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### ORIGINAL ARTICLE



# Periodontal conditions and association of periodontitis with oral-health-related quality of life in patients experiencing different episodes of bipolar disorder compared with healthy controls

Aysegul Sari<sup>1,2</sup> | M. Hanifi Kokacya<sup>3</sup> | Mark Ide<sup>2</sup>

<sup>1</sup>Department of Periodontology, Faculty of Dentistry, Hatay Mustafa Kemal University, Antakya, Hatay, Turkey

<sup>2</sup>Periodontology Unit, Centre for Host-Microbiome Interactions, King's College London Dental Institute, London, UK

<sup>3</sup>Department of Psychiatry, Faculty of Dentistry, Hatay Mustafa Kemal University, Antakya, Hatay, Turkey

### Correspondence

Aysegul Sari, Periodontology Unit, Centre for Host-Microbiome Interactions, Faculty of Dentistry, Oral and Craniofacial Sciences, Kings College London Guy's Hospital, Great Maze Pond, London SE1 9RT, UK. Email: aysegul.sari@kcl.ac.uk

### Abstract

**Aim:** The aim of the present cross-sectional study was to evaluate periodontal conditions and the association of periodontitis with oral-health-related quality of life (OHRQoL) in patients with a history of bipolar disorder.

**Materials and Methods:** A total of 160 participants were recruited in four groups for the study: 40 patients with euthymic episodes, 40 patients with depression, 40 patients with manic episodes and 40 systemically healthy individuals. Clinical periodontal parameters were recorded. Oral Health Impact Profile (OHIP-14) was used to measure the impact of oral health on the quality of life.

**Results:** Bipolar disorder groups exhibited generally higher clinical parameters compared with the control group (p < .05). OHIP-14 total score ( $\beta = 3.32$ , 95% confidence interval [CI]: 0.08–6.56, p = .044), functional limitation ( $\beta = .89$ , 95% CI: 0.27–1.49, p = .005) and physical pain ( $\beta = .64$ , 95% CI: 0.01–1.27, p = .046) were associated with bipolar depression episodes. Psychological discomfort was associated with the presence of generalized periodontitis ( $\beta = .76$ , 95% CI: 0.01–1.51, p = .047) and psychological disability was associated with the presence of stage III–IV ( $\beta = .83$ , 95% CI: 0.07–1.59, p = .033) and generalized ( $\beta = .75$ , 95% CI: 0.07–1.42, p = .029) periodontitis.

**Conclusions:** According to this study, a history of bipolar disorder episodes (exposure) may be associated with increased prevalence and severity of periodontitis and related reported OHRQoL impacts (outcomes). Bipolar depression episodes had a higher impact on OHRQoL than other bipolar episodes.

### KEYWORDS

bipolar disorders, oral-health-related quality of life, periodontal disease, periodontitis

### **Clinical Relevance**

*Scientific rationale for study*: Bipolar disorder is characterized by episodes of hypomania, mania and depression. This study aimed to evaluate periodontal conditions and the association of periodontitis with oral-health-related quality of life (OHRQoL) in patients who had different bipolar disorder episodes.

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Principal findings: This study confirmed that bipolar disorder can increase the risk of periodontitis. Periodontitis can negatively affect OHRQoL in patients with bipolar disorder.

Practical implications: Periodontal health should be considered in patients with bipolar disorder. Maintaining periodontal care and oral hygiene can improve the quality of life in these patients.

#### INTRODUCTION 1 |

Bipolar disorder is a serious mental disorder with fluctuating episodes. This disorder is characterized by episodes of hypomania, mania and depression (Grande et al., 2016) and affects more than 1% of the population of the world, regardless of nationality, ethnicity or socioeconomic status. Bipolar disorder is ranked as the second most common illness to affect the performance of daily roles in the WHO's World Mental Health surveys (Alonso et al., 2011). It is episodic and characterized by cognitive and functional impairment, reduces the quality of life of the individual and lasts for life (Martinez-Aran et al., 2007). There is some cumulative evidence that bipolar disorder is associated with immune reactions in the brain. low-grade chronic inflammation and excessive oxidative stress (Leboyer et al., 2012; Rege & Hodgkinson, 2013).

Periodontal diseases are associated with periodontal dysbiosis and disruption of tissue homeostasis (Darveau, 2010). Periodontal diseases were found to be linked to systemic diseases by bacteraemia and systemic inflammatory processes, including increases in oxidative stress (Ide et al., 2016; Sari et al., 2021). The association between periodontitis and cognitive and mental health such as dementia and major depressive disorders remains controversial (Gil-Montoya et al., 2015; Martínez et al., 2021). There are a few studies that evaluated the association between periodontal disease and bipolar disorder. Two previous studies suggest that the presence of periodontal disease can be predictive of a later diagnosis of bipolar disorder (Chang et al., 2020; Huang et al., 2020). The systemic impact of periodontal diseases can be linked to the inflammatory processes of bipolar disorder (Ball & Darby, 2022). On the other hand, one study showed that bipolar disorder had an association with a higher prevalence of periodontitis (Cunha et al., 2019). Psychiatric conditions such as stress can alter the immune system activity of periodontal diseases (Ball & Darby, 2022). Also, different episodes, the drug used and decreasing interest in self-care in bipolar disorders may affect the development and prognosis of periodontal disease.

General quality of life is associated with oral-health-related quality of life (OHRQoL). A deterioration in the general quality of life can be reflected in OHRQoL (Haag et al., 2017) OHRQoL focuses on the deterioration of psychosocial and physical conditions related to oral health (Baiju et al., 2017). Periodontal health is closely associated with OHRQoL by compromising facilities related to aesthetics and functions (Masood et al., 2019). It was noticed that periodontitis has a negative impact on OHRQoL (Ferreira et al., 2017; Needleman et al., 2004; Rawlinson et al., 2021). Severe periodontitis, which compromises aesthetics and function, has the most significant effect on OHRQoL (Ferreira et al., 2017). One study showed that higher periodontitis index scores and symptoms were associated with poorer OHQL scores (Needleman et al., 2004). Another study showed that OHRQoL was related to periodontitis in patients with end-stage renal disease (Oliveira et al., 2020). Also, it was reported that systemic diseases such as rheumatological diseases have a negative impact on OHRQoL (Schmalz et al., 2020). Patients with bipolar disorder have sub-syndromic or syndromic symptoms that affect their quality of life. Asymptomatic patients can be impaired in domains such as episode regulation, sleep, cognition, daily patterns, fitness condition, social skills, independence, education and work (Michalak & Murray, 2010). They have poor overall performance in cognitive and executive tasks associated with the quality of life (Cotrena et al., 2016). Different episodes of bipolar disorder that affect the general quality of life can have a negative impact on OHRQoL. Also, the impact of periodontitis on OHRQoL (Masood et al., 2019) may affect those with bipolar disorder.

To the best of our knowledge, there is no study evaluating whether periodontal disease affects OHRQoL in patients with bipolar disorder. We hypothesized that there is an association between periodontal disease and bipolar disorder and that periodontitis could also have a negative impact on OHRQoL in patients with bipolar disorder. Therefore, the aim of the present study was to evaluate the relationship between periodontal disease and different episodes of bipolar disorder and the association of periodontitis with OHRQoL in these patients compared with healthy controls.

#### MATERIALS AND METHODS 2

#### 2.1 Study population

A cross-sectional study was carried out as a joint collaboration between the Department of Psychiatry in the Faculty of Medicine and the Department of Periodontology in the Faculty of Dentistry at Hatay Mustafa Kemal University (HMKU), Hatay, Turkey. The study protocol was approved by the Ethics Committee for the Use of Human Subjects in Research of HMKU (Protocol No: 2018/116) and the study was carried out in accordance with the tenets of the Declaration of Helsinki. The study conforms to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies (von Elm et al., 2007).

A total of 219 individuals were examined from March 2019 to January 2021. Of these, 7 individuals refused to participate and 52 individuals met the exclusion criteria. Hence, 160 individuals (84 males and 76 females, aged 18-65 years) comprised the study population (Figure 1). The study protocol was explained to the



participants and written informed consent was received from each individual prior to enrolment. The study design was established with four participant groups. The study population included 120 patients with bipolar disorder who were undergoing medical or psychiatric treatment at the Department of Psychiatry, Faculty of Medicine, consisting of 40 patients with euthymic mood, 40 patients with depression and 40 patients with manic episodes. Forty systemically healty controls were recruited from the Department of Periodontology, Faculty of Dentistry. Recruitment was staged, focusing initially on those patients with a history of mania, and subsequently those in the other groups, aiming at matching them for age (the age criterion was ±3 years) and sex.

Inclusion criteria for study groups were patients aged ≥18 years, with body mass index (BMI) ≤25 kg/m<sup>2</sup> and more than 20 teeth. Exclusion criteria for study groups were as follows: patients who were pregnant; had any other systemic conditions that were considered risk factors for periodontal diseases such as kidney disease, diabetes, obesity and AIDS; were receiving orthodontic treatment or had

undergone antibiotic therapy or periodontal therapy in the past 6 months. Body weight (kg) divided by the square of height  $(m^2)$  was used for calculating BMI.

Individuals were assessed and diagnosed by a psychiatrist (M.H. K.) with experience in bipolar disorder management. The questionnaires administered for bipolar disorder diagnosis were the Young Scale (Young et al., 1978) (YMRS, for mania episode) and the Hamilton Scale (Hamilton, 1960) (HAMD, for depression episode). In addition, the Clinical Global Impressions Scale (CGI-s) was used to evaluate the severity for all groups with bipolar disorder (Guy & Cleary, 1976). These participants did not have any mental diseases and/or did not use psychotropic medications such as illicit drugs, antidepressants and anxiolytics. These data were confirmed from the medical records of the participants.

After obtaining formal written consent from the participants, their medical history was obtained. Demographic variables were collected, including education level, marital status, monthly income, place of residence, frequency of dental check-ups, toothbrushing 4 WILEY Periodontology

frequency, use of oral care products such as dental floss, interface brush and mouthwash, smoking status, smoking pack-years, and alcohol consumption.

#### 2.2 **Clinical periodontal parameters**

Upon confirmation of eligibility for enrolment in the study, clinical periodontal parameters including plaque index (PI) (Silness & Loe, 1964), gingival index (GI) (Loe, 1967), bleeding on probing (BOP) (presence/absence) (%) (Ainamo & Bay, 1975), probing pocket depth (PPD) (mm) and clinical attachment loss (CAL) (mm) were recorded from all participants during their visit to the Periodontology Department. Clinical periodontal measurements were performed at six sites on each tooth (mesio-buccal, midbuccal, disto-buccal, mesio-lingual, mid-lingual and disto-lingual locations), except for third molars, using a manual periodontal probe (Williams, Hu-Friedy, Chicago, IL, USA) by a single calibrated examiner (A.S.). Intra-examiner agreement was determined for CAL. Intra-examiner reproducibility was determined through repeated examinations of 10 subjects with a 1-h interval (intraclass corelation coefficient = 0.87).

Periodontal disease and conditions were diagnosed according to clinical and radiographic criteria proposed by the 2017 World Workshop on the Classifications of Periodontal and Peri-implant Disease and Conditions (Caton et al., 2018). Patients with an intact periodontium were included in this study of periodontal health and gingivitis cases. Individuals with a BOP score <10% without attachment loss and radiographic bone loss were considered to be periodontally healthy (Tonetti & Sanz. 2019). Individuals presenting with a BOP score ≥10% and all PPD ≤3 mm without attachment loss and radiographic bone loss were considered to suffer from gingivitis (Trombelli et al., 2018). The criteria for patients with periodontitis were (i) interdental CAL detectable at two or more non-adjacent teeth or (ii) buccal or oral CAL ≥3 mm with pocket depth >3 mm detectable at two or more teeth. The categorized greatest values of CAL for periodontitis severity were defined according to the periodontitis stages (Tonetti et al., 2018b). Mild periodontitis was defined as the presence of CAL 1-2 mm (Stage I); moderate periodontitis was defined as the presence of CAL 3-4 mm (Stage II); and severe periodontitis was defined as the presence of CAL ≥5 mm and with ≤4 teeth lost due to periodontitis (Stage III) and ≥5 teeth lost due to periodontitis (Stage IV) (Tonetti et al., 2018b). The extent of periodontitis was defined as localized (the presence of up to 30% of affected sites) and generalized (the presence of over 30% of affected sites) (Tonetti et al., 2018a). The extent of gingivitis was defined as localized (BOP score  $\geq$ 10% to  $\leq$ 30%) or as generalized (BOP score > 30%) (Trombelli et al., 2018). Mean PPD and CAL were also calculated.

Prevalence of sites with exceeding thresholds of PPD and CAL in patients with periodontitis was categorized. The site levels of PPD were categorized as ≥4. The site levels of CAL were categorized as ≥3 mm.

#### 2.3 **OHRQoL** measurement

The effect of OHRQoL was measured by the Turkish version of the Oral Health Impact Profile (OHIP-14) (Basol et al., 2014). The OHIP-14 is a multi-dimensional scale that measures the frequency of oralhealth-related problems. It has subgroups of seven different conceptual dimensions: functional limitation representing conditions such as difficulty in chewing; physical pain representing conditions such as discomfort eating foods and pain in the mouth; psychological discomfort representing conditions such as feeling tense and selfconscious;physical disability representing conditions such as unsatisfactory diet and interrupted meals; psychological disability representing conditions such as difficulty relaxing and embarrassment; social disability handicap refraining social activities; and handicap representing conditions such as disability of function. An ordinal scale scoring is used to quantify the answers as numbers: 0 = never, 1 = hardly ever, 2 = occasionally, 3 = fairly often and 4 = very often. Subgroup scores for each dimension are summed for obtaining the OHIP-14 total scores (Locker & Ouinonez, 2011).

#### 2.4 Statistical analysis

The primary study outcome was the comparison of periodontitis severity among the four groups. Because this was a novel study, we estimated the number as 40 per group. Post hoc power calculation (according to the parameter CAL for four groups) showed that 40 patients per group would give 99% power for an effect size f of 0.40 (standard deviation [SD]: 1.08) and  $\alpha = .05$ . Gpower package version 3.1 was used for post hoc power analysis.

The normality of the distribution of continuous variables was examined by the Shaphiro-Wilk test. Mean ± SDs and median and interquartile ranges were given as descriptive statistics. Comparing two groups for non-normally distributed data was done using the Mann-Whitney U test. More than two non-normally distributed variables were compared by performing the Kruskal-Wallis test, and post hoc pairwise multiple comparisons were done by the Dunn multiple comparison test. More than two normally distributed variables were compared by performing one-way ANOVA. Associations between categorical variables were tested using chi-squared tests; p-values were Bonferroni-corrected. To assess the correlations between numerical variables, Spearman's rank correlation coefficients were calculated. Furthermore, non-parametric models were used because the dependent values were with skewed distribution.

Generalized linear models were used to estimate the associations between either bipolar disorder groups or periodontitis severity (exposures) and OHIP-14 total and sub-items scores (outcomes), adjusting for age, sex, BMI, education level, monthly income, marital status, place of residence, frequency of dental check-ups, toothbrushing frequency, smoking and alcohol consumption. A single model was established for each outcome variable (OHIP-14 total and sub-items scores) and the exposure variables (bipolar disorder groups or periodontitis severity), adjusting for the same variables as described above.

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ABLE 1 Demographi	ic variables in bipolar disor	der and systemically healthy	/ groups.		
Variables	Euthymic group (n = 40)	Depression group $(n = 40)$	Mania group (n = 40)	Health group $(n = 40)$	p-Value
Age (years)	35.6 ± 14.98	35.63 ± 10.74	35.33 ± 11.68	35.65 ± 11.68	.933
BMI (kg/m <sup>2</sup> )	23.92 ± 1.26	24.22 ± 2.03	24.14 ± 2.32	23.9 ± 3.42	.599
Sex					
Male	21 (52.5)	21 (52.5)	21 (52.5)	21 (52.5)	1.000
Female	19 (47.5)	19 (47.5)	19 (47.5)	19 (47.5)	
Education level					
High school	29 (72.5) <sup>a</sup>	27 (67.5) <sup>b</sup>	28 (70) <sup>c</sup>	14 (35)	.001
University	11 (27.5) <sup>a</sup>	13 (32.5) <sup>b</sup>	12 (30) <sup>c</sup>	26 (65)	
Marital status					
Single	28 (70)	22 (55)	25 (62.5)	18 (45)	.131
Married	12 (30)	18 (45)	15 (37.5)	22 (55)	
Monthly income	()	( /	( /	( /	
<2500 t	22 (55) <sup>a</sup>	24 (60) <sup>b</sup>	26 (65) <sup>c</sup>	10 (25)	001
>2500 t	18 (45) <sup>a</sup>	16 (40) <sup>b</sup>	14 (35) <sup>c</sup>	30 (75)	1001
	10 (13)	10 (10)	11(03)	00(70)	
Village	5 (12 5)	5 (12 5)	3 (7 5)	2 (5)	046
Town	24 (40)	25 (62 5)	25 (42 5)	2 (3)	.040
City contro	24 (00)	20 (02.5)	23 (02.3)	13 (37.5)	
	11 (27.3)	10 (23)	12 (50)	23 (37.3)	
-requency of dental check-u	ps o (o)	0 (5)	0 (5)	0 (00 5)	0073
Every 6 months	0(0)	2 (5)	2 (5)	9 (22.5)	.007-
Annually	1 (2.5)	0 (0)	0(0)	1 (2.5)	
Irregular	39 (97.5)-	38 (95)	38 (95)	30 (75)	
oothbrushing frequency	0 (00 5)		4 (40)	0.(0)	0043
No	9 (22.5)	3 (7.5)	4 (10)	0(0)	.001*
Once a day	11 (27.5)	13 (32.5)	9 (22.5)	10 (25)	
More than once a	7 (17.5)ª	5 (12.5) <sup>6</sup>	8 (20) <sup>c</sup>	25 (62.5)	
Irregular	13 (32 5)	19 (47 5) <sup>b</sup>	19 (47 5) <sup>c</sup>	5 (12 5)	
lse of oral care products su	ch as dental floss interface brus	h and mouthwash	17 (47.3)	5 (12.5)	
Voc	2 (7 5) <sup>a</sup>	2 (5) <sup>b</sup>	1 (2 6)	10 (47 5)	001
No	3 (7.3)	2 (J)	1 (2.0)	17 (47.5)	.001
ino	37 (72.3)	30 (93)	36 (77.4)	21 (52.5)	
Maa	24 ((0)	24 (52 5)	20 (50)	22 (57 5)	700
res	24 (60)	21 (52.5)	20 (50)	23 (57.5)	./99
	16 (40)	19 (47.5)	20 (50)	17 (42.5)	
moking pack-years					
Never smoked	24 (60)	17 (42.5)	16 (40) <sup>c</sup>	31 (77.5)	.009
≤20 × 00	12 (30)	18 (45)	17 (42.5)	9 (22.5)	
>20	4 (10)	5 (12.5)	/ (17.5)	0 (0)	
Icohol consumption					
Yes	4 (10)	6 (15)	5 (12.5)	8 (20)	.062
No	36 (90)	34 (85)	35 (87.5)	32 (80)	
Mean YMRS	5 (1-8.5)	0 (0-2)	21 (19-25.9)	None	.001
Vean HAMD	4 (4-5)	6 (5-6)	6 (5-6)	None	.001
Mean CGI-s	3.5 (0-6)	16.5 (14-21)	0 (0-2)	None	.001

Note: Data are expressed as number (percentage) and mean ± standard deviation or median (25%-75% quantile). p-Values obtained from chi-square test for categorical variables with Bonferroni correction. p-Values obtained from Kruskal-Wallis test for non-parametric numerical variables and one-way ANOVA test for parametric numerical variables.

Abbreviations: BMI, body mass index; CGI-s, Clinical Global Impressions Scale; HAMD, Hamilton Scale; YMRS, Young Mania Rating Scale.

<sup>a</sup>Significant difference between health and euthymic groups (p < .05).

<sup>b</sup>Significant difference between health and depression groups (p < .05).

<sup>c</sup>Significant difference between health and mania groups (p < .05).

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Multi-collinearity was checked by calculating variance inflation factors (VIFs), and no variables with VIF >5 were identified. Statistical analysis was performed with SPSS for Windows version 24.0, and a p-value <.05 was accepted as statistically significant.

#### RESULTS 3

#### 3.1 **Demographic variables**

Table 1 reports the characteristics of the study population. There was no difference in age, sex or BMI among the groups (p = .933, .599, 1.000, respectively). Marital status, smoking and alcohol consumption were similar among the groups (p = .131, .799, .62, respectively). Education level (lower), monthly income (lower), place of residence, frequency of dental check-ups (irregular), toothbrushing frequency

(lower/irregular), use of oral care products such as dental floss, interspace brushes and mouthwash (lower) and smoking pack-years (never smoking was lower) were different for each bipolar disorder group compared with the systemically healthy group (p = .001, .001, .046,.007, .001, .001, .009, respectively). These variables were similar among the euthymic, depression and mania groups.

YMRS, HAMD and CGI-s scores were different among the bipolar groups (p = .001).

#### **Clinical periodontal findings** 3.2

Table 2 reports the periodontal conditions of the study groups. Periodontitis prevalence was different among the groups (p = .001). Periodontitis prevalence was higher (p = .020, .001, .040, respectively), and periodontal health prevalence was lower (p = .012, .001,

#### TABLE 2 Periodontal conditions in bipolar disorder and systemically healthy groups.

Euthymic group (n = 40) $4 (10)^{a}$ 12 (30) $24 (60)^{a}$	Depression group ( $n = 40$ ) 2 (5) <sup>b</sup> 8 (20)	Mania group (n = 40) 3 (7.5) <sup>c</sup>	Health group (n = 40) 16 (40)	<i>p</i> -Value
4 (10) <sup>a</sup> 12 (30) 24 (60) <sup>a</sup>	2 (5) <sup>b</sup> 8 (20)	3 (7.5) <sup>c</sup>	16 (40)	001
4 (10) <sup>a</sup> 12 (30) 24 (60) <sup>a</sup>	2 (5) <sup>b</sup> 8 (20)	3 (7.5) <sup>c</sup>	16 (40)	001
12 (30) 24 (60) <sup>a</sup>	8 (20)			.001
24 (60) <sup>a</sup>		14 (35)	13 (32.5)	
_ (+ +)	30 (75) <sup>b</sup>	23 (57.5) <sup>c</sup>	11 (27.5)	
4 (16.7)	5 (16.7)	10 (38.5)	1 (9.1)	.117
9 (37.5)	11 (36.7)	4 (15.4)	6 (54.5)	
10 (41.7)	9 (30)	7 (26.9)	4 (36.4)	
1 (4.2)	5 (16.7)	5 (19.2)	1 (4.2)	
6 (25)	9 (30)	10 (40)	3 (30)	.717
18 (75)	21 (70)	15 (60)	7 (70)	
1 (8.3)	1 (12.5)	O (O)	4 (30.8)	.098
11 (91.7)	7 (87.5)	14 (100)	9 (69.2)	
20.69 (0-56.84)	34.57 (7.74–53.39) <sup>b,d</sup>	16.37 (0-46.88)	0 (0-19.35)	.002
0 (0-22.33) <sup>a</sup>	13.1 (0–28.87) <sup>b</sup>	0 (0–20.77) <sup>c</sup>	0 (0-6.73)	.014
2 (1.61-2.57) <sup>a</sup>	2 (1.95–2.22) <sup>b</sup>	1.97 (1.72–2.3) <sup>c</sup>	1 (0.39–1.96)	.001
2.02 (1.65-2.93) <sup>a</sup>	2.03 (1.97-2.78) <sup>b</sup>	2 (1.71–2.47) <sup>c</sup>	1.2 (0.34–1.92)	.001
100 (72.32-100) <sup>a</sup>	100 (86.4–100) <sup>b</sup>	100 (75.37–100) <sup>c</sup>	35 (3.13-98.54)	.001
3.1 (2.23-3.82) <sup>a</sup>	3.35 (2.86–4.23) <sup>b</sup>	3.26 (2.75–3.79) <sup>c</sup>	2.18 (1.55-3.43)	.001
3.13 (2.23-3.82) <sup>a</sup>	3.36 (2.86-4.72) <sup>b</sup>	3.26 (2.75–3.9) <sup>c</sup>	2.18 (1.5-3.45)	.001
2 (0-6) <sup>a</sup>	2 (0–5) <sup>b</sup>	1 (0-4)	0 (0-2)	.036
	24 (60) <sup>a</sup> 4 (16.7) 9 (37.5) 10 (41.7) 1 (4.2) 6 (25) 18 (75) 11 (8.3) 11 (91.7) 20.69 (0-56.84) 0 (0-22.33) <sup>a</sup> 2 (1.61-2.57) <sup>a</sup> 2.02 (1.65-2.93) <sup>a</sup> 100 (72.32-100) <sup>a</sup> 3.1 (2.23-3.82) <sup>a</sup> 3.13 (2.23-3.82) <sup>a</sup>	12 (30)    8 (20)      24 (60) <sup>a</sup> 30 (75) <sup>b</sup> 4 (16.7)    5 (16.7)      9 (37.5)    11 (36.7)      10 (41.7)    9 (30)      1 (4.2)    5 (16.7)      6 (25)    9 (30)      18 (75)    21 (70)      11 (8.3)    1 (12.5)      11 (91.7)    7 (87.5)      20.69 (0-56.84)    34.57 (7.74-53.39) <sup>b.d</sup> 0 (0-22.33) <sup>a</sup> 13.1 (0-28.87) <sup>b</sup> 2 (1.61-2.57) <sup>a</sup> 2 (1.95-2.22) <sup>b</sup> 100 (72.32-100) <sup>a</sup> 100 (86.4-100) <sup>b</sup> 3.1 (2.23-3.82) <sup>a</sup> 3.35 (2.86-4.23) <sup>b</sup> 3.13 (2.23-3.82) <sup>a</sup> 3.36 (2.86-4.72) <sup>b</sup>	12 (30)    8 (20)    14 (35)      24 (60) <sup>a</sup> 30 (75) <sup>b</sup> 23 (57.5) <sup>c</sup> 4 (16.7)    5 (16.7)    10 (38.5)      9 (37.5)    11 (36.7)    4 (15.4)      10 (41.7)    9 (30)    7 (26.9)      1 (4.2)    5 (16.7)    5 (19.2)      6 (25)    9 (30)    10 (40)      18 (75)    21 (70)    15 (60)      1 (8.3)    1 (12.5)    0 (0)      11 (91.7)    7 (87.5)    14 (100)      20.69 (0-56.84)    34.57 (7.74-53.39) <sup>b.d</sup> 16.37 (0-46.88)      0 (0-22.33) <sup>a</sup> 13.1 (0-28.87) <sup>b</sup> 0 (0-20.77) <sup>c</sup> 2 (1.61-2.57) <sup>3</sup> 2 (1.95-2.22) <sup>b</sup> 1.97 (1.72-2.3) <sup>c</sup> 2.02 (1.65-2.93) <sup>a</sup> 2.03 (1.97-2.78) <sup>b</sup> 2 (1.71-2.47) <sup>c</sup> 100 (72.32-100) <sup>a</sup> 100 (86.4-100) <sup>b</sup> 100 (75.37-100) <sup>c</sup> 3.13 (2.23-3.82) <sup>a</sup> 3.35 (2.86-4.23) <sup>b</sup> 3.26 (2.75-3.9) <sup>c</sup> 3.13 (2.23-3.82) <sup>a</sup> 3.36 (2.86-4.72) <sup>b</sup> 3.26 (2.75-3.9) <sup>c</sup> 2 (0-6) <sup>a</sup> 2 (0-5) <sup>b</sup> 1 (0-4)	12 (30)8 (20)14 (35)13 (32.5)24 (60)a30 (75)b23 (57.5)c11 (27.5)4 (16.7)5 (16.7)10 (38.5)1 (9.1)9 (37.5)11 (36.7)4 (15.4)6 (54.5)10 (41.7)9 (30)7 (26.9)4 (36.4)1 (4.2)5 (16.7)5 (19.2)1 (4.2)6 (25)9 (30)10 (40)3 (30)18 (75)21 (70)15 (60)7 (70)1 (8.3)1 (12.5)0 (0)4 (30.8)11 (91.7)7 (87.5)14 (100)9 (69.2)20.69 (0-56.84)34.57 (7.74-53.39) <sup>b,d</sup> 16.37 (0-46.88)0 (0-19.35)0 (0-22.33)a13.1 (0-28.87)b0 (0-20.77)c0 (0-6.73)2 (1.61-2.57)b2 (1.95-2.22)b1.97 (1.72-2.3)c1 (0.39-1.96)2.02 (1.65-2.93)a2.03 (1.97-2.78)b2 (1.71-2.47)c1.2 (0.34-1.92)100 (72.32-100)a100 (86.4-100)b100 (75.37-100)c35 (3.13-98.54)3.1 (2.23-3.82)a3.35 (2.86-4.23)b3.26 (2.75-3.79)c2.18 (1.55-3.43)3.13 (2.23-3.82)a3.36 (2.86-4.72)b3.26 (2.75-3.9)c2.18 (1.5-3.45)2 (0-6)a2 (0-5)b1 (0-4)0 (0-2)

Note: Data are expressed as the number (percentage) and mean ± standard deviation or median (25%-75% quantile). p-Values obtained from chi-square test for categorical variables with Bonferroni correction. p-Values obtained from Kruskal-Wallis test for numerical variables and Dunn's multiple comparison tests for pairwise comparison.

Abbreviations: BOP, bleeding on probing; CAL, clinical attachment level; GI, gingival index; PI, plaque index; PPD, probing pocket depth.

<sup>a</sup>Significant difference between health and euthymic groups (p < .05).

<sup>b</sup>Significant difference between health and depression groups (p < .05).

<sup>c</sup>Significant difference between health and mania groups (p < .05).

<sup>d</sup>Significant difference between mania and depression groups (p < .05).

.040, respectively) in the euthymic, depression and mania groups compared with systemically healthy controls. There was no difference in gingivitis prevalence between the groups ( $p \ge .05$ ). The prevalence of periodontal diseases was similar among the euthymic, depression and mania groups ( $p \ge .05$ ). There were no differences in the severity (staging, p = .117) or extent (p = .717) of periodontitis, where present, between the groups. Likewise, the extent of gingivitis in patients with gingivitis was similar in all groups, although there was a tendency for the healthy controls to have more localized gingivitis (p = .098).

The percentage of sites with PPD  $\geq$ 4 mm was lower in the control and mania groups than in the depression group (p = .002, .0024, respectively). The percentage of sites with CAL  $\geq$ 3 mm was lower in the control group than in the euthymic, depression and mania groups (p = .11, .001, .024, respectively). PI, GI, BOP (%), PPD and CAL were higher in the bipolar groups than in the control group ( $p \geq .05$ ). There were more missing teeth in the euthymic and depression groups compared with controls (p = .009, .016, respectively).

Adjusted results of clinical periodontal parameters were shown by the generalized linear model analysis (Table S1). Bipolar disorder groups were associated with an increase in clinical parameters when compared with the control group (p < .05). There was no difference between the mania and control groups in the number of missing teeth (p = .202). These associations were found after adjusting for age, sex, BMI, education levels, monthly income, marital status, place of residence, frequency of dental check-ups, toothbrushing frequency, smoking and alcohol consumption.

### 3.3 | OHIP-14 scores

Table 3 reports the comparison of the overall OHIP-14 scores according to groups. Total OHIP-14, functional limitation and physical pain scores differed among the groups (p = .024, .001, .031,

respectively). The total OHIP-14 score was higher in the depression group compared with controls (p = .02). The control group showed lower functional limitation scores than the euthymic, depression and mania groups (p = .014, .04, .001, respectively). Physical pain was scored higher by those in the depression group than those in the euthymic and control groups (p = .049, .004, respectively). Otherwise, physical pain, psychological disability, social disability and handicap scores were not significantly different among the groups ( $p \ge .05$ ).

Table 4 reports the comparison of the overall OHIP-14 scores in patients with bipolar disorder according to the presence of periodontitis. The total score and psychological disability scores had a tendency to be higher for patients with periodontitis, but these and the scores for functional limitation, physical pain, social disability and handicap were similar regardless of absence or presence of periodontitis (p = .056, .054, .182, .173, .353, .197, respectively). Psychological discomfort and physical disability scores were higher in the presence of periodontitis (p = .033, .040, respectively).

### 3.4 | Correlations

The correlations between periodontal parameters and overall OHIP-14 and CGI-s scores in patients with bipolar disorder were shown (Table S2). There was a positive correlation between CAL and CGI-s in patients with bipolar disorder (r = .183) (p < .05). There were modest statistically significant positive correlations between each of the total score, functional limitation, physical pain, psychological discomfort, physical disability, psychological disability and handicap and the PPD score (r = .236, .194, .196, .291, .255, .190, respectively) (p < .05). There were also modest statistically significant positive correlations between each of the total score, functional limitation, physical pain, psychological discomfort, psychological disability, and handicap and

TABLE 3 Comparison of Oral Health Impact Profile (OHIP)-14 total and sub-item scores in bipolar disorder and systemically healthy groups.

Variable	Euthymic group (n = 40)	Depression group $(n = 40)$	Mania group (n = 40)	Health group ( $n = 40$ )	p- Value
OHIP-14 total score	6.5 (2-10)	8 (3.5–15)†	6 (3-14)	4 (1-9.5)	.024
Functional limitation	1 (0-2) <sup>a</sup>	2 (0–2) <sup>b</sup>	1 (0-2) <sup>c</sup>	0 (0–0)	.001
Physical pain	2.5 (1-3)	3 (2-4) <sup>b,d</sup>	2 (1.5-4)	2 (1-3)	.031
Psychological discomfort	1 (0-1.5)	1 (0-2)	1 (0-2)	0 (0-1)	.050
Physical disability	1 (0-2)	1 (0-2)	1 (0-2)	0 (0-1)	.091
Psychological disability	1 (0-1)	1 (0-2)	1 (0-2)	0 (0-1)	.312
Social disability	0 (0-1)	0 (0-1)	0 (0-1)	0 (0–0)	.781
Handicap	0 (0-1)	0 (0-1.5)	0 (0-1.5)	0 (0-1)	.181

Note: Data are expressed as median (25%–75% quantile). p-Values obtained from Kruskal–Wallis test for numerical variables, and Dunn's multiple comparison tests were performed for pairwise comparison.

<sup>a</sup>Significant difference between health and euthymic groups (p < .05).

<sup>b</sup>Significant difference between health and depression groups (p < .05).

<sup>c</sup>Significant difference between health and mania groups (p < .05).

<sup>d</sup>Significant difference between mania and depression groups (p < .05).

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8

	Periodontitis	Non-periodontitis	
Variables	(n = 43)	(n = 77)	p-Value
OHIP-14 total score	6 (3-11)	8 (3–17)	.056
Functional limitation	1 (0-2)	1 (0-2)	.182
Physical pain	2 (2-3)	3 (2-4)	.174
Psychological discomfort	0 (0-1)	1 (0-2)	.033
Physical disability	1 (0-1)	1 (0-2)	.040
Psychological disability	0 (0-1)	1 (0-2)	.054
Social disability	0 (0-1)	0 (0-1)	.353
Handicap	0 (0-1)	0 (0–2)	.197

TABLE 4 Comparison of Oral Health Impact Profile (OHIP)-14 total and subitem scores according to the presence of periodontitis in patients within the combined bipolar disorder groups.

Note: Data are expressed as median (25%-75% quantile). p-Values obtained from Mann-Whitney U test for numerical variables.

TABLE 5 Results from generalized linear models evaluating associations between bipolar disorder groups and the Oral Health Impact Profile (OHIP)-14 total and sub-item scores.

	Dependent variable	Independent variable	Median (25%–75% quantile)	Coefficient (95% CI)	<b>p</b> Adjusted
	OHIP-14 total score	Euthymic	6.5 (2-10)	-0.26 (-3.61 to 3.09)	.878
		Depression	8 (3.5–15)	3.32 (0.08-6.56)	.044
		Mania	6 (3-14)	1.86 (-1.42 to 5.14)	.267
		Health	4 (1-9.5)	1 (Reference)	
	Functional limitation	Euthymic	1 (0-2)	0.32 (-0.31 to 0.96)	.316
		Depression	2 (0–2)	0.89 (0.27-1.49)	.005
		Mania	1 (0-2)	0.51 (-0.11 to 1.12)	.11
		Health	0 (0-1)	1 (Reference)	
	Physical pain	Euthymic	2.5 (1-3)	-0.11 (-0.76 to 0.54)	.737
		Depression	3 (2–4)	0.64 (0.01-1.27)	.046
		Mania	2 (1.5-4)	0.17 (-0.47 to 0.81)	.61
		Health	2 (1-3)	1 (Reference)	
	Psychological discomfort	Euthymic	1 (0-1.5)	-008 (-0.76 to 0.59)	.066
		Depression	1 (0-2)	0.39 (-0.26 to 0.05)	.812
		Mania	1 (0-2)	0.47 (-0.19; 1.14)	.238
		Health	0 (0-1)	1 (Reference)	.166
	Physical disability	Euthymic	1 (0-2)	0.15 (-0.5 to 0.80)	.655
		Depression	1 (0-2)	0.39 (-0.23; 1.02)	.219
		Mania	1 (0-2)	0.29 (-0.34 to 0.93)	.365
		Health	0 (0-1)	1 (Reference)	
	Psychological disability	Euthymic	1 (0-1)	-0.15 (-0.65 to 0.36)	.432
		Depression	1 (0-2)	0.14 (-0.34 to 0.63)	.189
		Mania	1 (0-2)	0.01 (-0.48 to 0.50)	.781
		Health	0 (0-1)	1 (Reference)	
	Social disability	Euthymic	0 (0-1)	-0.15 (-0.65 to 0.36)	.572
		Depression	0 (0-1)	0.14 (-0.3 to 0.63)	.564
		Mania	0 (0-1)	0.01 (-0.48 to 0.51)	.965
		Health	0 (0–0.5)	1 (Reference)	
	Handicap	Euthymic	0 (0-1)	-0.13 (-0.65 to 0.39)	.620
		Depression	0 (0-1.5)	0.31 (-0.21 to 0.81)	.241
		Mania	0 (0-1.5)	0.30 (-0.21 to 0.81)	.255
		Health	0 (0-1)	1 (Reference)	

Note: pAdjusted obtained from generalized linear model adjusted for age, sex, body mass index, education levels, monthly income, marital status, place of residence, frequency of dental check-ups, toothbrushing frequency, smoking and alcohol consumption. Abbreviation: CI, confidence interval.

DHIP)-14 total and sub-item scores	in patients within combined bipola	ar disorder groups.		
Dependent variable	Independent variable	Median (25%–75% quantile)	Coefficient (95% CI)	р <sub>Аdju</sub>
OHIP-14 total score	Stage III-IV periodontitis	6 (3-9.5)	3.21 (-0.64 to 7.07)	.103
	Stage I–II periodontitis	7 (3–15)	2.03 (-1.44 to 5.51)	.252
	Non-periodontitis	6 (3-9.5)	1 (Reference)	
Functional limitation	Stage III-IV periodontitis	2 (0-2)	0.31 (-0.42 to 1.04)	.409
	Stage I–II periodontitis	1 (0-2)	0.08 (-0.58 to 0.74)	.807
	Non-periodontitis	1 (0-2)	1 (Reference)	
Physical pain	Stage III-IV periodontitis	2 (2-3)	0.47 (-0.25 to 1.97)	.201
	Stage I–II periodontitis	3 (2-4)	-0.18 (-0.67 to 0.64)	.956
	Non-periodontitis	2 (2-3)	1 (Reference)	
Psychological discomfort	Stage III–IV periodontitis	0 (0-1)	0.60 (-0.15 to 1.35)	.115
	Stage I–II periodontitis	1 (0-2)	0.60 (-0.08 to 1.28)	.115
	Non-periodontitis	1 (0-2)	1 (Reference)	
Physical disability	Stage III–IV periodontitis	1 (0-2)	0.41 (-0.28 to 1.10)	.246
	Stage I–II periodontitis	1 (0-3)	0.48 (-0.14 to 1.10)	.130
	Non-periodontitis	1 (0-1)	1 (Reference)	
Psychological disability	Stage III–IV periodontitis	1 (0-3)	0.83 (0.07-1.59)	.033
	Stage I–II periodontitis	1 (0-2)	0.56 (-0.13 to 1.25)	.112
	Non-periodontitis	0.5 (0-1)	1 (Reference)	
Social disability	Stage III–IV periodontitis	0 (0-1)	0.16 (-0.41 to 0.739)	.582
	Stage I–II periodontitis	0 (0-1)	0.18 (-0.33 to 0.69)	.497
	Non-periodontitis	0 (0-1)	1 (Reference)	
Handicap	Stage III-IV periodontitis	0 (0-2)	0. 43 (-0.18 to 1.04)	.167
	Stage I–II periodontitis	0 (0-2)	0.21 (-0.18 to 1.04)	.458
	Non-periodontitis	0 (0-1)	1 (Reference)	

TABLE 6 Results from generalized linear models evaluating associations between periodontitis severity and the Oral Health Impact Profile (OH

Note: pAdjusted obtained from generalized linear model adjusted for age, sex, body mass index, education levels, monthly income, marital status, place of residence, frequency of dental check-ups, toothbrushing frequency, smoking and alcohol consumption. Abbreviation: CI, confidence interval.

the CAL score (r = .257, .207, .218, .309, .271, .183, respectively) (p < .05). Finally, a modest statistically significant positive correlation existed between physical pain and the missing number of teeth (r = .199) (p < .05). Other correlations were not significant  $(p \ge .05)$ .

The plots with confidence intervals (CIs) for the OHIP-14 total score in bipolar episode groups are shown in Figure S1. There were positive correlations between PPD, CAL and the number of missing teeth and the OHIP-14 total score in the mania group (r = .324, .321,.325, respectively). There was no significant correlation in the euthymic and depression groups ( $p \ge .05$ ).

Further analyses showed positive correlations between total, functional limitation and handicap scores and the HAMD score in the depression group (r = .348, .380, .380, respectively). There was no correlation between the overall OHIP-14 scores and YMRS scores in the mania group ( $p \ge .05$ ).

Table 5 reports the associations between overall OHIP-14 scores and bipolar disorder episodes using a generalized linear model (n = 160). OHIP-14 total score  $(\beta = 3.32, 95\%$  CI: 0.08-6.56, p = .044), functional limitation ( $\beta = .89$ , 95% CI: 0.27–1.49, p = .005)

and physical pain ( $\beta$  = .64, 95% CI: 0.01–1.27, p = .046) were associated with bipolar depression episodes. These associations were adjusted for age, sex, BMI, education levels, monthly income, marital status, place of residence, frequency of dental check-ups, toothbrushing frequency, smoking and alcohol consumption.

Table 6 reports the associations between overall OHIP-14 scores and periodontitis stage using a generalized linear model in bipolar patients (n = 120). Psychological disability was associated with the presence of stage III-IV periodontitis ( $\beta = .83$ , 95% CI: 0.07-1.59, p = .033). These associations were adjusted for age, sex, BMI, education levels, monthly income, marital status, place of residence, frequency of dental check-ups, toothbrushing frequency, smoking and alcohol consumption.

#### DISCUSSION 4

This is the first study to evaluate the associations between periodontal conditions in patients with different episodes of bipolar disorder WILEY Journal of Clinical Periodontology

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and OHRQoL to the best of our knowledge. The results of the present study show that bipolar disorder episodes affect the presence of periodontal disease. The majority of clinical periodontal parameters were lower in the systemically healthy group compared with bipolar groups after taking into consideration confounding factors. The total OHIP-14, functional limitation and physical pain scores were adversely affected by depression episodes in patients with bipolar disorder. Psychological discomfort and psychological disability were related to periodontitis severity in patients with bipolar disorders.

Bipolar disorders are a life-long illness that is characterized by the repetition of different episodes and can lead to impairments in health and functionality-related quality of life (Rosa et al., 2008). The episode symptoms associated with these disorders can affect areas of social and occupational functioning and cause remarkable impairment and distress in many areas of personal life (Lu et al., 2020). The results of the present study showed that the education level (lower), monthly income (lower), place of residence (higher in outside of city), frequency of dental check-ups (irregular), toothbrushing frequency (lower) and use of oral care products such as dental floss (lower), interspace brushes and mouthwash (lower) were different for each bipolar disorder group compared with the systemically healthy group. Although there were no differences in smoking status and the number of pack-years when participants who smoked were separated according to the number of pack-years, the number of individuals who had never smoked was less in the depression and mania groups than in the healthy group. It was reported that bipolar disorder is associated with lower socio-economic status, which includes family income, education level and neighbourhood experience (Bradley & Corwyn, 2002; Lu et al., 2020). In agreement with the literature, our findings suggest that bipolar disorder is affected by the education level, monthly income and place of residence of patients (Bradley & Corwyn, 2002; Lu et al., 2020). A previous study had shown that patients with depressive episodes neglect oral care, leading to an increased risk of periodontal disease and dental caries (Sjögren & Nordström, 2000). The lower socio-economic status and the effect of changing episodes can lead to inadequate oral hygiene habits and dental check-ups. Also, smoking is higher in patients with bipolar disorder than in the general population (Heffner et al., 2011). This is related to the impact of smoking on serotonin levels and brain serotonergic function (Malone et al., 2003). Hence, these conditions are likely to have a significant deleterious effect by increasing the impact of a range of risk factors in terms of oral self-care and overall health behaviours and direct and indirect impacts on associated risk factors for periodontal diseases.

The link between bipolar disorder and periodontal diseases has been demonstrated (Cunha et al., 2019; Huang et al., 2020). Risk factors such as smoking, immune-inflammatory response and the gramnegative periodontopathogen pathway are potential mechanisms that are associated with both diseases (Cunha et al., 2019; Haditsch et al., 2020; Malone et al., 2003). Also, the loss of interest in self-care can cause poor oral hygiene. Worsening oral health in the long term in bipolar patients and subsequent advanced periodontal disease and caries have been reported (Gurbuz Oflezer et al., 2018). The present study showed that periodontitis prevalence was higher and

periodontal health prevalence was lower in each of the three bipolar disorder groups than in systemically healthy controls. The percentage of sites with PPD ≥4 mm was lower in the control group than in the bipolar disorder groups. The percentage of sites with CAL ≥3 mm was lower in the control and mania groups than in the depression group. The levels of periodontal disease present in the control group were similar to those reported in a previous study in a Turkish population (Ilhan et al., 2017). In this study, we only recruited participants with at least 20 teeth. This was to exclude the potential impact of previous tooth loss on disease severity assessment, especially given that it is often difficult to ascertain the exact reasons for such events. Furthermore, such a design also ensures that there will still be a range of active periodontitis exposures, and hence the impact of and relationship with the extent and severity of periodontal disease may be easier to determine. The findings of the present study suggest that nondepressive episodes can be associated with improved periodontal health, possibly related to more thorough self-care and better compliance with oral hygiene regimes, although the levels of the disease do tend to be worse compared with controls. In addition, bipolar groups were associated with an increase in most clinical parameters after considering confounding factors. A nationwide cohort study reported that bipolar disorder incidence rate was higher in those with periodontitis than in the controls (2.74 vs. 1.46 per 1000 person-years), after adjusting for confounding factors (Chang et al., 2020). Another study noticed that the incidence rate of bipolar disorder was higher in a chronic periodontitis group than in controls (adjusted odds ratio (OR): 1.46, 95% CI: 1.17-1.81) (Huang et al., 2020). A cross-sectional study showed that the prevalence of periodontitis was higher in patients with bipolar disorder than in controls (OR = 2.13, 95% CI: 1.39–3.27). Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans were higher in patients with periodontitis and bipolar disorder. Periodontitis was associated with the depressive phase of bipolar disorder (OR = 28.94; 95% CI: 4.44-177.27) (Cunha et al., 2019). The findings of the present study support those of the above studies. It suggests that patients with bipolar disorder tend to neglect oral care, leading to an increased risk of periodontal disease. The episodes of bipolar patients can make oral care a low priority in their lives and prevent awareness of their periodontal disease.

The episodes of bipolar disorder had negative effects on the quality of life (MacQueen et al., 2000; Vojta et al., 2001). To the best of our knowledge, there is no study in the literature that evaluated the relationship between bipolar disorder and OHRQoL. Results of the present study show that the total OHIP-14 score is higher in the depression group than in controls. The control group showed lower functional limitation scores than those in the euthymic, depression and mania groups. Physical pain was scored higher by those in the depression group compared with those in the euthymic and control groups. OHIP-14 total score ( $\beta = 3.32, 95\%$  CI: 0.08–6.56, p = .044), functional limitation ( $\beta = .89, 95\%$  CI: 0.27–1.49, p = .005) and physical pain ( $\beta = .64, 95\%$  CI: 0.01–1.27, p = .046) were associated with the bipolar depression episode. In psychiatrists' studies, in which they focused on bipolar patient groups, they reported that mania and hypomania were associated with decreased quality of life and that depressive episode was a stronger determinant of decreased quality of life (MacQueen et al., 2000; Vojta et al., 2001). Although the symptoms are fewer in euthymic episode than in other episodes, they are not asymptomatic. Decreased quality of life was first associated with this episode, but the depression episode showed a significantly lower QoL score (Vojta et al., 2001). A study showed the effect of subthreshold symptoms on functioning/disability and quality of life in patients with bipolar disorder (Bonnín et al., 2012). Another study reported that bipolar depression had a serious detrimental impact on the quality of life (Yatham et al., 2004). Also, the relationship between pain, depression and poor quality of life has been demonstrated (Stafford et al., 2007). Pain is often responsible for secondary depression through common pathophysiological mechanisms or cognitive mediators, and vice versa (Radat & Koleck, 2011). A study that evaluated functional and symptomatic outcomes in bipolar disorder reported that mania and depression are associated with poor functional outcomes (Kebede et al., 2006). Findings of the present study are in agreement with these results as regards total score and functional limitation scores. Similarly, depression episode had an association with some OHRQoL scores. It suggests that bipolar patients are more focused on the problem of functional limitation in relation to their oral health. Depression episode has a higher impact on OHROoL in bipolar disorder.

Periodontal disease negatively affects OHRQoL (Ferreira et al., 2017; Needleman et al., 2004). Though OHIP total score is the important variable for this study, we believe that sub-score results also offer useful insight. These variables can be important to facilitate comparisons with the methods used in previous studies (Gerritsen et al., 2010; Levin et al., 2018; Oliveira et al., 2020; Rebelo et al., 2016). It has been suggested that the association between tooth loss (possibly related to periodontal disease) and impaired QoL is related to loss of functional capacity and pain (Gerritsen et al., 2010). The present study showed that the total score and the psychological disability and discomfort score had a tendency to be higher for in patients with bipolar disorder with periodontitis. Also, psychological disability is associated with the presence of stage III–IV periodontitis ( $\beta$  = .83, 95% CI: 0.07–1.59, p = .033). Although there is no study that evaluated the association between periodontitis and OHRQoL in patients with bipolar disorder, some previous studies have evaluated the impact of periodontal disease on other systemic diseases. A study reported that periodontal disease affects OHRQoL in patients with systemic arterial hypertension (Rebelo et al., 2016). Oliveira et al. showed that severe periodontitis had an association with physical pain (risk ratio (RR) = 1.75, 95% CI: 1.08-2.83), psychological discomfort (RR = 1.81, 95% Cl: 1.09-3.00), physical disability (RR = 2.57, 95% Cl: 1.12-5.91) and psychological disability (RR = 2.58, 95% CI: 1.22-5.45) in patients with end-stage renal disease (Oliveira et al., 2020). On the other hand, in a study using the OHIP-49 scale, it was reported that there was no significant change in OHRQoL scores following periodontal treatment in patients with diabetes. This result was explained by the fact that diabetic patients were less concerned about their periodontal status than systemic healthy controls (Irani et al., 2015). The findings of the present study are compatible with those of the previous studies. Based on the results of the present

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study, it can be suggested that the prevalence and severity of periodontitis affect OHRQoL in patients with bipolar disorder. Furthermore, periodontitis severity can have an impact on patient-reported psycho-social outcomes regarding OHRQoL in depression episodes.

\*\*There was a positive correlation between CAL and CGI-s in patients with bipolar disorder. The correlation between these two parameters, which shows the severity of periodontitis and bipolar disease, may be an important finding to support the risk relationship between both diseases. Although cross-sectional design is a limitation for this interpretation, bipolar diseases can pose a risk for the development and progression of periodontal diseases, and vice versa. In addition, there were modest significant positive correlations between the total score, functional limitation, physical pain, psychological discomfort, physical disability, psychological disability and handicap with PPD and CAL scores in patients with bipolar disorder. A modest significant positive correlation was found to exist between physical pain and the number of missing teeth. All OHROoL scores except physical and social disability had a positive correlation with PPD and CAL, which indicate the severity of periodontitis. Also, OHIP total score was positively correlated with the mean PPD and mean CAL and the number of missing teeth in the mania groups when analyses were performed separately for different bipolar disorder episodes. A systematic review, involving 34 cross-sectional studies, showed that OHRQoL is negatively impacted by periodontal disease and that increased severity of the disease leads to a greater negative impact (Ferreira et al., 2017). Another study reported a positive correlation between higher OHROoL scores and the number of teeth with PPD = 5 mm (Needleman et al., 2004). These findings imply that the severity of periodontal disease negatively affects OHROoL in patients with bipolar disorder.

The cross-sectional design and blinding status were limitations of the present study. The periodontal examiner was not blinded to the patients with bipolar disorder and control participants. The selection of the control group that was applying for dental treatment can be another limitation. The frequency of dental visits might be influenced in this group. The prevalence of periodontitis is increasing in older population because of the cumulative and chronic nature of the disease (Eke et al., 2016). Thus, the low mean age of the participants (35 years) was another limitation. The distribution of periodontitis severity may not have included the more severe cases. Further studies, including longitudinal cohorts with larger study populations, are needed to explain the association between periodontal diseases and bipolar disorder and the effect of periodontitis on OHRQoL in patients with bipolar disorder.

Considering the findings of the present study, bipolar disorder, which makes it difficult to maintain the basic life needs of the patient, can lead to neglect of oral health. Periodontitis can be an additional burden for the already deteriorated quality of life in these patients. The present study highlights the importance of periodontal status determination in bipolar patients. Multidisciplinary approaches such as preventive oral health applications and periodontal treatments are important to provide the optimum oral health and quality of life in these patients. <sup>12</sup> WILEY Periodontolog

Within the limitations of this study, the results indicate that bipolar disorder episodes may be associated with the prevalence and severity of periodontitis and the reported OHRQoL. Bipolar patients are focused on functional limitations in relation to their oral health. Bipolar depression episode had a higher effect on OHRQoL.

### AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Data collection was performed by Aysegul Sari and M. Hanifi Kokacya. All authors contributed to the writing of the first draft of the manuscript and further revisions. All authors read and approved the final manuscript.

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### CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### ETHICS STATEMENT

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This work was approved by the Ethics Committee for the use of Human Subjects in Research, Hatay Mustafa Kemal University, Hatay, Turkey (Protocol No: 2018/116).

### ORCID

Aysegul Sari (D) https://orcid.org/0000-0001-6180-9776 M. Hanifi Kokacya 🕩 https://orcid.org/0000-0002-2961-7229 Mark Ide D https://orcid.org/0000-0002-6511-7803

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### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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