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Evaluation of periodontitis in hospital outpatients with major depressive disorder

A. C. O. Solis¹, A. H. Marques^{2,3}, C. M. Pannuti¹, R. F. M. Lotufo¹, and F. Lotufo-Neto³

¹Department of Stomatology, Discipline of Periodontics, School of Dentistry, University of São Paulo, São Paulo, Brazil

²Department of Epidemiology New York, Columbia University, New York, NY, USA

³Department and Institute of Psychiatry, School of Medicine, University of São Paulo, São Paulo, Brazil

Abstract

Background and Objective—Major depressive disorder (MDD) has been associated with alterations in the neuroendocrine system and immune function and may be associated with an increased susceptibility to cardiovascular disease, cancer and autoimmune/inflammatory disease. This study was conducted to investigate the relationship between periodontitis and MDD in a convenience sample of hospital outpatients.

Material and Methods—The sample consisted of 72 physically healthy subjects (36 outpatients with MDD and 36 age-matched controls [± 3 years]). Patients with bipolar disorder, eating disorders and psychotic disorders were excluded. Probing pocket depth and clinical attachment level were recorded at six sites per tooth. Depression was assessed by means of Structured Clinical Interview for DSM-IV.

Results—Extent of clinical attachment level and probing pocket depth were not different between controls and subjects with depression for the following thresholds: 3 mm (Mann-Whitney, $p = 0.927$ and 0.756); 4 mm (Mann-Whitney, $p = 0.656$ and 0.373); 5 mm (Mann-Whitney, $p = 0.518$ and 0.870); and 6 mm (Mann-Whitney, $p = 0.994$ and 0.879). Depression parameters were not associated with clinical attachment level 5 mm in this sample. Smoking was associated with loss of attachment 5 mm in the multi-variable logistic regression model (odds ratio = 6.99, 95% confidence interval = 2.00–24.43).

Conclusions—In this sample, periodontal clinical parameters were not different between patients with MDD and control subjects. There was no association between depression and periodontitis.

Keywords

depression; major depressive disorder; periodontitis; risk factor

The term depression has various meanings and can be applied to a symptom, syndrome or disease (1). Depression may refer to a normal mood fluctuation under normal conditions, or it may be associated with systemic medical conditions such as hypothyroidism or even be part of a mood disorder. Mood disorders are a group of clinical conditions characterized by a prominent mood polarization (such as elevated, irritable or depressed mood) accompanied by psychomotor and vegetative disturbances. Mood disorders occur in a periodic or cyclic manner and culminate in the impairment of the individual's functional capacity (1,2). Bipolar disorder and major depressive disorder (MDD) are two major psychiatric disorders classified as mood disorders in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) (2). Bipolar disorder is characterized by manic or hypomanic episodes (such as elevated or irritable mood) alone or in addition to a depressive episode (depressed mood). Conversely, MDD is characterized by the presence of one or more major depressive episodes and no manic or hypomanic episodes. A depressive episode is defined as depressed mood or loss of interest accompanied by at least four additional symptoms of depression (significant weight change without being on a diet, insomnia or hypersomnia, agitation or psychomotor retardation, fatigue or loss of energy, feelings of uselessness or guilt, reduced ability to think or concentrate, and recurrent thoughts about death) for at least 2 wk. According to these criteria, the symptoms may not be attributed to a general medical condition (2).

The lifetime prevalence of depression varies widely between countries. A recent study in 18 countries ($n = 89,037$ subjects) participating in the World Mental Health Survey Initiative reported lifetime prevalence rates ranging from 6.5% in China to 21% in France and 12 mo prevalence ranging from 2.2% in Japan to 10.4% in Brazil (3,4). In a study carried out in three Brazilian cities, the overall prevalence of depression was 2.8% in Brasília, 1.9% in São Paulo and 10.2% in Porto Alegre. These findings may reflect sociocultural and developmental differences between regions (5). Over the last few decades, depression has been associated with alterations in the neuroendocrine system and in immune functions (6–11). Although decreased immune activity has been observed in patients with depression, the clinical implications of these findings for diseases such as cancer and infectious diseases are still controversial. Moreover, the clinical relevance of these immunological alterations in the course of infectious diseases, especially periodontal disease, has not been well established (7).

Based on these observations, some investigators have evaluated the relationship between depressive symptoms and periodontal disease (12–17). Most of these studies have been performed on non-psychiatric populations, and have employed self-report questionnaires for the assessment of depression symptoms. Scales were used only to detect the presence and severity of depression symptoms, and were not used to provide diagnostic information. The DSM-IV applies a multiaxial approach to psychiatric diagnosis. For example, Axis I includes the primary psychiatric syndromes (e.g. depression, schizophrenia, social phobia and post-traumatic stress disorder). Axis II includes development and personality disorders, and Axis III includes clinically relevant general medical conditions (2). The other two axes are related to psychosocial stressors, and patient's level of function in a 0–100 point scale (Global Assessment of Functioning Scale). There is a need for more research to establish the

relationship between periodontal disease and depression. Therefore, the objective of the present study was to compare periodontal clinical parameters between patients with MDD and healthy controls without diagnosed depression.

Material and methods

Study sample

This study was conducted at the University of São Paulo, Brazil. Study subjects were recruited from patients, volunteers and hospital staff at the Institute of Psychiatry (Ipq-FMUSP). All subjects provided written consent to participate in the study. All participants were prescreened by telephone or personal interview and further assessed using the Structured Clinical Interview for DSM-IV (SCID) (18). Current severity of depression was evaluated with the Hamilton Depression Scale (HAM-D-31) (19). Subjects who reported any type of systemic alteration that might have hindered periodontal clinical examination were excluded, as were those with any of the following diagnoses: cardiovascular disease, diabetes and psychiatric Axis I disorders (delirium, dementia, schizophrenia, eating disorders, organic mental disorder, type 1 or 2 bipolar disorder, psychotic depression and schizoaffective disorder). Subjects with alcohol or drug dependence within 6 mo before the study, and those with a history of epilepsy, infectious or autoimmune disease were also excluded. Furthermore, we evaluated markers of immune activation in the sample, which included interleukin 6 and 1β levels in whole blood cultures. Strict exclusion criteria were necessary to determine the relationship between MDD and periodontal disease.

We selected a convenience sample of patients that met criteria for MDD based on SCID, in contrast to studies where patient selection was based only on self-reported scales.

Depression outpatients (case group)—To qualify for the study, depression outpatients were required to have one or more recurrent depressive episodes and a score of at least 15 points on the HAM-D-31. Patients were randomly selected from a larger group of available hospital outpatients. Patients were recruited by means of simple random sampling and from consecutive admission to the outpatient clinic from the Institute of Psychiatry.

Control group—Control subjects were recruited from hospital staff and volunteers who had no current MDD, delirium, dementia, schizophrenia, eating disorders, organic mental disorder, bipolar disorder (type 1 or 2), psychotic depression, schizoaffective disorder, history of alcohol or drug dependence within 6 mo before the study or history of epilepsy.

The period of recruitment of depression outpatients was July 2000–April 2002. Control subjects were selected during the same period, and an attempt was made to match subjects according to age (± 3 years), and as much as possible according to other demographic variables. The final sample was complete in November 2002. The sample size was determined by the principle of theoretical saturation (20).

Ethical issues

The project was approved by the ethics committees of the Department and Institute of Psychiatry, University of São Paulo, Brazil, and the School of Dentistry, University of São Paulo, Brazil.

Psychometric instruments

A diagnostic instrument and depression severity rating scales were used for this assessment. SCID version 2.0 based on DSM-IV criteria, was used for psychiatric diagnosis (18). Interviews were scheduled for 30 min and conducted by trained interviewers, to ensure proper psychiatric evaluation. Depression severity was assessed with the Hamilton Depression Rating Scale, which was designed to measure severity of depression in inpatients with previously diagnosed depression (19). There are four versions with 17, 21, 24 or 31 items. The items are assessed according to intensity and frequency within a specific period. We used the 31-item version to include symptoms of atypical depression, such as increased appetite and weight gain, and hypersomnia. The depressive syndrome was defined as chronic when symptoms were present for at least 2 years without remission lasting 2 mo or longer. Otherwise, it was classified as an acute episode.

Procedure

All participants underwent a standard physical examination and their medical history was documented. Clinical diagnoses were made by one experienced psychiatrist using the SCID. Patients with depression met the DSM-IV criteria for MDD. All participants were physically healthy. Psychiatric treatment was conducted according to the clinical needs of each patient and the availability of medication at the hospital. The participants were invited for periodontal clinical examination. CAL and probing pocket depth were measured at six sites per tooth, excluding the third molars, with an electronic (Florida probe) or manual probe (Hu-Friedy, PCPUNC). The frequency of missing teeth was also determined. The plaque index (PI) was used to record the presence of plaque (21) and gingival condition was evaluated with the gingival index (GI) (21,22). Intraexaminer agreement was evaluated by means of repeated measurements from the first examination during the study. Cohen's kappa coefficient was 0.972 for probing pocket depth and 0.972 for CAL (electronic probe, one patient), and 0.974 for probing pocket depth and 0.978 for CAL (manual probe, two patients), and 0.976 for probing pocket depth and 0.952 for CAL (manual/electronic probe, one patient). Dental treatment was offered and patients were referred to the dentistry service of Ipq-FMUSP. A flowchart of the study is presented in Fig 1.

Statistical analysis

Data were analyzed with the Minitab Statistical Package (Minitab Inc., version 16.0; Chicago, IL, USA) and Mstat 12 for Windows, version 12.02.00. The chi-squared test, Fisher exact test, *t*-test and Mann–Whitney test were used to compare the distribution of demographic and depression variables between cases and controls. The Mann–Whitney test was used to compare frequencies of subject-based and teeth-based probing pocket depth and CAL 3, 4, 5 and 6 mm. Univariable and multivariable logistic regression models were used to measure the association between the outcome variable (chronic periodontitis,

CAL ≥ 5 mm) and explanatory variables, which included age (> 35 years), gender, race, smoking (current or former), plaque (mean distribution frequency of teeth with PI ≥ 2 in 20% of the teeth), depression, MMD chronicity, MDD severity, MDD subtype and MMD (episode or disorder). Exposures with $p \leq 0.25$ in the univariable model were included in the multivariable model. The odds ratios and corresponding 95% confidence intervals were calculated. Differences at the 5% level were considered statistically significant.

Results

A total of 112 individuals who initially met the inclusion criteria were prescreened. Twenty-seven were excluded after SCID because they were not available for periodontal examination, refused clinical periodontal examination, or presented another psychiatric disorder (bipolar disorder). After periodontal evaluation, 12 participants with MDD and one control were excluded. Seven patients were edentulous (six MMD and one control), and three suffered from bipolar disorder (had an episode of hypomania soon after taking antidepressants). Two patients were removed from the MDD group because of alteration in the blood test and fibromyalgia (Fig. 1). Ten patients underwent periodontal evaluation during remission of depression, and two patients at the end of psychiatric treatment (3–4 mo later). PI and GI for the latter two patients were not included in the statistical analysis.

The final sample consisted of 72 subjects (36 depression outpatients and 36 healthy controls), who completed the clinical periodontal examination and the psychiatric interview. Demographic and socioeconomic data of the 72 patients are summarized in Table 1. Employment status ($p < 0.001$) and mean household income ($p = 0.001$) differed significantly between groups. Table 2 presents MDD and periodontal characteristics and Hamilton scores. Most of the patients with depression had more than one episode of depression (61.11%). Most cases of depression had melancholic features (66.67%), and 69.44% were classified as severe. Cutoff values for the Hamilton Depression Scale (17, 21 and 31) were significantly different between groups. Healthy controls and depression patients did not show differences in periodontal clinical parameters and missing teeth. Table 3 shows that mean values of probing pocket depth, CAL and GI differed significantly between smoking and nonsmoking patients. Furthermore, the frequencies of subject-based and teeth-based probing pocket depth and CAL for thresholds ≥ 3 , ≥ 4 , ≥ 5 and ≥ 6 mm were not different between groups (Tables 4 and 5). Smoking was associated with loss of attachment ≥ 5 mm in the multivariable logistic regression model (OR = 6.99, 95% CI = 2.00–24.43) (Table 3).

Discussion

Our study did not reveal an association between MDD and chronic periodontitis. Patients with MDD and controls did not show differences in periodontal clinical parameters (probing pocket depth, CAL, PI and GI). Similar probing pocket depth and CAL results were found for women with stress-related depression and exhaustion, evaluated with SCID (23) and for subjects with depression symptoms evaluated by self-report rating scales (14,16,17,24). Conversely, studies that have shown an association between periodontitis (CAL or probing

pocket depth) and depression evaluated patients based on self-report scales (13,25,26) or personality dimensions (26) and did not apply a diagnostic instrument.

One important aspect introduced in our study was the use of a diagnostic instrument (structured clinical interview) for psychiatric evaluation. This means that diagnostic categories (from DSM-IV) could be operational-ized with standardized interviews to facilitate replication of the study. Additionally, structured interview is the gold standard for classification of major psychiatric and personality disorders.

Personality disorders are clinical syndromes characterized by enduring patterns of inflexible and maladaptive thinking, feeling and acting that cause significant distress, impairment of social or occupational functions, or both. The symptoms are stable and of long duration and can be traced back at least to adolescence or early adulthood. Personality disorders do not result from alcohol or drug use or another psychiatric disorder. Therefore, personality disorder in the presence of an Axis I condition is difficult to diagnose. Clinicians are advised to observe patients over time to assess the degree to which other symptoms persist as Axis I symptoms remit (27).

We selected MDD from several types of stress-related disorders, because psychoneuroimmunology studies have shown that immunological and endocrine alterations in patients with MDD differ from those of subjects with post-traumatic stress disorder, personality disorders and/or a history of early adverse stressful events such as childhood maltreatment (7,8,28).

Patients with depression and control subjects had a similar distribution for most demographic and clinical variables such as gender, educational level, marital status, race, age, smoking status and body mass index. However, the greater proportion of females among depression patients in this study is consistent with studies that have shown a higher prevalence of MDD in women (4,29). Patients with depression also had a lower household income, probably because of the larger number of unemployed individuals in this group (Table 1). This finding is consistent with studies that have shown a higher prevalence of depression among unemployed compared to employed individuals (30) and can be explained by the debilitating nature of MDD.

Smoking was significantly associated with CAL and probing pocket depth in this sample (Tables 3 and 6, and supplementary material). These results are in accordance with well-designed Brazilian epidemiological studies (31,32). Therefore, it is relevant to point out that, in our sample, smoking status was similar between patients with MDD and controls, and GI was increased in smokers (Tables 1 and 3). Many studies have found that GI is lower in smokers (33,34), and others have shown that smoking is significantly more prevalent among individuals with depression mood disorders and anxiety disorders (36–46%) (35,36). Although smoking status did not differ according to PI (Table 3), higher levels of plaque were found in smokers. PI probably has an important effect on gingival inflammation.

Poorer oral hygiene was expected in patients with MDD. However, plaque was not different between groups (Table 2), and our results do not indicate an adverse effect of MDD on oral hygiene. Castro *et al.* emphasized that periodontal disease is more associated with

demographic and sociocultural variables of the Brazilian population than with psychosocial factors *per se* (17).

Periodontitis is a cumulative, chronic disease, whereas MDD is a chronic but intermittent disorder (4,29,37). The influence of this syndrome on periodontal disease is probably not relevant from an epidemiological point of view, although depressive episodes can be recurrent and can persist for weeks or months. MDD also has an earlier age of onset than chronic periodontal disease (4), is associated with being divorced or widowed, and is more prevalent in women (the female/male ratio is about 2 : 1) (3). Therefore, the impact of immunological alterations that might occur in MDD during the course of periodontal disease can be transitory and difficult to detect with the tools usually available for conventional clinical diagnosis. Additionally, depressive syndrome is a broad concept as classified by the DSM-IV. It means, for example, that this diagnosis can fit a girl who fights with her boyfriend and who presents sadness, loss of energy and other symptoms of depressive syndrome for more than 15 d, as well as patients with more severe forms of depression, which has been associated with biological alterations such as hyperactivity of the hypothalamic-pituitary-adrenal axis and activation of the innate immune response and inflammation (38–41). In this sense, some authors suggest that biological investigation of depression patients should include appropriate a structured interview that can classify depression based on its severity and subtypes, such as melancholic, atypical and psychotic. However, our study was designed to include patients with melancholic and atypical depression and to evaluate the association of these conditions with periodontal disease; the reduced sample size did not allow us to perform such analysis.

Our findings should be evaluated in the context of certain limitations. First, considering the epidemiological characteristics of MDD, we decided to conduct a study at the Institute of Psychiatry to focus on patients with MDD. Studies conducted at the psychiatry hospital differ from those performed in the community. All possible participants were initially prescreened by telephone or in-person interviews and further assessed with SCID. At that time it was difficult to determine, for example: (i) if the patient would meet the study's inclusion criteria; (ii) the severity of depressive symptoms; and (iii) ambulatory status (inpatient or outpatient). In addition, patients were required to undergo psychiatric treatment. These factors limited the number of participants. Second, although two healthy controls presented a Hamilton-D-17 score 7, 8 and 9 respectively, they did not meet clinical criteria for depressive syndrome. Despite these limitations, our results produced estimates that can be valuable for further meta-analyses.

In conclusion, we did not find an association between chronic periodontitis and MDD assessed by SCID. However, the influence of depression on periodontal disease should be further investigated in other countries to confirm these findings. Furthermore, we suggest that other studies oversample patients with melancholic and chronic depression.

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Fig. 1.
Study flowchart.

Table 1

Demographic and socioeconomic variables, smoking and body mass index of the groups

Variable		No depression (n = 36)	Major depressive disorder (n= 36)	p
Gender ^a	Female	30 (83.33%)	29 (80.56%)	0.759
	Male	6 (16.67%)	7 (19.44%)	
Education level ^a	Incomplete elementary school/Junior high school	7 (19.44%)	14 (38.89%)	0.148
	High school	20 (55.56%)	13 (36.11%)	
	College	9 (25.00%)	9 (25.00%)	
Marital status ^a	Married	17 (47.22%)	16 (44.44%)	0.813
	Divorced/detached/unmarried/alone and widow	19 (52.78%)	16 (55.56%)	
Employment status ^b	Unemployed	1 (2.78%)	19 (52.78%)	< 0.001 *
	Employed/retired	35 (97.22%)	17 (47.22%)	
Race ^a	Caucasian	22 (61.11%)	24 (66.67%)	0.624
	No caucasian	14 (38.89%)	12 (33.33%)	
Smoking ^a	Nonsmoking	24 (66.67%)	23 (63.89%)	0.804
	Smoker	12 (33.33%)	13 (36.11%)	
Age ^c	$\mu \pm$ SD (range)	36.75 $\pm$ 10.57 (18–58)	37.22 $\pm$ 10.13 (19–55)	0.847
Household income (Reais) ^d	$\mu \pm$ SD (range)	n = 33 2688.70 $\pm$ 3283.30 (376.00–15,000.00)	n = 36 1064.60 $\pm$ 782.10 (0.00–3500.00)	0.001 *
Body mass index ^d	$\mu \pm$ SD (range)	n = 30 24.99 $\pm$ 3.86 (19.72–34.62)	n = 34 24.84 $\pm$ 4.68 (18.75–35.15)	0.623

^a Chi-squared test.^b Fisher exact test.^c *t*-test.^d Mann–Whitney test (adjusted for ties).

* Statistically significant.

SD, standard deviation.

Table 2

Depression and periodontal characteristics of the groups

Variable		No depression (n = 36)	Major depressive disorder (n = 36)	p
Major depressive episode	MDE	–	14 (38.89%)	–
(MDE)/major depressive disorder (MDD)	MDD	–	22 (61.11%)	–
Chronicity	Acute	–	19 (52.78%)	–
	Chronic	–	17 (47.22%)	–
Severity	Severe	–	25 (69.44%)	–
	Light	–	11 (30.56%)	–
Subtype	Melancholic	–	24 (66.67)	–
	Atypical	–	12 (33.33)	–
HAM-D-17 ^a	μ ± SD (range)	n = 35 1.74 (±2.29) (0–9)	n = 35 23.82 (±6.50) (12–34)	< 0.000
HAM-D-21 ^a	μ ± SD (range)	n = 35 1.94 (± 2.42) (0–9)	n = 35 26.28 (± 7.14) (12–39)	< 0.000
HAM-D-31 ^a	μ ± SD (range)	n = 35 2.20 (±2.67) (0–10)	n = 35 34.74 (±8.18) (17–53)	< 0.000
Probing pocket depth ^a	μ ± SD	n = 36 2.46 (0.72)	n = 36 2.26 (0.46)	0.221
Clinical attachment level ¹	μ ± SD	n = 36 2.58 (0.91)	n = 36 2.48 (0.80)	0.430
Missing teeth ^a	μ ± SD	n = 36 4.36 (4.42)	n = 36 5.22 (5.45)	0.777
PI ^{a,b} (2)	μ ± SD	n = 30 29.67 (36.68)	n = 30 36.96 (38.64)	0.425
GI ^{a,b} (2)	μ ± SD	n = 29 52.00 (37.81)	n = 30 53.20 (38.70)	0.907

GI, gingival index; PI, plaque index; SD, standard deviation.

^a Mann-Whitney test (adjusted for ties).^b Mean distribution frequency of teeth with PI or GI 2.

Table 3

Periodontal clinical characteristics of the non-smoking and smoking groups

Variable		Nonsmoking <i>n</i> = 47	Smoking <i>n</i> = 25	<i>p</i>
Probing pocket depth ^a	μ ± SD	<i>n</i> = 47 2.09 (0.28)	<i>n</i> = 25 2.85 (0.76)	<i>p</i> < 0.000
Clinical attachment level ^a	μ ± SD	<i>n</i> = 47 2.17 (0.31)	<i>n</i> = 25 3.20 (1.12)	<i>p</i> < 0.000
Missing teeth ^a	μ ± SD	<i>n</i> = 47 5.10(5.53)	<i>n</i> = 25 4.20 (3.64)	0.985
PI ^{a,b} (2)	μ ± SD	<i>n</i> = 38 28.83 (33.35)	<i>n</i> = 22 41.07 (43.57)	0.526
GI ^{a,b} (2)	μ ± SD	<i>n</i> = 37 41.42 (36.85)	<i>n</i> = 22 71.44 (32.49)	0.002

GI, gingival index; PI, plaque index; SD, standard deviation.

^a Mann-Whitney test (adjusted for ties).^b Mean distribution frequency of teeth with PI or GI 2.

Table 4

Subject-based (prevalence), and teeth-based (extent) of clinical attachment level 3 mm, 4 mm, 5 mm and 6 mm in no depression and major depressive disorder groups

Variable	No depression (<i>n</i> = 36)	Major depressive disorder (<i>n</i> = 36)	<i>p</i>
Prevalence (% subjects)			–
3 mm	100%	100%	–
4 mm ^a	88.89%	97.22%	0.357
5 mm ^b	50%	58.33%	0.478
6 mm	30.56%	30.56%	–
Extent (% number of teeth)			
3 mm ^c ($\mu \pm$ SD)	80.66 (19.58)	81.78 (17.12)	0.927
4 mm ^c ($\mu \pm$ SD)	32.44 (31.05)	31.18 (31.11)	0.656
5 mm ^c ($\mu \pm$ SD)	16.32 (27.47)	16.95 (25.91)	0.518
6 mm ^c ($\mu \pm$ SD)	10.35 (22.86)	9.41 (19.93)	0.994

^aFisher exact test.

^bChi-squared test.

^cMann–Whitney test (adjusted for ties).

Table 5

Subject-based (prevalence), and teeth-based (extent) of probing pocket depths 3 mm, 4 mm, 5 mm and 6 mm in no depression and major depressive disorder groups

Variable	No depression (<i>n</i> = 36)	Major depressive disorder (<i>n</i> = 36)	<i>p</i>
Prevalence (% subjects)			
3 mm	100%	100%	–
4 mm	88.89%	88.89%	–
5 mm ^a	47.22%	50.00%	0.814
6 mm	30.56%	30.56%	–
Extent (% number of teeth)			
3 mm ^b ($\mu \pm$ SD)	79.32 (20.35)	78.71 (20.16)	0.756
4 mm ^b ($\mu \pm$ SD)	31.03 (30.44)	27.35 (29.98)	0.373
5 mm ^b ($\mu \pm$ SD)	15.59 (27.35)	13.17 (20.96)	0.870
6 mm ^b ($\mu \pm$ SD)	9.22 (19.99)	5.54 (11.61)	0.879

^a Chi-squared test.

^b Mann–Whitney test (adjusted for ties).

Table 6

Univariable and multivariate logistic regression analysis to measure the outcome variable (clinical attachment level ≥ 5 mm) and the explanatory variables, which included demographics, smoking, plaque and depression variables

Variables	Univariable			Multivariable		
	<i>p</i>	OR	95% CI	<i>p</i>	OR	95% CI
Age (> 35 years)	0.022	3.08	1.17–8.08	0.195	2.02	0.70–5.83
Gender (male)	0.980	0.98	0.30–3.28			
Race (no Caucasian)	0.652	1.25	0.47–3.30			
Smoking (smoker/former)	0.001	8.46	2.50–28.66	0.002	6.99	2.00–24.44
Plaque ($> 20\%$)	0.993	0.996	0.36–2.74			
Depression (yes)	0.478	1.40	0.55–3.55			
MDD chronicity						
Acute	0.853	1.11	0.37–3.38	–	–	–
Chronic	0.318	1.83	0.56–6.03	–	–	–
MDD severity						
Severe	0.442	1.50	0.53–4.21	–	–	–
Light	0.792	1.20	0.31–4.65	–	–	–
MDD subtype						
Melancholic	0.342	1.67	0.58–4.78	–	–	–
Atypical	1.000	1.00	0.27–3.69	–	–	–
MDD						
Episode	1.000	1.00	0.29–3.44	–	–	–
Disorder	0.313	1.75	0.59–5.19	–	–	–
MDD, major depressive disorder						