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Association among stress and depression in patients with advanced periodontitis: a cross-sectional study

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Abstract

Background: The relationship between psychological factors and the onset and progression of periodontal disease has recently attracted more academic attention. The purpose of the study was to evaluate the association between psychological stress and periodontitis The study was conducted out on patients with periodontitis.

Methods: All the patients included in the study were suffering from psychological stress and were referred to us by medical specialists, and they also showed clinical features of periodontal disease. Patients suffering from acute severe pain or system diseases were excluded. Periodontal exams were done out utilizing standard procedures. It was followed by Clinical Attachment Loss (CAL) diagnosis as a basis for evaluation of periodontal condition. Later psychosocial aspects were examined using globally approved questionnaires. The data were examined using chi square test and the Spearman correlation test with $p < 0.05$ considered as level of significance.

Results: Among the psychosocial factors identified in this study were anxiety, depression and chronic stress and methods to adapt stress were shown to have a significant relationship with CAL. Specifically, probing depth (PD) was significantly correlated with anxiety ($p<0.001$), depression ($p= 0.026$), stress ($p<0.001$); CAL was significantly correlated with elderly age ($p= 0.006$), anxiety ($p<0.001$), depression ($p= 0.026$) and stress ($p= 0.017$); bleeding on probing (BOP) was significantly correlated with depression ($p= 0.027$); plaque index (PI) was significantly correlated with anxiety ($p= 0.014$); gingival recession (REC) was significantly correlated with depression ($p= 0.016$) and stress ($p= 0.035$). The patients having severe periodontitis measured through CAL were found suffering from severe anxiety and they used more emotional focused coping methods frequently. Those with lower CAL used problem focussed coping methods frequently.

Conclusions: The results of this study demonstrated that the persistent financial stresses, depression, insufficient coping capacity and maladaptive personality dispositions were important risk factors for periodontal attachment loss.

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1. Introduction

Periodontitis is complex multifactorial disorder with high burden for health system caused by interaction of several genetic and environmental factors (Isola et al., 2022; Isola et al., 2023). About one third of the observed variance in the frequency of this condition is due to the genetic factors (Caetano et al., 2022; Li et al., 2022; Zhang et al., 2022; Zhou et al., 2015).

The more severe form of periodontitis is called periodontitis in which gingival tissue might pull away from the tooth resulting in bone loss, and tooth loss (Dionigi et al., 2022; Go et al., 2022; Hwang et al., 2022; Isola et al., 2019). About one third of the observed variance in the frequency of this condition is due to the genetic factors (Bunpeng et al., 2022; John et al., 2016; Larvin et al., 2022; Satomi et al., 2022; Zhan et al., 2020). This heritability index has been similar among different assessed populations and is increased with severity of the periodontitis. Genetic factors can regulate both the inflammatory responses in the affected tissues and the induced damage in the alveolar bone. The pathologic course of periodontitis is induced by pathogens such as *Porphyromonas Gingivalis* which are amassed in biofilm along the gingival margin and sulcus (Beikler et al., 2004; Mikuls et al., 2012; Olsen & Singhrao, 2018). The resultant inflammatory responses might destruct the periodontal ligament and the neighbouring bone leading to tooth loss (Chen et al., 2022; Lu et al., 2022; Petrenya et al., 2022), that, especially in patients with malocclusions or oral disorders should impact the overall self-esteem (Giudice et al., 2018; Leonardi et al., 2021; Lo Giudice et al., 2019; Loreto et al., 2020). Thus, genetic factors particularly those regulating the immune responses might affect the risk or severity of periodontitis. Recently, the existing relationships among physical and psychological factors appear to be central in literature. In these terms, psychological phenomena are studied in the light of their role in the onset, maintenance of physical conditions as in the field of psychosomatic research and as consequences of physical illness (Caputo et al., 2022; Catalano et al., 2019; Cooke, 2021; Martino et al., 2021; Myles & Merlo, 2022; Rasul et al., 2005; Sharpe & Curran, 2006). The relationship between psychological factors and the onset and progression of periodontal disease has recently attracted more attention. Because they target 2 crucial areas of interest surrounding an essential perio-systemic relationship, the most recent studies are significant (Alkan et al., 2022; Ju et al., 2022; Mombelli, 2018; Rahate et al., 2022; Zerr et al., 2015).

According to the Global Burden of Disease (GBD) Study, the impact of oral diseases ranks among the top 100 worldwide diseases on a list totalling 291 (Offenbacher et al., 2016; Righolt et al., 2018). It is well known that socioeconomic deprivation affects the occurrence of oral

diseases, and the interpretation of their impact (Alkan et al., 2022; A. Li et al., 2022; Umeizudike et al., 2022). However, the presence of oral diseases and unfavorable socioeconomic factors are not enough to explain the multidimensional and multifactorial oral health impact on quality of life, usually referred to as the oral health-related quality of life (OHRQoL) (Huang et al., 2022; Sengul et al., 2022).

Individualized medicine is gaining importance among physicians as a factor in providing patients with high-quality care. We are aware that several individual factors, including age, smoking, heredity, concurrent systemic illnesses, and dental hygiene, might affect the severity of periodontal disease and its response to therapy (Loos & Needleman, 2020; Suvan et al., 2020; Teughels et al., 2020). However, we are also aware that these factors do not fully account for the variances. There are therefore additional aspects at play, and it is undeniable that psychological factors have an impact on a variety of other health-related criteria (Flemmig et al., 1998; Loggner Graff et al., 2009). In this regard, the importance of stress, depression and periodontal disease have been reported as an important issues in patients with periodontitis that impact also the systemic self-esteem.

Over the last 10 years, some studies did not report any associations between stress, depression and periodontal disease, providing some lingering doubt regarding the strength of the associations. However, a recent systematic review has shown that positive study findings outnumber negative study findings by a 4:1 margin. Recent studies have shown convincing connections between stress and tooth loss, stress and attachment loss, stress/depression and disregard for oral hygiene, and elevated cortisol levels and pocket depth/tooth loss, demonstrating well-designed studies that confirm positive correlations between stress, depression, and periodontal disease (Bhardwaj et al., 2016; Ghasemzedah et al., 2017; Klionsky et al., 2016; Muniz et al., 2015). The molecular and behavioral underpinnings for this perio-systemic relationship are solidly supported by these investigations.

Frequent and repeated exposure to stressor(s) leads to wear and tear of the body's systems, resulting in what is known as allostatic load. In recent years, few studies examining the relationship between stress and periodontal diseases and *vice versa* have used an aggregate variable, including primary and secondary markers of allostatic load, as a biological marker of stress (Sabbah et al., 2018). While research on the relationship between allostatic load and periodontal disease is still developing, as most of the studies used cross-sectional data, this line of research presents a good opportunity for establishing a composite biological indicator as a risk factor for periodontal disease. Studies have shown that individuals under stresses are more

likely to smoke, less likely to brush their teeth, and less likely to visit a dentist all-important behavioral determinant of periodontal diseases (Krueger & Chang, 2008; Sheiham & Nicolau, 2005).

These findings have significant clinical ramifications because they suggest that treating psychological issues like stress and depression is a crucial component of overall preventive periodontal maintenance and, more importantly, may help prevent systemic inflammation in susceptible people from developing into oral inflammation. Information on a patient's psychological condition (stress levels related to employment, domestic, and other factors) is provided by the simple stress profile and depression scale utilized in one recent study.

Therefore, the objective of this study was to determine the effect of periodontitis on stress and depression, after considering for conditions of oral health, oral health-related behaviors and socioeconomic factors in adults. The main hypothesis was that periodontitis influenced the stress and depression in the enrolled sample. The null-hypothesis to be invalidated was that there was no impact of periodontitis on the development of stress and depression.

2. Materials and methods

2.1 Study participants

This cross-sectional retrospective study was conducted at the Unit of Periodontology, School of Dentistry, University of Catania, Catania, Italy. The local international review board approved the study protocol (215/21 - 19.10.21). Forty-nine patients, between the ages of 17 and 65 (mean age 46.8 ± 5.9 years) were enrolled. All of the patients experienced issues with psychological stress in addition to periodontitis.

2.2 Inclusions and exclusions criteria

For the present study, the inclusions criteria were: 1) aged >15 years old; 2) Diagnosis of periodontitis based on the new classification of periodontal disease (Tonetti et al., 2018). The exclusions criteria were: 1) Patients with significant pain or other medical conditions during the prior 6 months were not allowed to participate in the present trial and 2) non-compliant patients. Individuals lacking cognitive ability to answer the questions assessed during the interview. A survey was used to track psychological stress in the enrolled patients.

2.3 Questionnaires

The questionnaires used in the present study was the Symptom Check List (SCL 90) in order to evaluate ongoing stress. The Symptom Checklist-90-R (SCL-90-R) is a relatively brief self-report

psychometric instrument (questionnaire) published by the Clinical Assessment division of the Pearson Assessment & Information group. It is designed to evaluate a broad range of psychological problems and symptoms of psychopathology. It is also used in measuring the progress and outcome of psychiatric and psychological treatments or for research purposes. According to the overview given by the publisher, the SCL-90-R is normed on individuals 13 years and older. It consists of 90 items and takes 12–15 minutes to administer, yielding nine scores along primary symptom dimensions and three scores among global distress indices. The primary symptom dimensions that are assessed are somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and a category of "additional items" which helps clinicians assess other aspect of the symptoms (e.g. item 19, "poor appetite"). The three indices are global wellness index, hardiness, and symptom free. A high number of studies have been conducted demonstrating the reliability, validity, and utility of the instrument. It is one of the most widely used measures of psychological distress in clinical practice and research (Hjemdal et al., 2015).

2.4 Periodontal parameters

For the analysis of periodontal parameters, 2 calibrated physicians performed the periodontal charting. Probing depth (PD), bleeding on probing (BOP), gingival recession (REC) and plaque score (PI) were recorded in six sites per tooth for all teeth present, excluding wisdom teeth with a periodontal probe (De Soete et al., 2001). Clinical attachment loss (CAL) was calculated as the sum of PD values and gingival recession. The CEJ served as a reference for recession, which was registered as a positive value if the free gingival margin was apical to the CEJ, while it was recorded as a negative value if it was coronal to the CEJ. Each patient completed an anamnestic questionnaire reporting the eventual presence of any comorbidities (e.g., diabetes, hypertension, hypercholesterolemia, hypothyroidism, celiac disease, etc.), anxiety, depression and stress, all drugs usually taken, information on the lesion's onset and the possible degree of limitation felt in oral functions.

2.5 Statistical analysis

Numerical data were expressed as numbers and percentages. A non-parametric approach was used since analyzed variables were not normally distributed, as verified by the Kolmogorov–Smirnov test. The comparison between cases and controls was calculated using the Chi-Squared or exact Fisher test.

The Spearman correlation test was applied in order to assess the interdependence among variables. Statistical analyses were performed using SPSS 22.0 for the Windows package. A p-value smaller than 0.05 was considered to be statistically significant.

3. Results

Out of 75 patients referred to the unit of periodontics, 26 patients were excluded because did not present the inclusion criteria. For these reasons, 49 patients (22 males, 27 females) were finally enrolled. Table 1 illustrate the relative frequency distribution of demographic characteristics of enrolled subjects.

Table 1. Demographic characteristics of the study

Demographic Characteristics	Number (n= 49)	Percentage
Sex		
Male	22	44.9
Female	27	55.1
Age		
<20	5	10.2
20-40	8	16.3
40-60	21	42.9
60-70	11	22.4
<70	4	8.2
Married	27	55.1
Education		
Primary school	16	32.6
College	21	42.9
University	12	24.5
Occupation		
Retiree unemployed	5	10.2
Housewife	6	12.2
Worker	19	38.8
Self-employed	14	28.6
Employees	5	10.2
Clinical attachment loss levels (mm)		
0-1	4	8.2
1-2	6	12.2
2-3	12	24.5
3-4	14	28.6
4-6	19	38.8
<7	4	8.2

In the sample, 73.5% of patients were >40 years old, whole 42.9% had a college education, while 55.1% were married. Regarding occupation, 38.8% were workers, while 28.6 were self-employed (Table 1). When the patients 'psychological data were collected and classified based on degree of clinical attachment loss, the correlation of psychological factors with severity of clinical attachment loss was evaluated. Amongst evaluated psychological factors, anxiety,

depression, emotional focused coping behavior and chronic stress was present. The patients who suffered from severe attachment loss used emotional focused coping behavior more frequently when facing stressful situation.

When the patients 'psychological data were collected and classified based on degree of clinical attachment loss, the correlation of psychological factors with severity of clinical attachment loss was evaluated (Table 2). The presence of periodontitis, evaluated through different clinical parameters evidenced that PD was significantly correlated with anxiety ($p<0.001$), depression ($p= 0.026$), stress ($p<0.001$); CAL was significantly correlated with elderly age ($p= 0.006$), anxiety ($p<0.001$), depression ($p= 0.026$) and stress ($p= 0.017$); BOP was significantly correlated with depression ($p= 0.027$); PI was significantly correlated with anxiety ($p= 0.014$); REC was significantly correlated with depression ($p= 0.016$) and stress ($p= 0.035$) (Table 2).

Table 2. Correlation among periodontal parameters, stress and depression

	PD	**CAL**	**BOP**	**PI**	**REC**
Age	rs= 0.224; p= 0.149	rs= 0.055; p= 0.006	rs= -0.445; p= 0.187	rs= 0.125; p= 0.447	rs= 0.173; p= 0.324
Anxiety	rs= 0.418; p< 0.001	rs= 0.417; p< 0.001	rs= -0.237; p= 0.132	rs= 0.376; p= 0.014	rs= 0.364; p= 0.078
Depression	rs= 0.358; p= 0.026	rs= 0.225; p= 0.025	rs= -0.347; p= 0.027	rs= 0.191; p= 0.331	rs= 0.186; p= 0.016
Stress	rs= 0.554; p< 0.001	rs= 0.344; p< 0.017	rs= 0.066; p= 0.058	rs= 0.409; p= 0.007	rs= 0.385; p= 0.035

On the other hand, the group with attachment loss close to healthy level used problem focused coping behaviors more frequently while facing stressful events. Patients with lower level of anxiety showed less severe attachment loss in a significant manner and patients with lower score on chronic stress were found in better periodontal health.

4. Discussion

For the last many years dental professionals have been suggesting the presence of a relationship between psychosocial stress and periodontitis. It has been demonstrated that the clinical psychological factors and stress play a role in the etiology of several forms of diseases (Aggarwal et al., 2022; Barchetta et al., 2021; Bochicchio et al., 2023; Di Giacomo et al., 2019; Di Giuseppe et al., 2020; Frisone et al., 2021; Puşcaşu et al., 2022; Sheikh et al., 2019; Tolsa et al., 2022; Vita et al., 2020), including gingivitis and periodontitis (Mannem & Chava, 2012; Scandurra et al., 2021). Several epidemiological investigations demonstrated an increase in necrotizing periodontal diseases during times in which patients were subjected to stress (Li A. et al., 2022; Nair & Nisha, 2022; Ozturk & Ada, 2022). Other authors showed that individuals under high working load, bad marital status, occupational dissatisfaction (Gueiros et al., 2019; Hughes & Herrick, 2017), and high psychological strain caused by critical life event exhibited periodontal

destruction more frequently (Iram et al., 2019). Critical life events such as loss of spouse may cause a transitory immune suppression. Nevertheless, his association was dependent of the patients' favored coping strategy. In people with highly problem orientated coping manner, the study failed to show an association between stress and periodontal status (Lenk et al., 2022). Epidemiological studies have demonstrated that periodontitis does not affect all persons in the community in a comparable way. Some individuals offer risk characteristics that make them more vulnerable to acquire periodontal disease (Alani & Seymour, 2014; Amaliya et al., 2015; Fonseca et al., 2015; Grover et al., 2014; Lang, 2014). During recent years various epidemiological studies carried out in various countries revealed that periodontal diseases in different societies have a different prevalence (Antonoglou et al., 2015; Asa'ad et al., 2017; Cetin et al., 2022; Charupinijkul et al., 2022; Ghasemzedah et al., 2017; Ketharanathan et al., 2019; Klionsky et al., 2016; Lindner et al., 2022; Offenbacher et al., 2016). Inflammation is considered as the causative factor of in inflammatory process is the host's response to bacterial plaque which itself is under the influence of environmental and genetical factors (Akkaya et al., 2022), initiation and progress of periodontal infections are obviously potentiated by local and systemic situations called risk factors (Aarabi et al., 2018; Eapen et al., 2014; Jamali et al., 2018; Jimenez et al., 2022; Kim et al., 2018; Lenk et al., 2022). Currently, risk factors including colonization with particular pathogenic bacteria in gingival regions, systemic conditions related to low number of neutrophils, diabetes mellitus, smoking, and local factors are believed to be of importance in pathogenesis of periodontal disease. In addition to age (considering that the disease is most prevalent in elderly) and sex (also it is more prevalent in the males) recent studies refer to two risk-increasing factors of periodontal diseases including stress and coping behavior (Abada et al., 2022; Haffajee et al., 1997; Oliveira et al., 2009; Quirynen et al., 1999; Umeda et al., 1998; Wennstrom et al., 2005).

Regarding the importance of stress and the possibility of the influential role of other psychological factors and the way people face with stress, this study was aimed to investigate the association of periodontal disease with psychological variables (Fentoglu et al., 2022). Also, it was expected to demonstrate the association between stressful events of life and the clinical loss of periodontal attachment. In the present study the scale for categorization of periodontal diseases was based on clinical attachment loss (Esposito et al., 2004; Herrera et al., 2002; Jimenez et al., 2022; Konig et al., 2008; Pers et al., 2008; Yamada et al., 2006; Yamamiya et al., 2008). The questionnaires used in this study were internationally recognized and used in other studies performed. Moreover, each of these psychological tests were reliable and valid. These results

show that anxiety and other psychological factors effect CAL of and there was significant relationship between factors and the level of CAL.

The world health organization considers occupation as an intermediate determinant for health, and is directly connected to income and education level; therefore, it can also serve to determine access to health services and other resources (Frisone et al., 2021, Bolstad et al., 2022). The fact that these determinants did not reduce the influence of stress and depression may confirm the salutogenic assumption that socioeconomic factors would not change the individual perception of quality of life in adults.

The patients with higher mean CAL showed higher anxiety and depression scores. Regarding the nine psychological factors studied following SCL-90-R questionnaire scoring, only two factors namely problem focused coping and emotional focused coping behaviors were assessed. The result revealed likelihood of a higher usage of emotional focused coping in patients with higher CAL, in agreement with other reports (Santonocito et al., 2021a, Santonocito et al., 2021b, Santonocito et al., 2022).

The effort to direct oral health care actions toward a better, overall understanding of its benefits by human beings, considering their beliefs and the socioeconomic and cultural context, may help humanize oral health care and bring it closer to the population, reduce differences and promote long-lasting healthy oral behaviors (Amaliya et al., 2015; Antonoglou et al., 2015; Lo Giudice et al., 2022; Ronsivalle et al., 2023; Wu et al., 2016).

Increasing research reveals that periodontal disease-related inflammation can also be connected to rheumatoid arthritis, certain malignancies, preterm birth and dementia. Whilst the relationship between mental illness and poor oral health has been long documented, it has traditionally been interpreted as stemming from the poor self-care and lifestyle commonly observed in persons with poor mental health (Badersten et al., 1984; Soskolne et al., 1998; Torfason et al., 1979).

Typically, the finger has been pointed at factors such as negligent oral health care, poor diet, smoking and alcohol use. Stress can also reduce saliva volume and affect its composition, which can also contribute to poorer dental health (Ambili et al., 2005; Drisko, 2001; Loos, 2005; Mannisto et al., 1996).

In the other direction, any causal influence of poor oral health on mental health has been considered to be psychological, namely that dental disorders might lead to self-consciousness or negative ruminations about health or mortality, which in turn affect psychosocial functioning

and mood (Feller et al., 2020). However, current research demonstrates that chronic systemic inflammation directly affects neural systems and behaviour in very precise ways, which implies that the dental/mental health relationship is likely to be physiological as well as psychological. Increased peripheral cytokines directly affect the brain systems that are known to be involved in depression (such as the hypothalamus, hippocampus and prefrontal cortex), and reduces levels of serotonin, dopamine and norepinephrine in the brain, changes often correlated with mental illness.

Furthermore, inflammation reduces the production of brain-derived neurotrophic factor (BDNF), which is central to the creation of new neurons and synaptic connections (Klionsky et al., 2016). Experimentally, the administration of inflammatory agents leads directly to 'depressive behaviour' such as social withdrawal, reduced motivation and motor activity, and increased anxiety. Such behaviour is also correlated with natural levels of inflammatory markers in human individuals.

The negative effects of cortisol on immune defense mechanism also negatively influence the initiation and course of periodontitis. The results of the present study clearly demonstrate the relationship between depression and periodontitis. However, apart from age, gender and smoking the other demographic factors and socioeconomic characteristics such as education, lifestyle, nutritional status were not considered, which is one of the limitations of our study. Longitudinal studies with increased sample size emphasizing on clinical, neurophysiological, neuroendocrinological and psychopharmacological investigations would give conclusive evidence on the role of depression in progression of periodontitis (Lenk et al., 2022; Rahate et al., 2022; Wu et al., 2016).

According to data of this study, the patients with lower CAL, used problem focused coping behavior more frequently and the difference was shown to be significant. Also, the patients with lower CAL had lower anxiety level. In addition, while studying the correlation between CAL and chronic stress, it was demonstrated that a lower level of suffering from chronic stress was associated with lower clinical attachment loss.

The hypothesis that immunological processes may play a crucial role in the development of mental illnesses and their treatment is a fascinating topic of contemporary study. It is now known that widespread inflammation is a significant risk factor for depression and stress-mediated alterations in behavior. However, whilst periodontitis causes systemic inflammation, and various clinical studies do imply a causal link between periodontitis and depression, the idea

that periodontitis is a risk factor for depression is not definitively proven at present, and studies are ongoing.

The present study also has several limitations that should be considered. One is the limited number of enrolled patients, which could limit the results obtained, as well as the absence of a longitudinal evaluation that could better evaluate the impact of periodontitis on stress in the long term.

5. Conclusion

The findings of this study support the recent hypotheses in which psychological factors, particularly psychological stress and anxiety were shown to increase the risk of periodontal diseases. In the present study, PD and several clinical parameters of periodontitis were significantly correlated with anxiety, depression and stress, indicating a strict association between the extent of periodontitis and psychological aspects of well-being. The results suggest that stress and depression should be considered in further qualitative and interventional studies assessing the impact of oral health on quality of life. The data of the present status may also help future studies through designing interventional and preventive measures within the health system to improve the level of psychological health of the patients leading to managing stress more effectively. More studies are needed for further clarification of the relationship of psychological stress factors and their effect on clinical attachment loss or periodontal disease.

Ethical Approval

The international review board of the University of Catania approved the study protocol (215/21 - 19.10.21).

Data availability statement

Data are available upon reasonable request to the corresponding author

Conflict of interest statement

The authors declare that the research was conducted in the absence of any potential conflict of interest.

Authors' contribution

Conceptualization, G.I. and A.P.; methodology, A.P. and F.I.; validation F.I.; validation, A.C.; writing—original draft preparation, G.I., A.C., A.P.; writing—review and editing, G.I. All authors have read and agreed to the published version of the manuscript

References

1. Aarabi, G., Heydecke, G., & Seedorf, U. (2018). Roles of oral infections in the pathomechanism of atherosclerosis. *International Journal of Molecular Sciences*, *19*(7), 1978. https://doi.org/10.1038/s41598-019-42594-z

2. Abada, H. M., Hashem, A. A. R., Abu-Seida, A. M., & Nagy, M. M. (2022). The effect of changing apical foramen diameter on regenerative potential of mature teeth with necrotic pulp and apical periodontitis. *Clinical Oral Investigations*, 1-11. https://doi.org/10.1007/s00784-021-04159-1

3. Aggarwal, K., Gupta, J., Kaur, R. K., Bansal, D., & Jain, A. (2022). Effect of anxiety and psychologic stress on periodontal health: a systematic review and meta-analysis. *Quintessence International, 53*(2). https://doi.org/10.3290/j.qi.b2091191

4. Akkaya, H. Ü., Yılmaz, H. E., Narin, F., & Sağlam, M. (2022). Evaluation of galectin-3, peptidylarginine deiminase-4, and tumor necrosis factor-α levels in gingival crevicular fluid for periodontal health, gingivitis, and Stage III Grade C periodontitis: A pilot study. *Journal of Periodontology*, *93*(1), 80-88. https://doi.org/10.1002/JPER.21-0137

5. Alani, A., & Seymour, R. (2014). Systemic medication and the inflammatory cascade. *Periodontology 2000*, *64*(1), 198-210. https://doi.org/10.1111/j.1600-0757.2012.00454.x

6. Alkan, İ. İ., Akkaya, H. Ü., & Sağlam, M. (2022). The effectiveness of scaling and root planing with combined application of air polishing and Nd: YAG laser in periodontal pockets of stage III grade C periodontitis patients: a single-blinded randomized clinical trial. *Clinical Oral Investigations*, *26*(8), 5459-5469. https://doi.org/10.1007/s00784-022-04513-x

7. Amaliya, A., Laine, M. L., Delanghe, J. R., Loos, B. G., Van Wijk, A. J., & Van der Velden, U. (2015). Java project on periodontal diseases: periodontal bone loss in relation to environmental and systemic conditions. *Journal of clinical periodontology*, *42*(4), 325-332. https://doi.org/10.1111/jcpe.12381

8. Ambili, R., Santhi, W. S., Janam, P., Nandakumar, K., & Pillai, M. R. (2005). Expression of activated transcription factor nuclear factor-κB in periodontally diseased tissues. *Journal of periodontology*, *76*(7), 1148-1153. https://doi.org/10.1902/jop.2005.76.7.1148

9. Antonoglou, G. N., Suominen, A. L., Knuuttila, M., Ylöstalo, P., Ojala, M., Männistö, S., ... & Tervonen, T. (2015). Associations between serum 25-hydroxyvitamin d and periodontal pocketing and gingival bleeding: results of a study in a non-smoking population in Finland. *Journal of periodontology*, *86*(6), 755-765. https://doi.org/10.1902/jop.2015.140262

10. Asa'ad, F., Bollati, V., Pagni, G., Castilho, R. M., Rossi, E., Pomingi, F., ... & Rasperini, G. (2017). Evaluation of DNA methylation of inflammatory genes following treatment of chronic periodontitis: A pilot case–control study. *Journal of Clinical Periodontology*, *44*(9), 905-914. https://doi.org/10.1111/jcpe.12783

11. Badersten, A., Nilveus, R., & Egelberg, J. (1984). Effect of nonsurgical periodontal therapy: II. Severely advanced periodontitis. *Journal of clinical periodontology*, *11*(1), 63-76. https://doi.org/10.1111/j.1600-051x.1984.tb01309.x

12. Barchetta, S., Martino, G., Craparo, G., Salehinejad, M. A., Nitsche, M. A., & Vicario, C. M. (2021). Alexithymia is linked with a negative bias for past and current events in healthy humans. *International Journal of Environmental Research and Public Health, 18*(13), 6696. 12. https://doi.org/10.3390/ijerph1813669

13. Beikler, T., Abdeen, G., Schnitzer, S., Sälzer, S., Ehmke, B., Heinecke, A., & Flemmig, T. F. (2004). Microbiological shifts in intra-and extraoral habitats following mechanical periodontal therapy. *Journal of clinical periodontology*, *31*(9), 777-783. https://doi.org/10.1111/j.1600-051X.2004.00557.x

14. Bhardwaj, M., Deshmukh, R., Kaundal, M., & Reddy, B. K. (2016). Pharmacological induction of hemeoxygenase-1 activity attenuates intracerebroventricular streptozotocin induced neurocognitive deficit and oxidative stress in rats. *European Journal of Pharmacology*, *772*, 43-50. https://doi.org/10.1016/j.ejphar.2015.12.037

15. Bochicchio, V., Mezzalira, S., Maldonato, N. M., Cantone, E., & Scandurra, C. (2023). Olfactory-related quality of life impacts psychological distress in people with COVID-19: The affective implications of olfactory dysfunctions. *Journal of Affective Disorders, 323*, 741-747. https://doi.org/10.1016/j.jad.2022.12.049

16. Bolstad, A. I., Sehjpal, P., Lie, S. A., & Fevang, B. T. S. (2022). Periodontitis in patients with systemic lupus erythematosus: A nationwide study of 1,990 patients. *Journal of Periodontology*, *93*(3), 364-372. https://doi.org/10.1002/JPER.21-0181

17. Bunpeng, N., Boriboonhirunsarn, D., Boriboonhirunsarn, C., Sawangpanyangkura, T., & Tansriratanawong, K. (2022). Association between gestational diabetes mellitus and periodontitis via the effect of reactive oxygen species in peripheral blood cells. *Journal of Periodontology*, *93*(5), 758-769. https://doi.org/10.1002/JPER.21-0455

18. Caetano, A. J., D'Agostino, E. M., Sharpe, P., & Nibali, L. (2022). Expression of periodontitis susceptibility genes in human gingiva using single-cell RNA sequencing. *Journal of Periodontal Research*, *57*(6), 1210-1218. https://doi.org/10.1111/jre.13057

19. Caputo, A., Vicario, C. M., Cazzato, V., & Martino, G. (2022). Psychological Factors as Determinants of Medical Conditions, Volume II. *Frontiers in psychology, 13*, 865235. https://doi.org/10.3389/fpsyg.2022.865235

20. Catalano, A., Martino, G., Bellone, F., Papalia, M., Lasco, C., Basile, G., ... & Lasco, A. (2019). Neuropsychological assessment in elderly men with benign prostatic hyperplasia treated with dutasteride. *Clinical drug investigation*, *39*, 97-102. https://doi.org/10.1007/s40261-018-0720-7

21. Çetin, M. B., Sezgin, Y., Önder, C., & Bakirarar, B. (2022). The relationship between body mass index and stage/grade of periodontitis: A retrospective study. *Clinical Oral Investigations*, 1-9. https://doi.org/10.1007/s00784-021-04172-4

22. Charupinijkul, A., Arunyanak, S., Rattanasiri, S., Vathesatogkit, P., Thienpramuk, L., & Lertpimonchai, A. (2021). The effect of obesity on periodontitis progression: the 10-year retrospective cohort study. *Clinical Oral Investigations*, 1-8. https://doi.org/10.1007/s00784-021-04031-2

23. Chen, H., Wang, Z., He, Y., Peng, L., Zhu, J., & Zhang, X. (2022). Pyroptosis may play a crucial role in modifications of the immune microenvironment in periodontitis. *Journal of Periodontal Research*, *57*(5), 977-990. https://doi.org/10.1111/jre.13035

24. Cooke, D. J. (2021). The significance of life events as a cause of psychological and physical disorder. In *Psychiatric epidemiology* (pp. 67-80). Routledge. https://doi.org/10.1201/9781003134831-7

25. De Soete, M., Mongardini, C., Pauwels, M., Haffajee, A., Socransky, S., van Steenberghe, D., & Quirynen, M. (2001). One-stage full-mouth disinfection. Long-term microbiological results analyzed by checkerboard DNA-DNA hybridization. *Journal of Periodontology*, *72*(3), 374-382. https://doi.org/10.1902/jop.2001.72.3.374

26. Di Giacomo, D., Ranieri, J., Nasta, L., Moscato, S., Guerra, F., & Passafiume, D. (2019). Psychological distress in Interstitial Cystitis/Bladder Pain Syndrome: A cross-sectional study on emotional patterns. *Mediterranean Journal of Clinical Psychology*, *7*(2). https://doi.org/10.6092/2282-1619/2019.7.2135

27. Di Giuseppe, M., Miniati, M., Miccoli, M., Ciacchini, R., Orrù, G., Lo Sterzo, R., ... & Conversano, C. (2020). Defensive responses to stressful life events associated with cancer diagnosis. *Mediterranean Journal of Clinical Psychology*, *8*(1). https://doi.org/10.6092/2282-1619/mjcp-2384

28. Dionigi, C., Larsson, L., Difloe-Geisert, J. C., Zitzmann, N. U., & Berglundh, T. (2022). Cellular expression of epigenetic markers and oxidative stress in periodontitis lesions of smokers and non-smokers. *Journal of Periodontal Research*, *57*(5), 952-959. https://doi.org/10.1111/jre.13030

29. Drisko, C. H. (2001). Nonsurgical periodontal therapy. *Periodontology 2000*, *25*, 77-88. https://doi.org/10.1034/j.1600-0757.2001.22250106.x

30. Eapen, D. J., Manocha, P., Ghasemzadeh, N., Patel, R. S., Al Kassem, H., Hammadah, M., ... & Quyyumi, A. A. (2014). Soluble urokinase plasminogen activator receptor level is an independent predictor of the presence and severity of coronary artery disease and of future adverse events. *Journal of the American heart association*, *3*(5), e001118. https://doi.org/10.1161/JAHA.114.001118

31. Esposito, M., Coulthard, P., Thomsen, P., & Worthington, H. V. (2004). Enamel matrix derivative for periodontal tissue regeneration in treatment of intrabony defects: a Cochrane systematic review. *Journal of dental education*, *68*(8), 834-844. https://doi.org/10.1002/j.0022-0337.2004.68.8.tb03832.x

32. Feller, L., Feller, G., Ballyram, T., Chandran, R., Lemmer, J., & Khammissa, R. A. G. (2020). Interrelations between pain, stress and executive functioning. *British journal of pain*, *14*(3), 188-194. https://doi.org/10.1177/2049463719889380

33. Fentoğlu, Ö., Tülüceoğlu, E. E., & Orhan, H. (2022). Plasminogen gene polymorphisms [c. 924C> T and IVS 8+ 14 G> A] in periodontitis and familial Mediterranean fever: a case-control study. *Journal of Periodontal Research*, *57*(2), 371-380. https://doi.org/10.1111/jre.12966

34. Flemmig, T. F., Milian, E., Karch, H., & Klaiber, B. (1998). Differential clinical treatment outcome after systemic metronidazole and amoxicillin in patients harboring Actinobacillus actinomycetemcomitans and/or Porphyromonas gingivalis. *Journal of clinical periodontology*, *25*(5), 380-387. https://doi.org/10.1111/j.1600-051x.1998.tb02459.x

35. Frisone, F., Sicari, F., Settineri, S., & Merlo, E. M. (2021). Clinical psychological assessment of stress: a narrative review of the last 5 years. *Clinical Neuropsychiatry*, *18*(2), 91. https://doi.org/10.36131%2Fcnfioritieditore20210203

36. Fonseca, D. C., Cortelli, J. R., Cortelli, S. C., Miranda Cota, L. O., Machado Costa, L. C., Moreira Castro, M. V., ... & Costa, F. O. (2015). Clinical and microbiologic evaluation of scaling and root planing per quadrant and one-stage full-mouth disinfection associated with azithromycin or chlorhexidine: a clinical randomized controlled trial. *Journal of periodontology*, *86*(12), 1340-1351. https://doi.org/10.1902/jop.2015.150227

37. Ghasemzadeh, N., Hayek, S. S., Ko, Y. A., Eapen, D. J., Patel, R. S., Manocha, P., ... & Quyyumi, A. A. (2017). Pathway-specific aggregate biomarker risk score is associated with burden of coronary artery disease and predicts near-term risk of myocardial infarction and death. *Circulation: cardiovascular quality and outcomes*, *10*(3), e001493. https://doi.org/10.1161/CIRCOUTCOMES.115.001493

38. Go, H., Park, T., Shin, A. R., Jung, Y. S., Amano, A., Song, K. B., & Choi, Y. H. (2022). Validity of a combination of periodontal pathogens and salivary biomarkers as predictors of periodontitis. *Journal of Periodontal Research*, *57*(5), 1083-1092. https://doi.org/10.1111/jre.13048

39. Grover, V., Kapoor, A., Malhotra, R., & Kaur, G. (2014). Porphyromonas gingivalis antigenic determinants-potential targets for the vaccine development against periodontitis. *Infectious Disorders-Drug Targets (Formerly Current Drug Targets-Infectious Disorders)*, *14*(1), 1-13. https://doi.org/10.2174/1871526514666140827100930

40. Gueiros, L. A., France, K., Posey, R., Mays, J. W., Carey, B., Sollecito, T. P., ... & De Rossi, S. (2019). World Workshop on Oral Medicine VII: Immunobiologics for salivary gland disease in Sjögren's syndrome: A systematic review. *Oral diseases*, *25*, 102-110. https://doi.org/10.1111/odi.13062

41. Haffajee, A. D., Cugini, M. A., Dibart, S., Smith, C., Kent Jr, R. L., & Socransky, S. S. (1997). The effect of SRP on the clinical and microbiological parameters of periodontal diseases. *Journal of clinical periodontology*, *24*(5), 324-334. https://doi.org/10.1111/j.1600-051x.1997.tb00765.x

42. Herrera, D., Sanz, M., Jepsen, S., Needleman, I., & Roldán, S. (2002). A systematic review on the effect of systemic antimicrobials as an adjunct to scaling and root planing in periodontitis patients. *Journal of clinical periodontology*, *29*, 136-159. https://doi.org/10.1034/j.1600-051x.29.s3.8.x

43. Hjemdal, O., Roazzi, A., Dias, M. D. G. B., & Friborg, O. (2015). The cross-cultural validity of the Resilience Scale for Adults: a comparison between Norway and Brazil. *BMC psychology*, *3*, 1-9. https://doi.org/10.1186/s40359-015-0076-1

44. Huang, Y. F., Lin, K. C., Liu, S. P., Chang, C. T., Muo, C. H., Chang, P. J., ... & Wu, C. Z. (2022). The association between the severity of periodontitis and osteonecrosis of the jaw in patients with different cancer locations: A nationwide population-based study. *Clinical Oral Investigations*, *26*(5), 3843-3852. https://doi.org/10.1007/s00784-021-04175-1

45. Hughes, M., & Herrick, A. L. (2017). Digital ulcers in systemic sclerosis. *Rheumatology (Oxford)*, *56*(1), 14-25. https://doi.org/10.1093/rheumatology/kew047

46. Hwang, S. Y., Oh, H., Rhee, M. Y., Kang, S., & Kim, H. Y. (2022). Association of periodontitis, missing teeth, and oral hygiene behaviors with the incidence of hypertension in middle-aged and older adults in Korea: A 10-year follow-up study. *Journal of Periodontology*, *93*(9), 1283-1293. https://doi.org/10.1002/JPER.21-0706

47. Iram, S., Zahera, M., Wahid, I., Baker, A., Raish, M., Khan, A., ... & Khan, M. S. (2019). Cisplatin bioconjugated enzymatic GNPs amplify the effect of cisplatin with acquiescence. *Scientific Reports*, *9*(1), 13826. https://doi.org/10.1038/s41598-019-50215-y

48. Isola, G., Polizzi, A., Santonocito, S., Alibrandi, A., & Ferlito, S. (2019). Expression of salivary and serum malondialdehyde and lipid profile of patients with periodontitis and coronary heart disease. *International Journal of Molecular Sciences*, *20*(23), 6061. https://doi.org/10.3390/ijms20236061

49. Isola, G., Polizzi, A., Santonocito, S., Alibrandi, A., & Williams, R. C. (2022). Periodontitis activates the NLRP3 inflammasome in serum and saliva. *Journal of Periodontology*, *93*(1), 135-145. https://doi.org/10.1002/JPER.21-0049

50. Isola, G., Santonocito, S., Distefano, A., Polizzi, A., Vaccaro, M., Raciti, G., ... & Li Volti, G. (2023). Impact of periodontitis on gingival crevicular fluid miRNAs profiles associated with cardiovascular disease risk. *Journal of Periodontal Research*, *58*(1), 165-174. https://doi.org/10.1111/jre.13078

51. Jamali, N., Sorenson, C. M., & Sheibani, N. (2018). Vitamin D and regulation of vascular cell function. *American Journal of Physiology-Heart and Circulatory Physiology*, *314*(4), H753-H765. https://doi.org/10.1152/ajpheart.00319.2017

52. Jiménez, C., Garrido, M., Pussinen, P., Bordagaray, M. J., Fernández, A., Vega, C., ... & Hernández, M. (2021). Systemic burden and cardiovascular risk to Porphyromonas species in apical periodontitis. *Clinical Oral Investigations*, *26*, 993–1001https://doi.org/10.1007/s00784-021-04083-4

53. John, J., Saranathan, R., Adigopula, L. N., Thamodharan, V., Singh, S. P., Lakshmi, T. P., ... & Prashanth, K. (2016). The quorum sensing molecule N-acyl homoserine lactone produced by Acinetobacter baumannii displays antibacterial and anticancer properties. *Biofouling*, *32*(9), 1029-1047. https://doi.org/10.1080/08927014.2016.1221946

54. Ju, X., Harford, J., Luzzi, L., & Jamieson, L. M. (2022). Prevalence, extent, and severity of periodontitis among Australian older adults: Comparison of two generations. *Journal of periodontology*, *93*(9), 1387-1400. https://doi.org/10.1002/JPER.21-0458

55. Ketharanathan, V., Torgersen, G. R., Petrovski, B. É., & Preus, H. R. (2019). Radiographic alveolar bone level and levels of serum 25-OH-Vitamin D3 in ethnic Norwegian and Tamil periodontitis patients and their periodontally healthy controls. *BMC Oral Health*, *19*(1), 1-7. https://doi.org/10.1186/s12903-019-0769-6

56. Kim, O. S., Shin, M. H., Kweon, S. S., Lee, Y. H., Kim, O. J., Kim, Y. J., & Chung, H. J. (2018). The severity of periodontitis and metabolic syndrome in Korean population: The Dong-gu study. *Journal of periodontal research*, *53*(3), 362-368. https://doi.org/10.1111/jre.12521

57. Klionsky, D., Abdelmohsen, K., Abe, A., Abedin, M. J., Abeliovich, H., Arozena, A. A., ... & Bernassola, F. (2016). Guidelines for the use and interpretation of assays for monitoring autophagy. *Autophagy*, *12*(1), 1-222. https://doi.org/10.1080/15548627.2015.1100356

58. König, J., Schwahn, C., Fanghänel, J., Plötz, J., Hoffmann, T., & Kocher, T. (2008). Repeated scaling versus surgery in young adults with generalized advanced periodontitis. *Journal of periodontology*, *79*(6), 1006-1013. https://doi.org/10.1902/jop.2008.070380

59. Krueger, P. M., & Chang, V. W. (2008). Being poor and coping with stress: health behaviors and the risk of death. *American journal of public health*, *98*(5), 889-896. https://doi.org/10.2105/AJPH.2007.114454

60. Lang, N. P. (2014). Commentary: bacteria play a critical role in the etiology of periodontal disease. *Journal of periodontology*, *85*(2), 211-213. https://doi.org/10.1902/jop.2013.130699

61. Larvin, H., Kang, J., Aggarwal, V. R., Pavitt, S., & Wu, J. (2022). The additive effect of periodontitis with hypertension on risk of systemic disease and mortality. *Journal of Periodontology*, *93*(7), 1024-1035. https://doi.org/10.1002/JPER.21-0621

62. Lenk, M., Noack, B., Weidner, K., & Lorenz, K. (2022). Psychopathologies and socioeconomic status as risk indicators for periodontitis: a survey-based investigation in German dental practices. *Clinical Oral Investigations*, *26*(11), 2853–2862.https://doi.org/10.1007/s00784-021-04263-2

63. Leonardi, R., Ronsivalle, V., Lagravere, M. O., Barbato, E., Isola, G., & Lo Giudice, A. (2021). Three-dimensional assessment of the spheno-occipital synchondrosis and clivus after tooth-borne and bone-borne rapid maxillary expansion: A retrospective CBCT study using voxel-based superimposition. *The Angle Orthodontist*, *91*(6), 822-829. https://doi.org/10.2319/013021-86.1

64. Li, A., Du, M., Chen, Y., Marks, L. A., Visser, A., Xu, S., & Tjakkes, G. H. E. (2022). Periodontitis and cognitive impairment in older adults: The mediating role of mitochondrial dysfunction. *Journal of Periodontology*, *93*(9), 1302-1313. https://doi.org/10.1002/JPER.21-0620

65. Li, X., Guo, L., Sato, F., Kitayama, T., Tewari, N., Makishima, M., ... & Bhawal, U. K. (2022). Dec2 negatively regulates bone resorption in periodontitis. *Journal of Periodontal Research*, *57*(5), 1056-1069. https://doi.org/10.1111/jre.13046

66. Lindner, M., Arefnia, B., Ivastinovic, D., Sourij, H., Lindner, E., & Wimmer, G. (2022). Association of periodontitis and diabetic macular edema in various stages of diabetic retinopathy. *Clinical Oral Investigations*, *26*(1), 505-512. https://doi.org/10.1007/s00784-021-04028-x

67. Lo Giudice, A. L., Brewer, I., Leonardi, R., Roberts, N., & Bagnato, G. (2018). Pain threshold and temporomandibular function in systemic sclerosis: Comparison with psoriatic arthritis. *Clinical rheumatology, 37*, 1861-1867. https://doi.org/10.1007/s10067-018-4028-z

68. Lo Giudice, A. L., Nucera, R., Perillo, L., Paiusco, A., & Caccianiga, G. (2019). Is low-level laser therapy an effective method to alleviate pain induced by active orthodontic alignment archwire? A randomized clinical trial. *Journal of Evidence Based Dental Practice*, *19*(1), 71-78. https://doi.org/10.1016/j.jebdp.2018.11.001

69. Lo Giudice, A., Ronsivalle, V., Gastaldi, G., & Leonardi, R. (2022). Assessment of the accuracy of imaging software for 3D rendering of the upper airway, usable in orthodontic and craniofacial clinical settings. *Progress in Orthodontics*, *23*(1), 22. https://doi.org/10.1186/s40510-022-00413-8

70. Loggner Graff, I., Asklow, B., & Thorstensson, H. (2009). Full-mouth versus quadrant-wise scaling--clinical outcome, efficiency and treatment discomfort. *Swedish dental journal*, *33*(3), 105-113. https://www.ncbi.nlm.nih.gov/pubmed/19994560

71. Loos, B. G. (2005). Systemic markers of inflammation in periodontitis. *Journal of periodontology*, *76*, 2106-2115. https://doi.org/10.1902/jop.2005.76.11-S.2106

72. Loos, B. G., & Needleman, I. (2020). Endpoints of active periodontal therapy. *Journal of Clinical Periodontology*, *47*, 61-71. https://doi.org/10.1111/jcpe.13253

73. Loreto, C., Filetti, V., Almeida, L. E., La Rosa, G. R. M., Leonardi, R., Grippaudo, C., & Giudice, A. L. (2020). MMP-7 and MMP-9 are overexpressed in the synovial tissue from severe temporomandibular joint dysfunction. *European Journal of Histochemistry: EJH*, *64*(2). https://doi.org/10.4081/ejh.2020.3113

74. Lu, H., Wu, H., Yang, Y., Feng, X., Ma, X., Xie, Y., ... & Ye, W. (2022). Relationship between chronic periodontitis and inflammatory cytokines in patients undergoing maintenance hemodialysis. *Clinical Oral Investigations*, *26*(11), 6699-6709. https://doi.org/10.1007/s00784-022-04629-0

75. Mannem, S., & Chava, V. K. (2012). The effect of stress on periodontitis: A clinicobiochemical study. *Journal of Indian Society of Periodontology, 16*(3), 365. https://doi.org/10.4103/0972-124X.100912

76. Männistö, S., Virtanen, M., Mikkonen, T., & Pietinen, P. (1996). Reproducibility and validity of a food frequency questionnaire in a case-control study on breast cancer. *Journal of clinical epidemiology*, *49*(4), 401-409. https://doi.org/10.1016/0895-4356(95)00551-x

77. Martino, G., Caputo, A., Vicario, C. M., Feldt-Rasmussen, U., Watt, T., Quattropani, M. C., ... & Vita, R. (2021). Alexithymia, emotional distress, and perceived quality of life in patients with hashimoto's thyroiditis. *Frontiers in psychology*, *12*, 667237. https://doi.org/10.3389/fpsyg.2021.667237

78. Mikuls, T. R., Thiele, G. M., Deane, K. D., Payne, J. B., O'Dell, J. R., Yu, F., ... & Norris, J. M. (2012). Porphyromonas gingivalis and disease-related autoantibodies in individuals at increased risk of rheumatoid arthritis. *Arthritis & Rheumatism*, *64*(11), 3522-3530. https://doi.org/10.1002/art.34595

79. Mombelli, A. (2018). Microbial colonization of the periodontal pocket and its significance for periodontal therapy. *Periodontology 2000*, *76*(1), 85-96. https://doi.org/10.1111/prd.12147

80. Muniz, F. W. M. G., Nogueira, S. B., Mendes, F. L. V., Rösing, C. K., Moreira, M. M. S. M., de Andrade, G. M., & de Sousa Carvalho, R. (2015). The impact of antioxidant agents complimentary to periodontal therapy on oxidative stress and periodontal outcomes: A systematic review. *Archives of oral biology*, *60*(9), 1203-1214. https://doi.org/10.1016/j.archoralbio.2015.05.007

81. Myles, L., & Merlo, E. (2022). Elucidating the cognitive mechanisms underpinning behavioural activation. *International journal of psychological research, 15*(1), 126-132. https://doi.org/10.21500/20112084.5400

82. Nair, S., & Nisha, K. J. (2022). Evaluation of the effect of scaling and root planing on salivary and serum fetuin-A levels in patients with Stages II and III periodontitis. *Journal of Periodontology*, *93*(2), 179-188. https://doi.org/10.1002/JPER.21-0179

83. Offenbacher, S., Divaris, K., Barros, S. P., Moss, K. L., Marchesan, J. T., Morelli, T., ... & North, K. E. (2016). Genome-wide association study of biologically informed periodontal complex traits offers novel insights into the genetic basis of periodontal disease. *Human molecular genetics*, *25*(10), 2113-2129. https://doi.org/10.1093/hmg/ddw069

84. Oliveira, N. F., Damm, G. R., Andia, D. C., Salmon, C., Nociti Jr, F. H., Line, S. R., & De Souza, A. P. (2009). DNA methylation status of the IL8 gene promoter in oral cells of smokers and non-smokers with chronic periodontitis. *Journal of clinical periodontology*, *36*(9), 719-725. https://doi.org/10.1111/j.1600-051X.2009.01446.x

85. Olsen, I., & Singhrao, S. K. (2018). Importance of heterogeneity in Porhyromonas gingivalis lipopolysaccharide lipid A in tissue specific inflammatory signalling. *Journal of oral microbiology*, *10*(1), 1440128. https://doi.org/10.1080/20002297.2018.1440128

86. Öztürk, A., & Ada, A. O. (2022). The roles of ANRIL polymorphisms in periodontitis: A systematic review and meta-analysis. *Clinical Oral Investigations*, *26*, 1121–1135.https://doi.org/10.1007/s00784-021-04257-0

87. Pers, J. O., Saraux, A., Pierre, R., & Youinou, P. (2008). Anti–TNF-α immunotherapy is associated with increased gingival inflammation without clinical attachment loss in subjects with rheumatoid arthritis. *Journal of periodontology*, *79*(9), 1645-1651. https://doi.org/10.1902/jop.2008.070616

88. Petrenya, N., Hopstock, L. A., Holde, G. E., Oscarson, N., & Jönsson, B. (2022). Relationship between periodontitis and risk of cardiovascular disease: Insights from the Tromsø Study. *Journal of Periodontology*, *93*(9), 1353-1365. https://doi.org/10.1002/JPER.22-0004

89. Puşcaşu, A., Bolocan, A., Păduraru, D. N., Salmen, T., Bica, C., & Andronic, O. (2022). The implications of chronic psychological stress in the development of diabetes mellitus type 2. *Mediterranean Journal of Clinical Psychology*, *10*(2). https://doi.org/10.13129/2282-1619/mjcp-3544

90. Quirynen, M., Mongardini, C., Pauwels, M., Bollen, C. M., Van Eldere, J., & Van Steenberghe, D. (1999). One stage full-versus partial-mouth disinfection in the treatment of chronic adult or generalized early-onset periodontitis. II. Long-term impact on microbial load. *Journal of periodontology*, *70*(6), 646-656. https://doi.org/10.1902/jop.1999.70.6.646

91. Rahate, P. S., Kolte, R. A., Kolte, A. P., Lathiya, V. N., Gupta, M., & Chari, S. (2022). Evaluation of stress, serum, and salivary ghrelin and cortisol levels in smokers and non-smokers with Stage III periodontitis: A cross-sectional study. *Journal of Periodontology*, *93*(8), 1131-1140. https://doi.org/10.1002/JPER.21-0373

92. Rasul, F., Stansfeld, S. A., Hart, C. L., & Smith, G. D. (2005). Psychological distress, physical illness, and risk of coronary heart disease. *Journal of Epidemiology & Community Health, 59*(2), 140-145. https://doi.org/10.1136/jech.2004.019786

93. Righolt, A. J., Jevdjevic, M., Marcenes, W., & Listl, S. (2018). Global-, regional-, and country-level economic impacts of dental diseases in 2015. *Journal of dental research*, *97*(5), 501-507. https://doi.org/10.1177/0022034517750572

94. Ronsivalle, V., Venezia, P., Bennici, O., D'Antò, V., Leonardi, R., & Giudice, A. L. (2023). Accuracy of digital workflow for placing orthodontic miniscrews using generic and licensed open systems. A 3D imaging analysis of non-native. Stl files for guided protocols. *BMC Oral Health*, *23*(1), 494. https://doi.org/10.1186/s12903-023-03113-9

95. Sabbah, W., Gomaa, N., & Gireesh, A. (2018). Stress, allostatic load, and periodontal diseases. *Periodontology 2000*, *78*(1), 154-161. https://doi.org/10.1111/prd.12238

96. Santonocito, S., Polizzi, A., Ronsivalle, V., Palazzo, G., Sicari, F., Isola, G. (2021). Impact of periodontitis on systemic anxiety and oral health quality of life. *Mediterranean Journal of Clinical Psychology 9*(2). https://doi.org/10.13129/2282-1619/mjcp-3064

97. Santonocito, S., Indelicato, F., Polizzi, A., Palazzo, G. (2021). Impact of periodontitis and orthodontic treatment on dental anxiety and self-esteem. *Mediterranean Journal of Clinical Psychology, 9*(1). https://doi.org/10.6092/2282-1619/mjcp-2971

98. Santonocito, S., Palazzo, G., Francesco, I., Chaurasia, A., Isola, G. (2022). Effects induced by periodontal disease on overall quality of life and selfesteem. *Mediterranean Journal of Clinical Psychology, 10*(1). https://doi.org/10.13129/2282-1619/mjcp-3354

99. Satomi, K., Nishimura, K., & Igarashi, K. (2022). Semaphorin 3A protects against alveolar bone loss during orthodontic tooth movement in mice with periodontitis. *Journal of Periodontal Research*, *57*(5), 991-1002. https://doi.org/10.1111/jre.13038

100. Scandurra, C., Gasparro, R., Dolce, P., Bochicchio, V., Muzii, B., Sammartino, G., ... & Maldonato, N. M. (2021). The role of cognitive and non-cognitive factors in dental anxiety: A mediation model. *European Journal of Oral Sciences*, *129*(4), e12793. https://doi.org/10.1111/eos.12793

101. Şengül, V., Güney, Z., Kurgan, Ş., Önder, C., Serdar, M. A., & Günhan, M. (2022). Evaluation of salivary and serum methylated arginine metabolites and nitric oxide synthase in advanced periodontitis patients. *Clinical Oral Investigations*, *26*(7), 5061-5070. https://doi.org/10.1007/s00784-022-04479-w

102. Sharpe, L., & Curran, L. (2006). Understanding the process of adjustment to illness. *Social science & medicine, 62*(5), 1153-1166. https://doi.org/10.1016/j.socscimed.2005.07.010

103. Sheiham, A., & Nicolau, B. (2005). Evaluation of social and psychological factors in periodontal disease. *Periodontology 2000*, *39*, 118-131. https://doi.org/10.1111/j.1600-0757.2005.00115.x

104. Sheikh, S., Dahiya, S., Ansari, A. H., & Kumar, M. M. (2019). The association of quality of life between anxiety and depression in patients with chronic rheumatic heart disease. *Mediterranean Journal of Clinical Psychology, 7*(2). https://doi.org/10.6092/2282-1619/2019.7.2164

105. Soskolne, W. A., Chajek, T., Flashner, M., Landau, I., Stabholtz, A., Kolatch, B., & Lerner, E. I. (1998). An in vivo study of the chlorhexidine release profile of the PerioChipTM in the gingival crevicular fluid, plasma and urine. *Journal of clinical periodontology*, *25*(12), 1017-1021. https://doi.org/10.1111/j.1600-051x.1998.tb02407.x

106. Suvan, J., Leira, Y., Moreno Sancho, F. M., Graziani, F., Derks, J., & Tomasi, C. (2020). Subgingival instrumentation for treatment of periodontitis. A systematic review. *Journal of Clinical Periodontology*, *47*, 155-175. https://doi.org/10.1111/jcpe.13245

107. Teughels, W., Feres, M., Oud, V., Martín, C., Matesanz, P., & Herrera, D. (2020). Adjunctive effect of systemic antimicrobials in periodontitis therapy: A systematic review and meta-analysis. *Journal of Clinical Periodontology*, *47*, 257-281. https://doi.org/10.1111/jcpe.13264

108. Tolsa, M. D., & Malas, O. (2022). Re-exploring the connection between Emotional Intelligence, Anxiety, Depression, and Stress in adult population. *Mediterranean Journal of Clinical Psychology, 10*(1). https://doi.org/10.13129/2282-1619/mjcp-3291

109. Tonetti, M. S., Greenwell, H., & Kornman, K. S. (2018). Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *Journal of periodontology*, *89*, S159-S172. https://doi.org/10.1002/jper.18-0006

110. Torfason, T., Kiger, R., Selvig, K. A., & Egelberg, J. (1979). Clinical improvement of gingival conditions following ultrasonic versus hand instrumentation of periodontal pockets. *Journal of clinical periodontology*, *6*(3), 165-176. https://doi.org/10.1111/j.1600-051x.1979.tb02196.x

111. Umeda, M., Chen, C., Bakker, I., Contreras, A., Morrison, J. L., & Slots, J. (1998). Risk indicators for harboring periodontal pathogens. *Journal of periodontology*, *69*(10), 1111-1118. https://doi.org/10.1902/jop.1998.69.10.1111

112. Umeizudike, K. A., Lähteenmäki, H., Räisänen, I. T., Taylor, J. J., Preshaw, P. M., Bissett, S. M., ... & Sorsa, T. (2022). Ability of matrix metalloproteinase-8 biosensor, IFMA, and ELISA immunoassays to differentiate between periodontal health, gingivitis, and periodontitis. *Journal of Periodontal Research*, *57*(3), 558-567. https://doi.org/10.1111/jre.12985

113. Vita, R., Caputo, A., Quattropani, M. C., Watt, T., Feldt-Rasmussen, U., Puleio, P., ... & Martino, G. (2020). Quality of life in patients with hyperthyroidism: where do we stand?. *Mediterranean Journal of Clinical Psychology*, *8*(2). https://doi.org/10.6092/2282-1619/mjcp-2521

114. Wennström, J. L., Tomasi, C., Bertelle, A., & Dellasega, E. (2005). Full-mouth ultrasonic debridement versus quadrant scaling and root planing as an initial approach in the treatment of chronic periodontitis. *Journal of clinical periodontology*, *32*(8), 851-859. https://doi.org/10.1111/j.1600-051X.2005.00776.x

115. Wu, D. D., Li, S. H., Jin, L. Y., Jin, Y., Cui, Y. Y., Zhao, H., ... & Chen, H. B. (2016). Influencing factors of visual hallucinations in patients with Parkinson's disease and its relationship with sleep disorders. *Zhonghua yi xue za zhi*, *96*(13), 1016-1020. https://doi.org/10.3760/cma.j.issn.0376-2491.2016.13.007

116. Yamada, Y., Ueda, M., Hibi, H., & Baba, S. (2006). A novel approach to periodontal tissue regeneration with mesenchymal stem cells and platelet-rich plasma using tissue engineering technology: A clinical case report. *International Journal of Periodontics & Restorative Dentistry*, *26*(4), 363-9. https://www.ncbi.nlm.nih.gov/pubmed/16939018

117. Yamamiya, K., Okuda, K., Kawase, T., Hata, K. I., Wolff, L. F., & Yoshie, H. (2008). Tissue-engineered cultured periosteum used with platelet-rich plasma and hydroxyapatite in treating human osseous defects. *Journal of Periodontology*, *79*(5), 811-818. https://doi.org/10.1902/jop.2008.070518

118. Zerr, P., Vollath, S., Palumbo-Zerr, K., Tomcik, M., Huang, J., Distler, A., ... & Distler, J. H. (2015). Vitamin D receptor regulates TGF-β signalling in systemic sclerosis. *Annals of the rheumatic diseases*, *74*(3), e20-e20. https://doi.org/10.1136/annrheumdis-2013-204378

119. Zhan, Y., Lu, R., Meng, H., Hou, J., Huang, W., Wang, X. E., & Hu, W. (2020). Platelets as inflammatory mediators in a murine model of periodontitis. *Journal of Clinical Periodontology*, *47*(5), 572-582. https://doi.org/10.1111/jcpe.13265

120. Zhang, D., Zhao, C., Liu, Z., Ding, Y., Li, W., Yang, H., ... & Li, Y. (2022). Relationship between periodontal status and dyslipidemia in patients with type 2 diabetic nephropathy and chronic periodontitis: A cross-sectional study. *Journal of Periodontal Research*, *57*(5), 969-976. https://doi.org/10.1111/jre.13033

121. Zhou, J., He, Z., Yang, Y., Deng, Y., Tringe, S. G., & Alvarez-Cohen, L. (2015). High-throughput metagenomic technologies for complex microbial community analysis: open and closed formats. *MBio*, *6*(1), 10-1128. https://doi.org/10.1128/mBio.02288-14

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