Articles

Impact of periodontitis on systemic anxiety and oral health quality of life

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Abstract

Aim: The aim of the present study was to measure dental anxiety levels and oral health-related qualities of life (OHRQoL) in patients with periodontitis compared to healthy controls and to analyze their association with various demographic, clinical and periodontal parameters.

Methods: Fifty-five patients with periodontitis and 56 healthy controls were enrolled. Collected data included demographics, smoking habits, numerical rating scale (NRS), Corah's Dental Anxiety Scale (DAS) and Oral Health Impact Profile-14 (OHIP-14), DMFT index (Decayed, Missing and Filled Teeth), Plaque Index (PI), probing depth (PD), bleeding on probing (BOP), and radiographic bone loss.

Results: Periodontitis patients exhibited statistically significant higher scores in the total DAS and in almost of single DAS domains. Compared to the control group, periodontitis patients exhibited worse OHIP-14 global as well as in all individual OHIP-14 domains scores. Among both periodontitis and control patients, the physical pain domain was where the highest impact was recorded, while the lowest impact was recorded in the functional limitation domain.

Conclusion: Periodontitis patients were positively associated with higher levels of dental anxiety and worse OHRQoL. Self-perception of dental anxiety and OHRQoL should be regarded as an integral element in routine diagnostic work-up process of periodontal diseases. This study showed that for a nationally representative sample of the southern Italian population population, periodontal disease was significantly associated with the domains of OHRQoL.

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1. Introduction

Although various oral conditions are not fatal, they have significant impacts on the quality of life of individuals in terms of physical, social and psychological problems (Kim et al., 2018; Vita et al., 2020). The influence of oral health on quality of life and psychophysical well-being highlights their close association. This connection is demonstrated neurologically by the fact that one third of the brain circuits are used for chewing and swallowing (Dahlström & Carlsson, 2010). The connection of these aspects determines that the imbalance of even just one element causes the imbalance of the entire system, with repercussions on a psycho-physical level. Some disorders such as anxiety, depression, panic attacks could originate precisely from the cranio-cervical-nuchal compressions induced by craniomandibular imbalance (Jerolimov, 2009; Li et al., 2013; Yap et al., 2003).

Recent research from the University of Harvard (Komaroff, 2017) also showed that stress and emotional factors can damage the teeth and gums due to high cortisol levels and the onset of bad habits that cause the subject to neglect the fundamentals of periodontal hygiene. The recovery of oral health would therefore produce benefits not only on a physical level but also in terms of mental well-being, through the resolution of psychic conditions such as anxiety and depression (Conversano & Di Giuseppe, 2021; Frisone et al., 2021; Merlo et al., 2020, 2021; Paunica, 2016; Rawlinson et al., 2021; Shah et al., 2020; Vicario et al., 2020).

Among oral conditions, Global Burden of Disease study shows that severe periodontal disease is one of the most common oral conditions globally (Offenbacher et al., 2016; Righolt et al., 2018). Epidemiological studies from developed countries have frequently estimated that over 90% of the general population has some form of periodontal disease (Righolt et al., 2018; Shimizu et al., 2015; Shinjo et al., 2019).

Periodontal diseases have a significant impact on oral health-related quality of life (OHRQoL) (Isiekwe et al., 2016). In addition, individuals with periodontal disease have a negative perception of their oral health status and poorer quality of life when compared to healthy individuals (Carra et al., 2020; Righolt et al., 2018), as well as similar systemic diseases (Al-Harthi, 2013; Castro et al., 2020; Catalano et al., 2018; Conversano et al., 2020; Di Giuseppe et al., 2021; Marchini et al., 2021; Martino et al., 2021; Merlo, 2019a, 2019b; Merlo et al., 2020; Meusel, 2015).

While the impact of periodontal disease on overall OHRQoL has been assessed, there is a deficiency of knowledge in one important area: the impact of periodontal disease on specific OHRQoL domains at a population level. These studies included a small number of participants that were recruited using convenience sampling in a clinical setting rather than population-level

sampling (El Sayed et al., 2019). Additionally, an analysis adjustment for confounding factors such as dental caries and missing teeth was not performed; therefore, the findings may have been confounded (Ferreira et al., 2017).

It is important to measure the burden of periodontal disease on OHRQoL domains for reasons such as the identification of specific areas of intervention. In addition, key motives for individuals to seek treatment, such as functional limitation, psychological or social factors, may be identified (Borges Tde et al., 2013). It is also important to study the impact of periodontal disease on OHRQoL domains in non-treatment seeking population samples, such as a nationally representative sample.

Moreover, dental anxiety is an unreasonable apprehension of dental procedures, objects, or the context of dental procedure, usually associated with a significant physiological as well as emotional arousal. Population-based epidemiological surveys demonstrated that 5–20% of adults have dental anxiety, ranging from a mild sensation of apprehension to prominent anxiety and dental and general phobia (Merlo, 2019a, 2019b). Dental anxiety may lead to a vicious circle as suggested by Berggren & Meynert (1984), in which dental anxiety leads to avoidance of dental treatment which causes a deterioration of dental health, in turn leading to feelings of lower general well-being, vitality, guilt and shame, depression, social isolation, contentment, and a lower quality of life (Berggren & Meynert, 1984).

This may be important from a public health perspective, providing a broader evaluation of need assessment and assist with the planning of public health policy and prioritization of healthcare services, especially where public healthcare resources are limited (Settineri et al., 2018, 2019). It may, therefore, be valuable to assess the impact of periodontal disease on OHRQoL domains from a nationally representative sample, especially with regard to the possible effects of other clinical and socio-economic variables.

1.1 The current study

The aim of this study was to investigate the association of periodontal disease with the dental anxiety and OHRQoL and its domains among a southern Italian population.

2. Materials and Methods

2.1 Partecipants

The sample consisted of 56 patients with periodontitis who referred to the School of Dentistry at the University of Catania, Italy. The control group consisted of 55 patients matched for age and gender, with no history of periodontal disease.

All subjects between the ages of 18 and 50, with at least 20 teeth present were included in the study. The exclusion criteria concerned the presence of psychiatric disorders, drug abuse, taking sedative,

anxiolytic or analgesic drugs up to a week earlier, pregnancy or breastfeeding, and an acute dental or periodontal condition.

2.2 Materials

The psychological assessment included the following tools: the NPRS, Corah's Dental Anxiety Scale (DAS) (Corah et al., 1978), Oral Health Impact Profile (OHIP-14) (Johannsen et al., 2005).

The NPRS (or NRS scale) is an 11-point one-dimensional scale that assesses the intensity of pain in adults. The scale consists of a horizontal line, with an interval ranging from 0 to 10, corresponding respectively to "no pain" and "worst pain imaginable" (Breivik et al., 2008). The patient indicates the intensity of their pain verbally or by drawing a circle on the number that best describes it. As a one-dimensional measure, NPRS is more suitable for assessing current pain or pain felt in the last 24 hours, making it less appropriate for fluctuating symptoms. The score on this pain scale can range from 0 to 10 points: the higher the score, the greater the intensity of pain felt by the patient.

Corah's Dental Anxiety Scale (DAS) (Corah et al., 1978) is a specific instrument to measure dental anxiety. The total score, which ranges from 4 to 20, indicates the level of dental anxiety. The scale contains four multiple choice items dealing with the patient's subjective reaction to the dental situation: anticipating visit to the dental clinic; waiting in the dentist's office for treatment; waiting in the dental chair for drilling of teeth; waiting in the dental chair for scaling the teeth. Five possible answers that are in an ascending order, from 1 to 5, are provided; each carries a possible maximum score of 5, with a total possible maximum score of 20 for the entire scale. The Italian version of the DAS (Facco et al., 2008) also showed a very good internal consistency with Cronbach alpha =.883. Since the DAS score fails to capture additional information about other specific phobic stimuli, we evaluated the fear-causing nature of other phobic stimuli. Patients were asked to indicate whether each question evokes a fear response (yes or no). The questionnaire included the following phobic stimuli such as fear of dental injection, fear of the sound of the dental drill, and fear of having a foreign object in the mouth. Due to the current classification of dental phobia as BII phobia, we have evaluated that weather situations related to dental BII (i.e. dental injections) cause just as much anxiety as non-BII related situations (i.e. fear of the sound of the dental drill and fear to have a foreign body in the mouth).

Oral Health Impact Profile (OHIP-14) (Johannsen et al., 2005) was used to assess the oral health- related quality of life (OHRQoL). The OHIP-14 includes 14 items and seven conceptual domains of OHRQoL, calculated by adding the scores of the two corresponding items including: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap. For each OHIP-14 question, subjects were asked how frequently they had experienced the impact in the last 6 months, with values ranging from 0 to 4. Global OHIP-14 scores range from 0 (no adverse impact during previous month) to 56 (all 14 impacts experienced very often during the previous month). The Cronbach's alpha of the italian version was 0.90 (Corridore et al., 2013).

2.3 Procedure

Periodontitis was diagnosed according to American Academy of Periodontology guidelines, after a first visit. Once the diagnosis was confirmed, the subjects were required to complete a protocol consisting of several questionnaires, completed during a face-to-face interview.

The protocol consisted of a questionnaire in which demographics and smoking habits were collected and a set of observation tools. All patients were provided with explanations on the diagnosis, including the risk of tooth loss and the treatment option.

Clinical examinations were conducted with an oral mirror and a UNC-15 periodontal probe (University of North Carolina, USA), Hu-Friedy Manufacturing Co., Chicago, IL, USA. Vertical bilateral bitewings were included for the molar and premolar area combined with parallel periapical radiographs of the maxillary and mandibular incisors. Prior to the start of the study, a training and calibration session was performed for the examiners to ensure mutual agreement and correct interpretation of the measurements of the indices used in the study. Plaque Index Oral hygiene was assessed by Loe and Silness's Plaque Index (PI) (Loe et al., 1976). PI was calculated as the percentage of teeth with visible plaque on any tooth surface. For each tooth, the variables were recorded at six points around the tooth. The following variables were recorded as probing depth (PD), bleeding on probing (BOP), and radiographic bone loss.

2.4 Statistical analysis

The appropriate sample size was calculated to determine that at least 110 participants were needed, in two groups with a ratio of 0.65, to provide 80% statistical power to identify a 4.40-point difference in the overall OHIP score -14, with alpha set to 0.05 and an estimated standard deviation (SD) of 0.8 for using OHIP-14 scores as the primary outcome.

Continuous variables are presented as means and standard deviations, and categorical variables are presented as frequencies and percentages. Differences between groups were examined with a Pearson chi square for categorical variables and an analysis of variance (ANOVA) for numeric variables. Significance tests between DAS and OHIP-14 scores and the independent variables included Chi-square test, ANOVA, and t test. Based on the univariate results significant parameters were selected for multivariate linear regression analysis. Data were tabulated and statistical analyses performed using SPSS software version 21.0 (Chicago, IL, USA). Two-tailed level of statistical significance (α) was set at ≤ 0.05.

3. Results

All participants completed the study. There were no significant differences between the study groups regarding age, sex, and smoking habits, as well as regarding the current and the maximal NRS scores (Table 1). Periodontal status and caries experience of the study population are presented in Table 1.

Table 1. Demographic and periodontal characteristics of the enrolled patients

Parameter	Healthy Controls n= 56	Periodontitis n= 55	P Value
Male Gender, no.	30	32	0.089
Age, mean ± (SD)	51.5 (3.2)	52.1 (3.6)	0.125
N° cigarettes/day, mean ± (SD)	4 (1.5)	6 (3.2)	0.554
Current NRS, mean ± (SD)	1.3 (1.2)	1.9 (1.1)	0.066
Maximal NRS, mean ± (SD)	4.9 (1.4)	4.7 (2.3)	0.058
Probing depth, mean ± (SD)	2.31 (1.1)	3.65 (1.4)	0.005
Bleeding score, mean ± (SD)	19.36 (7.5)	55.42 (6.8)	0.003
Plaque index, mean ± (SD)	24.32 (11.6)	44.59 (12.6)	0.002
Decay teeth, mean ± (SD)	0.78 (0.5)	0.83 (0.6)	0.058
Missing teeth, mean ± (SD)	0.31 (0.2)	1.35 (0.5)	0.015
Filled teeth, mean ± (SD)	6.21 (3.2)	5.51 (2.8)	0.036
DMFT, mean ± (SD)	7.85 (2.1)	6.51 (1.9)	0.025

The periodontitis group exhibited statistically significant higher mean radiographic bone loss, probing depth, PI, and bleeding score, compared to control group (Table 2).

Table 2. Mean Dental anxiety scale (DAS) total and sub-scores, DAS categories, self-assessment of dental anxiety and phobic stimuli as indicated by patients with periodontitis and controls

Parameter	Variable	Healthy Controls n= 56	Periodontitis n= 55	P Value
Self-assessed dental anxiety, no.	Yes	15	18	0.325
	No	41	37	
Dental injections, no.	Yes	18	20	0.066
	No	38	35	
Dental drill noise, no.	Yes	5	14	0.033
	No	51	41	
DAS categories, mean ± (SD)	Mild anxiety	40	30	0.001
	Moderate anxiety	5	14	
	High anxiety	6	5	
	Phobia	5	6	
DAS 1st question, mean ± (SD)		2.5 (0.9)	2.8 (1.1)	0.019
DAS 2nd question, mean ± (SD)		1.7 (0.6)	2.3 (0.9)	0.007
DAS 3rd question, mean ± (SD)		1.9 (1.1)	2.5 (0.8)	0.019
DAS 4th question, mean ± (SD)		1.7 (0.9)	2.6 (1.1)	0.001
Total DAS score, mean ± (SD)		8.2 (2.3)	9.8 (2.1)	0.001

Patients with periodontitis exhibited statistically significant more missing (M) teeth, less filled (F) teeth, and lower global DMFT and periodontal scores compared to controls. Table 2 shows the mean DAS total and sub-scores. Compared to controls, periodontitis patients exhibited statistically significant higher scores in the DAS total as well as sub-scores, except from DAS 1st question. Moreover, there were statistically significant differences in the distribution of DAS categories between the periodontitis group and the control group (Table 2). The periodontitis group exhibited significantly higher percentage of patients with high anxiety compared to the control group (Table 2). No significant differences were observed between the groups regarding fear of dental injections and self-assessed dental anxiety.

There was an association, in all enrolled patients among total DAS as well as sub-scores with demographic parameters, smoking habits, NRS scores, periodontal status parameters, and DMFT scores.

Multivariate linear regression analysis of parameters reaching significantly significant association with the mean DAS total score revealed that significant risk factors for higher DAS total scores are being a patient in the periodontitis group (p = 0.015, B = − 1.118, S.E. = 0.563, β = − 0.2155, 95% confidence interval (CI)-2.409–0.017), higher current NRS scores (p = 0.007, B = 0.355, S.E. = 0.128, β = 0.284, 95% confidence interval: 0.105–0.442), maximal NRS scores (p = 0.018, B = 0.233, S.E. = 0.104, β = 0.242, 95% CI: 0.044–0.366), and higher PI scores (p = 0.005, B = 0.028, S.E. = 0.006, β = 0.235, 95% CI: 0.005–0.108).

Moreover, compared to controls, periodontitis patients exhibited worse scores in the OHIP-14 global as well as in all individual OHIP-14 domains scores (Table 3).

Table 3. Mean oral health impact profile (OHIP-14) global and domain scores among periodontitis patients compared to controls

OHIP-14	Group	Value	P-value
OHIP-14 global score	Control	6.89 (2.1)	0.001
	Periodontitis	11.89 (2.5)	
Functional limitation	Control	0.19 (0.2)	0.026
	Periodontitis	0.24 (0.2)	
Physical pain	Control	1.10 (0.3)	0.031
	Periodontitis	1.34 (0.4)	
Psychological disability	Control	0.48 (0.1)	0.023
	Periodontitis	0.89 (0.2)	
Social disability	Control	0.32 (0.1)	0.014
	Periodontitis	0.97 (0.2)	
Handicap	Control	0.28 (0.1)	0.004
	Periodontitis	0.55 (0.2)	

Less schooling years, smoking habits, higher current and maximal NRS scores, worse periodontal scores in all indexes, and more missing teeth were positively associated with worse OHIP-14 global scores. Multivariate linear regression analysis of parameters reaching significant association with the mean OHIP global scores revealed that significant risk factors for higher OHIP global scores are being a patient in the periodontitis group (p = 0.006, B = − 4.044, S.E. = 1.478, β = − 0.254, 95% confidence interval − 6.442 to − 1.235), higher current NRS scores

(p = 0.045, B = 0.554, S.E. = 0.245, β = 0.199, 95% CI 0.031–1.254), maximal NRS scores (p = 0.033, B = 0.545, S.E. = 0.236, β = 0.184, 95% CI: 0.058–0. 766), and higher PI scores (p = 0.005, B = 0.055, S.E. = 0.024, β = 0.233, 95% CI: 0.025–0.121). Worse mean DAS total score was positively associated with the physical pain, psychological discomfort, and psychological disability OHIP-14 domain scores.

4. Discussion

The present study addressed many important confounding factors such as demographics, pain scores, caries experience, and various periodontal parameters.

Compared to controls, the periodontitis group exhibited worse periodontal indices, including radiographic bone loss, probing depth, PI, and bleeding scores. The association between periodontitis and PI seems controversial in the literature: although Baer (Baer, 1971) suggested that juvenile periodontitis is not associated with significant amounts of plaque and calculus; this was not confirmed in the present study, as well as in other studies, who also reported higher PI among periodontitis patients compared to controls (Iqbal et al., 2015).

Compared to controls, periodontitis patients exhibited statistically significant higher scores in the DAS total as well as most subscores and higher percentage of patients with high anxiety, and they were more likely to fear of the dental drill noise and of foreign objects in the mouth. Johannsen et al. (2005) reported in their study of markers of periodontal disease that higher levels of self-reported every day anxiety were associated with deep pockets in smokers, and with gingival inflammation in non-smoking subjects without deep pockets. Worse periodontal indices were associated with higher DAS scores in the present study. Moreover, there could be influences of anxiety and periodontitis in specific subgroups included in the present study: younger humans with limited knowledge about the disease. Indeed, age and education, but not sex, were associated with total DAS score.

Furthermore, periodontitis patients exhibited worse OHIP-14 global scores as well as worse scores in all individual OHIP-14 domains. In fact, periodontal disease consequences, such as redness, bleeding on brushing, gingival recession, persistent halitosis, pain, tooth mobility, and tooth loss may compromise mastication, speech, swallowing, and smile esthetics, and consequently negatively affect self-esteem, quality of life and self-perception. These results are consistent with a study by Choi et al. (2017) for which the quality of life during an orthodontic treatment deteriorates temporarily and is often associated with psychological and relational discomforts. However, after the treatment, the quality of life improves, positively affecting self-esteem and individual well- being. Other studies also suggested improvements in self-esteem,

body image and the ability to socialize following orthodontic interventions (Kiyak, 2008; Mahmood & Kareem, 2013; Rahbar, 2001). These correlations support the importance of the oral sphere in psycho-physical well-being.

Worse periodontal scores in all indexes were positively associated with higher OHIP-14 global scores and most domain scores (Borges Tde et al., 2013). This is in line with other studies demonstrating that patients with severe periodontitis had significantly higher OHIP-14 values, and worse functional limitation, physical pain, physical incapacity, and psychological incapacity domain scores, than did those with mild/moderate periodontitis (Ehrenthal et al., 2016). The association to psychological domains was also demonstrated by others, for example, fewer teeth at the beginning of the treatment were related to higher scores of depressive symptoms, even when controlling for several covariates. Patients with higher attachment avoidance attended periodontal treatment later when diagnosed with chronic periodontitis and earlier with periodontitis (Graetz et al., 2013).

OHRQoL assessments may play an important role in clinical practice in terms of identifying needs, selecting therapies and monitoring patients' progress. A greater understanding of the consequences of periodontal disease and the effects of therapy are important on many fronts: in understanding and embracing patients' perceptions of the impact of their oral health on their lives, in planning periodontal care that addresses patients' needs and key concerns, in evaluating outcomes from periodontal treatment from the patients' perspective, and in drawing attention to the importance of periodontal care in society.

Qualitative research, which enables interpretation of patients' subjective experiences, can contribute to revealing overlooked or tricky details of conditions analyzed by quantitative studies by providing analyses of content from individual participant interviews. The term 'subjective' here indicates that the health condition is significant from patients' perspective and that interpretation of their subjective experiences could be applied as an essential means of assessing and explaining the consequences of the disease. This qualitative study endeavored to focus on the stories of periodontal patients and thoroughly observe their experiences of life with periodontal disease. The results from this study also demonstrated that not only the treatment of periodontal disease should be highlighted, but also to improve the OHRQoL for those with periodontal disease.

In conclusion, compared to controls, periodontitis patients were positively associated with higher levels of dental anxiety and worse OHRQoL. Self-perception of dental anxiety and OHRQoL should be an integral part of the routine diagnostic work-up procedure. It is essential,

from a public health perspective to establish communication between health professionals from the dental and behavioral fields, in order to implement a multidisciplinary team approach to treat dental anxiety, involving behavioral and psychological interventions. Patients must be aware of the importance of dental maintenance or have the motivation to visit dentists to receive regular dental care. Similar to the participants in this study, patients who are consistently involved in dental care feel proud of and recognize the benefits of maintaining high levels of dental hygiene. In other words, a desire to maintain a healthy oral cavity and enjoy the process would become the driving force for long-term planning for regular visits to the dentists. Furthermore, self-care based on professional brushing training has been shown to be even more important than maintenance several times a year. Customized dental health education programs focused on individual characteristics would be more appropriate for behavioral changes than the standard ones.

Conflict of Interest Statement

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

References

1. Al-Harthi, L. S., Cullinan, M. P., Leichter, J. W., & Thomson, W. M. (2013). The impact of periodontitis on oral health-related quality of life: A review of the evidence from observational studies. *Australian dental journal*, *58*(3), 274-277. https://doi.org/10.1111/adj.12076

2. Baer, P. N. (1971). The case for periodontosis as a clinical entity. *J Periodontol*, *42*(8), 516-520. https://doi.org/10.1902/jop.1971.42.8.516

3. Berggren, U., & Meynert, G. (1984). Dental fear and avoidance: causes, symptoms, and consequences. *J Am Dent Assoc*, *109*(2), 247-251. https://doi.org/10.14219/jada.archive. 1984.0328

4. Borges Tde, F., Regalo, S. C., Taba, M., Jr., Siessere, S., Mestriner, W., Jr., & Semprini, M. (2013). Changes in masticatory performance and quality of life in individuals with chronic periodontitis. *J Periodontol*, *84*(3), 325-331. https://doi.org/10.1902/jop.2012.120069

5. Breivik, E. K., Bjornsson, G. A., & Skovlund, E. (2000). A comparison of pain rating scales by sampling from clinical trial data. *Clin J Pain*, *16*(1), 22-28. https://doi.org/10.1097/00002508-200003000-00005

6. Breivik, H., Borchgrevink, P. C., Allen, S. M., Rosseland, L. A., Romundstad, L., Breivik Hals, E. K., ... & Stubhaug, A. (2008). Assessment of pain. *BJA: British Journal of Anaesthesia*, *101*(1), 17-24.

7. Carra, M. C., Detzen, L., Kitzmann, J., Woelber, J. P., Ramseier, C. A., & Bouchard, P. (2020). Promoting behavioural changes to improve oral hygiene in patients with periodontal diseases: A systematic review. *Journal of clinical periodontology*, *47*, 72-89. https://doi.org/10.1111/jcpe.13234

8. Castro, M. M., Ferreira, R. D. O., Fagundes, N. C., Almeida, A. P., Maia, L. C., & Lima, R. R. (2020). Association between psychological stress and periodontitis: a systematic review. *European journal of dentistry*, *14*(01), 171-179. https://doi.org/10.1055/s-0039-1693507

9. Catalano, A., Chilà, D., Bellone, F., Nicocia, G., Martino, G., Loddo, I., ... & Loddo, S. (2018). Incidence of hypocalcemia and hypercalcemia in hospitalized patients: Is it changing?. *Journal of clinical & translational endocrinology*, *13*, 9-13. https://doi.org/10.1016/j.jcte.2018.05.004

10. Choi, S. H., Cha, J. Y., Lee, K. J., Yu, H. S., & Hwang, C. J. (2017). Changes in psychological health, subjective food intake ability and oral health-related quality of life during orthodontic treatment. *Journal of Oral Rehabilitation, 44*(11), 860-869.

11. Conversano, C., & Di Giuseppe, M. (2021). Psychological factors as determinants of chronic conditions: clinical and psychodynamic advance. *Frontiers in Psychology*, *12*, 86. https://doi.org/10.3389/fpsyg.2021.635708

12. Conversano, C., Di Giuseppe, M., Miccoli, M., Ciacchini, R., Di Silvestre, A., Lo Sterzo, R., ... & Orrù, G. (2020). Retrospective Analyses of Psychological Distress and Defense Style Among Cancer Patients. *Clinical Neuropsychiatry*, *17*(4). 10.36131/cnfioritieditore20200403

13. Corah, N. L., Gale, E. N., & Illig, S. J. (1978). Assessment of a dental anxiety scale. *J Am Dent Assoc*, *97*(5), 816-819. https://doi.org/10.14219/jada.archive.1978.0394

14. Corridore, D., Campus, G., Guerra, F., Ripari, F., Sale, S., & Ottolenghi, L. (2013). Validation of the Italian version of the oral health impact profile-14 (IOHIP-14). *Annali di stomatologia*, *4*(3-4), 239.

15. Dahlström, L., & Carlsson, G. E. (2010). Temporomandibular disorders and oral health-related quality of life. A systematic review. *Acta Odontologica Scandinavica*, *68*(2), 80-85. https://doi.org/10.3109/00016350903431118

16. Di Giuseppe, M., Nepa, G., Prout, T. A., Albertini, F., Marcelli, S., Orrù, G., & Conversano, C. (2021). Stress, Burnout, and Resilience among Healthcare Workers during the COVID-19 Emergency: The Role of Defense Mechanisms. *International journal of environmental research and public health, 18*(10), 5258. https://doi.org/10.3390/ijerph18105258

17. Durham, J., Fraser, H. M., McCracken, G. I., Stone, K. M., John, M. T., & Preshaw, P. M. (2013). Impact of periodontitis on oral health-related quality of life. *Journal of dentistry*, *41*(4), 370-376. https://doi.org/10.1016/j.jdent.2013.01.008

18. Ehrenthal, J. C., Graetz, C., Plaumann, A., Dorfer, C. E., & Herzog, W. (2016). Number of teeth predict depressive symptoms in a longitudinal study on patients with periodontal disease. *J Psychosom Res*, *89*, 16-19. https://doi.org/10.1016/j.jpsychores.2016.08.002

19. El Sayed, N., Baeumer, A., El Sayed, S., Wieland, L., Weber, D., Eickholz, P., & Pretzl, B. (2019). Twenty years later: Oral health-related quality of life and standard of treatment in patients with chronic periodontitis. *J Periodontol*, *90*(4), 323-330. https://doi.org/10.1002/JPER. 18-0417

20. Facco, E., Zanette, G., & Manani, G. (2008). Italian version of Corah's Dental Anxiety Scale: normative data in patients undergoing oral surgery and relationship with the ASA physical status classification. *Anesthesia progress*, *55*(4), 109-115.

21. Ferreira, M. C., Dias-Pereira, A. C., Branco-de-Almeida, L. S., Martins, C. C., & Paiva, S. M. (2017). Impact of periodontal disease on quality of life: a systematic review. *J Periodontal Res*, *52*(4), 651-665. https://doi.org/10.1111/jre.12436

22. 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). doi.org/10.36131/cnfioritieditore20210203

23. Graetz, C., Ehrenthal, J. C., Senf, D., Semar, K., Herzog, W., & Dorfer, C. E. (2013). Influence of psychological attachment patterns on periodontal disease - a pilot study with 310 compliant patients. *J Clin Periodontol*, *40*(12), 1087-1094. https://doi.org/10.1111/jcpe.12159

24. Iqbal, P. S., Khan, S. N., Haris, M., Narayanan, M., Laju, S., & Kumar, S. S. (2015). Assessment of Systemic Inflammatory Markers in Patients with Aggressive Periodontitis. *J Int Oral Health*, *7*(Suppl 2), 48-51. https://www.ncbi.nlm.nih.gov/pubmed/26668481

25. Isiekwe, G. I., Sofola, O. O., Onigbogi, O. O., Utomi, I. L., Sanu, O. O., & daCosta, O. O. (2016). Dental esthetics and oral health-related quality of life in young adults. *Am J Orthod Dentofacial Orthop*, *150*(4), 627-636. https://doi.org/10.1016/j.ajodo.2016.03.025

26. Jerolimov, V. (2009). Temporomandibular disorders and orofacial pain. *Rad Hrvatske akademije znanosti i umjetnosti. Medicinske znanosti*, (504= 33), 53-77.

27. Johannsen, A., Asberg, M., Soder, P. O., & Soder, B. (2005). Anxiety, gingival inflammation and periodontal disease in non-smokers and smokers - an epidemiological study. *J Clin Periodontol*, *32*(5), 488-491. https://doi.org/10.1111/j.1600-051X.2005.00704.x

28. 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. *J Periodontal Res*, *53*(3), 362-368. https://doi.org/10.1111/jre.12521

29. Kiyak, H. A. (2008). Does orthodontic treatment affect patients' quality of life?. J*ournal of dental education,* 72(8), 886-894.

30. Komaroff, A. L. (2017). The Gut-Brain Connection. Harvard Health Letter, Retrieved from: www.health.harvard.edu/diseasesand-conditions/the-gut-brain-connection.

31. Li, Q., Zhang, M., Chen, Y. J., Zhou, Q., Wang, Y. J., & Liu, J. (2013). Psychological stress alters microstructure of the mandibular condyle in rats. *Physiology & behavior,* 110, 129-139

32. Loe, H., Schiott, C. R., Karring, G., & Karring, T. (1976). Two years oral use of chlorhexidine in man. I. General design and clinical effects. *J Periodontal Res*, *11*(3), 135-144. https://doi.org/10.1111/j.1600-0765.1976.tb00061.x

33. Mahmood, T. M. A., & Kareem, F. A. (2013). Psychological impact of dental aesthetics for Kurdish young adults seeking orthodontic treatment. *Scientific Journal Published by the College of Dentistry–University of Baghdad, 146*.

34. Marchini, F., Langher, V., Napoli, A., Balonan, J. T., Fedele, F., Martino, G., ... & Caputo, A. (2021). Unconscious loss processing in diabetes: associations with medication adherence and quality of care. *Psychoanalytic Psychotherapy*, 1-19. https://doi.org/10.1080/02668734.2021.1922492

35. 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*, 1295. https://doi.org/10.3389/fpsyg.2021.667237

36. Meusel, D. R., Ramacciato, J. C., Motta, R. H., Júnior, R. B. B., & Flório, F. M. (2015). Impact of the severity of chronic periodontal disease on quality of life. *Journal of oral science*, *57*(2), 87-94. https://doi.org/10.2334/josnusd.57.87

37. Merlo, E. M. (2019a). Adolescent phobia as a "mask object". *Mediterranean Journal of Clinical Psychology*, *7*(1). https://doi.org/10.6092/2282-1619/2019.7.2241

38. Merlo, E. M. (2019b). Opinion Article: The role of psychological features in chronic diseases, advancements and perspectives. *Mediterranean Journal of Clinical Psychology*, *7*(3). https://doi.org/10.6092/2282-1619/2019.7.2341

39. Merlo, E. M., Sicari, F., Frisone, F., Alibrandi, A., & Settineri, S. (2020). Personality types and dreaming in future health professionals: Effect of age and gender. *International Journal of Dream Research*, 160-172. https://doi.org/10.1080/000163501750266710

40. Merlo, E. M., Stoian, A. P., Motofei, I. G., & Settineri, S. (2021). The Role of Suppression and the Maintenance of Euthymia in Clinical Settings. *Frontiers in Psychology*, *12*, 1534. https://doi.org/10.3389/fpsyg.2021.677811

41. Offenbacher, S., Divaris, K., Barros, S. P., Moss, K. L., Marchesan, J. T., Morelli, T., Zhang, S., Kim, S., Sun, L., Beck, J. D., Laudes, M., Munz, M., Schaefer, A. S., & North, K. E. (2016). Genome-wide association study of biologically informed periodontal complex traits offers novel insights into the genetic basis of periodontal disease. *Hum Mol Genet*, *25*(10), 2113-2129. https://doi.org/10.1093/hmg/ddw069

42. Ozhayat, E. B. (2013). Influence of self-esteem and negative affectivity on oral health-related quality of life in patients with partial tooth loss. *Community Dent Oral Epidemiol*, *41*(5), 466-472. https://doi.org/10.1111/cdoe.12032

43. Păunică, I. (2016). Diagnostic and treatment difficulties in Crohn's disease. *Journal of Clinical and Investigative Surgery*, *1*(2), 47-53. 10.25083/2559.5555.12.4753

44. Rahbar, F. (2001). Changes in self-esteem and self-concept as a result of orthodontic treatment. University of Southern California.

45. Rawlinson, A., Vettore, M. V., Baker, S. R., & Robinson, P. G. (2021). Periodontal treatment, psychological factors and oral health-related quality of life. *Journal of Clinical Periodontology*, *48*(2), 226-236. https://doi.org/10.1111/jcpe.13405

46. Righolt, A. J., Jevdjevic, M., Marcenes, W., & Listl, S. (2018). Global-, Regional-, and Country- Level Economic Impacts of Dental Diseases in 2015. *J Dent Res*, *97*(5), 501-507. https://doi.org/10.1177/0022034517750572

47. Shah, H., Shah, R., Sanghani, H., & Lakhani, N. (2020). Health related quality of life (HRQoL) and its associated surgical factors in diabetes foot ulcer patients. *Journal of Clinical and investigative Surgery, 5*(2). https://doi.org/10.25083/2559-5555

48. Settineri, S., Frisone, F., Alibrandi, A., Pino, G., Lupo, N. J., & Merlo, E. M. (2018). Psychological Types and Learning Styles in Medical Education. *Mediterranean Journal of Clinical Psychology*, *6*(3). https://doi.org/10.6092/2282-1619/2018.6.2005

49. Settineri, S., Frisone, F., Alibrandi, A., & Merlo, E. M. (2019). Emotional Suppression and Oneiric Expression in Psychosomatic Disorders: Early Manifestations in Emerging Adulthood and Young Patients. *Frontiers in Psychology*, *10*. https://doi.org/ARTN 189710.3389/fpsyg. 2019.01897

50. Shimizu, S., Momozawa, Y., Takahashi, A., Nagasawa, T., Ashikawa, K., Terada, Y., Izumi, Y., Kobayashi, H., Tsuji, M., Kubo, M., & Furuichi, Y. (2015). A genome-wide association study of periodontitis in a Japanese population. *J Dent Res*, *94*(4), 555-561. https://doi.org/10.1177/0022034515570315

51. Shinjo, T., Ishikado, A., Hasturk, H., Pober, D. M., Paniagua, S. M., Shah, H., Wu, I. H., Tinsley, L. J., Matsumoto, M., Keenan, H. A., Van Dyke, T. E., Genco, R. J., & King, G. L. (2019). Characterization of periodontitis in people with type 1 diabetes of 50 years or longer duration. *J Periodontol*, *90*(6), 565-575.

52. Vicario, C. M., Nitsche, M. A., Salehinejad, M. A., Avanzino, L., & Martino, G. (2020). Time processing, interoception, and insula activation: a mini-review on clinical disorders. *Frontiers in Psychology*, *11*, 1893. https://doi.org/10.3389/fpsyg.2020.01893

53. 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