

Influence of psychological stress on the response to periodontal treatment: Systematic Review Protocol

Kelly Rocio Vargas Villafuerte, Luiz Henrique Palucci Vieira, Karina Oliveira Santos

Submitted to: JMIR Research Protocols on: January 26, 2024

Disclaimer: © **The authors. All rights reserved.** This is a privileged document currently under peer-review/community review. Authors have provided JMIR Publications with an exclusive license to publish this preprint on it's website for review purposes only. While the final peer-reviewed paper may be licensed under a CC BY license on publication, at this stage authors and publisher expressively prohibit redistribution of this draft paper other than for review purposes.

Table of Contents

Original Manuscript	4
	21
	21
	21
	22
	22.

Influence of psychological stress on the response to periodontal treatment: Systematic Review Protocol

Kelly Rocio Vargas Villafuerte^{1*} PhD; Luiz Henrique Palucci Vieira^{1*} Prof Dr, PhD; Karina Oliveira Santos^{2*} MSc

Corresponding Author:

Kelly Rocio Vargas Villafuerte PhD Universidad César Vallejo (UCV). Av. Argentina 1795 - Campus Callao, Lima, Perú Av. Argentina 1795 - Campus Callao, Lima – Perú.

Abstract

Background: The interaction between stress and periodontal treatment is a topic of growing interest, standing out as a field of research that sheds light on the complexity of oral health in individuals subjected to high levels of emotional stress.

Objective: To examine scientific evidence related to the influence of psychological stress on the response to periodontal treatment.

Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines will be followed, and the study is based on a formulation of PECO questions (Participants, Exposure, Comparators, Outcomes). This systematic review will involve a literature search covering studies published up to December 2023 and will include searching the PubMed, Web of Science, EBSCOHost, SCOPUS, ProQuest databases to identify relevant studies. After selection, data extraction and quality assessment of the included studies will be carried out using the Ottawa-Newcastle scale.

Results: The systematic review outlined by this protocol is expected to clearly integrate high-quality evidence on how psychological stress impacts the outcomes of periodontal treatment. This may provide valuable guidance for future research and assist clinical professionals in making decisions about the best treatment options for patients.

Conclusions: This review will help clarify how psychological factors, such as stress, influence periodontal treatment outcomes. Clinical Trial: Open Science Framework (OSF) Registries/Generalized Systematic Review Registration (Registry ID: https://osf.io/qfs6p).

(JMIR Preprints 26/01/2024:56765)

DOI: https://doi.org/10.2196/preprints.56765

Preprint Settings

- 1) Would you like to publish your submitted manuscript as preprint?
- ✓ Please make my preprint PDF available to anyone at any time (recommended).

Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users. Only make the preprint title and abstract visible.

No, I do not wish to publish my submitted manuscript as a preprint.

- 2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?
- ✓ Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).

Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

¹Universidad César Vallejo (UCV). Av. Argentina 1795 - Campus Callao, Lima – Perú. PE

²Universidade de São Paulo Bauru, São Paulo BR

^{*}these authors contributed equally

Original Manuscript

Influence of psychological stress on the response to periodontal treatment: Systematic Review Protocol

Kelly Rocio Vargas Villafuerte^{1,*} PhD; Luiz Henrique Palucci Vieira¹, PhD; Karina Oliveira Santos², MsC.

¹Universidad César Vallejo (UCV), Facultad de Ciencias de la Salud, Grupo de Investigación en Salud Integral Humana (GISIH), Campus Callao, 07001 Lima, Perú.

²Department of Biological Sciences, Bauru School of Dentistry, University of São Paulo (USP), Bauru 17012-901, Brazil.

*Corresponding Author: Kelly Rocio Vargas Villafuerte, PhD.

Address: Av. Argentina 1795 - Campus Callao, Universidad César Vallejo, Lima – Perú.

Postal Code: 07001, Callao.

Phone: +51(1)2024342

Fax: (01)-537-6006.

E-mail: kvargasvi@ucv.edu.pe

Abstract:

Background: The interaction between stress and periodontal treatment is a topic of growing interest. It stands out as a field of research that sheds light on the complexity of oral health in individuals

subjected to high levels of emotional stress.

Objective: To provide a protocol for a systematic review aiming at examine scientific evidence related to the influence of psychological stress on the response to periodontal treatment.

Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines will be followed, and the study is based on a formulation of PECO question (Participants, Exposure, Comparators, Outcomes). This systematic review will involve a literature search covering studies published from 2000 to January 2024 and will include searching the PubMed, Web of Science, EBSCOHost, SCOPUS, ProQuest databases to identify relevant studies. After selection, data extraction and quality assessment (Ottawa-Newcastle scale) of the included studies will be carried out.

Results: The present stage of the study consists of selecting studies for the systematic review as outlined by this protocol. The objective is to integrate high-quality evidence on how psychological stress impacts the outcomes of periodontal treatment. Depending on the number and methodological consistency of included studies, the results may be presented by meta-analysis or qualitative synthesis. The final results are expected by July 2024, with final manuscript submission planned for August 2024.

Conclusions: This review will help clarify how psychological factors, such as stress, influence the results of periodontal treatment, providing valuable guidelines for future research and helping clinicians make decisions about the best treatment options for patients.

Trial Registration: Open Science Framework (OSF) Registries/Generalized Systematic Review Registration (Registry ID: https://osf.io/qfs6p).

KEYWORDS: Psychological stress; periodontal disease; periodontal therapy; integral health

Introduction

Psychological stress represents an emotional and physiological response of the body to adverse stimuli, which occurs when a person perceives a situation or event as threatening to his or her coping resources [1] and can derive from various sources in everyday life, such as work problems, personal relationships, adverse economic situations, and these stressors influence well-being, behavior, and general health [2]. In its acute manifestation, its effect originates in the immune system [2, 3], while in its chronic form, it can lead to prolonged inflammatory processes that negatively impact both the immune and endocrine systems [4]. These effects contribute to the development of diseases such as diabetes mellitus, cardiovascular diseases, cold sores, lichen planus,

and periodontitis [4-6].

Periodontitis is a chronic inflammatory disease that affects the supporting tissues of the teeth. In its development and progression, dysbiosis (imbalance in the microbiota) and the host's immune-inflammatory response play fundamental roles [7]. Research has indicated a positive relationship between psychological stress and periodontal diseases [2, 8-10]. Stress can trigger changes in the immune system [2], characterized by an increase in the inflammatory response and a decrease in the body's immune defenses [3]. The presumed biological mechanisms affect the activity of stress axes, namely, the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS), leading to a subsequent dysregulation of the immune system [6]. Additionally, it has been observed that stress can lead to a reduction in saliva flow and its acidification, which, in turn, may increase the prevalence of periodontal diseases [8, 9].

Simultaneously, research has also demonstrated that stress has an adverse effect on periodontal treatment [2, 11, 12] and delays healing [13], indicating that stressed individuals do not show a reduction in periodontal clinical parameters [11]. Studies also suggest that stress triggers the production of substances such as cortisol/dehydroepiandrosterone (DHEA) [14] and catecholamines [3, 4], which can modulate bacterial growth in periodontal disease and the expression of virulence factors [4]. Additionally, factors like stress and anxiety can induce behavioral changes, such as poor oral hygiene, low-quality sleep, increased smoking [2, 3], as well as an inadequate diet [9] that includes foods rich in carbohydrates, sugar, and acids, further exacerbating periodontitis [9]. In this context, it seems crucial to consider and address psychological factors as an integral part of periodontal therapy [15].

Currently, there are systematic reviews on the impact of psychological factors, such as stress and anxiety, on periodontal health [16, 17] as well as on stress and depression as risk factors for periodontal diseases [8, 18]. However, systematic reviews addressing how psychological stress specifically affects the outcomes of periodontal treatment have not yet been conducted. Therefore, it is imperative to delve into this aspect and understand how this factor may influence periodontal treatment, that's the impact of psychological factors such as stress on periodontal treatment constitutes a highly relevant and complex aspect that demands a comprehensive approach to understanding how stress affects the immune response and patient behavior, which may influence the severity of periodontitis [5] and in the recovery capacity of periodontal tissue [13, 14].

The objective of this study is to provide a protocol for a systematic review intended to evaluate the influence of stress on the clinical outcome of periodontal treatment. The addressed PECO question will focus on: "What is the influence of psychological stress on the response to

periodontal treatment?"

Methods

Registration

This protocol was pre-registered in the Open Science Framework (OSF) Registries/Generalized Systematic Review Registration (Registry ID: qfs6p) [19]. The current protocol, as presented in its entirety below, follows the 2015 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (PRISMA-P) (Multimedia Appendix 1) [20]. It is also intended that this Systematic Review will contain the items of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), guidelines, 2020 version [21].

Electronic databases and Search strategy: The search will include all articles indexed in PubMed/NCBI (National Center for Biotechnology Information, US National Library of Medicine), Web of Science Core Collection (ClarivateTM), EBSCOHost, SCOPUS, and ProQuest published in the English language from January 2000 up to January 2024. In addition, we will consider also an additional exploration of the reference lists and bibliographies of all potential full-text articles.

EndNote software (EndNote X7.0.1, Thomson Reuters ©, NY, USA) will be used to facilitate reference management.

In Table 1 the search terms are presented exactly as it will be used in each specific database. A Boolean search strategy was elaborated, considering also those key terms previously used in existing systematic reviews [8, 16]. For the PubMed database, MeSH (Medical Subject Headings) terms were used to ensure a more comprehensive and precise search.

Table 1. The search strategy used exactly as entered into each specific database considered in the present review study.

PubMed

((((((((periodont*[Text Word]) OR periodontal therapy[MeSH Terms]) OR non-surgical periodontal therapy[MeSH Terms]) OR scaling[Text Word]) OR periodontal debridement[Text Word]) OR mechanical debridement[Text Word]) OR plaque removal[Text Word]) AND (((((stress[Text Word]) OR psychological stress[MeSH Terms])) OR emotional stress[Text Word]) OR chronic stress[Text Word]) OR job-related stress[Text Word]) AND (((control*[Text Word]) OR baseline[Text Word]) OR *stressed group*[Text Word]) AND (((probing depth[Text Word]) OR clinical attachment level[Text Word]) OR bleeding of probing[Text Word])

Web of Science

Periodont* OR Periodontal therapy OR Non-surgical periodontal therapy OR Scaling OR Periodontal debridement OR Mechanical debridement OR Plaque removal (Topic) AND Stress OR Psychological stress OR Emotional stress OR Chronic stress OR Job-related stress (Topic) AND Control* OR Baseline OR *Stressed group* AND Probing depth OR Clinical attachment level OR Bleeding of probing (Topic)

EBSCOHost

(Periodont* OR Periodontal therapy OR Non-surgical periodontal therapy OR Scaling OR Periodontal debridement OR Mechanical debridement OR Plaque removal) AND (Stress OR Psychological stress OR Emotional stress OR Chronic stress OR Job-related stress) AND (Control* OR Baseline OR *Stressed group*) AND (Probing depth OR Clinical Attachment level OR Bleeding of probing)

SCOPUS

(TITLE-ABS-KEY ("periodont*" OR "periodontal therapy" OR "non-surgical periodontal therapy" OR scaling OR "periodontal debridement" OR "mechanical debridement" OR "plaque removal") AND TITLE-ABS-KEY (stress OR "psychological stress" OR "emotional stress" OR "chronic stress" OR "job-related stress") AND TITLE-ABS-KEY (control* OR baseline OR "*stressed group*") AND TITLE-ABS-KEY ("probing depth" OR "clinical attachment level" OR "bleeding of probing"))

ProQuest

noft(Periodont* OR Periodontal therapy OR Non-surgical periodontal therapy OR Scaling OR Periodontal debridement OR Mechanical debridement OR Plaque removal) AND noft(Stress OR Psychological stress OR Emotional stress OR Chronic stress OR Job-related stress) AND noft(Control* OR Baseline OR Stressed group*) AND noft(Probing depth OR Clinical Attachment level OR Bleeding of probing)

Inclusion and exclusion criteria

Type of studies to be included: Cohort or cross-sectional studies, case-control studies; studies published in English are considered eligible. A targeted research query designed to enhance the literature search was formulated, outlining the assigned PECO measures as follows:

Population(P): Adult patients diagnosed with periodontitis and undergoing periodontal treatment [Prophylaxis and/or scaling and root planing (ultrasonic devices, curettes and polishing)].

Exposure(E): Psychological stress [Assessed by psychometric instruments - validated questionnaires to measure stress levels and/or studies that used biomarkers to assess stress (e.g. salivary cortisol)].

Comparison(C): Control group/ Patients with periodontitis without psychological stress [Assessed by psychometric instruments - validated questionnaires to measure stress levels and/or studies that

used biomarkers to assess stress (e.g. salivary cortisol)].

Outcomes measures(O): Clinical outcome of periodontal treatment.

Primary outcomes

Changes in probing pocket depth (PPD), and clinical attachment level (CAL) measured in mm. Changes in bleeding on probing (BOP), measured in percent.

Secondary outcomes

Changes in plaque index (PI) measured in percent.

Variables that will be considered for extraction includes, as for example, PPD, CAL, BOP and PI. Null-hypothesis significance tests may include independent samples t-test, Mann–Whitney U-test, Kruskal–Wallis test, ANOVA with posthoc, Linear regression models, Logistic regression models, and Multivariable ANCOVA. For the present review synthesis, the threshold for the significance will be pre-set at $p \le 0.05$.

Type of studies to be excluded: Observational studies (without mechanical debridement or professional plaque removal); studies, where patients received other adjuvant therapies (e.g.: Laser/probiotics or antibiotic use) or any type of periodontal treatment in the last 6 months; patients with systemic or autoimmune disorders, which influence treatment outcomes such as diabetes; pregnant or breastfeeding; patients using immunosuppressive drugs or drugs that affect the oral microbiome (e.g. antineoplastic or antiepileptic drugs); studies that did not go through ethics committee; letters, case reports, short communications; and studies in animal models and in vitro.

Selection of studies

The selection process will be in accordance with PRISMA guidelines. Data collection will be carried out using a specific spreadsheet, with parameters selected after a pilot study involving approximately ten included studies. Two reviewers, identified as participating researchers, will conduct the assessment independently. In case of disagreement, a third researcher with expertise in the field will resolve discrepancies.

If there is unclear or omitted information from the selected studies such as missing data or incomplete text, the authors will be contacted by e-mail and weekly attempts will be made for a maximum of five weeks. If there is no response from the authors, the study will be excluded. Studies meeting the inclusion criteria will undergo validation and data extraction.

Data extraction and evidence synthesis

The relevant data extracted from each study will be describing the designated PECO measures: author's name and date of publication; country; study design participant characteristics;

periodontal treatment; definition of psychological stress; stress diagnosis (stress scale or biomarkers used); clinical parameters (Probing depth, clinical attachment level, bleeding on probing and plaque index); monitoring and outcome measures of interest to the review (regular clinical monitoring to monitor the effectiveness of treatment), authors' conclusions and source of funding.

Subsequently, the "best evidence synthesis method" will be applied to classify the level of evidence [22]. It will be considered strong (consistent findings observed among multiple high-quality studies), moderate (consistent findings observed among multiple moderate-quality studies and/or one high-quality study), limited (findings provided by one moderate-quality study and/or only low-quality studies), conflicting (when inconsistent findings were observed) or 'no evidence' (when there were no available studies)[22]. Consistency will be assessed when \geq 75% of studies report results in the same direction, and inconsistency will be defined when < 75% of studies report results in the same direction.

Methodological quality and risk of bias assessments

Two authors (KRVV and KOS) will independently evaluate the methodological quality of each included study using the Newcastle-Ottawa Scale (NOS) [23]. This scale is specifically designed for non-randomized studies. The authors will employ a "star" system for each study, considering three main components: (1) quality of study participant selection, (2) comparability, and (3) exposure and outcome. The maximum score is 9 points for case-control studies and 10 points for cross-sectional studies. The total score will categorize the studies into three groups: (1) high quality (total score: 7 to 9/10), (2) moderate quality (total score: 4 to 6), and (3) low quality (total score: 0 to 3). To determine consistency, inter-rater agreement will be calculated using Cohen's kappa coefficient.

Moreover, the risk of bias (RoB) in the outcomes or interpretations will be independently determined for each included study. This will be done using the Risk of Bias Assessment Tool for Non-randomised Studies [24]. Each element will be evaluated as presenting low, high, or unclear risk concerning participant selection criteria, potential confounding variables, accuracy of exposure measurement, blinding of outcome assessments, handling of incomplete outcome data, and selective outcome reporting.

Results

The search, screening, and data extraction began in January 2024, following the established protocol. From the initial search to find previous reviews on the influence of psychological stress on periodontal treatment, no reviews were identified that had this objective, although we did find reviews on the association of psychological stress on periodontitis and about stress as a risk factor for

periodontitis (Table 2 and Table 3).

If there are a sufficient number of studies and no substantial variations in the methods used among them, the results may also be presented through a meta-analysis (quantitative synthesis). Regardless of whether the final manuscript meets the criteria for a quantitative synthesis, a qualitative synthesis will be conducted using the best evidence synthesis method. Additionally, a table with the main characteristics of the studies will be included.

We will also consider the statistical analyses used in the selected studies, including different types of regression models to adjust for confounding variables. This may include multiple linear regression for continuous dependent variables, multiple logistic regression for binary stages, and Multivariable ANCOVA. In addition, we will also include other statistical analyses, such as clarification analysis, as applicable.

The results are expected to be completed by July 2024, and the final manuscript of the systematic review is anticipated to be submitted in August 2024. The research is funded by the Research Support Fund of Cesar Vallejo University (reference number: Project ID 2762/2023).

Table 2. Some methods of review studies potentially address the influence of stress on periodontal treatment

Reference	Type of review	Guideline s	Date of searches/ inclusion	Databases considered
<mark>Peruzzo et al.</mark>	Systematic		January 1, 1990	MEDLINE and the
[18]			to April 1, 2006	Cochrane Oral Health
				Register
Botelho et al.	Systematic	PRISMA	<mark>up to September</mark>	Electronic general, open
[25]	and meta-		2017	access, regional, and
	<mark>analysis</mark>			grey literature databases
Decker et al.	Systematic Systematic Systematic	PECOS	up to December	MEDLINE (OVID),
[8]		framewor	2017	EMBASE (OVID), and
		k		Cochrane Central
				Register of Controlled
				Trials (Cochrane
				Library).
				The grey literature at the
				New York Academy of
				Medicine Grey Literature
				Report
Castro et al.	Systematic	PRISMA	<mark>until March 2018</mark>	PubMed, Scopus, Web

[16]				of Science, Lilacs, and
				Cochrane Library. The
				Google Scholar and
				OpenGrey were used as
				gray literature sources.
<mark>Badia et al.</mark>	Systematic	PRISMA	Until June 2021	MEDLINE,
[26]	and meta-			EMBASE and the
	<mark>analysis</mark>			Cochrane Library
<mark>Aggarwal et</mark>	Systematic		Until December	PubMed, Embase, and
al. [17]	and meta-		2019	Scopus
	<mark>analysis</mark>			

Table 3. Results of the initial search for review studies that potentially address the influence of stress on periodontal treatment

<mark>Reference Year</mark>	<mark>Aim</mark>	Results Programme Results Prog
Peruzzo et al. 2007	Review the evidence on	Eight studies (57.1%) found a
[18]	the influence of stress	positive outcome between
	and psychological factors	psychosocial factors/stress and
	on periodontal disease.	periodontal disease, four studies
		(28.5%) observed a positive
		outcome for some characteristics
		and a negative outcome for others,
		and two studies (14.2%) found a
		negative outcome between
		psychosocial factors/stress and
		periodontal disease.
Botelho et al. 2018	To systematically assess	A network meta-analysis was
[24]	whether periodontitis has	performed comparing salivary
	a meaningful effect on	cortisol response between chronic
	salivary cortisol,	and aggressive periodontitis
	reflecting changes in free	patients. Although the indirect
	blood cortisol levels	estimates were not statistically
		significant, the results were
		consistent with Bucher's test
		(p=0.99) and favored aggressive
		periodontitis regarding salivary

			continue vocas on the
			cortisol response. Overall, the
			salivary cortisol response in
			patients with aggressive
			periodontitis is, on average, 42%
			higher than in patients with
			chronic periodontitis (mean ratio
			[95% CI]: 1.42 [0.97-2.06],
Decker et al.	2020	To evaluate the impact of	p=0.99). Relationships between stress-
	2020	stress-related disorders	related disorders and serum and
[8]			
		on the progression of	salivary biomarkers such as
		periodontal disease and	cortisol, dehydroepiandrosterone
		evaluate the growing	(DHEA), chromogranin A (CgA),
		body of evidence of	and pro-inflammatory cytokines
		stress as a risk indicator	were identified.
		for periodontal disease	
Castro et al.	2020	progression. This systematic review	Three articles were selected by
Castro et ar.	2020	THIS SYSTEMATIC TEVIEW	
[16]			
[16]		aims to explore the	full text. Among them, two articles
[16]		aims to explore the relationship between	full text. Among them, two articles reported a positive association
[16]		aims to explore the relationship between psychological stress and	full text. Among them, two articles reported a positive association between psychological stress and
[16]		aims to explore the relationship between psychological stress and periodontitis by	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were
[16]		aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even
[16]		aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels and periodontal clinical	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even though two articles highlighted an
[16]		aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even though two articles highlighted an association between psychological
[16]		aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels and periodontal clinical	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even though two articles highlighted an association between psychological stress and the presence of a
[16]		aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels and periodontal clinical	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even though two articles highlighted an association between psychological stress and the presence of a possible modulatory pattern of
[16]		aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels and periodontal clinical	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even though two articles highlighted an association between psychological stress and the presence of a possible modulatory pattern of cortisol levels in clinical
[16]		aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels and periodontal clinical	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even though two articles highlighted an association between psychological stress and the presence of a possible modulatory pattern of cortisol levels in clinical parameters of periodontitis, more
[16]		aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels and periodontal clinical	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even though two articles highlighted an association between psychological stress and the presence of a possible modulatory pattern of cortisol levels in clinical parameters of periodontitis, more studies are necessary to elucidate
	2022	aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels and periodontal clinical parameters.	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even though two articles highlighted an association between psychological stress and the presence of a possible modulatory pattern of cortisol levels in clinical parameters of periodontitis, more studies are necessary to elucidate this question.
Badia et al.	2022	aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels and periodontal clinical parameters. To evaluate the literature	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even though two articles highlighted an association between psychological stress and the presence of a possible modulatory pattern of cortisol levels in clinical parameters of periodontitis, more studies are necessary to elucidate this question. The results of the meta-analysis
	2022	aims to explore the relationship between psychological stress and periodontitis by analyzing cortisol levels and periodontal clinical parameters.	full text. Among them, two articles reported a positive association between psychological stress and periodontitis. All articles were classified as low risk of bias. Even though two articles highlighted an association between psychological stress and the presence of a possible modulatory pattern of cortisol levels in clinical parameters of periodontitis, more studies are necessary to elucidate this question.

		<mark>periodontit</mark>	is and	its	two groups. There is a relationship
		progression	n, and	to	between psychological stress and
		<mark>evaluate cu</mark>	rrent evid	<mark>ence</mark>	the severity of periodontitis.
		of psychological stress as			This relationship must be
		a risk	factor	for	considered a possible risk factor
		<mark>periodonta</mark> l	disease u	<mark>sing</mark>	
		<mark>psychologi</mark>	<mark>cal</mark>		
		questionna	ires.		
Aggarwal et 2	. <mark>022</mark>	To assess t		<mark>ition</mark>	25 studies were selected for
al.[17]		between	psychol	<mark>ogic</mark>	systematic review and only 14
		stress, a	nxiety,	and	studies could be used for meta-
		<mark>periodontit</mark>	<mark>is.</mark>		analysis in three subsets. The
					pooled OR for stress and
					periodontitis was 1.78, which was
					statistically highly significant $(I^2 =$
					98.6%, P = 0.00). Mean salivary
					cortisol levels as a measure of
					stress in patients with periodontitis
					was 4.81 nmol/L (I ² = 98.0%, P =
					0.08). State-Trait Anxiety
					Inventory value was seen as -1.28
					$(I^2 = 0.0\%, P = .06)$ for state
					anxiety and -0.11 ($I^2 = 0.0\%$, P
					= .85) for trait anxiety in patients
					with periodontitis.

Discussion

Studies have shown a correlation between psychological stress and various inflammatory diseases [27, 28]. Research in the field of dentistry shows systematic reviews that explore the association between psychological stress and periodontitis [16, 17, 25], or psychological stress as a possible risk factor for periodontal diseases [8, 18, 26]. However, to date, no systematic review has focused on understanding how psychological stress specifically influences periodontal treatment outcomes.

There is evidence that psychological stress affects the body's inflammatory response [29, 30], which together may increase susceptibility to periodontal disease [16, 17, 31, 32] and hinder

adherence to periodontal treatment, resulting in slower healing and less favorable clinical outcomes [32, 33]. Therefore, it is hypothesized that the results of the selected studies confirm a significant influence of psychological stress on periodontal treatment. Patients with high levels of stress are likely to show worse periodontal treatment outcomes compared to those with lower levels of stress. One study [34] evaluated the effects of psychological stress on periodontitis healing in rats and the contribution of baseline fibroblast growth factor (fFGB) expression to the healing process and observed that psychological stress could delay periodontitis healing, which may be mediated in part by down-regulation of bFGF expression in the periodontal ligament. Therefore, it is important to investigate whether patients with elevated levels of psychological stress may require personalized, lifestyle-changing interventions to optimize treatment outcomes.

This review presents as a strength a rigorous methodology, which reinforces the validity of the results. In addition, this review will provide an updated, specific, and detailed view of how psychological stress directly affects periodontal treatment outcomes, highlighting the importance of considering psychosocial factors. However, there may be limitations to consider, such as variability in the measurement of psychological stress among the included studies, which may introduce bias.

For future research, it would be useful to explore the effectiveness of psychological interventions integrated into periodontal management to improve clinical outcomes. In addition, this review will identify other knowledge gaps, encouraging further studies to fill these gaps and thus improving the overall understanding of the topic, which will benefit clinical practice in the future.

To maximize the impact of these findings, several dissemination strategies are planned. These include publication in high-impact scientific journals and collaborations with dental professional societies to promote the integration of these findings into clinical practice. In addition, educational materials and workshops for oral health professionals will be developed, highlighting the importance of addressing psychological stress in periodontal treatment.

Conclusions

This review will provide current information on how psychological stress affects the outcome of periodontal treatment, the results of which can serve as a basis for creating broader health strategies aimed at addressing psychosocial factors in promoting oral health.

Acknowledgments

Funding Information: Fondo de Apoyo a la Investigación de la Universidad César Vallejo (IdProyecto #2762- 14/11/2023).

Conflicts of interest

None declared.

Abbreviations

OSF: Open Science Framework

PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses

RoB: Risk of bias tiab: Title/Abstract

TI: record's title field

TI,AB,IF: searches for online in the title, abstract, and keywords fields

Author Contributions

Conceptualization: K.R.V.V.; methodology: K.R.V.V., L.H.P.V., and K.O.S.; investigation: K.R.V.V.,

L.H.P.V. and K.O.S.; writing —original draft preparation: K.R.V.V. and L.H.P.V.; writing—review

and editing: K.R.V. V., L.H.P.V. and K.O.S.; supervision, data curation, project administration and

funding acquisition: K.R.V.V.

Multimedia Appendix 1

PRISMA-P checklist for the present systematic review protocol.

References

- 1. Corridore D, Saccucci M, Zumbo G, Fontana E, Lamazza L, Stamegna C, et al. Impact of Stress on Periodontal Health: Literature Revision. Healthcare (Basel, Switzerland). 2023 May 22;11(10). PMID: 37239803. doi: 10.3390/healthcare11101516.
- 2. Wimmer G, Köhldorfer G, Mischak I, Lorenzoni M, Kallus KW. Coping with stress: its influence on periodontal therapy. Journal of periodontology. 2005 Jan;76(1):90-8. PMID: 15830642. doi: 10.1902/jop.2005.76.1.90.
- 3. Zhang H, Chen B, Pan C, Zhang A. To evaluate the serum cortisol, salivary cortisol, and serum interleukin-1 B level in patients of chronic periodontitis with smoking and stress and without smoking and stress. Medicine. 2021 Aug 6;100(31):e26757. PMID: 34397819. doi: 10.1097/md.00000000000026757.
- 4. Ball J, Darby I. Mental health and periodontal and peri-implant diseases. Periodontology 2000. 2022 Oct;90(1):106-24. PMID: 35913583. doi: 10.1111/prd.12452.
- 5. Marruganti C, Gaeta C, Romandini M, Ferrari Cagidiaco E, Parrini S, Discepoli N, et al. Multiplicative effect of stress and poor sleep quality on periodontitis: A university-based cross-sectional study. Journal of periodontology. 2023 Jul 21. PMID: 37477025. doi: 10.1002/jper.23-0209.
- 6. Seizer L, Schubert C. On the Role of Psychoneuroimmunology in Oral Medicine. International dental journal. 2022 Dec;72(6):765-72. PMID: 36184323. doi: 10.1016/j.identj.2022.07.002.

7. Caton JG, Armitage G, Berglundh T, Chapple ILC, Jepsen S, Kornman KS, et al. A new classification scheme for periodontal and peri-implant diseases and conditions - Introduction and key changes from the 1999 classification. Journal of periodontology. 2018 Jun;89 Suppl 1:S1-s8. PMID: 29926946. doi: 10.1002/jper.18-0157.

- 8. Decker A, Askar H, Tattan M, Taichman R, Wang HL. The assessment of stress, depression, and inflammation as a collective risk factor for periodontal diseases: a systematic review. Clinical oral investigations. 2020 Jan;24(1):1-12. PMID: 31677052. doi: 10.1007/s00784-019-03089-3.
- 9. Goyal S, Gupta G, Thomas B, Bhat K, Bhat GJIpj. Stress and periodontal disease: The link and logic!! 2013;22(1):4.
- 10. Wimmer G, Janda M, Wieselmann-Penkner K, Jakse N, Polansky R, Pertl C. Coping with stress: its influence on periodontal disease. Journal of periodontology. 2002 Nov;73(11):1343-51. PMID: 12479640. doi: 10.1902/jop.2002.73.11.1343.
- 11. Vettore M, Quintanilha RS, Monteiro da Silva AM, Lamarca GA, Leão AT. The influence of stress and anxiety on the response of non-surgical periodontal treatment. Journal of clinical periodontology. 2005 Dec;32(12):1226-35. PMID: 16268999. doi: 10.1111/j.1600-051X.2005.00852.x.
- 12. Kloostra PW, Eber RM, Wang HL, Inglehart MR. Surgical versus non-surgical periodontal treatment: psychosocial factors and treatment outcomes. Journal of periodontology. 2006 Jul;77(7):1253-60. PMID: 16805690. doi: 10.1902/jop.2006.050302.
- 13. Glaser R, Kiecolt-Glaser JK, Marucha PT, MacCallum RC, Laskowski BF, Malarkey WB. Stress-related changes in proinflammatory cytokine production in wounds. Archives of general psychiatry. 1999 May;56(5):450-6. PMID: 10232300. doi: 10.1001/archpsyc.56.5.450.
- 14. Lee YH, Suk C, Shin SI, Hong JY. Salivary cortisol, dehydroepiandrosterone, and chromogranin A levels in patients with gingivitis and periodontitis and a novel biomarker for psychological stress. Frontiers in endocrinology. 2023;14:1147739. PMID: 37113482. doi: 10.3389/fendo.2023.1147739.
- 15. Goh V, Hassan FW, Baharin B, Rosli TI. Impact of psychological states on periodontitis severity and oral health-related quality of life. Journal of oral science. 2022 Jan 19;64(1):1-5. PMID: 34690248. doi: 10.2334/josnusd.21-0267.
- 16. Castro MML, Ferreira RO, Fagundes NCF, Almeida A, Maia LC, Lima RR. Association between Psychological Stress and Periodontitis: A Systematic Review. Eur J Dent. 2020 Feb;14(1):171-9. PMID: 32069501. doi: 10.1055/s-0039-1693507.
- 17. Aggarwal K, Gupta J, Kaur RK, Bansal D, Jain A. Effect of anxiety and psychologic stress on

periodontal health: a systematic review and meta-analysis. Quintessence Int. 2022 Jan 7;53(2):144-54. PMID: 34595909. doi: 10.3290/j.qi.b2091191.

- 18. Peruzzo DC, Benatti BB, Ambrosano GM, Nogueira-Filho GR, Sallum EA, Casati MZ, et al. A systematic review of stress and psychological factors as possible risk factors for periodontal disease. J Periodontol. 2007 Aug;78(8):1491-504. PMID: 17668968. doi: 10.1902/jop.2007.060371.
- 19. Vargas Villafuerte KR, Palucci Vieira LH, Santos KO. Influence of psychological stress on the response to periodontal treatment: Systematic Review Protocol. The Open Science Framework (OSF). Published 2024-05-01. https://osf.io/qfs6p. [access date 2024-01-19].
- 20. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ (Clinical research ed). 2015 Jan 2;350:g7647. PMID: 25555855. doi: 10.1136/bmj.g7647.
- 21. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ (Clinical research ed). 2021 Mar 29;372:n71. PMID: 33782057. doi: 10.1136/bmj.n71.
- van Tulder M, Furlan A, Bombardier C, Bouter L. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. Spine. 2003 Jun 15;28(12):1290-9. PMID: 12811274. doi: 10.1097/01.Brs.0000065484.95996.Af.
- 23. Luchini C, Stubbs B, Solmi M, Veronese NJWJoM-A. Assessing the quality of studies in meta-analyses: Advantages and limitations of the Newcastle Ottawa Scale. 2017;5(4):80-4.
- 24. Kim SY, Park JE, Lee YJ, Seo HJ, Sheen SS, Hahn S, et al. Testing a tool for assessing the risk of bias for nonrandomized studies showed moderate reliability and promising validity. Journal of clinical epidemiology. 2013 Apr;66(4):408-14. PMID: 23337781. doi: 10.1016/j.jclinepi.2012.09.016.
- 25. Botelho J, Machado V, Mascarenhas P, Rua J, Alves R, Cavacas MA, et al. Stress, salivary cortisol and periodontitis: A systematic review and meta-analysis of observational studies. 2018;96:58-65.
- 26. Badia II, Aparicio LC, Aranda MR, Illueca FA, Roldán ALJJoID, Research M. Assessment of Psychological Stress as a Risk Factor for Periodontal Disease: Systematic Review and Meta-Analysis. 2022;15(3):1330-9.
- 27. Labanski A, Langhorst J, Engler H, Elsenbruch S. Stress and the brain-gut axis in functional and chronic-inflammatory gastrointestinal diseases: A transdisciplinary challenge. Psychoneuroendocrinology. 2020 Jan;111:104501. PMID: 31715444. doi:

- 10.1016/j.psyneuen.2019.104501.
- 28. Wynne B, McHugh L, Gao W, Keegan D, Byrne K, Rowan C, et al. Acceptance and Commitment Therapy Reduces Psychological Stress in Patients With Inflammatory Bowel Diseases. Gastroenterology. 2019 Mar;156(4):935-45.e1. PMID: 30452919. doi: 10.1053/j.gastro.2018.11.030.
- 29. Schneider KM, Blank N, Alvarez Y, Thum K, Lundgren P, Litichevskiy L, et al. The enteric nervous system relays psychological stress to intestinal inflammation. Cell. 2023 Jun 22;186(13):2823-38.e20. PMID: 37236193. doi: 10.1016/j.cell.2023.05.001.
- 30. Lwin MN, Serhal L, Holroyd C, Edwards CJ. Rheumatoid Arthritis: The Impact of Mental Health on Disease: A Narrative Review. Rheumatology and therapy. 2020 Sep;7(3):457-71. PMID: 32535834. doi: 10.1007/s40744-020-00217-4.
- 31. Rettori E, De Laurentiis A, Zorrilla Zubilete M, Rettori V, Elverdin JC. Anti-inflammatory effect of the endocannabinoid anandamide in experimental periodontitis and stress in the rat. Neuroimmunomodulation. 2012;19(5):293-303. PMID: 22777139. doi: 10.1159/000339113.
- 32. Decker AM, Kapila YL, Wang HL. The psychobiological links between chronic stress-related diseases, periodontal/peri-implant diseases, and wound healing. Periodontology 2000. 2021 Oct;87(1):94-106. PMID: 34463997. doi: 10.1111/prd.12381.
- 33. Horan MP, Quan N, Subramanian SV, Strauch AR, Gajendrareddy PK, Marucha PTJB, behavior,, et al. Impaired wound contraction and delayed myofibroblast differentiation in restraint-stressed mice. 2005;19(3):207-16.
- 34. Zhao YJ, Li Q, Cheng BX, Zhang M, Chen YJ. Psychological stress delays periodontitis healing in rats: the involvement of basic fibroblast growth factor. Mediators of inflammation. 2012;2012:732902. PMID: 23326020. doi: 10.1155/2012/732902.

Supplementary Files

Untitled.

URL: http://asset.jmir.pub/assets/250999b1bac3ab085953d209ba9f7d63.docx

Untitled.

URL: http://asset.jmir.pub/assets/bd27c8df4b07f64ef69ccd7854b5306c.doc

Multimedia Appendixes

Untitled.

URL: http://asset.jmir.pub/assets/26acc544497fadcd229069ecc89c89c8.doc