

Association of periodontitis and psoriasis: a systematic review and meta-analysis

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Abstract

Background: Psoriasis and periodontitis are chronic inflammatory diseases with shared etiopathogenic aspects and risk factors. This systematic review (SR) aims to assess the impact of periodontitis on the risk of psoriasis.

Methods: Prospective and retrospective studies were included in this review. MEDLINE, EMBASE, and LILACS databases were searched up to Feb 2021. Odds ratio (OR) and standard error (SE) values of the studied groups were converted to LogOR, and the results of individual studies were grouped using a fixed-effects model. A modified version of the Newcastle-Ottawa (NOS) scale was used to assess the risk of bias of retrospective and prospective studies.

Results: From a total of 169 articles initially searched, eight articles were included in this systematic review (SR). Of these, five retrospective studies were included in the meta-analysis. The overall meta-analysis demonstrated that individuals with periodontitis have 61% increased odds of psoriasis compared to individuals with periodontal health (OR = 1,61; 95% CI = 1,23 to 2,11, Heterogeneity: $I^2 = 0\%$, $p = 0,0005$).

Conclusion: Psoriatic patients with periodontal disease have a higher risk of psoriasis than periodontally healthy individuals. Because of the limitations, we cannot yet establish a causal relationship between these two inflammatory diseases.

Keywords: Psoriasis. Periodontal disease. Systematic review.

Introduction

Periodontitis is a highly prevalent chronic inflammatory disease characterized by a dysregulated host inflammatory response to dysbiotic biofilms (Papapanou *et al.*, 2018). Clinical aspects of periodontitis include periodontal pocket depth formation, bleeding on probing, and clinical attachment loss (Meuric *et al.*, 2017; Yost *et al.*, 2015).

The periodontal disease exhibits a linkage to several systemic illnesses and disabilities (Jepsen *et al.*, 2018), which can be explained mainly by the fact that periodontitis patients present increased bacteremia and higher levels of inflammatory biomarkers in serum when compared with periodontally healthy individuals (Jepsen *et al.*, 2018; Sanz e Winkelhoff, Van, 2011). In this context, epidemiological studies demonstrated that periodontal disease is associated with poor glycemic

control in diabetic patients (Genco e Borgnakke, 2013), adverse pregnancy outcomes (Chambrone *et al.*, 2011), ventilator-associated pneumonia (Raghavendran, Mylotte e Scannapieco, 2007) and autoimmune diseases (Ambrosio *et al.* 2017) such as psoriasis (Skudutyte-Rysstad *et al.*, 2014).

Psoriasis is a chronic, immune-mediated, genetic-based inflammatory dermatosis that affects around 1.5% of the Caucasian population (Ferrándiz *et al.*, 2001; Nevitt e Hutchinson, 1996). It is characterized by skin alterations and considerably impairs the patient's quality of life (Sabat *et al.*, 2007). Chronic plaque psoriasis (CPP) is the most common type and is represented by demarcated, erythematous, and scaly lesions (Nestle, Kaplan e Barker, 2009). The number of epithelial cells increases due to tissue inflammation, which leads to a quick cycle of immaturity epithelial cells desquamation. The hyperplasia of the epidermis combined with the marked desquamation clinically determines its clinical aspect (Sabat *et al.*, 2007).

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The evolution of a psoriatic lesion is based on a complex interaction between environmental and genetic factors. Psoriasis has been linked to smoking (Armstrong, Harskamp e Armstrong, 2013), alcoholism (Gupta *et al.*, 1993), and stress (Kouris *et al.*, 2017). In addition, the systemic state of chronic inflammation seems to determine a bidirectional relationship with several systemic and oral pathologies (Binus *et al.*, 2012) (Procaccini *et al.*, 2011; Versini *et al.*, 2014); Armstrong, Harskamp e Armstrong, 2013; Mehta *et al.*, 2010).

Both psoriasis and periodontal disease involve an exaggerated immune response in epithelial surfaces and a dysregulation of the host inflammatory response (Cutler e Jotwani, 2006; Preus *et al.*, 2010; Sabat *et al.*, 2007). In psoriasis and periodontitis, the state of systemic inflammation revealed by increased serum levels of pro-inflammatory biomarkers and oxidative stress represents a possible link between these conditions (Borska *et al.*, 2017; Miranda *et al.*, 2019). (Hussain *et al.*, 2016; Tóthová e Celec, 2017). Oxidative stress occurs when there is an imbalance between oxidative free radicals and anti-oxidative mechanisms. It plays a crucial role in the pathogenesis of psoriasis, exerting an anti-proliferative function in keratinocytes, which leads to the abnormal proliferation of keratinocytes and the development of the signs and symptoms of the disease (Tóthová e Celec, 2017).

Thus, psoriasis and periodontitis are chronic inflammatory diseases with shared etiopathogenic aspects and risk factors. This systematic review (SR) aims to assess the impact of periodontitis on the risk of psoriasis. The following focused question was addressed: “Do individuals with periodontitis present an increased risk for psoriasis when compared with periodontally healthy individuals?”.

Materials and Methods

This systematic review followed the preferred reporting items for systematic reviews and meta-analysis (PRISMA) of observational studies (MOOSE). The protocol was previously registered in the International Prospective Register of Systematic Reviews (CRD:42020205338).

Eligibility criteria

Observational studies were included (retrospective and prospective studies) according to the following requirements: a) original studies published in English; b) data showing the number of psoriatic patients with and without periodontitis; c) outcome data of the assessment of psoriasis severity on patients with and without periodontal disease; and d) odds ratio for the association between psoriasis and periodontitis.

Narrative analyses, case series, case reports, and in vitro and animal studies were excluded. In addition, studies that did not include a control group with systemically healthy individuals were excluded.

Search strategy

An electronic literature search was performed on the MEDLINE, EMBASE, and LILACs databases up to February 2021. The following search strategy was used: (psoriatic or psoriasis) AND (periodontitis or gingivitis or periodontal disease or attachment loss).

In the first phase, two independent reviewers (ISOC and MRF) selected titles and abstracts used by the search strategy. The disagreements were resolved by the decision of a third reviewer (ESR). In the second phase, they reviewed the selected articles' full texts that met the inclusion criteria or those with unclear information in the title and abstract. The reasons for the rejection of the studies were recorded for each report.

Data extraction

The following items were extracted from publications that met inclusion criteria: author, year, country, study design, sample size, follow-up, the definition of periodontitis and psoriasis, assessment of psoriatic and periodontitis patients, odds for psoriasis or periodontitis, assessment of the severity of psoriasis, results, conflict of interest and source of funding.

Risk of bias

A modified version of the Newcastle-Ottawa (NOS) scale was used (Sendyk *et al.* 2016).

NOS was adapted with seven questions for the Retrospective studies and ten questions for the Prospective study, assessing sample size calculation, representativeness of the psoriatic patients, selection of psoriatic patients, ascertainment of patients with periodontitis, source of patients without periodontitis, assessment of clinical outcomes, description of clear inclusion/exclusion criteria; comparability; outcomes and statistics.

The scores of retrospective studies ranged from 0 to 10. Studies with 7-10 stars were rated as having a low risk of bias, 5-6 stars moderate risk of bias, and < 5 high risk of bias. The scores of prospective studies ranged from 0 to 11. Studies with 7-11 stars were rated as having a low risk of bias, 5-6 stars moderate risk of bias, and < 5 high risk of bias.

Summary measures and synthesis of results

Studies that presented the number of psoriatic and systemically healthy patients with and without periodontitis or the Odds ratio (OR) for psoriasis/periodontitis were included in the meta-analysis. Analyses were

performed using a software package (Review Manager software, version 5.3, The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark). OR and standard error (SE) values of the studied groups were converted to LogOR, and the results of individual studies were grouped using a fixed-effects model. The meta-analysis used the inverse variance method and the DerSimonian-Laird estimator for Tau. The pooled results were estimated using OR and 95% confidence intervals (CIs). The heterogeneity analysis was performed by the I² test. Since only one prospective study was included in the present systematic review, the meta-analysis was conducted only for retrospective studies.

Results

Search results

Records identified through electronic database searching strategies and manual searches resulted in the identification of a total of one hundred and sixty-nine articles. One hundred and seventy-eight (178) were excluded after the title and abstract screening. In the second phase, 16 articles were selected for full-text reading (Antal

et al., 2014; Fadel *et al.*, 2013; Ganzetti *et al.*, 2014; Gheorghita *et al.*, 2016; Keller e Lin, 2012; Lazaridou *et al.*, 2013; Mendes *et al.*, 2019; Nakib *et al.*, 2013; Painsi *et al.*, 2017; Preus *et al.*, 2010; Sarac *et al.*, 2017; Sezer *et al.*, 2016; Skudutyte-Rysstad *et al.*, 2014; Su *et al.*, 2017; Woeste *et al.*, 2019). Sixteen were excluded for the following reasons: one study has a cross-sectional design, one focused on smoking patients (Antal *et al.*, 2014; Fadel *et al.*, 2013); three studies did not have sufficient information (Preus *et al.*, 2010; Sezer *et al.*, 2016; Woeste *et al.*, 2019); two studies did not have a control group without psoriasis, and systemically health individuals (Painsi *et al.*, 2017; Su *et al.*, 2017) and one study (Gheorghita *et al.*, 2016) was not possible to download the article. A total of 8 articles (Ganzetti *et al.*, 2014; Keller e Lin, 2012; Lazaridou *et al.*, 2013; Mendes *et al.*, 2019; Nakib *et al.*, 2013; Sarac *et al.*, 2017; Sharma, Raman e Pradeep, 2014; Skudutyte-Rysstad *et al.*, 2014) were included in this review. It was possible to include 5 (Ganzetti *et al.*, 2014; Keller e Lin, 2012; Lazaridou *et al.*, 2013; Mendes *et al.*, 2019; Skudutyte-Rysstad *et al.*, 2014) of these in the meta-analysis (Figure 1).

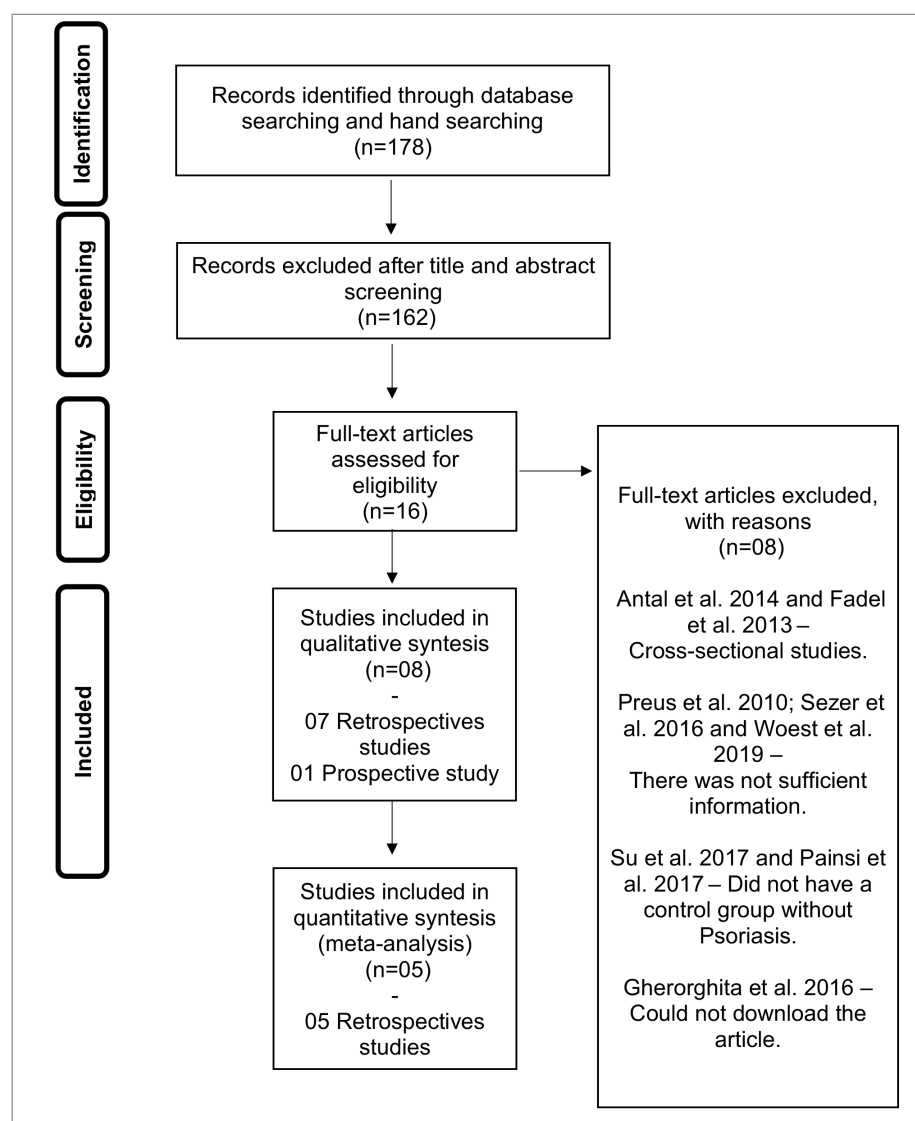


Figure 1. Flow-chart

Included studies

Retrospective studies

Seven retrospective studies were included (Ganzetti *et al.*, 2014; Keller *et al.*, 2012; Lazaridou *et al.*, 2013; Mendes *et al.*, 2019; Sarac *et al.*, 2017; Skudutyte-Rysstad *et al.*, 2014). Their characteristics are shown in Table 1; 231.985 individuals of both sexes, ranging from 19,6 to 62,2 years, were included. All studies evaluated

the exposure (periodontitis) by clinical examination. Regarding the outcome, the psoriasis diagnosis and severity were evaluated by clinical examination (Ganzetti *et al.*, 2014; Lazaridou *et al.*, 2013; Mendes *et al.*, 2019; Sarac *et al.*, 2017; Skudutyte-Rysstad *et al.*, 2014); clinical examination confirmed with histopathological and immunofluorescence exam (Sharma, Raman *et al.*, Pradeep, 2014) and medical record (Keller *et al.*, 2012).

Table 1. Characteristics of the retrospective studies.

Author (Country)	Subjects characteristics	Subjects characteristics	Definition of Psoriasis	Outcome assessment	Main findings	Conflict of interest and source funding
Ganzetti <i>et al.</i> 2014 (Italy)	28 men and 22 women, mean age 44.7 ± 11.5 years from Clinical of Dermatology of Ancona. The control group comprised 45 healthy gender and age-matched individuals. Retrospective Study	Chronic periodontitis was considered localized or generalized (>30% of sites involved). Severity was characterized by the amount of clinical attachment loss.	The diagnosis of psoriasis was made following PASI.	Assessment of patients: - Psoriatic: Clinical examination - With periodontitis: clinical examination Follow up: 10 months	Test group (psoriatic patients): 50 Periodontitis: n = 22 Without periodontitis: n = 28 Control group (control): 45 Periodontitis: n = 2 Without periodontitis: n = 43 Periodontal health may reduce the risk factors triggering psoriasis.	All authors state that they do not have any conflict of interest related to the submitted work. Editorial assistance was provided by Mary Hineson behalf of Health Publishing and Services Srl and funded by Pfizer Italia.
Keller <i>et al.</i> 2012 (Taiwan)	230.730 patients (110.430 man and 120.300 woman) age/mean: 39.2 ± 16.2 from Taiwan National Health Research Institute Retrospective Study	Patients who had at least two consensus diagnoses of Chronic Periodontitis. There was no further information.	Patients that received a diagnosis of psoriasis. There was no further information.	Assessment of patients: - Psoriatic: Medical record - With periodontitis: clinical examination Follow up: 5 years Recommended intervals of SPT: 2 visits per year	Test group (periodontitis patients): N=115.365 Psoriasis incidence in 5 years: n=10823. Control group (control without periodontitis): N=115.365 Psoriasis incidence in 5 years: n = 706 Hazard Ratio of psoriasis during the 5-year follow-up period for patients with Chronic periodontitis was 1.54 (95% CI 1.40–1.69).	Authors declared no conflict of interest.
Lazaridou <i>et al.</i> 2013 (Greece)	200 patients (114 woman and 88 man) age/ Mean: 57.2 ± 5 from Hospital of Skin and Venereal Diseases Retrospective Study	Radiologic confirmation of bone loss. Community Periodontal Index scoring was used for the classification of periodontitis	Biopsy confirmed Chronic Plaque Psoriasis with duration of the disease for at least 6 months. Patients with chronic plaque psoriasis were sub classified further on the basis of PASI scores.	Assessment of patients: - Psoriatic: clinical examination - With periodontitis: clinical examination Follow up: 5 months	Test group (psoriatic patients) = 100 Periodontitis= 27 Without periodontitis= 73 Control group (healthy patients) = 100 Periodontitis= 10 Without periodontitis= 90 Significant correlations between psoriasis and periodontitis (OR = 3.329, 95%CI: 1.513–7.324, P = 0.003)	Authors declared no conflict of interest. No funding sources supported this work.
Mendes <i>et al.</i> 2019 (Brazil)	756 patients (463 woman and 293 man) Age/Mean: 46.71 ± 7.0 from Department of Dermatology of Clinics Hospital and from the Center of Specialized Medicine, Teaching and Research. Retrospective Study	Periodontitis was defined according to the American Academy of Periodontology	PASI was used and were made available in all medical records of the patients.	PASI was used and were made available in all medical records of the patients.	Test group (psoriatic patients) = 397 Periodontitis = 183 Without periodontitis = 214 Control group (healthy patients) = 240 Periodontitis = 119 Without periodontitis = 121 Individuals with psoriasis presented a chance 1.72 higher of having periodontitis than controls (OR = 1.72; 95% CI 1.28–2.32; p < 0.001).	The authors declare that are no conflicts of interest. This study was supported by the National Council of Scientific and Technological Development–CNPq, Brazil (Productivity research grants #307034/2015-1; #307024/2015-6 and #402158/2016-4) and grants from FAPEMIG.

Table 1. (Continuation) Characteristics of the retrospective studies.

Author (Country)	Subjects characteristics	Subjects characteristics	Definition of Psoriasis	Outcome assessment	Main findings	Conflict of interest and source funding
Sarac <i>et al.</i> 2017 (Turkey)	152 patients (97 woman and 55 man) - Age group test: 34.43 ± 14.4 and Age group control: 30.80 ± 11.19 - from Faculty of Medicine, Department of Dermatology, Inonu University	Periodontal disease was classified according to the system of Community Periodontal Index of Treatment Needs.	Psoriasis was defined according to PASI.	Assessment of patients: - Psoriatic: clinical examination - With periodontitis: clinical examination Follow up: 10.5 years	Test group (psoriatic patients) = 76 Periodontitis = 15 Without periodontitis = 61 Control group = 76 Periodontitis = 6 Without periodontitis = 70 The periodontal disease may impact psoriasis as a chronic infectious.	Authors declared no conflict of interest.
	Retrospective Study					
Sharma <i>et al.</i> 2014 (India)	68 patients (31 woman and 37 man) - Age group test: 34.58 ± 3.47 years and Age group control: 34.34 ± 3.11 years) from Department of Dermatology, Bangalore Medical College and Research Institute, Bangalore.	Periodontitis was defined as subjects with ≥ 2 interproximal sites with Pocket depth ≥ 5 mm or ≥ 2 interproximal sites with attachment loss ≥ 4 mm with radiographic evidence of bone loss	The diagnosis for patients with psoriasis were based on case history, clinical examination and confirmed with histopathological as well as immunofluorescence. The severity of psoriasis was assessed and recorded by PASI.	Assessment of patients: - Psoriatic: case history, clinical examination and confirmed with histopathological as well as immunofluorescence - With periodontitis: clinical examination Follow up: 4 months	The study showed higher presence of Chronic Periodontitis in psoriasis group compared with healthy subjects. Significant relationship between Pocket Depth and severity of psoriasis and between attachment loss and severity of psoriasis were found	Authors declared no conflict of interest.
	Retrospective Study					
Skudutyte-Rysstad <i>et al.</i> 2014 (Norway)	171 patients (72 woman and 99 man) age 22-66 years from Faculty of Dentistry, University of Oslo and the Dermatology Department, Oslo University Hospital-Rikshospitalet, Norway.	Periodontitis was defined according to the case definitions for surveillance of periodontitis proposed by the Centers for Disease Control and Prevention and the American Academy of Periodontology.	Their psoriasis diagnosis was verified by PASI.	Assessment of patients: - Psoriatic: clinical examination - With periodontitis: clinical examination Follow up: 15 months	Test group (psoriatic patient) = 50 Periodontitis = 21 Without periodontitis = 29 Control group (healthy patients) = 121 Periodontitis = 22 Without periodontitis = 99 The prevalence of periodontitis was significantly higher in psoriasis individuals compared to healthy controls.	Authors declared no conflict of interest.
	Retrospective Study					

PASI: Psoriasis area and severity index.

Prospective study

Only one of the eight included studies was prospective (Nakib *et al.*, 2013). The characteristics are shown in Table 2. The study followed 81,378 individuals of both sexes, mean age of 64 years, and subjects were followed for ten years. A self-reported questionnaire assessed exposure (periodontitis) and outcome (psoriasis severity).

Methodological assessment

Retrospective studies

NOS domains were used to assess the quality of the retrospective studies included. Of the seven retrospective

studies (Table 3), five were considered to have a low risk of bias (Ganzetti *et al.*, 2014; Lazaridou *et al.*, 2013; Mendes *et al.*, 2019; Sharma, Raman e Pradeep, 2014; Skudutyte-Rysstad *et al.*, 2014) and two moderate risk (Keller e Lin, 2012; Sarac *et al.*, 2017).

Prospective study

The risk of bias from the prospective study is shown in Table 4, and the study was considered to have a moderate risk of bias (Nakib *et al.*, 2013).

Table 2. Characteristics of the prospective studies.

Author (Country)	Subjects characteristics	Subjects characteristics	Definition of Psoriasis	Outcome assessment	Main findings	Conflict of interest and source funding
Nakib et al. 2013 (EUA)	81.378 patients Age/Mean 64 years from Nurses' Health Study. Prospective Study	Self-reported history of bone loss.	Self-reported physician-diagnosed psoriasis through 2008. Participants were asked to complete the Psoriasis Screening Tool.	- Psoriasis: self-report, questionnaire - Periodontitis: self-report, questionnaire Follow up: 10 years	History of periodontal bone loss increased the risk of developing psoriasis in 47%, when compared to those without periodontal bone loss.	Dr Abrar A. Qureshi has received a grant from Amgen/Pfizer to evaluate 'Biomarkers in psoriasis and psoriatic arthritis'. He also serves as a consultant for Abbott, Centocor, Novartis and the Centers for Disease Control and Prevention. The other authors report no conflicts of interest.

Table 3. Methodological quality of the retrospectives studies.

	Selection (maximum 5)	Comparability (maximum 2)	Outcome (maximum 2)	Statistics (maximum 1)	Total (maximum 10)
Ganzetti et al. 2014	4 ★	2 ★	1 ★	0 ★	7 ★
Keller et al. 2012	4 ★	0 ★	1 ★	1 ★	6 ★
Lazaridou et al. 2013	3 ★	2 ★	3 ★	1 ★	8 ★
Mendes et al. 2019	5 ★	2 ★	2 ★	1 ★	10 ★
Sarac et al. 2017	4 ★	1 ★	2 ★	0 ★	5 ★
Sharma et al. 2014	5 ★	1 ★	2 ★	1 ★	9 ★
Skudutyte-Rysstad et al. 2014	5 ★	2 ★	2 ★	1 ★	10 ★

Scores ranged from 0 to 10 stars. Studies with 7-10 stars were arbitrarily rated as low risk of bias, 5-6 stars moderate risk of bias and < 5 high risk of bias.

Table 4. Methodological quality of the prospective study.

	Selection (maximum 5)	Comparability (maximum 2)	Outcome (maximum 2)	Statistics (maximum 1)	Total (maximum 10)
Nakib et al., 2013	2★	1 ★	1 ★	1 ★	5 ★

Scores ranged from 0 to 11 stars. Studies with 7-11 stars were arbitrarily rated as low risk of bias, 5-6 stars moderate risk of bias and < 5 high risk of bias.

Pooled outcomes

Retrospective studies

The overall meta-analysis demonstrated that individuals with periodontitis have 61% increased odds of psoriasis compared to individuals with periodontal health (OR = 1,61; 95% CI = 1,23 to 2,11, Heterogeneity: I² = 0%, p = 0,0005), (Figure 2).

Prospective study

A descriptive analysis of the prospective study showed that during the 10-year follow-up period, the history of periodontal bone loss increased the risk of developing psoriasis when compared with periodontally healthy patients.

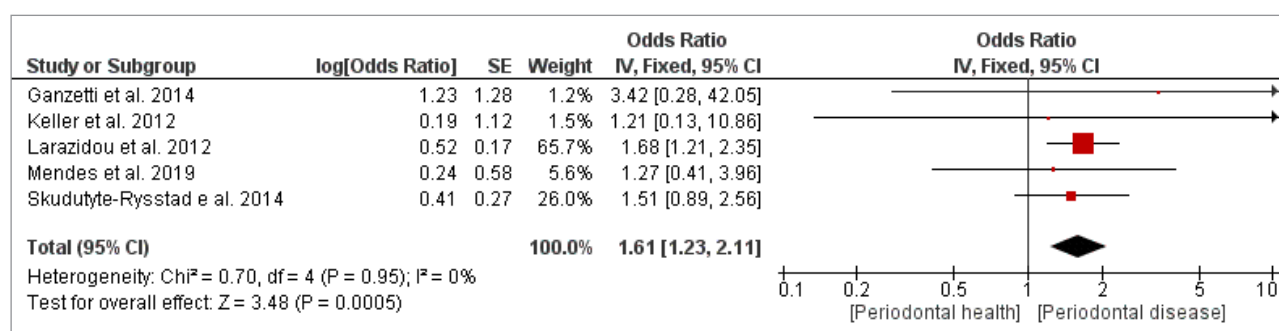


Figure 2. Forest plot.

Discussion

The main results of the present SR indicate that individuals with periodontitis may have an increased risk of psoriasis when compared with periodontally healthy individuals.

An overall meta-analysis from retrospective studies demonstrated that individuals with periodontitis have a 61% increased risk of psoriasis compared to those with periodontal health. This result is in accordance with previous reviews (Ungprasert, Wijarnpreecha, Wetter, 2017; Zhang *et al.*, 2020), which found 55% and 2.87 times increased risk of psoriasis, respectively.

Noteworthy, some differences should be pointed out. 1) The search strategy from Ungprasert, Wijarnpreecha e Wetter, 2017 was carried out about five to six years ago, and since then, the base of evidence has improved (Mendes *et al.*, 2019); 2). Both previous reviews (Ungprasert, Wijarnpreecha e Wetter, 2017; Zhang *et al.*, 2020), included prospective and retrospective studies in the same overall meta-analysis, dividing into subgroups by study designs. In the present review, we chose to combine only the retrospective studies in the meta-analysis, leaving only one prospective study, which was not included in the meta-analysis. This decision was based on the Cochrane handbook (Higgins *et al.*, 2019), which does not recommend combining prospective and retrospective studies in the same analysis due to several methodological differences and possible bias involved; and 3) The more recent SR, (Zhang *et al.*, 2020), included in their meta-analysis one study with a control group of not systemically health individuals (with chronic spontaneous urticaria) (Painsi *et al.*, 2017) and one study that focused on smoking patients (Antal *et al.*, 2014). Since the above-mentioned studies would substantially increase heterogeneity, we decided not to include them in the present SR.

The molecular mechanisms that may explain the association between periodontitis and psoriasis found herein are the state of systemic inflammation revealed by increased serum levels of pro-inflammatory cytokines in periodontitis and psoriasis patients; and the

oxidative stress, which plays a major role in the pathogenesis of both diseases (Tóthová e Celec, 2017; Zhang *et al.*, 2019). In addition, both are chronic inflammatory diseases that share the same risk factors, such as smoking (Armstrong *et al.*, 2014; Leite *et al.*, 2018), alcoholism (Gupta *et al.*, 1993; Wang *et al.*, 2016), stress (Botelho *et al.*, 2018; Kouris *et al.*, 2017) and obesity (Moura-Grec *et al.*, 2014; Procaccini *et al.*, 2011; Versini *et al.*, 2014).

All prospective and retrospective studies included in the present SR had their methodological quality assessed by a modified version of the NOS scale (Campos *et al.*, 2021; Sendyk *et al.*, 2017). The qualitative assessment considered the sample size calculation, representativeness of the sample, ascertainment of exposure, management of confounding factors, outcome assessment, and valid statistical analysis. Meeting these criteria is essential for the studies' bias control, and its failure may have impacted the results. In our quality assessment, most retrospective studies were considered to have a low risk of bias (Ganzetti *et al.*, 2014; Lazaridou *et al.*, 2013; Mendes *et al.*, 2019; Sharma, Raman e Pradeep, 2014; Skudutyte-Rysstad *et al.*, 2014), and there was no study rated as high risk of bias. The only prospective study (Nakib *et al.*, 2013) was rated as moderate risk. Although most studies included did not present a high risk of bias, some points should be addressed. An important point is that only the retrospective studies were included in the meta-analysis, which are associated with bias and heterogeneity. In fact, in retrospective analysis, we do not know the patient's periodontal and systemic condition when the psoriasis was installed, making it difficult to prove the cause-effect relationship of the diseases. In addition, there were several methodological differences among the included studies (Ganzetti *et al.*, 2014; Keller e Lin, 2012; Lazaridou *et al.*, 2013; Mendes *et al.*, 2019; Sarac *et al.*, 2017; Sharma, Raman e Pradeep, 2014; Skudutyte-Rysstad *et al.*, 2014), as regards periodontal disease assessment and classification; and therefore, the results of the present SR should be interpreted with caution. Further, other limitations of

this SR include the low number of studies on this topic. Because of the above-mentioned limitations, we cannot yet establish a causal relationship between these two inflammatory diseases.

Importantly, a preliminary search was conducted to find randomized clinical trials (RCT) on the effect of periodontal treatment on psoriasis condition. However, only one randomized clinical trial on this topic has been found (Yarkac, Ogrum e Gokturk, 2020). This RCT showed that periodontal therapy improved the psoriasis condition measured by the Psoriasis Area and Severity Index in patients with both diseases and decreased several salivary inflammatory biomarkers. The results from this RCT corroborate with the present SR, which found an association between these conditions; however, more RCTs should be conducted on this topic in order to improve the strength of evidence and confirm or not the cause-relationship of these diseases.

This study demonstrated an association between periodontal disease and psoriasis. Despite the weak evidence on the topic, clinicians should monitor their patients' periodontal health to provide oral health and, secondarily, possibly prevent the risk of psoriasis. Further prospective studies and randomized clinical trials on this topic should be carried out.

Conclusions

The present SR indicates that individuals with periodontitis may have an increased risk of psoriasis compared to periodontally healthy individuals. Because of the limitations, we cannot yet establish a causal relationship between these two inflammatory diseases.

References

- Antal M, Braunitzer G, Mattheos N, Gyulai R, Nagy K. Smoking as a permissive factor of periodontal disease in psoriasis. *PLoS One*. 2014 Mar 20;9(3):e92333. doi: 10.1371/journal.pone.0092333. Erratum in: *PLoS One*. 2014;9(10):e110975.
- Armstrong AW, Harskamp CT, Armstrong EJ. The association between psoriasis and hypertension: a systematic review and meta-analysis of observational studies. *J Hypertens*. 2013 Mar;31(3):433-42; discussion 442-3.
- Armstrong AW, Harskamp CT, Dhillon JS, Armstrong EJ. Psoriasis and smoking: a systematic review and meta-analysis. *Br J Dermatol*. 2014 Feb;170(2):304-14.
- Binus AM, Han J, Qamar AA, Mody EA, Holt EW, Qureshi AA. Associated comorbidities in psoriasis and inflammatory bowel disease. *J Eur Acad Dermatol Venereol*. 2012 May;26(5):644-50.
- Borska L, Kremlacek J, Andrys C, Krejsek J, Hamakova K, Borsky P, Palicka V, Rehacek V, Malkova A, Fiala Z. Systemic Inflammation, Oxidative Damage to Nucleic Acids, and Metabolic Syndrome in the Pathogenesis of Psoriasis. *Int J Mol Sci*. 2017 Oct 25;18(11):2238.
- Botelho J, Machado V, Mascarenhas P, Rua J, Alves R, Cavacas MA, Delgado A, João Mendes J. Stress, salivary cortisol and periodontitis: A systematic review and meta-analysis of observational studies. *Arch Oral Biol*. 2018 Dec;96:58-65.
- Campos ISO, de Freitas MR, Costa FO, Cortelli SC, Rovai ES, Cortelli JR. The Effects of Patient Compliance in Supportive Periodontal Therapy on Tooth Loss: A systematic Review and Meta-analysis. *J Int Acad Periodontol*. 2021 Jan 1;23(1):17-30.
- Chambrone L, Pannuti CM, Guglielmetti MR, Chambrone LA. Evidence grade associating periodontitis with preterm birth and/or low birth weight: II: a systematic review of randomized trials evaluating the effects of periodontal treatment. *J Clin Periodontol*. 2011 Oct;38(10):902-14.
- Cutler CW, Jotwani R. Dendritic cells at the oral mucosal interface. *J Dent Res*. 2006 Aug;85(8):678-89.
- Fadel HT, Flytström I, Calander AM, Bergbrant IM, Heijl L, Birkhed D. Profiles of dental caries and periodontal disease in individuals with or without psoriasis. *J Periodontol*. 2013 Apr;84(4):477-85.
- F Ferrándiz C, Bordas X, García-Patos V, Puig S, Pujol R, Smandía A. Prevalence of psoriasis in Spain (Epiderma Project: phase I). *J Eur Acad Dermatol Venereol*. 2001 Jan;15(1):20-3.
- Ganzetti, G.; Campanati, A.; Santarelli, A.; Pozzi, V.; Molinelli, E.; Minnetti, I.; Brisigotti, V.; Procaccini, M.; Emanuelli, M.; Offidani, A. Periodontal Disease: An Oral Manifestation of Psoriasis or an Occasional Finding? *Drug Development Research*, 2014, 75: S46-S49.
- Genco RJ, Borgnakke WS. Risk factors for periodontal disease. *Periodontol 2000*. 2013 Jun;62(1):59-94.
- Gheorghita D, Antal MA, Nagy K, Kertesz A, Braunitzer G. Smoking and Psoriasis as Synergistic Risk Factors in Periodontal disease. *Fogorv Sz*. 2016 Dec;109(4):119-124.
- Gupta MA, Schork NJ, Gupta AK, Ellis CN. Alcohol intake and treatment responsiveness of psoriasis: a prospective study. *J Am Acad Dermatol*. 1993 May;28:730-2.
- Higgins, J. P. T.; Thomas, J.; Chandler, J.; Cumpston, M.; Li, T.; Page, M. J.; Welch, V. A. *Cochrane handbook for systematic reviews of interventions*, 2019, 5.1.0 ed. [s.l.] The Cochrane Collaboration.

- Hussain T, Tan B, Yin Y, Blachier F, Tossou MC, Rahu N. Oxidative Stress and Inflammation: What Polyphenols Can Do for Us? *Oxid Med Cell Longev*. 2016;**2016**:7432797.
- Jepsen, S.; Caton, JG; Albandar, JM; Bissada, NF; Bouchard, P; Cortellini, P; Demirel, K; Sanctis, M; Ercoli, C; Fan, J; Geurs, NC; Hughes, FJ; Jin, L; Kantarci, A; Lalla, E; Madianos, PN; Matthews, D; McGuire, MK; Mills, MP; Preshaw, PM; Reynolds, MA; Sculean, A; Susin C; West, NX; Yamazaki, K. Periodontal manifestations of systemic diseases and developmental and acquired conditions: Consensus report of workgroup 3 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of periodontology*, 2018, **89**: S237-S248.
- Keller JJ, Lin HC. The effects of chronic periodontitis and its treatment on the subsequent risk of psoriasis. *Br J Dermatol*. 2012 Dec;**167**(6):1338-44.
- Kouris A, Platsidaki E, Kouskoukis C, Christodoulou C. Psychological parameters of psoriasis. *Psychiatriki*. 2017 Jan-Mar;**28**(1):54-59.
- Lazaridou E, Tsikrikoni A, Fotiadou C, Kyrmanidou E, Vakirlis E, Giannopoulou C, Apalla Z, Ioannides D. Association of chronic plaque psoriasis and severe periodontitis: a hospital based case-control study. *J Eur Acad Dermatol Venereol*. 2013 Aug;**27**(8):967-72.
- Leite FRM, Nascimento GG, Scheutz F, López R. Effect of Smoking on Periodontitis: A Systematic Review and Meta-regression. *Am J Prev Med*. 2018 Jun;**54**(6):831-841.
- Mehta NN, Azfar RS, Shin DB, Neimann AL, Troxel AB, Gelfand JM. Patients with severe psoriasis are at increased risk of cardiovascular mortality: cohort study using the General Practice Research Database. *Eur Heart J*. 2010 Apr;**31**(8):1000-6.
- Mendes VS, Cota LOM, Costa AA, Oliveira AMSD, Costa FO. Periodontitis as another comorbidity associated with psoriasis: A case-control study. *J Periodontol*. 2019 Apr;**90**(4):358-366.
- Meuric V, Le Gall-David S, Boyer E, et al. Signature of Microbial Dysbiosis in Periodontitis. *Appl Environ Microbiol*. 2017;**83**(14):e00462-17.
- Miranda TS, Heluy SL, Cruz DF, da Silva HDP, Feres M, Figueiredo LC, Duarte PM. The ratios of pro-inflammatory to anti-inflammatory cytokines in the serum of chronic periodontitis patients with and without type 2 diabetes and/or smoking habit. *Clin Oral Investig*. 2019 Feb;**23**(2):641-650.
- Moura-Grec PG, Marsicano JA, Carvalho CA, Sales-Peres SH. Obesity and periodontitis: systematic review and meta-analysis. *Cien Saude Colet*. 2014 Jun;**19**(6):1763-72.
- Moura-Grec PG, Marsicano JA, Carvalho CA, Sales-Peres SH. Obesity and periodontitis: systematic review and meta-analysis. *Cien Saude Colet*. 2014 Jun;**19**(6):1763-72.
- Nakib S, Han J, Li T, Joshipura K, Qureshi AA. Periodontal disease and risk of psoriasis among nurses in the United States. *Acta Odontol Scand*. 2013 Nov;**71**(6):1423-9.
- Nestle FO, Kaplan DH, Barker J. Psoriasis. *N Engl J Med*. 2009 Jul 30;**361**(5):496-509.
- Nevitt GJ, Hutchinson PE. Psoriasis in the community: prevalence, severity and patients' beliefs and attitudes towards the disease. *Br J Dermatol*. 1996 Oct;**135**(4):533-7.
- Painsi C, Hirtenfelder A, Lange-Asschenfeldt B, Quehenberger F, Wolf P: The Prevalence of Periodontitis Is Increased in Psoriasis and Linked to Its Inverse Subtype. *Skin Pharmacol Physiol* 2017;**30**:324-328.
- Papapanou PN, Sanz M, Buduneli N, Dietrich T, Feres M, Fine DH, Flemmig TF, Garcia R, Giannobile WV, Graziani F, Greenwell H, Herrera D, Kao RT, Kebschull M, Kinane DF, Kirkwood KL, Kocher T, Kornman KS, Kumar PS, Loos BG, Machtei E, Meng H, Mombelli A, Needleman I, Offenbacher S, Seymour GJ, Teles R, Tonetti MS. Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Periodontol*. 2018 Jun;**89** Suppl 1:S173-S182.
- Preus HR, Khanifam P, Koltveit K, Mørk C, Gjermo P. Periodontitis in psoriasis patients: a blinded, case-controlled study. *Acta Odontol Scand*. 2010 May;**68**(3):165-70.
- Procaccini C, Carbone F, Galgani M, La Rocca C, De Rosa V, Cassano S, Matarese G. Obesity and susceptibility to autoimmune diseases. *Expert Rev Clin Immunol*. 2011 May;**7**(3):287-94.
- Raghavendran K, Mylotte JM, Scannapieco FA. Nursing home-associated pneumonia, hospital-acquired pneumonia and ventilator-associated pneumonia: the contribution of dental biofilms and periodontal inflammation. *Periodontol 2000*. 2007;**44**:164-77.
- Sabat R, Philipp S, Höflich C, Kreutzer S, Wallace E, Asadullah K, Volk HD, Sterry W, Wolk K. Immunopathogenesis of psoriasis. *Exp Dermatol*. 2007 Oct;**16**(10):779-98.
- Sabat R, Philipp S, Höflich C, Kreutzer S, Wallace E, Asadullah K, Volk HD, Sterry W, Wolk K. Immunopathogenesis of psoriasis. *Exp Dermatol*. 2007 Oct;**16**(10):779-98.

- Sanz M, van Winkelhoff AJ; Working Group 1 of Seventh European Workshop on Periodontology. Periodontal infections: understanding the complexity--consensus of the Seventh European Workshop on Periodontology. *J Clin Periodontol*. 2011 Mar;38 Suppl 11:3-6.
- Sarac G, Kapicioglu Y, Cayli S, Altas A, Yologlu S. Is the periodontal status a risk factor for the development of psoriasis? *Niger J Clin Pract*. 2017 Apr;20(4):474-478.
- Sendyk DI, Rovai ES, Pannuti CM, Deboni MC, Sendyk WR, Wennerberg A. Dental implant loss in older versus younger patients: a systematic review and meta-analysis of prospective studies. *J Oral Rehabil*. 2017 Mar;44(3):229-236.
- Sezer U, Şenyurt SZ, Gündoğar H, Erciyas K, Üstün K, Kimyon G, Kırtak N, Taysı S, Onat AM. Effect of Chronic Periodontitis on Oxidative Status in Patients With Psoriasis and Psoriatic Arthritis. *J Periodontol*. 2016 May;87(5):557-65.
- Sharma A, Raman A, Pradeep AR. Association of chronic periodontitis and psoriasis: periodontal status with severity of psoriasis. *Oral Dis*. 2015 Apr;21(3):314-9.
- Skudutyte-Rysstad R, Slevolden EM, Hansen BF, Sandvik L, Preus HR. Association between moderate to severe psoriasis and periodontitis in a Scandinavian population. *BMC Oral Health*. 2014 Nov 26;14:139.
- Su NY, Huang JY, Hu CJ, Yu HC, Chang YC. Increased risk of periodontitis in patients with psoriatic disease: a nationwide population-based retrospective cohort study. *PeerJ*. 2017 Nov 16;5:e4064.
- Tóthová L, Celec P. Oxidative Stress and Antioxidants in the Diagnosis and Therapy of Periodontitis. *Front Physiol*. 2017 Dec 14;8:1055.
- Ungprasert P, Wijarnpreecha K, Wetter DA. Periodontitis and risk of psoriasis: a systematic review and meta-analysis. *J Eur Acad Dermatol Venereol*. 2017 May;31(5):857-862.
- Versini M, Jeandel PY, Rosenthal E, Shoenfeld Y. Obesity in autoimmune diseases: not a passive bystander. *Autoimmun Rev*. 2014 Sep;13(9):981-1000.
- Wang J, Lv J, Wang W, Jiang X. Alcohol consumption and risk of periodontitis: a meta-analysis. *J Clin Periodontol*. 2016 Jul;43(7):572-83.
- Woeste S, Graetz C, Gerdes S, Mrowietz U. Oral Health in Patients with Psoriasis-A Prospective Study. *J Invest Dermatol*. 2019 Jun;139(6):1237-1244.
- Ucan Yarkac F, Ogrum A, Gokturk O. Effects of non-surgical periodontal therapy on inflammatory markers of psoriasis: A randomized controlled trial. *J Clin Periodontol*. 2020 Feb;47(2):193-201.
- Yost S, Duran-Pinedo AE, Teles R, Krishnan K, Frias-Lopez J. Functional signatures of oral dysbiosis during periodontitis progression revealed by microbial metatranscriptome analysis. *Genome Med*. 2015 Apr 27;7(1):27.
- Zhang X, Gu H, Xie S, Su Y. Periodontitis in patients with psoriasis: A systematic review and meta-analysis. *Oral Dis*. 2020 Aug 27.
- Zhang Y, Li Z, Ma Y, Mu Z. Association of total oxidant status, total antioxidant status, and malondialdehyde and catalase levels with psoriasis: a systematic review and meta-analysis. *Clin Rheumatol*. 2019 Oct;38(10):2659-2671.