

Assessment of Psychological Stress as a Risk Factor for Periodontal Disease: Systematic Review and Meta-Analysis

Iris Iborra Badia¹, Lydia Calabuig Aparicio², Manuel Rodríguez Aranda³,
Francisco Alpiste Illueca⁴, Andrés López Roldán^{5*}

1. Associate Professor of the Master of Periodontics and Osseointegration Programme, Periodontics Unit., Department of Stomatology, School of Medicine and Dentistry, Universitat de València (University of Valencia).
2. Student in the Master of Periodontics and Osseointegration Programme, Periodontics Unit, Department of Stomatology, School of Medicine and Dentistry, University of Valencia.
3. Lecturer in the Master's Programme in Periodontics and Osseointegration, Periodontics Unit, Department of Stomatology, School of Medicine and Dentistry, University of Valencia.
4. Director of the Master of Periodontics and Osseointegration Programme, Periodontics Unit. Department of Stomatology, School of Medicine and Dentistry, University of Valencia.
5. Part-time Instructor in the Periodontics and Osseointegration Unit, Department of Stomatology, School of Medicine and Dentistry, University of Valencia.

Abstract

Our objective is to get a new perspective on the impact of psychological stress on periodontitis and its progression, evaluating the current evidence of psychological stress as a risk factor for periodontal disease through the use of psychological questionnaires.

A systematic review was conducted with observational cross-sectional, case-control, cohort studies and clinical trials. The selected studies had to include at least two periodontal variables and evaluate their relationship with psychological stress. An electronic search of various databases was performed by two independent researchers to obtain the most relevant articles published up to June 2021. Sixteen articles were included in the final qualitative synthesis. 93,7% observed a positive relationship between psychological stress and periodontitis, and the clinical attachment level was the periodontal parameter most related to stress. A meta-analysis was then performed to compare the questionnaire results of healthy individuals with those of individuals with periodontitis.

The results of the meta-analysis did not show statistically significant differences between the two groups. There is a relationship between psychological stress and the severity of periodontitis. This relationship must be considered a possible risk factor. Questionnaires on psychological stress could be used in the future as a possible clinical tool.

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Introduction

Periodontitis is an inflammatory disease produced by bacterial biofilms that presents as a loss in the clinical attachment level (CAL). When gingival inflammation begins, bleeding on probing (BOP) is the main tool for the diagnosis of periodontitis¹. However, the onset and progression of periodontitis is characterised by loss of interdental attachment and

radiographically detectable alveolar bone loss: periodontal pockets ≥ 3 mm and BOP $\geq 10\%$ ². Although the bacterial biofilm itself plays a fundamental role in the development of periodontitis, it alone is not sufficient to explain the progression of the disease³. Age, smoking, genetic factors, socioeconomic status, systemic diseases and psychological stress have been identified as other risk factors for periodontitis⁴.

At present, stress is considered one of the most prevalent pathologies in the population. It consists of a physiological and/or biological reaction of the organism that prompts various defence mechanisms against a situation that is perceived as threatening or demanding⁴. Short-term stress provokes adaptive changes that allow the organism to cope with this series of external threats. Problems arise when overloads fatigue

*Corresponding author:

Iris Iborra Badia,
Associate Professor of the Master of Periodontics and Osseointegration Programme, Periodontics Unit., Department of Stomatology, School of Medicine and Dentistry, Universitat de València (University of Valencia).
E-mail: iris.iborrabadia@gmail.com

the organism, leading to de-adaptive changes "pathology". The first situation is considered normal and is called stress, while the second is known as distress; however, it is common for studies to apply the term stress to the second situation. The origin of the stressor determines whether the stress is physical or mental, and its duration determines whether it is acute or chronic⁵.

There are two main pathways through which stress can affect periodontal disease: changes in health behaviour "direct pathway", pathophysiological changes "indirect pathway" or a combination of both⁶. The main stress-related changes in health habits are poor oral hygiene and increased smoking. Regarding pathophysiological changes, the impact of stress on the immune system is widely known, and chronic stress can lead to the breakdown of homeostasis between the oral microflora and the host immune system. Alterations in the "immuno-neuro-endocrine complex" are observed based on nerve fibre junctions of the autonomic nervous system and the hypothalamus-pituitary-adrenal axis which disrupt plasma levels of cortisol and cytokines (IL-1 β , IL-6, IL-8)⁷.

Therefore, the objective of this review was to assess the impact of psychological stress on periodontitis by evaluating the current evidence of psychological stress as a risk factor for periodontitis through the use of psychological questionnaires.

Materials and methods

The PRISMA-P checklist (Preferred Reporting Items for Systematic Review and Meta-analysis) was followed in preparing the protocol of this systematic review, and the 27 items for systematic reviews and meta-analysis were used⁸. In addition, this systematic review was registered in PROSPERO and was assigned the following number: CRD42020191069 (International Prospective Register of Systematic Reviews hosted by the National Institute for Health Research, University of York, Centre for Reviews and Dissemination).

Objective of The Review

The objective of this systematic review was to verify the relationship between psychological stress and periodontitis using different periodontal parameters. A research

question was developed to aid in the literature search, which applied the following PECO measures:

Participants (P): adults > 18 years without relevant systemic diseases

Exposure (E): patients with high levels of stress, evaluated using specialised psychological questionnaires

Comparison (C): patients without stress

Outcomes (O): existence of a relationship between the results of the psychological stress questionnaires and the clinical periodontal variables: probing depth (PD), CAL, BOP, plaque index (PI), gingival index (GI) and tooth loss. CAL was the principal variable examined.

Databases Used for Article Extraction

The literature search was performed by two independent researchers (I.I and L.C) at the University of Medicine and Dentistry of Valencia from February 2020 to June 2021. The following electronic databases were searched: MEDLINE, EMBASE and the Cochrane Library (Cochrane Central Register of Controlled Trials). All articles published in these databases until June 2021 were reviewed. The two independent researchers (L.C and I.I) reviewed the titles, abstracts and full texts of the identified articles. In all of the articles identified, the following data were considered: publication status, year of publication, observational study design, characteristics of the participants and study groups, methodological characteristics, the approach used to evaluate periodontitis and the presence/absence of psychological stress and, finally, the results.

Selection Criteria

Study Inclusion Criteria

Studies in humans

Studies with patients older than 18 years with periodontitis

Observational studies (cohort studies, case-control studies, cross-sectional and longitudinal studies) and clinical trials

Studies that evaluated at least two different periodontal variables: PD, CAL, BOP, PI, GI and tooth loss.

Studies that evaluated psychological variables through the use of psychological questionnaires

Study Exclusion Criteria

Other systematic reviews
Literature reviews
Animal studies
Studies that did not use psychological questionnaires to measure psychological stress
Studies that evaluated physical stress and not psychological stress
Studies that evaluated stress at a specific time point (acute stress) and not chronic stress

Data Extraction

The two reviewers were trained and calibrated (II and LC). Articles that met the inclusion criteria were selected for data extraction. The two reviewers included the full texts of the potentially relevant articles and evaluated them independently for each search. Any disagreement was resolved through discussion and with the help of a third reviewer specialising in the subject (AL). Finally, the main variables were summarised in a table (Table 1).

Analysis of The Methodological Quality of The Studies Selected for Data Extraction

The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of each of the cohort, case-control and cross-sectional studies that was included. Thirteen publications scored at least 7 points out of 9 and, therefore, were considered high quality. Two publications were considered medium quality due to a score lower than 7 points out of 9, while one publication was considered very low quality due to a score of 4.

Summary of Measures and Synthesis of Outcomes

For the meta-analysis of the results, articles that used the same psychological stress questionnaires (LES and SCL-90R) were chosen, and the different groups were divided according to CAL. Individuals with a CAL loss of 0 mm to 3 mm were included in the periodontally healthy group, and individuals with a CAL loss of > 4 mm were included in the unhealthy group or the group with periodontitis.

While the values provided by the different authors were measured using different scales since they used different versions (extended or abbreviated versions) of the different psychological questionnaires, this problem did not preclude the meta-analysis; however, it did require working with a standardised mean

difference (SMD). Different meta-analyses were performed according to the psychological stress questionnaire used: one meta-analysis was performed to compare the outcomes of the Life Events Scale (LES) questionnaire between periodontally healthy and unhealthy individuals and another meta-analysis to compare the outcomes of the Symptom Check List-Revised (SCL-90R) questionnaire between periodontally healthy and sick individuals.

For the study of heterogeneity, the I^2 index (percentage of variability of the estimated effect that can be attributed to the heterogeneity of the true effects) and the corresponding statistical *Dixon's Q test* for nullity were performed. The level of significance used in the analyses was 5% ($\alpha = 0,05$).

Results

Results of Search and Selection

The search of the electronic databases identified 642 articles (345 PubMed, 288 EMBASE, 9 Cochrane). After duplicate articles were discarded, the titles and abstracts of 188 articles were reviewed; 150 were excluded, leaving 38 articles for full evaluation (Figure 1).

Analysis of The Results

Of the 16 articles included in the review, 15 articles (93,7%) claimed a significant association between psychological stress and periodontitis, while one article (the remaining 6,3%), did not describe any association.

Figure 2 shows the psychological tests most often used in the articles included in this review and the number of articles that used them; the LES⁹⁻¹² and the SCL-90R^{9,10,13} were the most commonly used.

33% of the articles found a significant association between PD and stress¹³⁻¹⁷, 53% of the articles found a relationship between CAL and stress^{9,10, 13-15, 17, 18, 19, 20}. In 20% of the articles, there was a relationship between BOP and stress level^{16, 17, 21}. In 33% of the articles, there was a statistically significant association between PI and stress^{13, 19, 22-24}. 20% of the articles noted an association between GI and stress^{17, 19, 25}. Finally, no significant association was found in any of the 16 articles between the number of teeth and the level of stress.

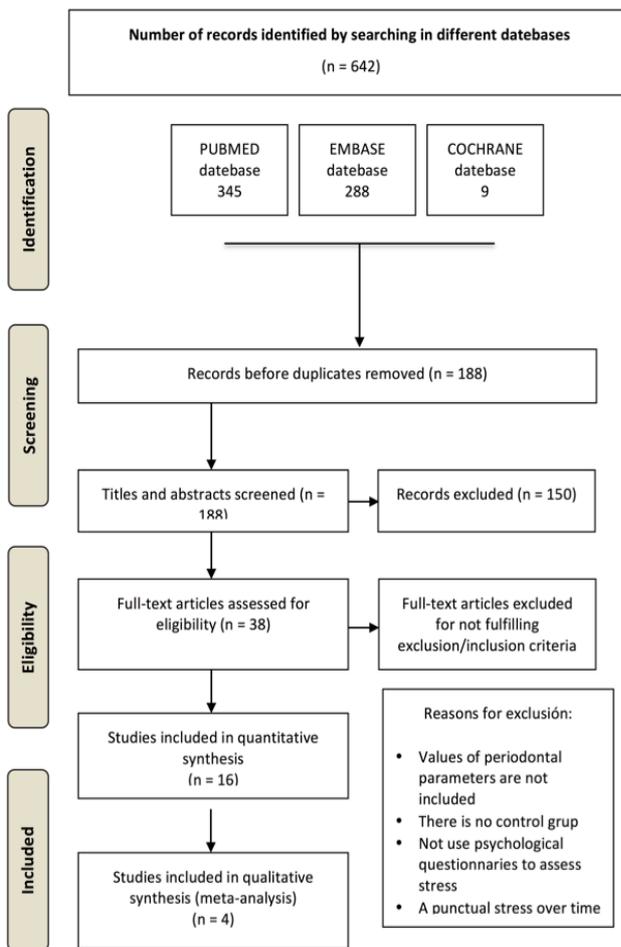


Figure 1. Flowchart (PRISMA format).

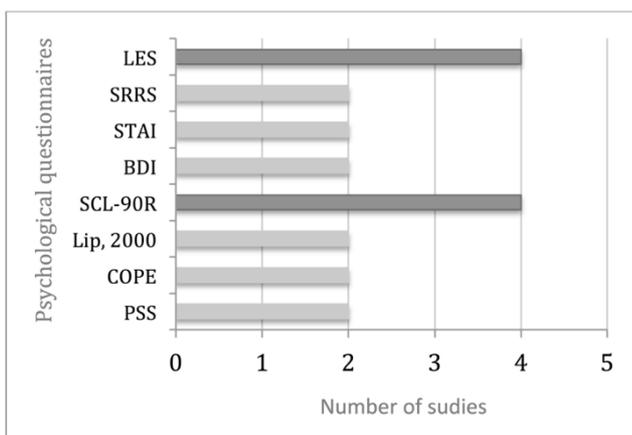


Figure 2. Most frequently used psychological questionnaires.

Therefore, we can affirm that CAL is the periodontal parameter that is most related to psychological stress according to the articles included in this review. The results of this review indicate that there is a significant relationship between psychological stress assessed by

questionnaires and periodontitis assessed by periodontal clinical parameters. Only one article found no positive association between stress and periodontitis¹¹.

Once the fifteen articles selected for the final qualitative synthesis of this systematic review were analysed, a meta-analysis was conducted to compare the outcomes of the most commonly used psychological stress questionnaires (LES and SCL-90R) and their relationship with periodontitis. There were some differences among the articles, such as the use of different versions of the questionnaire (extended or abbreviated), periodontitis subgroups that varied among the articles and the reporting of standard deviation (SD) by some authors and standard error (SE) by others.

The objective of the present systematic review focused on comparing patients who presented psychological stress with patients who did not present psychological stress and determining how stress relates to periodontitis. The articles selected for the meta-analysis used the same psychological stress questionnaires (LES and SCL-90R), but due to the large number of psychological variables analysed, the authors of these articles divided the individuals in their sample according to the loss of CAL, grouping them into a periodontally healthy group and a periodontally sick group. For this reason, the present meta-analysis focused on assessing the psychological stress of individuals differentiated into two groups: periodontally healthy and periodontally unhealthy.

Meta-Analysis of The LES Questionnaire Results

The 95% confidence interval (-0,19 0,21) clearly included 0; therefore, there is not enough statistical evidence to say that periodontally healthy and sick people have different psychological scores ($p = .928$). $I^2 = 42.1\%$ was obtained. This degree of heterogeneity was moderate, which indicates that the three authors' results were consistent with one another and increases the reliability of the meta-analysis results. In fact, the p -value = .178 confirms that the heterogeneity in the analysis is practically zero.

The estimated difference between periodontally sick and healthy individuals was .009 (Figure 3).

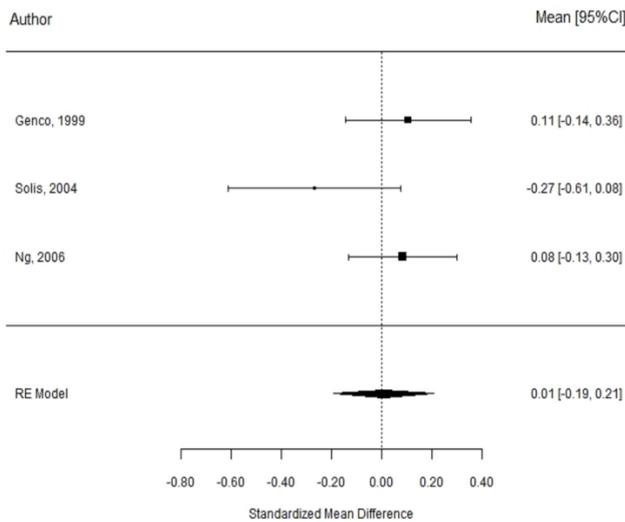


Figure 3. Outcomes of the meta-analysis of the LES questionnaire results (healthy vs. sick): standardised mean difference (smd), standard error (se), 95% confidence interval, z-test (p-value).

Meta-Analysis of The SCL-90R Questionnaire Results

In this case, the estimated difference between periodontally healthy and sick individuals was .106. The 95% confidence interval included 0; therefore, there is not enough statistical evidence to say that periodontally healthy and sick individuals have different psychological scores ($p = .206$) (Figure 4). Heterogeneity was not notable ($I^2 = 0\%$).

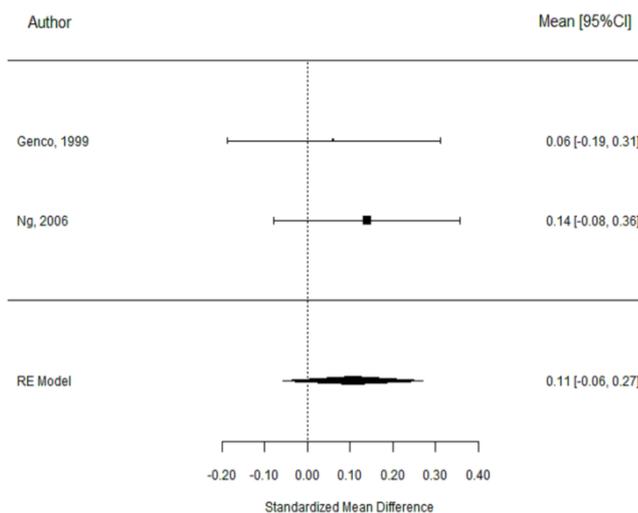


Figure 4. Outcomes of the meta-analysis of the SCL-90R questionnaire results (healthy vs. sick): standardised mean difference (smd), standard error (se), 95% confidence interval, z-test (p-value).

Discussion

Given the relationship between negative effect of stress and immune function, it is not surprising that over the past several decades a variety of studies have reported links between psychological stress and periodontal disease²⁶⁻²⁹. Chronic inflammatory diseases, such as periodontitis, have a complex pathogenesis and a multifactorial etiology, involving complex host-parasite interactions³¹. Genetic variations in genes encoding the molecular components of the host immune defense, coupled with specific bacterial species in the subgingival plaque, set the stage for individual differences in risk for periodontitis^{30,31}. A substantial body of evidence indicates that chronic psychological stress and ineffective coping can influence the onset and progression of many chronic diseases, including periodontitis³²⁻³⁴.

Evaluation of Periodontal Parameters

Two studies observed that financial stress, child-related stress and coping with emotions and problems increased in conjunction with increases in attachment loss, reporting a significant relationship between stress and periodontitis^{9,10}. In one of the studies, it was observed that individuals with work stress had higher PD values than individuals with family stress; however, this relationship was not significant. On the other hand, individuals with family stress had higher CAL values than individuals with work stress did, but in this case, the relationship was significant ($p = .001$)¹⁷. Some authors concluded that a PD > 4 mm and moderate CAL had a significant relationship with high levels of stress and anxiety ($p < 0,05$), and thus, stress and anxiety could be an important predictor of periodontitis¹⁷. However, the objective of the present systematic review was to assess the levels of psychological stress and not the levels of anxiety.

Regarding oral hygiene, some authors found a statistically significant relationship of family stress and stressful events with bacterial plaque levels ($p = .05$) levels of gingival inflammation ($p = .008$)^{13, 19}. Finally, a statistically significant relationship was found between work stress ($p < .04$), economic problems ($p < .0001$) and insecure work ($p = .003$) and the PI²⁴.

Evaluation of Psychological Stress

Another limitation of this systematic review was the heterogeneity of the questionnaires used to measure psychological stress: although a significant relationship was observed in most studies between periodontitis and psychosocial factors and each article evaluated psychological stress differently, resulting in bias in the results.

The psychosocial factors assessed depended on the test used. The most evaluated factors were daily stressors, such as work stress, financial stress, domestic stress, being single and child-related stress (assessed by the LES). Additionally, coping with problems and emotions (based on the COPE Inventory) and different symptoms, such as anxiety, somatisation, interpersonal sensitivity, psychoticism, depression, hostility, paranoid ideas, phobic anxiety and compulsive obsession (measured with the Brief Symptom Inventory (BSI) and the SCL-90R), were important.

Another drawback that we found when compiling the results was that many of the articles did not collect data from the administered questionnaires^{14, 15, 21, 23, 24}.

On a related note, since stress was measured through questionnaires, it is possible that the incorrect information was obtained, because the respondent either misinterpreted the questions or did not answer them honestly; thus, the resulting data regarding the epidemiological relationship between stress and periodontitis may not correspond to reality. Similarly, stress is not experienced in the same way by everyone. It depends on social support, if available, and may decrease if support can be obtained from family and friends². In addition, stress is less a product of the presence of stressors than how a person manages those stressors. This may explain why one of the selected articles found no relationship between stress and periodontitis¹¹.

Conclusions

There is an evident association between psychological stress and periodontitis, and CAL was the periodontal parameter that was most related to psychosocial factors. However, this systematic review presents a series of limitations due to the different methodologies used in the 16 studies, including the size and age range of the samples, the measurement of periodontal parameters, the definition of periodontitis and, most importantly, the evaluation and definition of psychological stress. Nonetheless, most of the articles analysed the same periodontal variables: PD, CAL, BOP, PI, GI and tooth loss.

Regarding the meta-analysis, the outcomes did not show statistically significant differences in psychological stress between the two groups (periodontally healthy and unhealthy). Although the results of our review were positive, more studies are required to investigate the relationship between psychological stress and periodontitis using a standardised protocol to streamline and homogenise the stress questionnaires and to define a single type of psychological stress; more reliable and accurate results could be obtained by isolating the variable "psychological stress".

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Declaration of Interest

The authors have explicitly declared that there are no conflicts of interest directly related to this article.

STUDY DESIGN	TYPE OF STUDY	SAMPLE Size and sample characteristics	METHODOLOGY	RESULTS
Minneman et al., (1995)	Longitudinal	217	Psychological tests: EPQ (Eysenck's personality questionnaire) on personality traits OIAS (Organizational and individual assessment survey) on tolerance to stress, change, work stress and life stress variables.	A significant relationship was observed between personality traits and stress tolerance. Gingival inflammation was related to tolerance to change and anxiety; and oral soft tissue pathology with physical stress.
Genco et al., (1999)	Cross Sectional	1426	Psychological tests: LES (Life Events Scale) SCL-90R (Hopkins Symptom checklist 90 revised) BSI (Brief Symptom Inventory) COPE (The COPE Inventory questionnaire on coping styles and strategies) Hasses and Uplifts	Only financial stress was significantly associated with greater attachment loss and alveolar bone loss, so there is a relationship between financial stress and periodontal disease.
Hugoson et al., (2002)	Cross Sectional	298	Psychological tests: Questionnaire on demographic and socioeconomic status LES Psychosocial factors and stress	Age, bacterial plaque index, smoking, marital status, and traumatic life events increase the risk of severe periodontal disease. The relationship between the welfare state and the place of control was also positive.
Mengel et al., (2002)	Cases and controls	40 cases 40 controls	Psychological tests: Questionnaire carried out in cooperation with the Department of Medical Sociology of the University of Marburg on family and work stress	There is no significant relationship between IL-1 β , IL-6, cortisol, and psychological stress. Only in untreated patients with aggressive generalized periodontitis IL-6 was significant and there was a slight correlation with attachment loss. In all patients with aggressive generalized periodontitis family stress and smoking were associated with attachment loss. In untreated aggressive generalized periodontitis patients smoking was associated with IL-1 β , and in controls there was a moderate relationship between smoking and IL-6 levels.
Vettore et al., (2003)	Cases and controls	79	Psychological tests: SSI (Stress Symptom Inventory) stress and anxiety scale. SRRS (Social Readjustment Rating Scale) measures the number of stressful events in the last 12 months. STAI (State-Trait Anxiety Inventory) anxiety scale	All periodontal parameters, except bacterial plaque index, were significant in the three groups. The SRRS and the STAI were not significant between the 3 groups.
Solis et al., (2004)	Cross Sectional	160	Psychological tests: Self-Report Psychiatric Screening Questionnaire-20 STAI BDI (Beck Depression Scale) LES modified by Savoia BHS BHS (Beck Hopelessness Scale)	There is no statistically significant relationship between periodontitis patients and anxiety, stress, and depression.

Trombelli et al., (2005)	Longitudinal	96	Psychological tests: CECS (Hardiness scale and Courtauld Emotional Control Scale) Questionnaire on personality traits and coping mode VAS (Visual Analogue Scale) MSPSS (multidimensional scale of perceived social support) LES (Life experiences survey)	The MSPSS questionnaire showed a positive association with bacterial plaque index. No relationship was observed between gingival index and psychological variables, but a positive relationship was observed between crevicular fluid levels and psychological variables.
Hilgert et al., (2006)	Cross Sectional	235	Psychological tests: Lipp, 2000 (Lipp Stress Symptom Inventory for Adults)	Cortisol shows a positive association with periodontitis after adjusting for the variables of age, sex, oral hygiene, bleeding on probing, smoking and Lipp, 2000. The different phases of stress, cortisol, and the extent and severity of periodontitis were not significant.
Ng et al., (2006)	Cross Sectional	1000	Psychological tests: LEQ (Life Events Questionnaire) SRRS (Schooler's Scale of Daily Life Problems) SCL-90 DASS-S (Scale of depression, anxiety and stress reduced version) DASS-T (Depression, Anxiety and Stress Scale Long Version) COPE	Work and financial stress, depression, anxiety, and inadequate coping are significant risk indicators for severe insertion loss. No relationship was observed between stress measured with LEQ and SRRS with attachment loss and other periodontal parameters.
Chiou et al., (2010)	Cross Sectional	1764	Psychological tests: CHQ-12 (12-item Chinese health questionnaire)	Psychosocial factors and smoking were associated with attachment loss, but not with the periodontal index. Individuals with CHQ-12 ≥ 6 had a higher odds ratio for attachment loss if they were smokers.
Mannem et al., (2012)	Cross Sectional	111	Psychological tests: Lipp, 2000	Chronic periodontitis showed a significant relationship with hypercortisolemia, job strain, financial problems, clinical stress syndrome, bacterial plaque index, and uninsured work.
Laforgia et al., (2015)	Cases and controls	54 cases 54 controls	Psychological tests: IRLE (interview on recent events) SCL-90 BDI	There is a significant difference between the mean bleeding on probing obtained in periodontal and healthy subjects and between periodontitis and the mean SCL-90 values of both groups.
Jaiswal et al., (2016)	Cases and controls	20 cases 20 controls	Psychological tests: PSS (perceived stress scale)	Elevated cortisol levels and psychological stress are positively related to chronic periodontitis. Cortisol increased in stressed individuals with chronic periodontitis.
Radeef, Faisal, 2017	Cases and controls	159 73% periodontitis 27% gingivitis	Psychological tests: DASS-21 (scale of depression, anxiety and stress)	Patients with advanced periodontitis showed higher mean scores of emotional disturbances in the form of depression, anxiety and stress symptoms, although it was not statistically significant.
Coelho et al., (2019)	Cross Sectional	621	Psychological tests: PSS	There was only a statistically significant relationship between stress and probing depth ≥ 4 mm. After adjusting for age, sex, school level, smoking habit, lung disease, and body mass index, there was a relationship between stress and probing depth > 4 mm, between stress and insertion level > 5 mm, and between stress and probing depth. periodontitis.

Petit et al., (2021)	Clinical Trial	54	Psychological tests: Depression, Anxiety and Stress Scale (DASS-42) Scale coping questionnaire (TSC)	According to DASS-stress scale, 2.4% patients were considered suffering from mild stress, 11,8% from moderate stress and 4,8% from severe to extremely severe stress. DASS-stress score was associated to worsened of the outcomes of periodontal treatment regarding the evolution of BOP (OR=1,02, p<.05) and mean PD (p<.05). When coping strategies were evaluated, patients exhibiting high score of negative coping were more prone to having worse results after periodontal treatment.
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Table 1. Characteristics of the included studies.

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