GI
Buduneli et al., 2011b	D/C	FM/ST	PD/GI/CAL/AL	Özdemir et al., 2016	D/C	FM/ST	PD/GI/AL
Canakci et al., 2009	D/C	ST	OH/GI/PD/AL	Özmeric et al., 2000	D/C	NI	PD
Cetinkaya et al., 2013	D/C	FM/ST	PD/GI/CAL/AL	Öztürk et a., 2016	D/C	FM/ST	PD/GI/RAL/CAL
Chakraborty et al., 2014	T/I	FM/ST	PD/GI/AL	Papathanasiou et al.,	D/C	FM/ST	PD/GI/CAL/AL
Chen et al., 2010	D/C	FM/ST	PD/GI/AL	Pawar & Mehta, 2015	D/I	NI	1999 Classification
Chen et al., 2016	D/C	STS	PD/GI/RAL/CAL	Peicic et al., 2012	D/C	NI	PD/GI/RAL/CAL
Choonharuangdej et al.,2011	D/C	ST	1999 Classification	Pereira et al., 2013	D/C	FM/ST	PD/GI/RAL/CAL/AL
Cifcibasi et al., 2015	D/C	FM/ST	1999 Classification	Pinho et al., 2009	D/I	NI	PD/CAL
Dede et al., 2013	T/I	FM/ST	OH/GI/PD/CAL	Pinho et al., 2018	D/L	FM/ST	1999 Classification
Dede et al., 2016	T/I	FM/ST	PD/GI/RAL/AL	Purwar et al., 2015a	D/C	FM/ST	OH/GI/PD/CAL/AL
Deepika & Saxena, 2013	D/L	NI	PD/GI/CAL/AL	Purwar et al., 2015b	T/I	FM/ST	1999 Classification
Devanoorkar et al., 2012	T/I	NI	PD/GI/RAL/CAL	Qi et al., 2013	D/C	FM/ST	PD/CAL/RAL
Duarte et al., 2010	T/I	FM/ST	PD/GI/RAL/CAL	Roberts et al., 2015	T/I	NI	PD/GI/RAL/AL
Duzagac et al., 2016	T/I	FM/ST	PD/GI/RAL/CAL	Sakallıoğlu et al., 2008	D/C	FM/ST	GI/CAL
Emingil et al., 2006	D/C	ST	PD/GI/RAL/CAL/AL	Sánchez et al., 2013	D/I	NI	Page & Eke (2007)
Eren et al., 2016	D/C	FM/ST	PD/GI/RAL/CAL	Silva et al, 2010	D/C	NI	PD/CAL
Ertugrul et al., 2013a	D/C	FM/ST	PD/GI/RAL/CAL	Silva et al, 2014	T/I	FM/ST	PD/GI/CAL
Ertugrul et al., 2013b	D/C	NI	PD/GI/CAL	Staudte et al.,2005	P/I	FM/ST	NI
Figueiredo et al.,2002	D/C	ST	PD	Surna et al.,2009	D/C	NI	1999 Classification
Fujita et al., 2012	D/C	STS	PD/GI/CAL	Swaminathan et al., 2013	D/C	FM/ST	AL/CAL
Fukushima et al., 2017	D/I	ST	GI//CAL/AL	Tabari et al., 2014	D/C	NI	PD/GI/CAL/AL
Gamel et al., 2017	D/C	FM/ST	1999 Classification	Tamaki et al., 2009	T/I	FM/ST	OH/GI/PD/CAL
Ghallab et al., 2015	D/C	FM/ST	OH/GI/PD/CAL/AL	Tarannum & Faizuddin,	D/C	FM/ST	PD/GI/CAL
Gharbi et al., 2019	D/C	NI	PD/CAL/AL	Tarannum & Faizuddin,	D/C	FM/ST	PD/GI/CAL
Gheren et al., 2008	D/I	FM/ST	PD/CAL	Tasdemir et al., 2020	D/C	ST	1999 Classification
Gokhale et al., 2013	P/I	NI	PD/GI/CAL	Taskan et al., 2019	D/C	ST	2017 Classification
Gokhale et al., 2014	D/C	NI	PD/GI/CAL	Teles et al., 2012	D/L	FM/ST	PD/GI/CAL
Guentsch et al., 2014	T/I	NI	PD/CAL	Tezel et al., 2005	T/I	NI	GI//CAL/RAL
Gupta et al., 2015	D/C	NI	PD/CAL	To et al., 2015	D/C	STS	1999 Classification
Hartenbach et al., 2018	T/I	FM/ST	PD/GI/CAL	Toker et a., 2012	T/I	ST	PD/GI/RAL/CAL
Haytural et al., 2015	D/C	NI	PD/GI/CAL	Toyman et al., 2015	D/C	ST	PD/GI/CAL
Hendek et al., 2015	D/C	FM/ST	1999 Classification	Tripathi et al., 2018	D/C	NI	PD/CAL
İlgenli et al., 2006	D/C	ST	PD/GI/RAL/CAL/AL	Trivedi et al., 2014	D/C	FM/ST	PD/GI/CAL/AL
Ishizuka et al., 2017	D/C	STS	PD, GI	Türkoğlu et al., 2009	D/C	FM/ST	PD/GI/RAL/CAL
Jaradat et al., 2013	D/C	NI	PD/GI/RAL/AL	Türkoğlu et al., 2010	D/C	FM/ST	PD/GI/CAL/AL
Javed et al., 2014	D/C	FM/ST	PD/GI/CAL	Türkoğlu et al., 2011	D/C	FM/ST	PD/CAL
Katarkar et al., 2015	D/C	NI	1999 Classification	Tüter et al., 2002	T/I	NI	PD
Keles et al., 2014	D/C	FM/ST	PD/GI/RAL/CAL/AL	Tüter et al., 2013	T/I	ST	1999 Classification
Kerdvongbundit et al.,2003	T/I	ST	NI	Vinayak & Vandana,	D/C	STS	PD/GI/CAL
Khongkhunthian et al., 2013	D/C	NI	1999 Classification	Wang et al., 2013	D/C	NI	PD/CAL/RAL/AL
Khongkhunthian et al., 2014	D/C	STS	GI//CAL/AL	Wei et al., 2004	D/C	ST	PD/GI/AL
Konopka et al., 2012	T/I	ST	1999 Classification	Wei et al.,2010	T/I	NI	PD/GI/AL
Köseoğlu et al., 2015	D/C	FM/ST	PD/GI/CAL/AL	Yang et al., 2018	D/C	ST	1999 Classification
Kumar et al., 2014	P/C	FM/ST	AL/CAL	Zheng et al., 2006	D/C	FM/ST	PD/GI/RAL/CAL

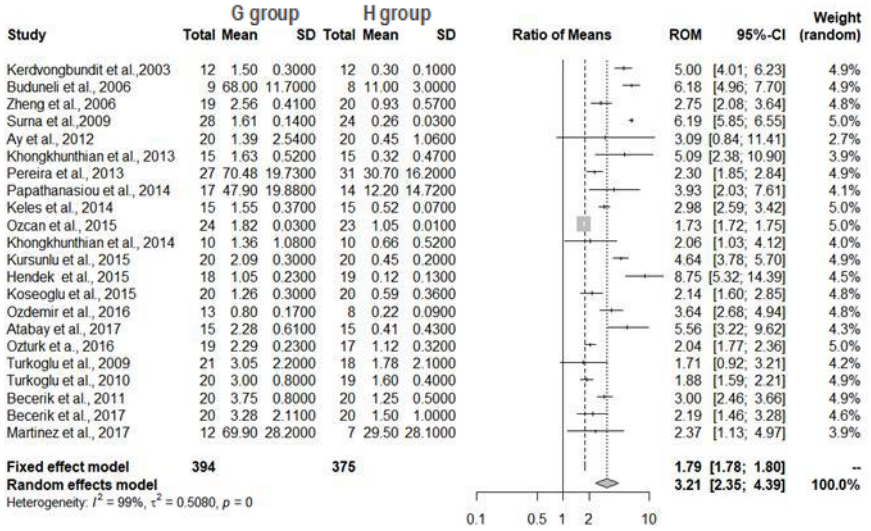
Legends: AL=attachment loss, C=cross-sectional, CAL=clinical attachment level, D=diagnosis, FM=full-mouth, GI=gingival index, I=intervention, L=longitudinal, NI=not informed, OH=oral hygiene, PD=probing depth, PR=prevention, RAL= radiographic alveolar bone loss, ST=partial teeth, STS=partial teeth site, T=treatment. Source: The Authors.

Figure 2. Meta-analysis evaluation and forest plot showing the ratio of mean of all included studies with plaque index for H and P group (n =101).



Source: The Authors.

Figure 3. Meta-analysis evaluation and forest plot showing the ratio of mean of all included studies with plaque index for H and G group (n =22).



Source: The Authors.

Concerning to PI-SL (n=158), H group (n=60; MRAW 0.52; 95% CI 0.42-0.63) differed from G group (n=23; MRAW 1.58; 95% CI 1.28-1.89) and P group (n=75; MRAW 1.83; 95% CI 1.67-1.98), although it was not possible to distinguish the G from the P group, due to the intersecting confidence intervals. The same findings were observed in the PI-% (n=51: H=23, G=5 and P=23) meta-analysis, there were dissociations between H group and G and P group, as well as, intersecting confidence intervals between G and P group. The meta-analysis of the periodontal indexes showed that the only PD was able to distinguish all periodontal condition (H: MRAW 1.73, 95% CI 1.51–1.95; G: MRAW 2.22, 95% CI 2.05–2.40, and P: MRAW 4.49, 95% CI 4.28–4.71). The GI-LS and BOP, similarly to PI, only dissociate H group from G and P groups, with intersecting confidence intervals between G and P group. Otherwise, for CAL, the P group (MRAW 5.04, 95% CI 4.72–5.35) was distinguished from H (MRAW 1.25, 95% CI 1.12–1.37) and G (MRAW 1.32, 95% CI 0.83–1.82) groups (Table 2).

Table 2. Evaluated indexes meta-analysis and periodontal outcomes.

		PI-SL (n = 158)	PI-% (n = 51)	GI-LS (n=144)	BOP (%) (n=129)	PD (mm) (n=236)	CAL (mm) (n=183)
H group	n	60	23	57	53	103	65
	MRAW	0.52 [c]	22.4 [c]	0.34 [c]	5.25 [c]	1.73 [c]	1.25 [c]
	95% CI	0.42-0.63	14.8-30.0	0.29–0.40	4.42–6.08	1.51–1.95	1.12–1.37
G group	n	23	5	17	16	27	22
	MRAW [a]	1.58 [c]	68.5 [c]	1.47 [c]	47.41 [c]	2.22 [c]	1.32 [c]
	95% CI	1.28-1.89	56.9-80.2	1.14–1.81	33.97–60.86	2.05–2.40	0.83–1.82
P group	n	75	23	70	60	106	96
	MRAW	1.83 [c]	68.4 [c]	1.86 [c]	62.10 [c]	4.49 [c]	5.04 [c]
	95% CI	1.67-1.98	61.9-74.9	1.77–1.94	60.64–63.56	4.28–4.71	4.72–5.35

Legend: [c] = p<0.01., n = sample, MRAW = Untransformed raw mean, CI = confidence interval, BOP = bleeding on probing, PD = probing depth, CAL = clinical attachment level. Source: The Authors.

4. Discussion

Our systematic review summarizes the evidence of the quantitative association of dental plaque index with periodontal conditions associated with plaque. The meta-analysis showed that there is a tendency that higher PI correspond to a progressive periodontal breakdown. In the meta-analysis of the different PI type, this progressive association was also demonstrated in PI-SL. Despite that, regardless of the index used, we were not able to distinguish G group from P group.

The search strategy was developed to be extensive and, as expected, resulted in a large number of studies. The intention was to select the largest number of data to improve the validation of the results obtained. Systematic searching limited to PubMed could be not sufficient to identify all relevant references, however the amount of included studies in meta-analysis was substantial. Besides that, some studies indicate that the gains from searching sources beyond others databases are modest (van Enst *et al.*, 2014; Rice *et al.*, 2016) and the expected number of relevant studies was big enough (Halladay *et al.*, 2015).

In order to reduce bias of confounding, selected studies did not include smoking and comorbidities since there is sufficient evidence to suggest that periodontal disease and systemic health have a two-way relationship (Tonetti *et al., 2018*; Hegde & Awan, 2019; Bascones-Martínez *et al.*, 2009) and smoking was associated with periodontitis and its severity (Tonetti *et al., 2018*; Goel *et al.*, 2021; Genco & Borgnakke, 2013). In addition, non-plaque induced gingival and periodontal diseases and conditions were also excluded, based on primary etiology (Tonetti *et al., 2018*; Armitage, 1999).

The variables that could explain heterogeneity can be divided in (1) related to design and (2) related to the study population (Delgado-Rodríguez & Sillero-Arenas, 2018). It was possible a study objective and design interference, that does not were observed in the meta-regression analysis. Further studies may consider improving the study design by including larger sample size and longer follow-up (6 months or more), with at least a control group and a disease group outcome, in order to identify the eventual plaque accumulation pattern even introducing hygiene instructions.

Due to the individual characteristics of the different studies and populations studied, a high level of heterogeneity could be expected in a meta-analysis of observational studies (Sutton *et al.*, 2000). For this reason, we used random models, which produced broader confidence intervals and the inferences can be generalized for the set of studies from which the sample was obtained (Hedges & Vevea, 1998). Subgroup analysis was also used to explore heterogeneity. Despite that, as the prevalence studies involve several peculiarities because of the population itself (Gimenez *et al.*, 2016) the high level of heterogeneity could not be reduced in this systematic review.

The Classification of Periodontal Diseases is constantly evolving due to knowledge about physiopathology of periodontal diseases. Even though the criteria for periodontal classification differ among studies, we expect that possible diagnostic interferences would have the same contribution in all analyzed indexes. Furthermore, the purpose of this review is the determination of a clinically significant threshold, not to establish PI as a periodontal diagnosis method.

The ideal index should have a clear purpose; be intelligible; provide easily available data, with minimal modification, and understandable. It should reflect both the health problem and ability of the society to solve it, and also how society defines health (Larson, 1991). The PI methods have the advantages of being relatively easy to perform and requiring a minimum of time and equipment. However, there are disadvantages, including a lack of sensitivity, especially at the extremes of low and high amount of plaque. In addition, all of these methods are nonlinear, semi-quantitative, subjective and could be a reflection of the moment, not a pattern. Even that, PI has become the mainstay for use in studies that assess the efficacy of antiplaque agents (Scannapieco, 1995; Godard *et al.*, 2011).

Despite the primary etiological factor of periodontal damage is the host-mediated inflammatory and immune responses to the accumulation of microbial plaque and its diffusible enzymes, the lifestyle (unbalanced diet and smoking) along with bad oral hygiene, represent the main factors promoting the upset of the harmonious equilibrium of the oral

microbiome, especially in individuals with genetic and epigenetic susceptibility. Educating patients on a culture of oral prevention and using efficient plaque treatment strategies that maintain the natural diversity of resident microbiota should represent the main goals in the prevention and treatment of periodontal disease (Di Stefano *et al.*, 2022).

The effects of oral hygiene on periodontitis were analyzed by Lertpimonchai *et al.* (2017), through a systematic review and meta-analysis, suggesting a dose-response relationship between oral hygiene and periodontitis, with a 2- to 5-fold increase in the risk of developing periodontitis in individuals with reasonable and poor oral hygiene, respectively compared to those with good hygiene. Hygiene was assessed through a categorization common to other studies, in which PI greater than 2 was classified as poor and PI between 1 and 2, reasonable. Considering these values, the P group' PI-SL of 1.83 (CI = 1.67 - 1.98), could be classified as values corresponding to reasonable hygiene. In addition, considering this review, an IP-SL up to 0.7 can be classified as good oral hygiene, from 0.7 to 1.6 reasonable and above 1.6 should be considered as poor.

Regarding periodontal disease progression, Haffajee *et al.* (1991) found that the plaque level was strongly associated with risk of periodontal attachment loss. Using predictive analysis techniques, they proposed the following: a PI from 0% to 50% low risk of attachment loss (adequate hygiene), PI from 51% to 75% medium risk (poor hygiene) and PI from 76% to 100% high risk (inadequate hygiene). Using the values obtained in this meta-analysis: (1) the H group PI-% ≤30%; (2) G group with PI-% between 57% to 80% and; (3) P group PI-% of 62% to 75%. Based on the PI-% obtained in the meta-analysis, a PI below 30% represents adequate hygiene (or indicating health); from 31% to 60% poor hygiene (indicating gingivitis), and up to 61% we can classify it as inadequate hygiene (indicating periodontitis).

In a 24-year longitudinal study in Stockholm, poor oral hygiene, characterized by plaque accumulation, was also associated with an increase in premature death from cancer (OR = 1.79). In that study, people who continued alive had an average of PI 0.67 (± 0.46) and people who died had 0.87 (± 0.62). Current mean PI-SL for H group was 0.52 (CI = 0.42 - 0.63), is in accordance with the study by Söder *et al.* (2012) which allowed us to conclude that maintaining a plaque index below 0.63 is effective to health promotion and preventing chronic diseases.

The present review has limitations that should be considered. Most of the included studies were cross-sectional, which could make a causal inference difficult. Besides that, visible plaque reflects the moment, could not necessarily reflect habit, but one's ability to remove plaque; in other words, individuals with gingivitis or periodontitis may not present visible plaque during the examination, which may influence the diagnosis. Added to the fact that (1) periodontal disease is multifactorial and not always keeping a plaque index below the recommended may be enough to prevent its development and; (2) most gingivitis does not progress to periodontitis. Nevertheless, gingivitis is a prerequisite for periodontitis, and managing gingivitis is a vital primary prevention strategy to prevent periodontitis (Chapple *et al.*, 2018).

Future randomized clinical trials, which include groups of individuals with disease and without periodontal disease in order to represent a real situation of the population, with plaque index data and periodontal parameters; should clarify this issue. Despite this, PI from longitudinal studies, depending on time interval, may indicate the intervention effect instead a pattern.

The meta-analysis found an association between PI and periodontal outcomes, whereas that association was not capable to quantitatively distinguish G from P group. The comparison with other periodontal parameters evaluated in this review resulted in: (1) only the PS was able to differentiate the three groups accurately; (2) IG-LS and BOP, as PI, can be used to differentiate healthy individuals from those with some periodontal disease (G or P) and; (3) CAL can distinguished periodontal disease from periodontal health or gingivitis. Taking into account, PI must be combined with other clinical parameters to perform differential diagnoses of gingivitis and periodontitis.

The strengths of this study are the inclusion of different age groups in 22 countries in all continents, leading to a global sample of 6,157 individuals. In addition, there was no restriction for language or year of publication and the high quality of the data included should ensure the validity of our findings.

5. Conclusion

This systematic review and meta-analysis found a three times fold increase in PI associated with disease groups (gingivitis and periodontitis), compared to healthy group. These results would raise awareness with regard to the dental plaque control, resulting in the reduction in health burden caused by periodontal diseases maintaining a plaque index below 0.7 or 30%. Public health policies, such as health promotion strategies, population-based health prevention strategies, and the development of technological devices focused on self-monitoring the PI, should be implemented.

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References

Ainamo J. & Bay I. (1975, December). Problems and proposals for recording gingivitis and plaque. Int Dent J. 25(4):229-35.

Airila-Mansson S., Soder B. & Klinge B. (2005). Bone height changes in individuals with periodontal disease: a 17-year prospective longitudinal study. Journal of Clinical Periodontology. 32(7):822-827.

Akalin F. A., Toklu E. & Renda N. (2005). Analysis of superoxide dismutase activity levels in gingiva and gingival crevicular fluid in patients with chronic periodontitis and periodontally healthy controls. Journal of Clinical Periodontology. 32(3):238-243.

Akpinar A., Toker H., Ozdemir H., Bostanci V. & Aydin H. (2013). The effects of non-surgical periodontal therapy on oxidant and anti-oxidant status in smokers with chronic periodontitis. Archives of Oral Biology. 58(6):717-723.

Anovazzi G., Finoti L. S, Corbi S. C. T., Kim Y. J., Marcaccini A. M., Gerlach R. F.,et al. (2013). Interleukin 4 haplotypes of susceptibility to chronic periodontitis are associated with IL-4 protein levels but not with clinical outcomes of periodontal therapy. Human Immunology. 74(12):1688-1695.

Armitage G. C. (1999, December). Development of a classification system for periodontal diseases and conditions. Ann Periodontol. 4(1):1-6.

Atabay V. E., Lutfioğlu M., Avci B., Sakallioglu E. E. & Aydoğdu A. (2017). Obesity and oxidative stress in patients with different periodontal status: a casecontrol study. Journal of Periodontal Research. 52(1): 51-60.

Ay Y. Z., Sütçü R., Uskun E., Bozkurt F. & Berker E. (2009). The impact of the IL-11:IL-17 ratio on the chronic periodontitis pathogenesis: a preliminary report. Oral Diseases. 15(1):93-99.

Ay Z. Y., Kırzıoğlu F. Y., Öztürk M. O., Sütçü R. & Kapucuoğlu N. (2012). The gingiva contains leptin and leptin receptor in health and disease. Odontology. 100(2):222-231.

Balci Yuce H., Karatas Ö., Tulu F., Altan A. & Gevrek F. (2018, October). Effect of diabetes on collagen metabolism and hypoxia in human gingival tissue: a stereological, histopathological, and immunohistochemical study. Biotechnic & Histochemistry. 65-73.

Baltacıoğlu E., Kehribar M. A., Yuva P., Alver A., Atagün Ö. S., Karabulut E. & Akalın F. A. (2014a). Total Oxidant Status and Bone Resorption Biomarkers in Serum and Gingival Crevicular Fluid of Patients With Periodontitis. Journal of Periodontology. 85(2):317-326.

Baltacıoğlu E., Yuva P., Aydın G., Alver A., Kahraman C., Karabulut E. & Akalın F. A. (2014b). Lipid Peroxidation Levels and Total Oxidant/Antioxidant Status in Serum and Saliva From Patients With Chronic and Aggressive Periodontitis. Oxidative Stress Index: A New Biomarker for Periodontal Disease? Journal of Periodontology. 85(10):1432-1441.

Banu S., Jabir N. R., Mohan R., Manjunath N. C., Kamal M. A., Vinod Kumar K. R., et al. (2015). Correlation of Toll-Like Receptor 4, Interleukin-18, Transaminases, and Uric Acid in Patients With Chronic Periodontitis and Healthy Adults. Journal of Periodontology. 86(3):431-439.

Bascones-Martínez A., Muñoz-Corcuera M. & Meurman J. H. (2009, December). Odontogenic infections in the etiology of infective endocarditis. Cardiovasc Hematol Disord Drug Targets. 9(4):231-5.

Becerik S., Afacan B., Oztürk V. O., Atmaca H. & Emingil G. (2011). Gingival crevicular fluid calprotectin, osteocalcin and cross-linked N-terminal telopeptid levels in health and different periodontal diseases. Dis Markers. 31(6):343-52.

Becerik S., Öztürk V. Ö., Celec P., Kamodyova N., Atilla G. & Emingil G. (2017, November). Gingival crevicular fluid and plasma oxidative stress markers and TGM-2 levels in chronic periodontitis. Archives of Oral Biology. 83:47-54.

Bhardwaj S., Prabhuji M. L. V. & Karthikeyan B. (2015). V. Effect of non-surgical periodontal therapy on plasma homocysteine levels in Indian population with chronic periodontitis: a pilot study. Journal of Clinical Periodontology. 42(3):221-227.

Borenstein M., Hedges L. V., Higgins J. P. & Rothstein H. R. (2010, April). A basic introduction to fixed-effect and random-effects models for meta-analysis. Res Synth Methods. 1(2):97-111.

Bostanci V., Toker H., Senel S., Ozdemir H. & Aydin H. (2014). Effect of Chronic Periodontitis on Serum and Gingival Crevicular Fluid Oxidant and Antioxidant Status in Patients With Familial Mediterranean Fever Before and After Periodontal Treatment. Journal of Periodontology. 85(5):706-712.

Bostanci V., Toker H., Senel S., Poyraz O., Akpinar A., Görgün E. P. & Bakar O. (2016). Evaluation of IL-1β, IL-1ra, and IL-10 levels and outcome of periodontal therapy in chronic periodontitis with familial Mediterranean fever. Clinical Oral Investigations. 21(1):469-475.

Buduneli N., Kardessler L., Issik H., Willis C. S., Hawkins S. I., Kinane D. F. & Scott D. A. (2006). Effects of smoking and gingival inflammation on salivary antioxidant capacity. Journal of Clinical Periodontology. 33(3):159-164.

Buduneli N., Larsson L., Bıyıkoğlu B., Renaud D. E., Bagaitkar J. & Scott D. A. (2011a). Fatty Acid Profiles in Smokers with Chronic Periodontitis. Journal of Dental Research. 90(1):47-52.

Buduneli N., Özçaka Ö. & Nalbantsoy A. (2011b). Salivary and Plasma Levels of Toll-Like Receptor 2 and Toll-Like Receptor 4 in Chronic Periodontitis. Journal of Periodontology. 82(6):878-884.

Çanakçi C. F., Çanakçi V., Tatar A., Eltas A., Sezer U., Çiçek Y. & Oztas S. (2009). Increased salivary level of 8-hydroxydeoxyguanosine is a marker of premature oxidative mitochondrial DNA damage in gingival tissue of patients with periodontitis. Archivum Immunologiae et Therapiae Experimentalis. 57(3):205-211.

Cetinkaya B., Guzeldemir E., Ogus E. & Bulut S. (2013). Proinflammatory and Anti-Inflammatory Cytokines in Gingival Crevicular Fluid and Serum of Patients With Rheumatoid Arthritis and Patients With Chronic Periodontitis. Journal of Periodontology. 84(1):84-93.

Chakraborty S., Tewari S., Sharma R. K. & Narula S. C. (2014). Effect of Non-Surgical Periodontal Therapy on Serum Ferritin Levels: An Interventional Study. Journal of Periodontology. 85(5):688-696.

Chapple I. L. C., Mealey B. L., Van Dyke T. E., Bartold P. M., Dommisch H., Eickholz P., et al. (2018, June). Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol. 89(Suppl 1):S74-S84.

Chen H., Zheng P., Zhu H., Zhu J., Zhao L., El Mokhtari N. E., et al. (2010). Platelet-activating factor levels of serum and gingival crevicular fluid in nonsmoking patients with periodontitis and/or coronary heart disease. Clinical Oral Investigations. 14(6):629-636.

Chen S. S., Wang K., Zhao J., Wu W. C., Wu Y. F. & Zhao L. (2016). Increased expression of triggering receptor expressed on myeloid cells 1 and 2 in inflamed human gingiva. Journal of Periodontal Research. 52(3): 512-521.

Choonharuangdej S., Chutinet A. & Kuphasuk Y. (2010). Crevicular Porphyromonas gingivalis-specific immunoglobulin A levels in healthy and periodontitisaffected Thai cohorts. Journal of Investigative and Clinical Dentistry. 2(1):43-50.

Cifcibasi E., Ciblak M., Kiran B., Badur S., Firatli E., Issever H. & Cintan S. (2015). The Role of Activated Cytotoxic T Cells in Etiopathogenesis of Periodontal Disease: Does It Harm or Does It Heal?. Scientific Reports. 5(1).

Dede O. F., Özden F. O. & Avcı B. (2013). 8-Hydroxy-Deoxyguanosine Levels in Gingival Crevicular Fluid and Saliva in Patients With Chronic Periodontitis After Initial Periodontal Treatment. Journal of Periodontology. 84(6):821-828.

Dede O. F., Balli U., Doğan B. Ş. & Güven B. (2016). Interleukin-32 levels in gingival crevicular fluid and saliva of patients with chronic periodontitis after periodontal treatment. Journal of Periodontal Research. 52(3):397-407.

Deepika P. C. R., & Saxena R.M. (2013, April). Comparison of glycosylated hemoglobin levels in severe periodontitis patients and healthy controls: a study in an Indian population. Quintessence Int. 44(4):319-25.

Delgado-Rodríguez M., & Sillero-Arenas M. (2018, October). Systematic review and meta-analysis. Med Intensiva (Engl Ed). 42(7):444-453.

Devanoorkar A., Dwarakanath C. D., Gundanavar G., Kathariya R. & Patil S. R. (2012). Evaluation of serum resistin levels in periodontal health and disease and effects of non surgical periodontal therapy on its levels. Dis Markers. 32(5):289-94.

Di Stefano M., Polizzi A., Santonocito S., Romano A., Lombardi T. & Isola G. (2022, May). Impact of Oral Microbiome in Periodontal Health and Periodontitis: A Critical Review on Prevention and Treatment. Int J Mol Sci. 5;23(9):5142.

Duarte, P. M., da Rocha M., Sampaio E., Mestnik M. J., Feres M., Figueiredo L. C., et al. (2010). Serum Levels of Cytokines in Subjects With Generalized Chronic and Aggressive Periodontitis Before and After Non-Surgical Periodontal Therapy: A Pilot Study. Journal of Periodontology. 81(7):1056-1063.

Duzagac E., Cifcibasi E., Erdem M. G., Karabey V., Kasali K., Badur S. & Cintan S. (2016). Is obesity associated with healing after non-surgical periodontal therapy? A local vs. systemic evaluation. Journal of Periodontal Research. 1(5):604–612.

Emingil G., Kuula H., Pirila E. & Atilla G., Sorsa T. (2006). Gingival crevicular fluid laminin-5 gamma2-chain levels in periodontal disease. Journal of Clinical Periodontology. 33(7):462-468.

Eren G., Türkoğlu O., Atmaca H. & Atilla G. (2016). Evaluation of gingival crevicular fluid cyclophilin a and extracellular matrix metalloproteinase inducer levels in different periodontal diseases. Archives of Oral Biology. 68: 162-166.

Ertugrul A. S., Dikilitas A., Sahin H., Alpaslan N., Bozoglan A. & Tekin, Y. (2013a). Gingival crevicular fluid levels of human beta-defensins 1 and 3 in subjects with periodontitis and/or type 2 diabetes mellitus: a cross-sectional study. Journal of Periodontal Research. 48(4):475-482.

Ertugrul A. S., Arslan U., Dursun R. & Sezgin Hakki S. (2013b). Periodontopathogen profile of healthy and oral lichen planus patients with gingivitis or periodontitis. International Journal of Oral Science. 5(2):92–97.

Figueiredo L. C., Rosetti E. P., Marcantonio E., Marcantonio R. A. C. & Salvador S. L. (2002). The Relationship of Oral Malodor in Patients With or Without Periodontal Disease. Journal of Periodontology. 73(11):1338-1342.

Fujita Y., Ito H., Sekino S. & Numabe Y. (2012). Correlations between pentraxin 3 or cytokine levels in gingival crevicular fluid and clinical parameters of chronic periodontitis. Odontology. 100(2):215-221.

Fukushima H., et al. (2017). PAR-2 expression in the gingival crevicular fluid reflects chronic periodontitis severity. Braz oral res. (31).

Gamel E. B., Hashim N. T., Satti A. & Gismalla B. G. (2017). Salivary TNFα levels in groups of subjects with rheumatoid arthritis and chronic periodontitis. BMC Res Notes. 10:34.

Genco R. J. & Borgnakke W. S. (2013, June). Risk factors for periodontal disease. Periodontol 2000. 62(1):59-94.

Ghallab N. A., Amr E. M. & Shaker O. G. (2015). Expression of Leptin and Visfatin in Gingival Tissues of Chronic Periodontitis With and Without Type 2 Diabetes Mellitus: A Study Using Enzyme-Linked Immunosorbent Assay and Real-Time Polymerase Chain Reaction. Journal of Periodontology. 86(7):882-889.

Gharbi A., Hamila A., Bouguezzi A., Dandana A., Ferchichi S., Chandad F., et al. (2019). Biochemical parameters and oxidative stress markers in Tunisian patients with periodontal disease. BMC Oral Health. 19(1):225.

Gheren L. W., Cortelli J. R., Rodrigues E., Holzhausen M. & Saad W. A. (2008). Periodontal therapy reduces arginase activity in saliva of patients with chronic periodontitis. Clinical Oral Investigations. 12(1):67-72.

Gimenez T., Bispo B. A., Souza D. P., Viganó M. E., Wanderley M. T., Mendes F. M., et al. (2016, October). Does the Decline in Caries Prevalence of Latin American and Caribbean Children Continue in the New Century? Evidence from Systematic Review with Meta-Analysis. PLoS One. 21;11(10):e0164903.

Godard A., Dufour T. & Jeanne S. (2011, December). Application of self-regulation theory and motivational interview for improving oral hygiene: a randomized controlled trial. J Clin Periodontol. 38(12):1099-105.

Goel K., Sharma S., Baral D. D. & Agrawal S. K. (2021, February). Current status of periodontitis and its association with tobacco use amongst adult population of Sunsari district, in Nepal. BMC Oral Health. 12;21(1):66.

Gokhale N. H., Acharya A. B., Patil V. S., Trivedi D. J. & Thakur S. L. A. (2013). Short-Term Evaluation of the Relationship Between Plasma Ascorbic Acid Levels and Periodontal Disease in Systemically Healthy and Type 2 Diabetes Mellitus Subjects. Journal of Dietary Supplements. 10(2):93-104.

Gokhale N. H., Acharya A. B., Patil V. S., Trivedi D. J., Setty S. & Thakur S. L. (2014). Resistin Levels in Gingival Crevicular Fluid of Patients With Chronic Periodontitis and Type 2 Diabetes Mellitus. Journal of Periodontology. 85(4):610-617.

Greene J. C., & Vermillion J. R. (1964, January). The Simplified Oral Hygiene Index. J Am Dent Assoc. 68:7-13.

Guentsch A., Pfister W., Cachovan G., Raschke G., Kuepper H., Schaefer O. & Eick S. (2014). Oral prophylaxis and its effects on halitosis-associated and inflammatory parameters in patients with chronic periodontitis. International Journal of Dental Hygiene. 12(3):199-207.

Gupta N., Gupta N. D., Gupta A., Khan S. & Bansal N. (2015). Role of salivary matrix metalloproteinase-8 (MMP-8) in chronic periodontitis diagnosis. Frontiers of Medicine. 9(1):72-76.

Haffajee A. D., Socransky S. S., Lindhe J., Kent R. L., Okamoto H. & Yoneyama T. (1991, February). Clinical risk indicators for periodontal attachment loss. J Clin Periodontol. 18(2):117-25.

Halladay C. W., Trikalinos T. A., Schmid I. T., Schmid C. H. & Dahabreh I. J. (2015, September). Using data sources beyond PubMed has a modest impact on the results of systematic reviews of therapeutic interventions. J Clin Epidemiol. 68(9):1076-84.

Hartenbach F. A. R. R., Silva-Boghossian C. M. & Colombo A. P. V. (2018, January). The effect of supragingival biofilm re-development on the subgingival microbiota in chronic periodontitis. Archives of Oral Biology. (85):51-57.

Haytural O., Yaman D., Ural E. C., Kantarci A. & Demirel K. (2015). Impact of periodontitis on chemokines in smokers. Clinical Oral Investigations. 19(5):979-986.

Hedges L. V., & Vevea J. L. (1998). Fixed- and random-effects models in meta-analysis. Psychological Methods. 3(4):486-504.

Hegde R., & Awan K. H. (2019, June). Effects of periodontal disease on systemic health. Dis Mon. 65(6):185-192.

Hendek M. K., Erdemir E. O. & Kisa U. (2015). Evaluation of Salivary Procalcitonin Levels in Different Periodontal Diseases. Journal of Periodontology. 86(6):820-826.

Hozo S. P., Djulbegovic B. & Hozo I. (2005, April). Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol. 20;5:13.

İlgenli T., Vardar-Sengul S., Gürkan A., Sorsa T., Stackelberg S., Köse T & Atilla G. (2006). Gingival crevicular fluid matrix metalloproteinase-13 levels and molecular forms in various types of periodontal diseases. Oral Diseases. 12(6):573-579.

Ishizuka M., Kato R., Moriya Y., Noguchi E., Koide Y., Inoue S., et al. (2017). Changes in apolipoprotein B and oxidized low-density lipoprotein levels in gingival crevicular fluids as a result of periodontal tissue conditions. Journal of Periodontal Research. 52(3):594-602.

Jaradat S., Hoder-Przyrembel C., Cubillos S., Krieg N., Lehmann K., Piehler S., et al. (2013). Beta-defensin-2 Genomic Copy Number Variation and Chronic Periodontitis. Journal of Dental Research. 92(11):1035-1040.

Javed F., Ahmed H. B., Saeed A., Mehmood A. & Bain C. (2014). Whole Salivary Interleukin-6 and Matrix Metalloproteinase-8 Levels in Patients With Chronic Periodontitis With and Without Prediabetes. Journal of Periodontology. 85(5):e130-e135.

Katarkar A., Saha A., Mukherjee S., Kundu D., Bandyopadhyay P. & Chaudhuri K. (2015). Telomerase Expression in Individuals With Chronic and Aggressive Periodontitis. Journal of Periodontology. 86(5):656-665.

Keles Z. P., Keles G. C., Avci B., Cetinkaya B. O. & Emingil G. (2014). Analysis of YKL-40 Acute-Phase Protein and Interleukin-6 Levels in Periodontal Disease. Journal of Periodontology. 85(9):1240–1246.

Kerdvongbundit V., Vongsavan N., Soo-ampon S. & Hasegawa A. (2003). Microcirculation and micromorphology of healthy and inflamed gingivae. Odontology. 91(1):19-25.

Khongkhunthian S., Techasatian P., Supanchart C., Bandhaya P., Montreekachon P., Thawanaphong S. & Krisanaprakornkit S. (2013). Elevated Levels of a Disintegrin and Metalloproteinase 8 in Gingival Crevicular Fluid of Patients With Periodontal Diseases. Journal of Periodontology. 84(4):520-528.

Khongkhunthian S., Kongtawelert P., Ongchai S., Pothacharoen P., Sastraruji T., Jotikasthira D. & Krisanaprakornkit S. (2014, August). Comparisons between two biochemical markers in evaluating periodontal disease severity: a cross-sectional study. BMC Oral Health. 30;14:107.

Konopka Ł., Pietrzak A. & Brzezińska-Błaszczyk E. (2012). Effect of scaling and root planing on interleukin-1β, interleukin-8 and MMP-8 levels in gingival crevicular fluid from chronic periodontitis patients. Journal of Periodontal Research. 47(6):681-688.

Köseoğlu S., Sağlam M., Pekbağrıyanık T., Savran L. & Sütçü R. (2015). Level of Interleukin-35 in Gingival Crevicular Fluid, Saliva, and Plasma in Periodontal Disease and Health. Journal of Periodontology. 86(8):964-971.

Kumar K. R. V, Ranganath V., Naik R., Banu S. & Nichani A. S. (2014). Assessment of high-sensitivity C-reactive protein and lipid levels in healthy adults and patients with coronary artery disease, with and without periodontitis - a cross-sectional study. Journal of Periodontal Research. 49(6): 836-844.

Kurşunlu S. F., Öztürk V. Ö., Han B., Atmaca H. & Emingil G. (2015). Gingival crevicular fluid interleukin-36β (-1F8), interleukin-36γ (-1F9) and interleukin-33 (1F11) levels in different periodontal disease. Archives of Oral Biology. 60(1):77-83.

Kurtiş B., Tüter G., Serdar M., Akdemir P., Uygur C., Firatli E. & Bal B. (2005). Gingival Crevicular Fluid Levels of Monocyte Chemoattractant Protein-1 and Tumor Necrosis Factor-Alpha in Patients With Chronic and Aggressive Periodontitis. Journal of Periodontology. 76(11):1849-1855.

Kwon T., Lamster I. B. & Levin L. (2021, December). Current Concepts in the Management of Periodontitis. Int Dent J. 71(6):462-476.

Laddha R., Mahajania M., Khadse A., Bajaj R., Jawade R. & Choube S. (2018, October). Assessment of Sirtuin 3 and Sirtuin 4 Level in Patients with Diabetes Mellitus and Periodontitis: A Clinical Study. J Contemp Dent Pract. 19(10):1199-1203.

Lakshmanan R., Jayakumar N. D., Sankari M., Padmalatha O. & Varghese S. (2014). Estimation of Pentraxin-3 Levels in the Gingival Tissues of Chronic and Aggressive Periodontitis Participants: An In Vivo Study. Journal of Periodontology. 85(2):290-297.

Larson J. S. (1991). The measurement of health: concepts and indicators. Greenwood.

Leite S. A. M., Casanovas R. C., Rodrigues V. P., Pereira A. F. V., Ferreira T. C. A. Nascimento F. R F., et al. (2019, September). The effect of nonsurgical periodontal therapy on hepcidin and on inflammatory and iron marker levels. Braz Oral Res. 9;33:e055.

Lertpimonchai A., Rattanasiri S., Arj-Ong Vallibhakara S., Attia J. & Thakkinstian A. (2017, December). The association between oral hygiene and periodontitis: a systematic review and meta-analysis. Int Dent J. 67(6):332-343.

Lihala R., Jayaram P., Chatterjee A. & Joshi A. (2019). Effect of non-surgical periodontal therapy on stress and salivary Chromogranin-A levels: A clinicobiochemical study. Indian Journal of Dental Research. 30(2):213-218.

Lin Y. C., Wu C. Y., Chang L. Y., Chen C. C., Chen H. H., Lai Y. L. & Hung S. L. (2017). Levels of high-mobility group box-1 in gingival crevicular fluid in nonsmokers and smokers with chronic periodontitis. Journal of the Formosan Medical Association. 116(12):933-939.

Löe H., & Silness J. (1963). Periodontal disease in pregnancy. I. Prevalenceand severity. Acta Odontol Scand. 21:533-51.

Mahajani M. J., Jadhao V. A., Wankhade P. S., Samson E., Acharya V. D. & Tekale P. D. (2017, November). Effect of Periodontal Therapy on Crevicular Fluid Interleukin-18 Level in Periodontal Health and Disease in Central Maharashtra (India) Population. J Contemp Dent Pract. 1;18(11):1085-1089.

Mariggio M. A., Guida L., Laforgia A., Santacroce R., Curci E., Montemurro P. & Fumarulo R. (2001). Nicotine effects on polymorphonuclear cell apoptosis and lipopolysaccharide-induced monocyte functions. A possible role in periodontal disease? Journal of Periodontal Research. 36(1):32-39.

Martinez G. L., Majster M., Bjurshammar N., Johannsen A., Figueredo C. M. & Boström E. A. (2017). Salivary Colony Stimulating Factor-1 and Interleukin-34 in Periodontal Disease. Journal of Periodontology. 88(8):e140-e149.

Muthu J., Muthanandam S., Mahendra J., Namasivayam A., John L. & Logaranjini A. (2015). Effect of Nonsurgical Periodontal Therapy on the Glycaemic Control of Nondiabetic Periodontitis Patients: A Clinical Biochemical Study. Oral Health Prev Dent. 13(3):261-6.

Naiff P. F., Ferraz R., Cunha C. F., Orlandi P. P., Boechat A. L., Bertho Á. L. & Dos-Santos M. C. (2014). Immunophenotyping in Saliva as an Alternative Approach for Evaluation of Immunopathogenesis in Chronic Periodontitis. Journal of Periodontology. 85(5):e111-e120.

Nguyen T. T., Ngo L. Q., Promsudthi A. & Surarit R. (2016). Salivary oxidative stress biomarkers in chronic periodontitis and acute coronary syndrome. Clinical Oral Investigations. 21(7):2345-2353.

Nimcharoen T., Aung W. P. P., Makeudom A., Sastraruji T., Khongkhunthian S., Sirinirund B., et al. (2019, January). Reduced ADAM8 levels upon non-surgical periodontal therapy in patients with chronic periodontitis. Archives of Oral Biology. 97:137-143.

Nogueira-Filho G., Rosa B. T., Santos P. F., Tunes U. R., Freire S. M., Meyer R. & Darveau R. P. (2014). Whole-Blood Cultures From Patients With Chronic Periodontitis Respond Differently to Porphyromonas gingivalis but not Escherichia coli Lipopolysaccharide. Journal of Periodontology. 85(2):e18-e23.

Novakovic N., Todorovic T., Rakic M., Milinkovic I., Dozic I., Jankovic S., et al. (2014). Salivary antioxidants as periodontal biomarkers in evaluation of tissue status and treatment outcome. Journal of Periodontal Research. 49(1):129-136.

Özçaka Ö., Nalbantsoy A. & Buduneli N. (2010). Salivary osteocalcin levels are decreased in smoker chronic periodontitis patients. Oral Diseases. 17(2):200-205.

Özcan E., Saygun N. I., Serdar M. A. & Kurt N. (2015). Evaluation of the salivary levels of visfatin, chemerin, and progranulin in periodontal inflammation. Clinical Oral Investigations. 19(4):921-928.

Özdemir B., Özmeric N., Elgün S. & Barış E. (2016). Smoking and gingivitis: focus on inducible nitric oxide synthase, nitric oxide and basic fibroblast growth factor. Journal of Periodontal Research. 51(5): 596-603.

Özmeriç N., Elgün S. & Uraz A. (2000). Salivary arginase in patients with adult periodontitis. Clinical Oral Investigations. 4(1):21-24.

Öztürk V. Ö., Belibasakis G. N., Emingil G. & Bostanci N. (2016). Impact of aging on TREM-1 responses in the periodontium: a cross-sectional study in an elderly population. BMC Infectious Diseases. 16(1).

Papathanasiou E., Teles F., Griffin T., Arguello E., Finkelma M., Hanley J. & Theoharides T. C. (2014). Gingival crevicular fluid levels of interferon-γ, but not interleukin-4 or -33 or thymic stromal lymphopoietin, are increased in inflamed sites in patients with periodontal disease. Journal of Periodontal Research. 49(1):55-61.

Pawar D. D. & Mehta D. S. (2015, May). Effect of phase 1 periodontal therapy on gingival crevicular fluid levels of matrix metalloproteinases-3 and -13 in chronic periodontitis patients. J Investig Clin Dent. 6(2):118-24.

Pejcic A., Kesic L., Ilic S., Pesic Z. & Mirkovic D. (2012). Association between chronic periodontitis and serum lipid levels. Military Medical and Pharmaceutical Journal of Serbia. 69(9):771-777.

Pereira A. L., Franco G. C., Cortelli S. C., Aquino D. R., Costa F. O., Raslan S. A. & Cortelli J. R. (2013). Influence of Periodontal Status and Periodontopathogens on Levels of Oral Human β-Defensin-2 in Saliva. Journal of Periodontology. - 84(10):1445-1453.

Pinho M. N., Oliveira R. D. R., Novaes Jr A. B. & Voltarelli J. C. (2009). Relationship between periodontitis and rheumatoid arthritis and the effect of non-surgical periodontal treatment. Brazilian Dental Journal. 20(5):355-364.

Pinho R. C. M, Dias R. S. A. M., Bandeira F., Rodrigues J. K. F., da Silva R. C., et al. (2019, February). Polymorphisms of the vitamin D receptor gene (FOKI, CDX2, and GATA) and susceptibility to chronic periodontitis in diabetic and non-diabetic individuals: A case-control study. J Investig Clin Dent. 10(1):e12370.

Purwar P., Khan M. A., Mahdi A. A., Pandey S., Singh B., Dixit J. & Sareen S. (2015). Salivary and Serum Leptin Concentrations in Patients With Chronic Periodontitis. Journal of Periodontology. 86(4):588-594.

Purwar P., Khan M. A., Gupta A., Mahdi A. A, Pandey S., Singh B., et al. (2015). The effects of periodontal therapy on serum and salivary leptin levels in chronic periodontitis patients with normal body mass index. Acta Odontologica Scandinavica. 73(8):633-641.

Qi Y., Feng W., Song A., Song H., Yan S., Sun Q. & Yang P. (2013). Role of Serum IL-23/IL-17 Axis in the Relationship Between Periodontitis and Coronary Heart Disease. The International Journal of Periodontics and Restorative Dentistry. 33(2):185-191.

Quigley G. A. & Hein J. W. (1962, July). Comparative cleansing efficiency of manual and power brushing. J Am Dent Assoc. 65:26-9.

Rice D. B., Kloda L. A., Levis B., Qi B., Kingsland E. & Thombs B. D. (2016, August). Are MEDLINE searches sufficient for systematic reviews and meta-analyses of the diagnostic accuracy of depression screening tools? A review of meta-analyses. J Psychosom Res. 87:7-13.

Richardson W. S., Wilson M. C., Nishikawa J. & Hayward R. S. (1995, Nov-Dec). The well-built clinical question: a key to evidence-based decisions. ACP J Club. 123(3):A12-3.

Roberts H. M., Ling M. R., Insall R., Kalna G., Spengler J., Grant M. M & Chapple I. L. C. (2015). Impaired neutrophil directional chemotactic accuracy in chronic periodontitis patients. Journal of Clinical Periodontology. 42(1):1-11.

Sakallıoğlu E. E., Lütfioğlu M., Sakallıoğlu U., Dıraman E. & Keskiner İ. (2008). Fluid dynamics of gingiva in diabetic and systemically healthy periodontitis patients. Archives of Oral Biology. 53(7):646-651.

Sánchez G., Miozza V., Delgado A., & Busch L. (2013). Relationship between salivary mucin or amylase and the periodontal status. Oral Diseases. 19(6):585-591.

Scannapieco F. A. (1995, June). Monitoring the efficacy of plaque control methods. Periodontol 2000. 8:24-41.

Silness J. & Löe H. (1964, February). Periodontal Disease in Pregnancy. II. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand. 22:121-35.

Silva D. G., Stevens R. H., Macedo J. M. B., Albano R. M., Falabella M. E. V., Fischer R. G., et al. (2010). Presence of Helicobacter pylori in supragingival dental plaque of individuals with periodontal disease and upper gastric diseases. Archives of Oral Biology. 55(11): 896-901.

Silva H. A. B., Alves E. V. T., Spolidório L. C., Neto J. B. C., Eichler R. S., Carvalho M. H. C. & Holzhausen M. (2014). Expression of Protease Activated Receptor-1 in Chronic Periodontitis. Journal of Periodontology. 85(12):1763-1769.

Söder B., Yakob M., Meurman J. H., Andersson L. C. & Söder P. Ö. (2012, June). The association of dental plaque with cancer mortality in Sweden. A longitudinal study. BMJ Open. 11;2(3):e001083.

Staudte H., Sigusch B. W. & Glockmann E. (2005). Grapefruit consumption improves vitamin C status in periodontitis patients. British Dental Journal. 199(4):213-217.

Surna A., Kubilius R., Sakalauskiene J., Vitkauskiene A., Jonaitis J., Saferis V. & Gleiznys A. (2009). Lysozyme and microbiota in relation to gingivitis and periodontitis.Med Sci Monit. 15(2):CR66-73.

Sutton A. J., Abrams K. R., Jones D. R., Sheldon T. A. & Song F. (2000). Methods for Meta-Analysis in Medical Research. New York, NY:John Wiley.

Swaminathan V., Prakasam S., Puri V. & Srinivasan M. (2013, December). Role of salivary epithelial toll-like receptors 2 and 4 in modulating innate immune responses in chronic periodontitis. Journal of Periodontal Research. 48(6):757-65.

Tabari Z. A., Azadmehr A., Nohekhan A., Naddafpour N. & Ghaedi F. B. (2014). Salivary Visfatin Concentrations in Patients With Chronic Periodontitis. Journal of Periodontology. 85(8):1081-1085.

Tamaki N., Tomofuji T., Ekuni D., Yamanaka R., Yamamoto T. & Morita M. (2009). Short-Term Effects of Non-Surgical Periodontal Treatment on Plasma Level of Reactive Oxygen Metabolites in Patients With Chronic Periodontitis. Journal of Periodontology. 80(6):901-906.

Tarannum F. & Faizuddin M. (2016). Association between lipoxin A4 and interleukin-12 in gingival crevicular fluid: a preliminary investigation. Journal of Periodontal Research. 52(2): 210-217.

Tarannum F. & Faizuddin M. (2017). Effect of Alox-15 Polymorphism on GCF Levels of Lipoxin-A4 in Chronic Periodontitis: A Preliminary Study. Braz Dent J. 28(2).

Taşdemir Z., Etöz M., Köy Ö., Soydan D. & Alkan A. (2020, January). Masseter muscle thickness and elasticity in periodontitis. Journal of Oral Science. 29;62(1):43-47.

Taskan M. M., Karatas O., Yuce B. H., Kara I. G., Gevrek F. & Yarkac U. F. (2019, June). Hypoxia and collagen crosslinking in the healthy and affected sites of periodontitis patients. Acta Odontologica Scandinavica. 77(8):600-607.

Teles F. R., Teles R. P., Uzel N. G., Song X. Q., Torresyap G., Socransky S. S. & Haffajee A. D. (2012). Early microbial succession in redeveloping dental biofilms in periodontal health and disease. Journal of Periodontal Research. 47(1):95-104.

Tezel A., Yucel O., Orbak R., Kara C., Kavrut F., Yagiz H. & Sahin T. (2005). The gingival crevicular fluid ciprofloxacin level in subjects with gingivitis and periodontitis, and its effects on clinical parameters. Journal of Periodontal Research. 40(5):395-400.

To T. T., Gümüş P., Nizam N., Buduneli N. & Darveau R. P. (2015). Subgingival Plaque in Periodontal Health Antagonizes at Toll-Like Receptor 4 and Inhibits E-Selectin Expression on Endothelial Cells. Infection and Immunity. 84(1):120-126.

Toker H., Akpınar A., Aydın H. & Poyraz O. (2012). Influence of smoking on interleukin-1beta level, oxidant status and antioxidant status in gingival crevicular fluid from chronic periodontitis patients before and after periodontal treatment. Journal of Periodontal Research. 47(5):572-577.

Tonetti M. S., Greenwell H. & Kornman K. S. (2018, December). Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. J Periodontol. 2018 Jun;89 Suppl 1:S159-S172. doi: 10.1002/JPER.18-0006. Erratum in: J Periodontol. 89(12):1475.

Toyman U., Tüter G., Kurtiş B., Kıvrak E., Bozkurt Ş., Yücel A. A. & Serdar M. (2015). Evaluation of gingival crevicular fluid levels of tissue plasminogen activator, plasminogen activator inhibitor 2, matrix metalloproteinase-3 and interleukin 1-β in patients with different periodontal diseases. Journal of Periodontal Research. 50(1):44-51.

Tripathi V., Singh S. T., Sharma V., Verma A., Singh C. D. & Gill J. S. (2018, March). Assessment of Lipid Peroxidation Levels and Total Antioxidant Status in Chronic and Aggressive Periodontitis Patients: An in vivo Study. J Contemp Dent Pract. 19(3):287-291.

Trivedi S., Lal N., Mahdi A. A., Mittal M., Singh B. & Pandey S. (2014). Evaluation of Antioxidant Enzymes Activity and Malondialdehyde Levels in Patients With Chronic Periodontitis and Diabetes Mellitus. Journal of Periodontology. 85(5):713-720.

Trombelli L., Farina R., Silva C. O. & Tatakis D. N. (2018, June). Plaque-induced gingivitis: Case definition and diagnostic considerations. J Periodontol. 89 Suppl 1:S46-S73.

Turesky S., Gilmore N. D. & Glickman I. (1970). Reduced plaque formation by the chloromethyl analogue of Victamine C. J Periodontol. 41:41-3.

Türkoğlu O., Emingil G., Kütükçüler N. & Atilla G. (2009). Gingival Crevicular Fluid Levels of Cathelicidin LL-37 and Interleukin-18 in Patients With Chronic Periodontitis. Journal of Periodontology. 80(6):969-976.

Türkoğlu O., Emingil G., Kütükçüler N. & Atilla G. (2010). Evaluation of Gingival Crevicular Fluid Adrenomedullin and Human Neutrophil Peptide 1–3 Levels of Patients With Different Periodontal Diseases. Journal of Periodontology. 81(2):284-291.

Türkoğlu O., Kandiloğlu G., Berdeli A., Emingil G. & Atilla G. (2011). Antimicrobial peptide hCAP-18/LL-37 protein and mRNA expressions in different periodontal diseases. Oral Diseases. 17(1):60-67.

Tüter G., Özdemir B., Kurtiş B., Serdar M., Yücel A. A. & Ayhan E. (2013). Short term effects of non-surgical periodontal treatment on gingival crevicular fluid levels of tissue plasminogen activator (t-PA) and plasminogen activator inhibitor 2 (PAI-2) in patients with chronic and aggressive periodontitis. Archives of Oral Biology. 58(4):391-396.

Tüter G., Kurtiş B. & Serdar M. (2002). Effects of Phase I Periodontal Treatment on Gingival Crevicular Fluid Levels of Matrix Metalloproteinase-1 and Tissue Inhibitor of Metalloproteinase-1. Journal of Periodontology. 73(5):487-493.

van der Weijden G. A. & Hioe K. P. (2005). A systematic review of the effectiveness of self-performed mechanical plaque removal in adults with gingivitis using a manual toothbrush. J Clin Periodontol. 32 Suppl 6:214-28.

van Enst W. A., Scholten R. J., Whiting P., Zwinderman A. H. & Hooft L. (2014, November). Meta-epidemiologic analysis indicates that MEDLINE searches are sufficient for diagnostic test accuracy systematic reviews. J Clin Epidemiol. 67(11):1192-9.

Vinayak M. J. & VandanaIndian K. L. (2007, Jan-Mar). The detection of eight putative periodontal pathogens in adult and rapidly progressive periodontitis patients: an institutional study. J Dent Res. 18(1):6-10.

Wan X., Wang W., Liu J. & Tong T. (2014, December). Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 19;14:135.

Wang H., Luo Z., Lei L., Sun Z., Zhou M., Dan H., et al. (2013). Interaction Between Oral Lichen Planus and Chronic Periodontitis with Th17-Associated Cytokines in Serum. Inflammation. 36(3):696-704.

Wei D., Zhang X. L., Wang Y. Z., Yang C. X. & Chen G. (2010). Lipid peroxidation levels, total oxidant status and superoxide dismutase in serum, saliva and gingival crevicular fluid in chronic periodontitis patients before and after periodontal therapy. Australian Dental Journal. 55(1):70-78.

Wei P. F., Ho K. Y., Ho Y. P., Wu Y. M., Yang Y. H. & Tsai C. C. (2004). The investigation of glutathione peroxidase, lactoferrin, myeloperoxidase and interleukin- 1beta in gingival crevicular fluid: implications for oxidative stress in human periodontal diseases. Journal of Periodontal Research. 39(5):287-293.

Yang J., Zhu Y., Duan D., Wang P., Xin Y., Bai L., et al. (2018, December). Enhanced activity of macrophage M1/M2 phenotypes in periodontitis. Archives of Oral Biology. 96:234-242.

Zheng P., Chen H., Shi S., Jepsen S. & Eberhard J. (2006). Periodontal parameters and platelet-activating factor levels in serum and gingival crevicular fluid in a Chinese population. Journal of Clinical Periodontology. 33(11):797-802.