



ASSOCIATION BETWEEN PERIODONTAL DISEASE AND DEPRESSION

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Abstract

Background & Objectives: Periodontitis is a chronic, multifactorial, polymicrobial disease causing inflammation in the supporting structures of the teeth. Depression is associated with a chronic, low-grade inflammatory response, activation of cell-mediated immunity, and compensatory anti-inflammatory reflex system, as well as an augmentation of oxidative and nitrosative stress, which contribute to neuroprogression in the disorder. The inflamed periodontal pocket can, be a significant source of inflammatory and pathogen-derived mediators, which can cause neuro inflammation leading to depression. The aim of the study is to know if there is an association between Periodontal disease and depression.

Methods: The study group consisted of 500 patients visiting the general outpatient department (OPD) of Malabar dental college. Periodontal parameters like Plaque index, Gingival index, maximum probing depth, and maximum clinical attachment loss were measured. Based on the clinical findings they were divided into three groups, namely healthy, gingivitis, and periodontitis group. To those patients Beck's depression inventory was given. To correlate the association between different forms of periodontal disease and depression was evaluated.

Results & Discussion: All the participants completed the study. The results showed that depressive scores are increased in periodontitis group than in the healthy and gingivitis group (p value <0.001) and was found to be highly statistically significant

Key words: periodontitis, gingivitis, depression.

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INTRODUCTION

Periodontal disease refers to the inflammatory processes that occur in the tissues surrounding the teeth in response to bacterial accumulations, or dental plaque, on the teeth. The bacterial accumulations cause an inflammatory response from the body. The chronic and progressive bacterial infection of the gums leads to alveolar bone destruction and loss of tissue attachment to the teeth. Periodontal disease has many states or stages, ranging from easily treatable gingivitis to irreversible severe periodontitis. Periodontal disease is increased by several risk factors: cigarette smoking; systemic diseases; medications such as steroids, anti-epilepsy drugs and cancer

therapy drugs; ill-fitting bridges; crooked teeth and loose fillings; pregnancy; and oral contraceptive use. In addition to these variables, any medical condition that triggers host antibacterial defense mechanisms, such as human immunodeficiency virus (HIV) infection, diabetes, and neutrophil disorders, will likely promote periodontal disease.¹

Within the past 10 years, many studies have been published indicating a positive or negative relationship between periodontal disease and various systemic disorders and diseases. Depending on the outcome of the studies, a positive correlation reflects a strong case for the relationship as opposed to a negative or no

correlation. Significant associations between periodontal disease and cardiovascular disease, diabetes mellitus, preterm low birth weight, and osteoporosis have been discovered, bridging the once-wide gap between medicine and dentistry. Researchers have hypothesized the etiologic role of periodontitis in the pathogenesis of these systemic illnesses. Therefore, patients diagnosed with periodontal disease may be at higher risk due to a compromised immune system. Infectious and opportunistic microbes responsible for periodontal infection may thus bring a burden onto the rest of the body. Furthermore, these microbes can release products that elicit an inflammatory response. Periodontal lesions are recognized as continually renewing reservoirs for the systemic spread of bacterial antigens, Gram-negative bacteria, cytokines, and other proinflammatory mediators.²

Depression, a disabling psychiatric disorder, manifests with depressed mood, vegetative symptoms, and cognitive impairment, and could impair the personal life quality and physical function.³

Periodontal disease and depression are sharing common risk factors within the context of the wider socio-environmental milieu and adopting a collaborative approach (e.g., the common risk factor approach) is more rational than one that is disease specific. The prevalence and severity of both periodontitis and depression, are associated with several social determinants such as older age, low socioeconomic status, low educational level, and ethnicity.⁴

Both psychosocial and biological mechanisms are supposed to link a chronic inflammatory disease like periodontitis and development of major depression⁴

To the best of our knowledge no studies till date have assessed the relationship between different forms of periodontal disease and onset of depression in India. So we wanted to test the strength of association between periodontal disease and depression. We hypothesized that periodontal disease can lead to depression

AIMS AND OBJECTIVES

AIM: To assess relationship between periodontitis and depression in patients attending the general out patient department (OPD) of Malabar dental college.

OBJECTIVES

1. To assess the level of depression by using Beck's depression inventory scoring scale in healthy, gingivitis and periodontitis patients.

2. To correlate the association between different forms of periodontal disease and depression

METHODOLOGY

This cross-sectional experimental study was conducted in the General out patient department (OPD), Malabar Dental College & Research Centre, Edappal and the study subjects were selected based on the following inclusion and exclusion criteria.

INCLUSION CRITERIA

- Both male and female patients above 25 years
- Subjects with clinically healthy gingiva should have tissue that demonstrates an absence, or very low level, of clinical indicators of inflammation such as BoP. (Lang & Bartold 2018)
- Subjects diagnosed with gingivitis should include erythema, edema, bleeding, tenderness, and enlargement. (Murakami et al 2018)
- Subjects diagnosed with periodontitis should have
 - a) interdental clinical attachment loss (CAL) detectable at ≥ 2 non adjacent teeth.
 - b) buccal or oral CAL ≥ 3 mm with pocketing > 3 mm is detectable at ≥ 2 teeth. (Tonetti et al 2018)

EXCLUSION CRITERIA

- Patients on antibiotic treatment and have undergone periodontal treatment 6 months before examination.
- Pregnancy or lactation
- Subjects on antidepressants, tranquilizers or sedatives.
- Diabetic patients
- Smokers

SAMPLE SIZE DETERMINATION

$$N = \frac{Z_{\alpha/2}^2 \times p \times (1-p) \times D}{E^2}$$

$Z_{\alpha/2}$ = Normal deviate for two-tailed hypothesis = 1.96

P = proportion or prevalence (from previous studies) = 64%

D = Design effect = 2

E = Margin of error = 10%

N (sample size) = 500

CLINICAL EVALUATION AND TREATMENT PROCEDURE

The nature and purpose of the study was explained to the patients and an informed consent was obtained from each participant recruited in to this study. Basic demographic details and clinical

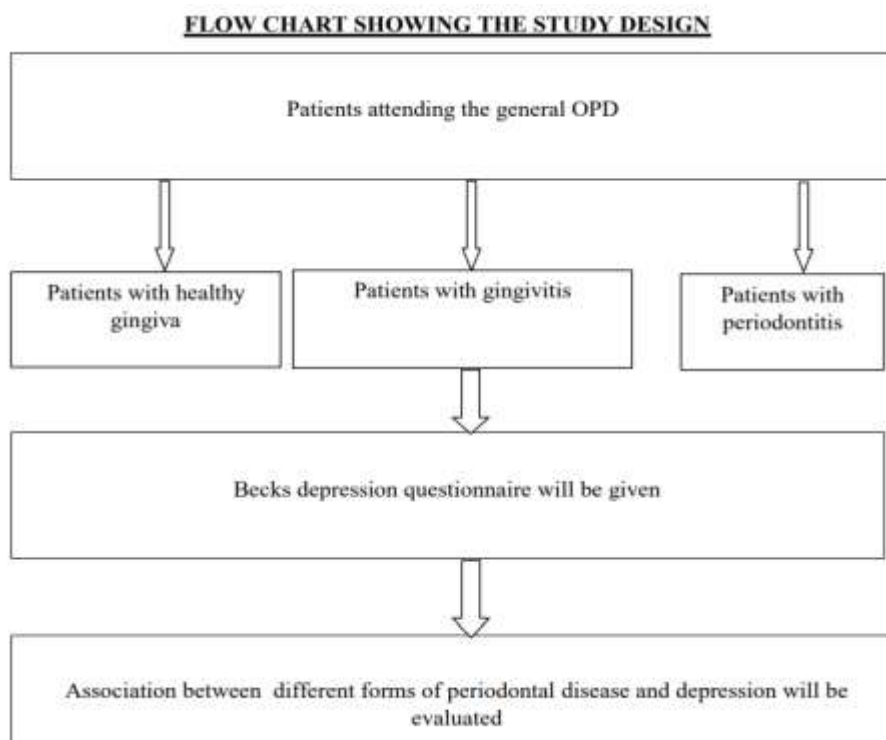
parameters like number of teeth present and periodontal parameters like

- I. Plaque index- PI (Silness J and Loe H 1964)
- II. Gingival index - GI (Loe H and Silness J 1963)
- III. Probing Pocket Depth (PD)
- IV. Clinical attachment level (CAL) will be recorded.

The same patients will be given the Becks depression inventory scoring scale ,and the correlation between different forms of periodontal disease and depression will be evaluated.

The patients who visited the general OPD of Malabar dental college were examined . PI and GI index noted along with maximum probing depth and maximum clinical attachment level were also measured . These patients were given Becks depression inventory which is in a multiple choice format. Adding up the scores for all of the twenty-one questions, the single total score is produced indicating the intensity of the depression. Associations between different forms of periodontal disease and depression will be evaluated.

CLINICAL TREATMENT PROCEDURE



Statistical methods

All statistical procedures were performed using Statistical Package for Social Sciences (SPSS)20.0. Calculations for power (80%) of study was performed before commencement of the study. All quantitative variables expressed in mean and standard Deviation. Qualitative variables be expressed in percentages. Shapiro-Wilk test was used for testing the normality assumption of the data. Chi square and independent student t test will be used for association between two independent variables. One way ANOVA followed by LSD post hoc test was used to find association between different levels of association and outcome variables. Pearson correlation will be used for correlating

between periodontitis and depression scores. Probability value($p < 0.05$) was considered statistically significant

RESULTS

A total number of 500 subjects, comprising of 266 males and 234 females participated through out in this study.

Presence of plaque was measured in all the three groups. The mean value in healthy group was 0.08, in gingivitis group it was 0.45, and in periodontitis group it was 0.59. A significant increase in the plaque scores was seen between the groups, ($p < .001$), which was found to be highly statistically significant. (table 1)

Table 1
Association between different forms of periodontal disease and PI

PI	Mean	SD	F value	P value
HEALTHY	0.08 ^{ab}	0.04	75.19	<0.001**
GINGIVITIS	0.45 ^{bc}	0.34		
PERIODONTITIS	0.59 ^{bc}	0.39		

Gingival index

Presence of bleeding was measured in all the three groups ,the mean value in health group was 0.0, in gingivitis group was 0.56, and in

periodontitis group was 0.95. A significant increase in bleeding scores was seen between the groups,(p<.001) which was found to be highly statistically significant.(table 2)

Table 2
Association between different forms of periodontal disease and GI

GI	Mean	SD	F value	P value
HEALTHY	0.00	0.0	62.83	<0.001**
GINGIVITIS	0.56	0.42		
PERIODONTITIS	0.95	0.63		

Probing depth

The mean probing depth was measured in all the three groups.In healthy and in gingivitis group it was 3mm,and in periodontitis group it was 5.54mm.

A significant increase in probing depth was seen between the groups ,(p<.001) which was found to be highly statistically significant.(table 3)

Table 3
Association between different forms of periodontal disease and MAX PD

MAX PD	Mean	SD	F value	P value
HEALTHY	3.00 ^a	.00	64.76	<0.001**
GINGIVITIS	3.00 ^b	.00		
PERIODONTITIS	5.54 ^{ab}	1.27		

Clinical attachment loss

The mean clinical attachment loss was measured in all the three groups. In healthy and in gingivitis group it was 0 mm,and in periodontitis group it

was 4.19mm . A significant increase was seen between the groups ,(p<.001) which was found to be highly statistically significant. (table 4)

Table 4
Association between different forms of periodontal disease and MAX CAL

MAX CAL	Mean	SD	F value	P value
HEALTHY	0.00 ^a	0.00	93.98	<0.001**
GINGIVITIS	0.00 ^b	0.00		
PERIODONTITIS	4.19 ^{ab}	1.58		

One way ANOVA followed by LSD post hoc test ;*p value <0.05 is statistically significant;** <0.001 is statistically highly significant

Depression

The mean depressive score obtained in the healthy group was 2.83, in gingivitis group was 5.44 and in periodontitis group was 11.5 There was an

increase in depressive scores from healthy , gingivitis and in periodontitis group.(p<.001) which was found to be highly statistically significant.(table 5)

Table 5

Association between different forms of periodontal disease and depression score

	Mean	SD	F value	P value
HEALTHY	2.83	4.11	48.16	<0.001**
GINGIVITIS	5.44	5.94		
PERIODONTITIS	11.5	8.78		

One way ANOVA followed by LSD post hoc test ;*p value <0.05 is statistically significant;** <0.001 is statistically highly significant

When depression scores was compared between periodontitis and non periodontitis group, the

depression scores in non periodontitis group was 4.51 and in periodontitis group was 11.5 (table6)

Table 6

Association of depression between periodontitis and non periodontitis group

	Mean	SD	F value	P value
NO PERIODONTITIS	4.51	5.50	10.69	<0.001**
PERIODONTITIS	11.5	8.78		

Independent t test ;*p value <0.05 is statistically significant;** <0.001 is statistically highly significant

In the healthy group, we can see that majority of the individuals 92.6% belong to the score between 0 to 10, while 6.3% of individuals belong to the score 11-16, and just 1.1% belonged to the score ranging from 21-30.

In gingivitis group also we can see that majority of individuals 83.7% belong to the score level between 0 to 10, while 9.3% of individuals belong to the score 11-16, 4.7% and 2.3% of the individuals belonged to the scores between 17-20 and 21-30 respectively.

In both the groups it is clearly seen that, no one has gone above the score of 31, which is indicative of severe depression

While when we consider the periodontitis group, only half the population, that is 50.2% belong to the score between 0 to 10, while the rest belong to the scores above 11, which is considered to have depressive symptoms. In that 31.3% of individuals belong to the score between 11-16 18.5% of the individuals also fall in the scores above 17, which is very high compared to healthy and gingivitis group.

We can also see that depressive scores are increased in periodontitis group than in the healthy and gingivitis group ($p < .001$) which was found to be highly statistically significant. (table 7)

Table 7

Association of periodontitis with different scores of depression

SCORE		GINGIVITIS	HEALTHY	PERIODONTITIS
1-10	N	144	88	117
	%	83.7%	92.6%	50.2%
11-16	N	16	6	73
	%	9.3%	6.3%	31.3%
17-20	N	8	0	13
	%	4.7%	0.0%	5.6%
21-30	N	4	1	23
	%	2.3%	1.1%	9.9%
31-40	N	0	0	6
	%	0.0%	0.0%	2.6%
≥40	N	0	0	1
	%	0.0%	0.0%	0.4%
TOTAL	N	172	95	233
	%	100.0%	100.0%	100.0%

Chi square value is 70.16; p value <0.001**

From table 8, we can see that there is a positive correlation between periodontitis and depression.

Table 8

Correlation between periodontitis and depression score

Pearson Correlations			
		Depression Score	Periodontitis
Depression Score	Pearson Correlation	1	0.471**
	Sig. (2-tailed)		.000
	N	500	500
Periodontitis	Pearson Correlation	0.471**	1
	Sig. (2-tailed)	.000	
	N	500	500

** . Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

Periodontitis is an infectious disease and the risk factors affecting the host can modify its onset and progression⁵

A robust, and presumably causal, association exists between stressful life events and major depressive episodes. The neurobiology underlying stress and depression is thought to result from molecular and cellular abnormalities that interact with genetic and environmental factors⁶

Several pathophysiologic mechanisms may explain the association of chronic stress and depression with systemic diseases^{7,8,9,10}. Studies demonstrated that stress and depression are associated with atrophy and loss of function of limbic brain regions that control mood and depression, including the prefrontal cortex and the hippocampus.^{11,12,13}

Moreover, animal studies suggested that chronic stress induces vascular inflammation through elevations in circulating proinflammatory cytokines⁶.

Periodontitis per se is a low-grade chronic inflammation, but it causes or hastens the other chronic systemic inflammatory diseases, including atherosclerosis, cardiovascular diseases, diabetes, and rheumatoid arthritis¹⁴.

Various clinical studies also imply a causal relationship between periodontitis and major depression^{15,16}. Distress experienced by patients with periodontitis significantly correlated with the progression of periodontitis¹⁷.

Periodontitis can be classified as gingivitis, when the inflammation is localized in the gingival tissues, or it may assume a more severe destructive form, with the inflammatory process reaching deeper connective and bone tissue, causing bone and attachment loss, that may ultimately lead to tooth loss.¹⁷

Chronic stress and depression can mediate risk and progression of periodontitis through change in health-related behaviors such as oral hygiene, smoking, and diet⁶. Also, as periodontitis got chronic, the occurrence of depression increased¹⁷. Hence, the present study is performed to determine whether there is an association between periodontal disease and depression.

Numerous screening tools have been specifically designed to identify depressive symptoms or possible presence of depression and self-reporting measures have been advocated as a simple, expeditious and inexpensive method to ameliorate detection. Studies have demonstrated the reliability of utilizing self-reporting depression/depressive symptoms for research purpose, hence the Beck's depression inventory, which is one of the most prevalent

depression/depressive symptoms screening measures was used in the present study¹⁸

In this cross-sectional study, the relationship between psychological and periodontal variables were investigated in a consecutive sample of 500 subjects aged 25-66 years. This study design is often used to investigate the association between risk factors and disease prevalence in situations where less is known about the form or type of association¹⁹.

Studies with similar design were conducted by other authors, using however, different target populations, threshold scores and indices to positively identify the disease^{20,21,22}. Studies conducted by other authors^{23,24} also applied different self-report scales as instruments to measure psychological variables (Minnesota Multiphasic Personality Inventory, Modifiers and Perceived Stress Scale, Brief Symptom Inventory) as well as different psychological variables (stress, anxiety, depression). These differences may limit the comparisons between the investigations.²⁵

Lack of microbial control may lead to an imbalance between the microbiota and the host due to a markedly increased microbial mass and/or increased virulence of the microorganisms present. Such alterations in the host-parasite equilibrium may result in transient episodes of tissue destruction and in the long term, to cumulative damage to the periodontal tissues.²⁶ Researches on the epidemiology of periodontal disease has demonstrated a close correlation between periodontal disease and oral debris^{27,28}. There is a substantial amount of evidence to the effect that, bacterial plaque and calculus are the most common direct causes of periodontal disease²⁹. In the present study a statistically increased plaque value is seen in periodontitis group compared to the healthy and gingivitis group, and this finding corroborates well with previous observations by Lertpimonchai et al where in their systematic review and meta-analysis it was seen that fair to poor oral hygiene increases the risk of periodontitis by two- to five-fold³⁰. Previous studies by Norderyd et al in 1999 states that percentage of supra gingival plaque, gingival inflammation, and deepened periodontal pockets (>4 mm) at baseline were related to severe periodontal disease. Associations with severe periodontal disease experience have previously been found for age, smoking, and supra gingival plaque in a cross-sectional sample from Jonko ping County³¹.

There is also a significant increase in gingival index scores in the periodontitis group which

clearly shows that the validity of gingival bleeding as a clinical tool can be taken not only for the diagnosis of periodontal disease, but also in the detection of its activity and progression which could be established by correlating the GI scores, which was supported by the study done by, Muthukumar et al in 2014³². The results of the study by Lang et al 1986 indicated that pockets with a probing depth of > 5 mm had a significantly higher incidence of BOP³³ which is seen in periodontitis patients and studies by Joss et al in 1994 found that the patients with the highest mean BOP showed the biggest number of sites losing probing attachment³⁴. The association between BOP (bleeding on probing), important sign of clinical inflammation, and periodontal destruction has been studied by Claffey N, Schatzle and by Lang et al^{35,36,37}. The obtained results from the study by Luigi Checchi 2009 confirm and corroborate the importance of BOP as indicator of subgingival deposits, which is supported in our study where periodontitis patients have more plaque and gingival bleeding compared to the healthy and gingivitis group³⁸. A significant increase in probing attachment level is the gold standard for the measurement of periodontal disease activity at a site³⁹. The observations by Goodson in 1984 indicate that attachment loss precedes radiographic evidence of crestal alveolar bone loss during periods of periodontal disease activity⁴⁰. PD was associated with subsequent ABD (alveolar bone density) and ABH (alveolar bone height) loss⁴¹. While considering probing depth and attachment loss, there will be an increased probing depth and attachment loss seen in the periodontitis patients compared to the healthy and gingivitis patients. These findings are in agreement with results from previous studies by Sundararajan, et al, Himanshu Aeran, which was also seen in our study.^{18,42}

The studies by Majumder et al also found a significant correlation between probing depth, missing teeth, and clinical attachment loss, which can lead to periodontal disease⁴³.

Pearson correlation analysis (controlling for the effects of age, and gender) reveal significant positive correlation between the severity of periodontal disease (PD, CAL) and depression determined by means of Beck's depression inventory

Our findings are in agreement with the majority of the literature. Studies by Moss et al., 1996, reveals that depression was associated with a more rigorous course of periodontitis⁴⁴.

Although emotional disorder may increase the risk of chronic periodontitis, the mechanism

remains unclear. On one hand, the altered emotional status would change the health-related behaviors, such as oral hygiene, oral health examination, smoking, and diet, which might increase the risk of periodontitis⁴⁵.

Depressed patients neglect oral hygiene and professional regular dental care due to reduced motivation and interest⁴⁶. Depression is also associated with unhealthy habits such as smoking and alcohol dependence, two factors that are also known to increase one's risk for chronic periodontitis³².

As gingival inflammation is often associated with dental plaque⁴⁷ it was considered to be of interest how life in depression can relate to plaque accumulation. Previous studies by Kurer et al 1995 have shown that Mean depression score was related with plaque accumulation⁴⁶. A study by Klages et al 2005 have shown that Subjects with more depression showed same plaque accumulation but more gingival inflammation¹⁵. Johanssen et al in 2007 demonstrated that the depressed patient had significantly higher inflammation and deeper pocket⁴⁸.

We hypothesized that the possible mechanism of the increased risk of depression in periodontitis patients may be associated with neuroinflammation and disturbed serotonin synthesis. Distress was noted in patients with periodontitis, and psychological stress is associated with the outcome and progression of periodontitis^{49,50}. Periodontitis is a disease showing low-grade systemic inflammation and releasing proinflammatory cytokines, including IL-1b, IL-6, and TNF-a, into systemic circulation⁵¹. Furthermore, psychological stress in patients with periodontitis exhibited a disturbed HPA axis and related hypercortisolism, which affects immune dysfunction and neuroinflammation and may result in subsequent development of depression^{52,53}. By contrast, proinflammatory cytokines could induce indoleamine 2,3-dioxygenase secretion reducing the availability of tryptophan and disturbing serotonin synthesis⁵⁴. Moreover, increased tryptophan catabolites are anxiogenic and depressogenic, which is ascribed to clinical manifestations of depression⁵⁵. Moreover, increased tryptophan catabolites are anxiogenic and depressogenic, which is ascribed to clinical manifestations of depression⁵⁶. To summarize, the aforementioned condition could be considered as neuroprogression leading to subsequent depression. Thus, periodontitis is a risk factor for developing depression³.

The results of our study were in agreement with various previous studies. Studies by Monteiro da Silva et al 1996 in a Case control study ,found that there was a significantly increased depression in the rapidly progressive periodontitis group compared to routine chronic adult periodontitis and control group²³ .Another study by Genco et al 1999 in a cross sectional study revealed an increase in CAL was significantly associated with depression. Depression and financial strain were significant predictor of CAL⁵⁷ .

Ng et al, 2006 stated that subjects with more severe CAL had a greater depression score than the periodontally healthy subject⁵⁸ .

In our study, we got a positive correlation between depression and periodontitis. The cases with higher depression score showed significantly higher PD, CAL, scoring as compared to controls and patients showing lower depression score. Similar results were reported by Sundararajan S. et al. who reported direct co relation between severity of periodontitis and severity of depression in patients¹⁸.The studies by Belting et al 1961 has suggested that the severity of periodontal disease was significantly greater among the psychiatric patients than the control group⁵⁹ . Studies by saletu 2005 confirm depressive mood as a relevant pathogenetic factor for periodontitis⁶⁰ .Decreased cerebral monoamine and increased cortisol levels lead to depression, which in turn, at the behavioural level, is responsible for a lack of dental hygiene, which is supported by in increased plaque index in our periodontal patients⁶⁰ . Johannsen et al. observed that women with stress-related depression had more plaque accumulation, GI and increased levels of IL-6 and cortisol in gingival cervicular fluid (GCF), compared with normal controls. They suggested that depression might affect immune function, leading to impaired periodontal health⁶¹ .

On the other hand, some other studies failed to find a strong association between depression, anxiety and hopelessness with periodontitis.The results of study by Anttila et al. who investigated the relationship of depressive symptoms to edentulousness, dental health and dental health behaviour in a Finnish population, using the Zung Self-Rating Depression Scale (ZSDS), found no association between depressive symptoms and dental caries, periodontal status or number of teeth⁶².Castro et al. following a case-control study in Brazil using four inventories for psychological assessment, also found no significant association between psychosocial factors and periodontal disease⁶³ . Study by

Mendes at al showed no significant association between depression and periodontal disease⁶⁴.There was no statistically significant association between susceptibility to depression symptoms and periodontal parameters, including PD by the studies by Abahneh et al⁶⁵ . Studies by Solis et al who used the same depression scale (BDI) as in our study showed that patients with depression symptoms were not at a greater risk of developing established periodontitis²⁵ .

However, 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. Another limitation could be that the questionnaires were very long and subjects felt rather tired completing them. Misinterpretation and misunderstanding of questionnaire items would have occurred

CONCLUSION

The aim of this study was to to assess relationship between periodontitis to depression in patients attending the general OPD of Malabar dental college. A total of 500 participants were enrolled in the study.The age of the participants were in the range of 24-66 years. Patients were randomly selected from the oral medicine department ,and they were classified into three groups the healthy group, the gingivitis group and the periodontitis group based on the clinical findings. To those patients, a self reported becks depression inventory questionnaire was provided.The levels of depression in healthy,gingivitis and periodontitis patients were assessed with this questionnaire.The present study found a positive correlation between periodontitis and depression.

The present study again highlights that periodontitis can cause neuroinflammation induced by systemic inflammation associated with periodontitis; or evoked by direct invasion of periodontal pathogen and their inflammatory products into the brain,leading to depression. Future longitudinal studies and clinical trials can be aimed for obtaining more insight evidence toward the association between clinical depression and periodontitis. Instead of self-report scales, structured and detailed interviews can be integrated into the studies to prevent subjective bias in answering the questions.

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