Prevalence of periodontitis in patients with inflammatory bowel disease: a case-control study in an Italian population

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Word count: 2.940

Tables and figures: 5

Conflict of interest and source of funding:

The authors do not have any financial interests, either directly or indirectly, in the information listed in the paper.

Abstract *(English version)*

Aim: To estimate the prevalence of periodontitis in patients with Crohn's disease (CD) or ulcerative colitis (UC) and age- and gender-matched controls without inflammatory bowel disease (IBD).

Material and Methods: One hundred eighty IBD (117 CD, 60 UC, 3 IBD-unclassified) and 180 healthy controls were compared for their periodontitis diagnosis (CDC/AAP case definition) and full-mouth periodontal parameters. In addition, explorative logistic regression models were performed.

Results: Significantly more patients with IBD had periodontitis (85.6% vs 65.6%, $p<0.001$) and severe periodontitis (36.7% vs 25.6%, $p<0.001$) than controls. Differences were higher in the 35-50 and 51-65 age groups, without significant changes between CD and UC. IBD subjects presented chances ~3.5 higher of having moderate/severe periodontitis ($p<0.001$). Significant variables associated with periodontitis in the whole sample were older age, presence of IBD, and higher full-mouth plaque scores; whereas in the IBD group they were gender (male), IBD-associated surgery, IBD duration and localization (pancolitis). Positive risk indicators for IBD were periodontitis severity and higher bleeding scores, while smoking was negatively associated with UC.

Conclusions: Relevant associations between IBD and periodontitis were found, being modified by CD and UC clinical characteristics. Preventive and therapeutic strategies involving the gum-gut axis should be enforced in IBD patients.

Keywords: Gum-gut axis, Inflammation, Inflammatory disorders, Diagnosis, Oral health.

Abstract *(versione italiana)*

Obiettivo: Stimare la prevalenza della parodontite nei pazienti affetti da morbo di Crohn (CD) o rettocolite ulcerosa (UC) rispetto ad un gruppo di controllo, appaiato per età e per genere, privo di malattie infiammatorie intestinali (IBD).

Materiali e Metodi: Centottanta pazienti con IBD (117 CD, 60 UC e 3 con IBD indifferenziato) e 180 controlli sani sono stati confrontati sulla base della loro diagnosi di parodontite (definizione CDC/AAP) e dei parametri parodontali rilevati full-mouth. Inoltre, sono stati costruiti modelli esplorativi di regressione logistica.

Risultati: Un numero più elevato di pazienti con IBD presentava parodontite (85.6% vs 65.6%, $p<0.001$) e parodontite severa (36.7% vs 25.6%, $p<0.001$) rispetto ai controlli. Le differenze erano più marcate nelle fasce di età tra i 35-50 e i 51-65 anni, e rimanevano significative anche considerando separatamente CD e UC. Gli individui con IBD avevano una probabilità ~3 e ~4.5 volte più elevata di avere, rispettivamente, parodontite moderata e severa. Le variabili associate in modo significativo alla parodontite nell'intero campione erano età più avanzata, presenza di IBD, e percentuali più elevate di indice di placca. Se si prendevano in esame solo i pazienti con IBD, il genere (uomo), pregressi interventi chirurgici intestinali, la durata di malattia e la localizzazione di IBD (pancolite) erano associati in modo significativo con la presenza di parodontite. Dall'altro lato, la severità della parodontite e valori più elevati dell'indice di sanguinamento erano le variabili associate positivamente con IBD, mentre il tabagismo era associato negativamente con UC.

Conclusioni: È presente un'associazione significativa tra IBD e parodontite, modificata da alcune caratteristiche cliniche specifiche di CD e UC. Di conseguenza, dovrebbero essere implementate rilevanti strategie preventive e terapeutiche lungo l'asse oro-intestinale nei pazienti con questo tipo di disordini infiammatori.

Introduction

Inflammatory bowel disease (IBD) is a group of chronic and relapsing disorders of the gastrointestinal tract, Crohn's disease (CD) and Ulcerative Colitis (UC) being the main forms. IBD represents a significant health problem, with prevalence of about 187/100.000 and incidence of 12/100.000 in Italy (Tursi et al. 2013). The pathogenesis of IBD is not yet fully elucidated, involving genetic predisposition, environmental factors, gut microbial dysbiosis and dysregulated immune response (De Souza et al. 2017). The most common symptoms are abdominal cramps, vomiting, bloody diarrhea, urge to evacuate, tenesmus, fatigue, and weight loss, characterized by phases of quiescence and phases of flare-up of the disease (Ribaldone et al. 2019). CD can present with deep lesions of the gastrointestinal wall from the mouth to the anus, whereas UC affects the mucosa of the colon and rectum in a continuous way, with presence of erythema, erosions, and ulcers (Actis et al. 2019). Besides intestinal inflammatory activity and complications, which may require surgical treatment, extra-intestinal manifestations in IBD can occur in joints, skin, eyes, and mouth (Ribaldone et al. 2020; Rosso et al. 2021).

Periodontitis represents the sixth most common human disease, affecting up to 10% of the world population in its more severe forms (GBD 2020). On the top of being the main cause leading to tooth loss in the adults, chronic gum infection/inflammation underpinning periodontitis may lead to relapsing bacteremia, elevation of the systemic low-grade inflammatory burden, autoimmune dysregulations, and bacterial translocation to lower respiratory tract and digestive system (Hajishengallis and Chavakis 2021). In the light of these mechanisms, periodontitis has been robustly associated with a wide range of systemic diseases, including cardiovascular diseases, diabetes, rheumatoid arthritis, and gastrointestinal diseases (Genco and Sanz 2020; Baima et al. 2022a).

Following recent evidence that oral and gut environments are closely related under the microbiological and immunological perspective, a plausible bidirectional association between periodontitis and IBD is receiving growing scientific interest (Kitamoto et al. 2020a; Baima et al. 2021). Recent meta-epidemiologic data indicated that IBD was associated with a significantly increased risk of periodontitis compared to non-IBD patients (Papageorgiou et al. 2017; Zhang et al. 2021). However, most of the available literature presented arbitrary case definitions for periodontitis, inaccurate assessment of the outcomes, uneven samples of IBD and non-IBD patients, and the risk of residual confounders in the analyses (Grössner-Schreiber et al. 2006; Brito et al. 2008; Vavricka et al. 2013; Tan et al. 2021).

Therefore, the primary aim of this study was to investigate the prevalence of periodontitis in a sample of patients with CD and UC compared to an age and gender-matched control group of patients without IBD. The secondary aim was to explore the association between IBD activity and other disease characteristics including systemic markers of inflammation with the severity of periodontitis.

Materials and Methods

Patient selection

This case-control study was conducted in accordance with the Helsinki Declaration and approved by the Institutional Ethical Committee of the "AOU Città della Salute e della Scienza" of Turin (cod.: 00066/2021), and it complies with the STROBE guidelines. All participants signed an informed consent to undergo physical and periodontal examination.

Individuals treated as outpatients for IBD at the Department of Medical Sciences, University of Turin, were consecutively recruited from September 2020 to December 2021. The diagnosis of either CD or UC was confirmed by previously established clinical, radiological and endoscopic criteria (ECCO Guidelines 2021). Moreover, histological findings also had to be confirmative or compatible with this diagnosis. The same number of non-IBD subjects randomly selected from the C.I.R. Dental School, University of Turin, were compared with the study patients. Patients with IBD (cases) and the control group were recruited from the same population (Turin, North Italy). The control group and patients with IBD were matched referring to age, sex and ethnicity.

The following inclusion criteria were considered: (i) at least 18 years of age; (ii) having at least 6 teeth; (iii) availability of measurements of routine IBD-related laboratory tests made (C-reactive protein, calprotectin). Exclusion criteria were: (i) diabetes mellitus; (ii) intake of drugs known to affect gingival tissues; (iii) periodontal therapy in the past 3 months; (iv) pregnancy or lactation; and (v) diagnosis of following pathologies: cancer, human immunodeficiency virus/AIDS, liver/kidney failure.

Clinical examination

Participants were required to complete a questionnaire to obtain information on socio-demographic characteristics (gender, age, ethnicity, education), general health behavior (daily smoking and dietary habits, alcohol consumption), and oral hygiene behavior (frequency of dental examinations and professional oral hygiene sessions, toothbrushing frequency, use of interdental devices).

Baseline characteristics also included years from IBD diagnosis, localization and extraintestinal manifestations, previous surgery (ostomy or bowel resection), hypertension, C-reactive protein (CRP), and fecal calprotectin. Disease activity of CD was assessed using Harvey-Bradshaw index (HBI) (Peyrin-Biroulet et al. 2016), whereas disease activity of UC was assessed using the partial Mayo Score (PMI) (Lewis et al. 2008).

Patients received standard medical treatment including corticosteroids (prednisone or oral budesonide), immunosuppressants (e.g., azathioprine), amino-salicylate (e.g. 5-ASA), target therapies (e.g., anti-TNF, vedolizumab, ustekinumab) and antibiotics as mono- or combination therapy. None of the patients of the control group received any of the above-mentioned medical treatments.

Periodontal examination

The intra-oral examinations were conducted using a dental chair and included the presence of plaque and periodontal measurements [bleeding on probing (BoP), probing pocket depth (PPD), recession (Rec), clinical attachment loss (CAL)].

Full-mouth PPD, BoP, Rec and CAL were assessed at six sites per tooth, excluding third molars. The total percentages of sites exhibiting bacterial plaque or BoP were expressed as full mouth plaque score (FMPS) and full mouth-bleeding score (FMBS), respectively. The number of missing teeth was also recorded. All measurements were performed by means of a periodontal probe with 1-mm markings (PCP-UNC 15, Hu-Friedy, Chicago, IL, USA) and the readings were recorded to the nearest 1 mm. The PPD was measured from the gingival margin to the base of the probable sulcus/pocket. The presence or absence of BoP was recorded after 30 seconds. The CAL represented the distance between the cementoenamel junction (CEJ) and the base of the probable sulcus/pocket. In case a restoration extended apically to the CEJ or an abrasion was present at the tooth cervix, the position of the CEJ was estimated by extrapolating the position of the CEJ from the adjacent teeth. Measurements were taken by two calibrated examiners throughout the study for patients with IBD and controls, achieving substantial inter – examiner reproducibility (k ranging from 0.72 to 0.86, $p<0.001$) for all the variables analyzed.

The presence of periodontitis was defined according to the criteria proposed by Centers for Disease Control and Prevention/American Academy of Periodontology (CDC/AAP) for epidemiologic surveys (Page and Eke 2007, Page et al. 2012). Therefore, moderate periodontitis was defined as at least 2 interproximal sites with attachment loss ≥ 4 mm (not on the same tooth) or at least 2 interproximal sites with PPD ≥ 5 mm, also not on the same tooth.

The presence of at least 2 interproximal sites with attachment loss ≥ 6 mm (not on the same tooth) and at least 1 interproximal site with PPD ≥ 5 mm indicated severe periodontitis. If neither moderate nor severe periodontitis applied, no/mild periodontitis was recorded.

Statistical analysis

Sample size calculation was based on an expected prevalence of periodontitis of 85% among IBD individuals compared to 70% among non-IBD controls (Brito et al. 2008) using the Fleiss method through the OpenEpi software (version 3.01, Boston, USA). Based on an alpha error of 0.05, a power of 0.90, and a case–control ratio of 1:1, a total of 360 individuals (180 cases and 180 controls) were enrolled.

Descriptive analysis such as frequencies, percentages and mean with standard deviation (SD) or median with interquartile (IQR) was used where appropriate. The Shapiro–Wilk test and Q-Q normality plots were applied to verify the normal distribution of quantitative variables. The homogeneity of variances was assessed by the Levene test. The $\chi 2$ test was used to evaluate any potential association between categorical variables and the independent t-test (for variables with Gaussian distribution) and the Mann-Whitney U-test (for variables without a Gaussian distribution) to assess differences of quantitative variables between case and control groups and between CD and UD subjects.

Explorative multiple logistic regression models were developed to identify risk indicators of IBD (yes vs. no) and total periodontitis (yes vs. no) among all the enrolled subjects and for different IBD diagnosis. Selection of potential statistically (p value < 0.25 in the univariate analyses) and clinically relevant variables was conducted (Bursac et al. 2008). Data were presented as odds ratio (OR) and 95% confidence intervals (CI). The significance level was set at 5% (p <0.05) and statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS), version 25.0 software (Chicago, IL, USA).

Results

A total of 180 IBD patients (117 CD, 60 UC, 3 IBD-unclassified -> IBD-U) and 180 age- and gender- matched controls were enrolled. Data from the 3 IBD-U patients were pooled within the total IBD sample, although they were not included in the subgroup analyses.

Table 1 provides descriptive statistics of the study participants, both overall and categorized for IBD types. All participants were Caucasian, with a mean age of 48.4 (± 15.3)

years in the case group and 47.8 (± 14.3) years in the control group. No statistically significant differences were found for any socio-demographic variable between healthy and diseased individuals, nor between the different IBD manifestations. All participants had a balanced diet, with none to moderate alcohol consumption. Significant differences were found among groups with respect to oral hygiene habits, with IBD patients reporting higher flossing habits and frequencies of professional hygiene recalls than controls ($p<0.001$). When comparing CD and UC patients, the latter had received less surgical interventions and smoked less ($p<0.05$).

Periodontal parameters are reported in Table 2. The number of teeth did not differ between patients with IBD versus healthy controls. A significantly higher prevalence of periodontitis was found for IBD patients compared to controls (85.6% vs 65.6%; $p<0.001$). Both moderate (48.9% vs 40.0%) and severe periodontitis (36.7% vs 25.6%) were more frequent in IBD patients ($p<0.001$) than controls, without any significant differences between CD and UC. As expected, PPD and CAL values, as well as number of deep pockets (PPD ≥ 5 mm) were significantly higher than IBD-free subjects.

Periodontal data stratified by age are reported in Table 3. Individuals aged between 36 and 50 years presented a significantly higher prevalence of moderate and severe periodontitis ($p<0.005$), higher CAL and PPD values, as well as a higher number of deep pockets compared to controls ($p<0.05$). Moreover, individuals aged between 51 and 65 suffered from severe periodontitis more frequently than age-matched controls, also showing higher CAL values (both $p<0.05$).

Table 4 shows four final logistic regression models with significant positive predictors and adjusted OR estimates for periodontitis (dependent variable) stratified by IBD forms. (a) Model 1 (all sample)—age, FMPS, and presence of IBD; (b) Model 2 (only IBD)—age, male sex, IBD-associated surgery, IBD localization (ileum + colon); Model 3 (only CD)—age, male sex, FMBS, CD localization (ileum + colon); Model 4 (only UC)—age, UC localization (pancolitis), UC duration (negative predictor).

Table 5 shows three final logistic regression models with significant variables and adjusted OR estimates for IBD, CD, and UC (dependent variables). (a) Model 1 (IBD)—moderate and severe periodontitis as well as higher FMBS were significant positive predictors of IBD, while light smoking decreased the odds of having the condition; (b) Model 2 (CD) and Model 3 (UC) confirmed the previous associations, except for smoking that was negatively associated only to UC.

Discussion

The current study revealed that the prevalence of periodontitis and severe periodontitis is significantly higher in IBD patients compared to age- and gender- matched healthy controls. Even if subgroup analyses often lack power, in the study sample the association was the strongest in the age group from 35 to 50 years and it remained significant from 51 to 65 years. Individuals with IBD consistently presented with significantly worse periodontal clinical parameters, while no differences were encountered between CD and UC.

This case-control study confirms the findings from previous meta-analyses which found a significantly higher prevalence of periodontitis in patients with both CD and UC (Papageorgiou et al. 2017; She et al. 2020). The present data are highly concordant with the results of Brito et al. (2008), who found higher prevalence of periodontitis of 82% in CD, 90% in UC, and 68% in controls. Conversely, some other studies failed to produce evidence for a correlation between IBD and periodontal disease. Grössner-Schreiber et al. (2006) observed no distinct periodontal diagnosis between cases and controls, despite patients with IBD having slightly more sites with CAL ≥ 4 mm. Moreover, a recent study with a similar design found that the frequency of periodontal diseases did not significantly differ among IBD and non-IBD groups, as determined by the Dutch Periodontal Screening Index (Tan et al. 2021). These conflicting results may arise from different periodontitis case definitions and thresholds employed. Moreover, using simplified periodontal screening examinations or partial mouth assessments pose the risk of underestimating the disease, especially in younger populations (Romano et al. 2019). Indeed, the present study used a full-mouth examination protocol and it was the first to apply the CDC/AAP classification system. These criteria have been recommended when investigating systemic periodontal linkages (Holfreter et al. 2015). In an attempt to minimize misclassification, solely CDC/AAP algorithms for moderate/severe periodontitis were implemented and only patients with a minimum number of 6 teeth were enrolled (Romano et al. 2021).

IBD are complex diseases, with their development and progression being influenced by (epi)genetic determinants and environmental factors leading to a disturbed host-microbiome interplay (Jostins et al. 2012). Since several of these IBD-relevant influences are also risk factors for periodontitis (Papageorgiou et al. 2017), multiple logistic models were built for the first time to explore their relative contribution. Within the present sample, having IBD was an independent risk indicator for periodontitis, together with increasing age and FMPS. Individuals with IBD presented a chance ~3 and ~4.5 higher of having moderate and severe periodontitis, respectively. Besides male sex, the extension of the gut mucosal inflammation was a significant predictor of periodontitis in both CD and UC. It may be hypothesized that a

more severe inflammatory burden of IBD may correlate with periodontal damage. Contrary to most studies, we determined clinical disease activity by established scores (HBI and PMI) and biochemical markers. Nevertheless, these scores were not associated with periodontitis. It has to be remarked that the present sample was composed of outpatients with IBD with current remission or in low activity phase. Indeed, most of them had a long history of medical treatment with immunosuppressants and a consistent group already underwent intestinal resection. Since longer disease duration and IBD-associated surgery were negatively associated with periodontitis, it may be speculated that having IBD under control may play a protective role.

When the inverse inferential pathway was explored, the probability of having IBD appeared associated with the severity of periodontitis and the increasing of the bleeding score. Interestingly, either being a light or a heavy smoker was negatively associated with UC, but it did not have an effect on CD. Paradoxically, cigarette smoking appears to decrease the risk for UC in epidemiologic studies, although the mechanisms involved have not yet fully been clarified (Bastida and Beltrán 2011).

Both periodontitis and IBD develop from a disproportionate mucosal inflammatory response to microbial dysbiosis in susceptible patients (Nishida et al. 2018; Hajishengallis and Chavakis 2021). The fact that IBD and periodontitis were more significantly associated in the middle age categories (36-50 and 51-65 years) can point to an increased inflammatory reactivity in patients with immune-mediated diseases, which is also indicated by a higher FMBS compared to similar levels of biofilm accumulation and higher oral hygiene care in patients with IBD. It can be thus hypothesized that both UC and CD patients possess a hyper-inflammatory phenotype at the oral mucosal level, which may be consistent with the pathogenesis of the gut disease (Kitamoto et al. 2020a). Recent available evidence suggests different plausible pathways of interaction between periodontitis and IBD along the gum-gut axis, including the hematogenous, the enteral, and the immunological routes (Baima et al. 2022). Indeed, both periodontal pathobionts and orally-primed Th17 cells can translocate to the intestinal tract, where they can activate the inflammasome in colonic macrophages, exacerbating mucosal inflammation (Kitamoto et al. 2020b).

Compared to the previous investigations, the present study relies on the standards for reporting periodontitis prevalence and severity, a larger sample size, and the presence of a well-balanced control group. Furthermore, the regression models firstly identified explorative risk indicators for the IBD-periodontitis interrelationship. Limitations worth mentioning are related to the sample of patients that may be considered not representative of the whole population, since recruited in two university-based IBD and dental centers located in Northern Italy. This

may limit the generalizability of the present findings. Furthermore, due to the multifactorial etiology of both diseases, the risk of residual confounders in the analyses could not be ruled out. Although the current case definition for epidemiological surveys was employed, it would be interesting to confirm these findings using the most updated criteria for periodontitis clinical classification (Tonetti et al. 2018).

Conclusions

Overall, the present study demonstrated a relevant association between IBD and periodontitis, particularly in the 36-50 age category. Despite CD or UC patients having the same prevalence of periodontitis, some disease-specific variables were found to modify the association, such as the extension of the gut mucosal inflammation and the history of treatment. Both clinicians and public health administrators should consider that IBD patients may benefit from tailored interdisciplinary preventive and therapeutic programs involving the gum-gut axis.

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Table 1. Patient and Disease Characteristics

	IBD (n = 180)	**CD** (n = 117)	**UC** (n = 60)	**Controls** (n = 180)
Male (n, %)	102 (56.7)	61 (52.1)	39 (65.0)	103 (57.2)
Age at examination (mean ± SD)	48.4 ± 15.3	47.9 ± 13.6	49.3 ± 17.8	47.8 ± 14.3
Education level				
Low (n, %)	51 (34.7)	35 (36.8)	13 (32.0)	71 (39.4)
Intermediate (n, %)	73 (49.7)	44 (46.3)	27 (54.0)	74 (41.1)
High (n, %)	23 (15.6)	16 (16.8)	7 (14.0)	35 (19.4)
IBD duration (mean ± SD)	15.8 ± 10.9	16.5 ± 10.5	14.9 ± 11.8	NA
Disease activity				
Partial Mayo (mean ± SD)	NA	NA	1.31 ± 1.69	NA
HBI (mean ± SD)	NA	3.27 ± 2.87	NA	NA
IBD-associated surgery (n, %)	80 (44.4)	65 (55.6)	15 (25.0)[a]	NA
CRP mg/L (mean ± SD)	6.2 ± 10.8	5.1 ± 8.9	8.2 ± 13.6	NA
Fecal calprotectin µg/g (mean ± SD)	388.7 ± 641.3	369.9 ± 652.7	408.8 ± 624.5	NA
Localization (n, %)				
E1	NA	NA	6 (10.0)	NA
E2	NA	NA	15 (25.0)	NA
E3	NA	NA	39 (65.0)	NA
L1	NA	45 (38.5)	NA	NA
L2	NA	19 (16.2)	NA	NA
L3	NA	53 (45.3)	NA	NA
Extraintestinal manifestation (n, %)	18 (10.2)	14 (12.0)	4 (6.9)	NA
Drugs (n, %)				
Systemic steroids	12 (6.7)	7 (6.0)	4 (6.7)	NA
Budesonide	31 (17.2)	14 (12.0)	17 (28.3)	NA
Targeted therapies	48 (26.7)	36 (30.8)	11 (18.3)	NA
Aminosalicylates	116 (64.4)	73 (62.4)	41 (68.3)	NA
Oral health practices				
Flossing (n, %)	119 (66.1)[b]	76 (65.0)	41 (68.3)	62 (34.4)
Brushing frequency (n, %)				
≤ once/day	23 (13.1)	16 (14.0)	5 (8.5)	29 (16.1)
twice/day	98 (55.7)	63 (55.3)	34 (57.6)	80 (44.4)
≥ three times/day	55 (31.3)	35 830.7)	20 (33.9)	71 (39.4)
Regular scaling frequency (n, %)				

sporadically	94 (54.0) [b]	62 (54.4)	31 (54.4)	114 (63.3)
once/year	28 (16.1)	18 (15.8)	10 (17.5)	54 (30.0)
≥ twice/year	52 (29.9)	34 (29.8)	16 (28.1)	12 (6.7)
Smoking (n, %)				
No	131 (72.8)	78 (66.7)	52 (86.7)[a]	116 (64.4)
Light	20 (11.1)	17 (14.5)	2 (3.3)	31 (17.2)
Heavy	29 (16.1)	22 (18.8)	6 (10.0)	33 (18.3)

Abbreviations: IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; HBI, Harvey-Bradshaw Index; CRP, C-reactive protein; NA, not assessable.
[a], CD vs UC $p<0.05$; [b], IBD vs controls $p<0.05$

Table 2. Group comparison of patients with IBD and controls with regards to periodontal parameters

	IBD (n = 180)	**CD** (n = 117)	**UC** (n = 60)	**Controls** (n = 180)
Diagnosis				
No/mild periodontitis (%)	26 (14.4)[a]	17 (14.5)	9 (15.0)	62 (34.4)
Moderate periodontitis (%)	88 (48.9)[a]	59 (50.4)	28 (46.7)	72 (40.0)
Severe periodontitis (%)	66 (36.7)[a]	41 (35.0)	23 (38.3)	46 (25.6)
Moderate/severe periodontitis (%)	154 (85.6)[a]	100 (85.4)	51 (85.0)	118 (65.6)
Periodontal parameters				
N of teeth (median, IQR)	26 (4)	26 (5)	26 (4)	26 (5)
FMPS (median, IQR)	60.7 (42.3)	57.4 (43.2)	64.3 (42.8)	47.9 (43.1)
FMBS (median, IQR)	27.5 (25.8)	26.9 (20.7)	31.1 (34.9)	33.6 (40.5)
PPD (median, IQR)	3.0 (0.8)[a]	3.0 (0.8)	3.0 (0.7)	2.6 (0.6)
CAL (median, IQR)	3.1 (0.9)[a]	3.0 (0.9)	3.1 (0.7)	2.7 (0.7)
N PPD ≥ 5 mm (median, IQR)	8.0 (14.5)[a]	7.0 (16.5)	8.5 (13.8)	4.0 (16.0)

Abbreviations: IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; FMPS, full.mouth plaque score; FMBS, full-mouth bleeding score; PPD, probing pocket depth; CAL, clinical attachment level; IQR, interquartile range.
[a], IBD vs controls $p<0.001$; [b], CD vs UC $p<0.05$

Table 3. Group comparison of patients with IBD and controls with regards to periodontal parameters stratified by age

	Age 18-35		Age 36-50		Age 51-65		Age > 65	
	IBD (n = 38)	**Controls** (n = 38)	**IBD** (n = 59)	**Controls** (n = 62)	**IBD** (n = 56)	**Controls** (n = 54)	**IBD** (n = 27)	**Controls** (n = 26)
Diagnosis								
No/mild periodontitis (%)	14 (36.8)	19 (50.0)	7 (11.9)	25 (40.3)	4 (7.1)	14 (25.9)	1 (3.7)	4 (15.4)
Moderate periodontitis (%)	22 (57.9)	15 (39.5)	35 (59.3)	26 (41.9)	22 (39.3)	20 (37.0)	9 (33.3)	11 (42.3)
Severe periodontitis (%)	2 (5.3)	4 (10.5)	17 (28.8)	11 (17.7)	30 (53.6)	20 (37.0)	17 (63.0)	11 (42.3)
Moderate/severe periodontitis (%)	24 (63.2)	19 (50.0)	52 (88.2)	37 (59.6)	52 (92.9)	40 (74.0)	26 (99.3)	22 (84.6)
p-value	NS		0.002		0.022		NS	
Periodontal parameters								
N of teeth (median, IQR)	28 (1)	28 (4)	27 (3)	27 (3)	24 (5)	24 (5)	24 (5)	22 (13)
p-value	NS		NS		NS		NS	
FMPS (median, IQR)	53.9 (32.5)	46.4 (35.9)	52.5 (40.5)	44.5 (36.0)	72.6 (39.2)	53.7 (50.5)	66.7 (49.9)	60.4 (61.7)
p-value	NS		NS		NS		NS	
FMBS (median, IQR)	24.5 (24.8)	32.4 (42.5)	28.7 (26.8)	29.4 (39.1)	30.4 (27.9)	36.1 (37.9)	26.6 (22.9)	40.4 (61.0)
p-value	NS		NS		NS		NS	
Mean PPD (median, IQR)	3.0 (0.9)	2.5 (0.6)	3.0 (0.7)	2.6 (0.5)	3.0 (0.5)	2.7 (0.6)	3.0 (1.1)	2.9 (0.6)
p-value	NS		0.011		NS		NS	
Mean CAL (median, IQR)	3.0 (1.0)	2.6 (0.5)	3.1 (0.8)	2.6 (0.6)	3.1 (0.6)	2.8 (0.9)	3.3 (1.2)	3.1 (1.1)
p-value	NS		0.002		0.021		NS	
N PPD ≥ 5 mm (median, IQR)	2.5 (6.5)	1.5 (6.2)	9.0 (20.0)	3.0 (11.2)	10.5 (20.8)	7.0 (26.2)	9.0 (11.0)	12.5 (19.2)
p-value	NS		0.027		NS		NS	

Abbreviations: IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; NS, non-statistically significant ($p > 0.05$); FMPS, full-mouth plaque score; FMBS, full-mouth bleeding score; PPD, probing pocket depth; CAL, clinical attachment level; IQR, interquartile range.

[a], IBD vs controls $p<0.001$; [b], CD vs UC $p<0.05$

Table 4. Final explorative logistic regression models for moderate/severe periodontitis

Models and variables	OR	95% (CI)	p-value
Model 1	**Periodontitis all sample** (dichotomous)		
Age	1.05	1.02-1.06	<0.001
IBD			
No	1		
Yes	3.52	2.00-6.21	<0.001
FMPS	1.02	1.01-1.03	0.003
Model 2 [b]	**Periodontitis only IBD** (dichotomous)		
Gender			
Female	1		
Male	3.42	1.27-9.24	0.015
Age	1.07	1.03-1.12	<0.001
IBD-associated surgery			
No	1		
Yes	0.028	0.10-0.79	0.016
IBD localization			
Colon	1		
Ileum	1.79	0.52-6.15	0.354
Ileum + colon	3.39	1.00-11.53	0.05
Model 3 [b]	**Periodontitis only CD** (dichotomous)		
Gender			
Female	1		
Male	3.70	1.02-13.48	0.047
Age	1.07	1.02-1.12	0.009
FMBS	1.03	1.00-1.06	0.030
CD localization			
Colon (L2)	1		
Ileum (L1)	2.98	0.68-13.14	0.149
Ileum + colon (L3)	7.07	1.50-33.46	0.014
Model 4 [a]	**Periodontitis only UC** (dichotomous)		
Age	1.29	1.07-1.56	0.008
UC duration	0.79	0.65-0.98	0.028
CD localization			
Localized (E1-E2)	1		

Pancolitis (E3)	21.65	1.11-420.16	0.042

Abbreviations: IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; FMPS, full-mouth plaque score; FMBS, full-mouth bleeding score.

[a] , adjusted for gender and smoking status.

Table 5. Final explorative logistic regression models for IBD, CD and UC

Models and variables	OR	95% (CI)	p-value
Model 1	**IBD** (dichotomous)		
Smoking status			
Non-smoker	1		
Light smoker	0.49	0.26-0.94	0.031
Heavy smoker	0.69	0.38-1.24	0.212
Periodontal diagnosis			
No/mild periodontitis	1		
Moderate periodontitis	3.21	1.80-5.72	<0.001
Severe periodontitis	4.48	2.30-8.73	<0.001
FMBS (%)	1.01	1.00-1.02	0.023
Model 2	**CD** (dichotomous)		
Smoking status			
Non-smoker	1		
Light smoker	0.71	0.35-1.41	0.322
Heavy smoker	0.96	0.51-1.82	0.900
Periodontal diagnosis			
No/mild periodontitis	1		
Moderate periodontitis	3.13	1.62-6.05	0.001
Severe periodontitis	4.01	1.92-8.38	<0.001
FMBS (%)	1.01	1.00-1.02	0.048
Model 3	**UC** (dichotomous)		
Smoking status			
Non-smoker	1		
Light smoker	0.14	0.03-0.63	0.010
Heavy smoker	0.34	0.13-0.90	0.030
Periodontal diagnosis			
No/mild periodontitis	1		
Moderate periodontitis	3.14	1.32-7.47	0.010
Severe periodontitis	4.43	1.66-11.81	0.003
FMBS (%)	1.01	0.99-1.03	0.090

Abbreviations: IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; FMBS, full-mouth bleeding score.
Models adjusted for age, sex and education level.