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# Increased risks of dental caries and periodontal disease in Chinese patients with inflammatory bowel disease

Limin Zhang[1], Xiang Gao[2], Jiamin Zhou[1], Shan Chen[1], Jinxin Zhang[3], Yingfan Zhang[4], Baili Chen[4] and Junying Yang[1]

*[1]Department of Stomatology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China; [2]Department of Gastroenterology, The Center for Inflammatory Bowel Disease, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China; [3]School of Public Health, Sun Yat-sen University, Guangzhou, Guangdong, China; [4]Department of Gastroenterology, the Center for Inflammatory Bowel Disease, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China.*

**Objectives:** Inflammatory bowel disease (IBD) may be associated with oral diseases, but few relevant studies have been reported in China. This study aimed to compare the prevalence, severity and extent of dental caries and periodontal disease in Chinese IBD patients and healthy controls. **Materials and methods:** In this cross-sectional study, questionnaires and oral examinations were completed for 389 IBD patients [265 with Crohn's disease (CD) and 124 with ulcerative colitis (UC)] and 265 healthy controls based on the established criteria of the World Health Organization. Tobit regression, multiple linear regression and logistic regression were performed to analyse the data. **Results:** After adjusting for confounders, the decayed, missing and filled surfaces indices were significantly increased in the CD and UC patients compared with those in the controls ($P < 0.001$). Patients with CD [odds ratio (OR) = 4.27, 95% confidence interval (95% CI): 2.63–6.95, $P < 0.001$] and UC (OR = 2.21, 95% CI: 1.24–3.94, $P = 0.007$) had significantly higher risks of dental caries than controls. Significantly higher percentages of sites with probing pocket depth $\geq 5$ mm and clinical attachment loss $\geq 4$ mm were observed in CD and UC patients compared with controls ($P < 0.001$). A fully adjusted model revealed that CD and UC were risk indicators for periodontitis (OR = 4.46, 95% CI: 2.50–7.95, $P < 0.001$; OR = 4.66, 95% CI: 2.49–8.71, $P < 0.001$, respectively). No significant differences in dental caries and periodontal disease were observed between the CD and UC patients. **Conclusions:** Chinese IBD patients have a higher prevalence, severity and extent of dental caries and/or periodontal disease than controls, and require oral health education and multidisciplinary treatment.

***Key words:** Dental caries, periodontal disease, inflammatory bowel disease, Crohn's disease, ulcerative colitis*

## INTRODUCTION

Dental caries and periodontal disease are the two most prevalent forms of chronic oral diseases, and not only affect oral physiological function and physical appearance but are also associated with systemic diseases, including diabetes, cardiovascular diseases, osteoporosis and respiratory diseases[1,2]. In recent years, a number of reports have examined the association between oral diseases and digestive diseases, especially inflammatory bowel disease (IBD)[4,5].

Inflammatory bowel disease is a chronic intestinal inflammatory illness comprising two main disease entities—Crohn's disease (CD) and ulcerative colitis (UC)—the aetiology and pathogenesis of which are not fully clear, although the immune system, genetics and environmental factors have all been found to play a role[6]. According to epidemiological studies, the prevalence and incidence of IBD in North America and northern Europe are the highest in the world[7]. As the economic status and dietary structures of the general public continue to improve in developing countries, the incidence of IBD in Asia has gradually increased[8]. In China, the incidences of UC and CD are approximately 1.18/100,000 and 0.40/100,000[9]. IBD preferentially manifests in the second and fourth decades of life, and can affect any part of the gastrointestinal tract. Clinical manifestations of IBD include abdominal pain, diarrhoea, fever, haematochezia and perianal abscesses[10]. In addition, the course of IBD is usually lengthy and can be accompanied by a variety of systemic diseases that compromise the physical and mental health of patients and impose tremendous economic burdens on patients and the medical system[11].

Approximately 16.7%–40% of IBD patients have at least one extraintestinal manifestation, and the oral cavity is one of the most frequently affected areas[4]. In 1969, Dudeney[12] first reported granulomatous inflammation of the buccal mucosa in a CD patient. Since then, multiple studies have confirmed that IBD patients have an increased prevalence of dental caries, periodontitis, some oral mucosal diseases and oral symptoms compared with non-IBD patients[13–15]. However, some studies have reported different conclusions[16,17]. Widely varying prevalence rates of oral manifestations in CD and UC patients have been reported, ranging from 0.5% to 37%, and these manifestations may precede, coincide with, or follow the onset of intestinal symptoms[18,19]. Few large-scale clinical studies of the association between IBD and oral diseases among Chinese populations are available[20,21]. Thus, in the present study, we aimed to compare the prevalence, severity and extent of dental caries and periodontal disease between Chinese IBD patients and healthy controls, and to identify related risk factors. The results will provide guidance on oral health education and multidisciplinary treatment for IBD patients, with the ultimate goal of relieving the burden of IBD and improving patients' quality of life.

## MATERIALS AND METHODS

### Study design and sample

This cross-sectional study was registered and reviewed in the Chinese Clinical Trial Register (ChiCTR1800018971), and was conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki. The study was approved by the Ethics Committee of the First Affiliated Hospital of Sun Yat-sen University [no. (2018) 216]. The participants enrolled in this study signed written informed consent forms before beginning the investigations. The sample was determined using *Power Analysis and Sample Size* (PASS) version 12 (NCSS, Kaysville, UT, USA) with a 0.05 significance level and an 80% power based on the results of previous studies[13–15]. We collected data from 389 outpatients or inpatients with IBD (265 with CD and 124 with UC) in the Center for Inflammatory Bowel Disease of the First Affiliated Hospital and the Sixth Affiliated Hospital of Sun Yat-sen University from March 2018 to April 2019. The diagnosis and evaluation of IBD activity were based on the Third European Evidence-based Consensus on Diagnosis and Management of Crohn's Disease and Ulcerative Colitis[22,23]. During the same period, 265 age- and sex-matched healthy individuals with no symptoms or signs of IBD were selected as controls at the two hospitals. All participants were older than 18 years. The exclusion criteria were as follows: those who refused or whose families refused participation in this study; those who had cognitive impairments; those who were diagnosed with other systemic diseases; those who were pregnant or lactating; those who were edentulous or had fixed orthodontic appliances; and those who had undergone periodontal treatments or who had been taking antibiotics within the preceding 3 months.

### Questionnaires

According to 'Oral Health Survey: Basic Methods' published by the WHO (5th edition)[24] and the Fourth Oral Health Survey in China[25], a questionnaire was designed that included the following items: age, sex, level of education, smoking status, dietary habits, oral hygiene behaviours, the year of IBD diagnosis, types of medications used, and other factors. The questionnaires were distributed on-site to the participants by trained investigators (J.M. Zhou, S. Chen and Y.F. Zhang) who provided instructions for filling out the forms and collected the completed surveys.

### Oral examinations

All permanent teeth (except for the third molars) of each participant were examined by the same dentist (L.M. Zhang) using a mouth mirror and a periodontal probe (PCPUNC1561-15mm, Hu-Friedy, Chicago, IL, USA) based on the 'Oral Health Survey: Basic Methods' published by WHO (5th edition)[24]. Various parameters were recorded as follows: the numbers of decayed, missing and filled teeth (DMFT); decayed teeth (DT); missing teeth (MT); filled teeth (FT); decayed, missing and filled surfaces (DMFS); decayed surfaces (DS); missing surfaces (MS); filled surfaces (FS); probing pocket depth (PD); clinical attachment loss (CAL); bleeding on probing (BOP); gingival recession (GR); the gingival index (GI); the plaque index (PLI); and the calculus index (CI). PD, CAL, GR and BOP were measured at six sites on each tooth (mesial, distal and middle sites of the buccal and lingual sides). The GI and PLI were evaluated at four sites per tooth (disto-buccal, mid-buccal, mesio-buccal and mid-lingual), and the CI was examined at the buccal and lingual surfaces of each tooth. For each individual, the mean values for the individual measurements were calculated and regarded as the representative value for that participant. The diagnostic criterion for periodontitis is $\geq 2$ interproximal sites with CAL $\geq$ 3 mm, and $\geq 2$ interproximal sites with PD $\geq 4$ mm (not on the same tooth), or $\geq 1$ site with PD $\geq$ 5 mm[26]. A standard consistency test was performed by the dentist (L.M. Zhang) prior to the clinical examination. The kappa values for the status of dental caries and PD were 0.88 and 0.74, respectively.

### Statistical analyses

Statistical analyses were performed using the software packages SPSS version 25 (IBM, Armonk, NY, USA) and R version 3.5.3 (The R Foundation for Statistical Computing, Auckland, New Zealand). For continuous variables, data are presented as the means and standard deviations or as medians and interquartile ranges, and groups were compared using an analysis of variance or the Kruskal–Wallis test depending on the presence or absence of a normal distribution, respectively. Count data are reported as percentages or ratios, and intergroup comparisons were conducted using the $\chi^2$ test or the Kruskal–Wallis test. For univariate analyses, Tobit regression models or multiple linear regression models were used to compare differences in dental caries and periodontal parameters among the CD and UC patients and controls after adjusting for confounders including age, sex, education level, smoking and the daily frequency of toothbrushing according to the type of data. Tobit regression models were used to compare differences in the mean values of the DMFT, DMFS, DT, MT, FT, DS, MS, FS, CAL and GR, as well as the percentages of sites with a PD $\geq 4$ mm and 5 mm, CAL $\geq 3$ mm and 4 mm, and GR $\geq 1$ mm and 2 mm among the three groups after adjusting for the confounders mentioned above. The mean values of PD, GI and PLI and the percentages of sites with BOP and CI were converted into dependent variables through a logarithmic transformation. Then, multiple linear regression models were used to compare differences in those dependent variables among the three groups after adjusting for the confounders mentioned above. Binary logistic regression analyses were used to determine the associations of CD and UC (independent variable) with dental caries or periodontitis (dependent variable) after adjusting for the confounders mentioned above. The enter method was used to select the important independent variables, including CD, UC, age, sex, education level, smoking and the daily frequency of toothbrushing. A $P$-value $< 0.05$ was considered statistically significant. Adjusted odds ratios (ORs) and their 95% confidence intervals (95% CIs) were reported. The parameters associated with dental caries and periodontal disease were compared among the three groups using Bonferroni correction.

## RESULTS

### Study populations

Ultimately, 654 participants were included in this study, 265 of whom had CD (170 males and 95 females, with an age range of 18–68 years), while 124 had UC (75 males and 49 females, with an age range of 18–75 years) and 265 served as controls (150 males and 115 females, with an age range of 19–67 years). The demographic data of these participants are presented in *Table 1*. No differences were found among the three groups regarding age ($P = 0.298$) and sex ($P = 0.206$). No significant differences in disease activity or the time of diagnosis were observed between CD and UC patients ($P > 0.05$). The dietary habits of these participants are shown in *Table 2*. The frequency of daily meals did not differ significantly among the three groups ($P = 0.443$), and patients with CD and UC consume fewer sugary foods than controls ($P \leq 0.001$).

### Dental caries assessment

The prevalence of dental caries was higher in IBD patients than in controls (85.6% *vs.* 68.0%, $P < 0.001$), and the values were 87.5% and 81.5% in CD and UC patients, respectively. The mean value of DMFT was increased in IBD patients compared with controls (mean difference: 2.71, 95% CI: 2.18–3.25, $P < 0.001$). The dental caries status of these participants are listed in *Table 3*. According to Tobit regression analyses, the mean DMFT, DMFS, DT, DS and MT were all significantly higher in CD and UC patients than those in controls after adjusting for confounding factors ($P < 0.05$). No significant differences in the above parameters for dental caries were observed between the CD and UC patients ($P > 0.05$).

### Periodontal disease assessment

A higher prevalence of periodontitis was observed in IBD patients than in controls (37.5% *vs.* 19.2%, $P < 0.001$), and the values were 31.3% and 50.8% in CD and UC patients, respectively. The periodontal status of the participants are listed in *Table 4*. After adjusting for confounding factors, the mean PD, CAL, GI and PLI, and the percentages of sites with a PD $\geq$ 5 mm, CAL $\geq 4$ mm, GR $\geq 2$ mm, BOP and a CI were all increased in CD and UC patients compared with those in controls ($P < 0.001$). Significant differences in the parameters of periodontal disease were not observed between patients with CD and UC ($P > 0.05$).

**Table 1** Demographics of the study population

| Variables | Controls ($n$ = 265) | CD ($n$ = 265) | UC ($n$ = 124) | $P$-value |
|---|---|---|---|---|
| Age (years), M (IQR) | 26 (25–47) | 29 (25–38) | 39 (27–40) | 0.298* |
| Gender, $n$ (%) | | | | 0.206† |
| Male | 150 (56.6) | 170 (64.2) | 75 (60.5) | |
| Female | 115 (43.4) | 95 (35.8) | 49 (39.5) | |
| Education, $n$ (%) | | | | **< 0.001†** |
| Less than junior college | 78 (29.4) | 119 (44.9) | 80 (64.5) | |
| Junior college or more | 187 (70.6) | 146 (55.1) | 44 (35.5) | |
| Smoking, $n$ (%) | | | | **0.003†** |
| Current smoker | 22 (8.3) | 21 (7.9) | 14 (11.3) | |
| Ex-smoker | 17 (6.4) | 36 (13.6) | 23 (18.5) | |
| Non-smoker | 226 (85.3) | 208 (78.5) | 87 (70.2) | |
| Frequency of tooth-brushing per day, $n$ (%) | | | | **< 0.001†** |
| < 2 times | 57 (21.5) | 111 (41.9) | 54 (43.5) | |
| ≥ 2 times | 208 (78.5) | 154 (58.1) | 70 (56.5) | |
| Active disease, $n$ (%) | – | 96 (36.2) | 49 (39.5) | – |
| Time of diagnosis (years), $n$ (%) | | | | – |
| < 3 years | – | 130 (49.1) | 61 (49.2) | |
| 3–9 years | – | 105 (39.6) | 48 (38.7) | |
| > 9 years | – | 30 (11.3) | 15 (12.1) | |
| Pharmacotherapy, $n$ (%) | | | | – |
| Untreated | 265 (100.0) | 17 (6.4) | 4 (3.2) | |
| Under salicylate therapy | – | 26 (9.8) | 68 (54.8) | |
| Under corticosteroids therapy | – | 10 (3.8) | 18 (14.5) | |
| Under immunosuppressant therapy | – | 106 (40.0) | 27 (21.8) | |
| Under biological therapy | – | 106 (40.0) | 7 (5.7) | |

CD, Crohn's disease; M (IQR), median (interquartile range); UC, ulcerative colitis.
$P$: the significance of differences among the controls and patients with CD and UC. Significant results ($P < 0.05$) are highlighted in bold.
*Kruskal–Wallis test.
†$\chi^2$ test.

### Binary logistic regression analysis

The results of binary logistic regression analyses are presented in *Table 5*. After adjustment for confounding factors, including age, sex, education level, smoking and the daily frequency of tooth-brushing, the risk of dental caries was increased for IBD patients compared with that for controls (OR = 3.45, 95% CI: 2.25–5.31, $P < 0.001$). CD, UC, female sex and tooth-brushing less than twice per day were risk indicators for dental caries ($P < 0.05$). Moreover, compared with controls, the risk of periodontitis was increased in IBD patients (OR = 4.54, 95% CI: 2.66–7.76, $P < 0.001$), and the risk indicators for periodontitis were CD, UC and age ($P < 0.001$). A further analysis of patients with CD and UC revealed that the activity, duration and drug treatment of IBD were not risk indicators for dental caries and periodontitis.

## DISCUSSION

A meta-analysis of nine cross-sectional surveys revealed that the DMFT index of IBD patients was significantly greater than that of non-IBD patients (mean difference: 3.85), which did not include Chinese IBD patients[13]. To investigate the prevalence of dental caries among Chinese IBD patients, we conducted this study and found that the DMFT index in IBD patients was 2.71-higher than that in controls. Grössner-Schreiber *et al.*[16] reported a 2.37-times higher risk of dental caries in German IBD patients than that in controls. Our study found similar results, as the risk of dental caries was 3.45 times higher in IBD patients than in controls. We found that the mean values for DMFT, DMFS, DT, DS and MT were higher in patients with CD and UC than in controls, consistent with the findings of most previous studies[27,28].

One of the major manifestations of IBD is food intolerance, which may also be one of the causes of the disease[30]. In our survey, the common poorly tolerated foods among IBD patients were dairy products, fried food, spicy food and cold food, similar to the results of a Korean study[31]. However, the positive percentage of food intolerance in IBD patients (52.4%) in our study was lower than in a report from Spain, which found that 77% of patients avoided some foods to prevent disease relapse[32]. In addition, surveys in other countries have found that IBD patients often adopt a diet of small, frequent meals and tend to consume more refined carbohydrates and sugary food, which was considered one of the causes of caries susceptibility in IBD patients[29,33,34]. By contrast, in our study, the frequency of daily meals did not differ significantly among the three groups, and patients with CD and UC may consume fewer sugary foods than controls. Currently, most investigators

**Table 2** Dietary habits of the study population

| Variables | Controls *n* (%) | CD *n* (%) | UC *n* (%) | *P* | *P*1 | *P*2 | *P*3 |
|---|---|---|---|---|---|---|---|
| Meal frequency per day | | | | 0.443 | | | |
| ≤ 2 times | 33 (12.5) | 34 (12.8) | 13 (10.5) | | | | |
| 3 times | 214 (80.8) | 204 (77.0) | 97 (78.2) | | | | |
| 4 times | 14 (5.3) | 21 (7.9) | 13 (10.5) | | | | |
| 5 times | 4 (1.5) | 6 (2.3) | 1 (0.8) | | | | |
| Consumption of more meals per day but less food at each meal | | | | 0.072 | | | |
| Never | 33 (12.5) | 17 (6.4) | 14 (11.3) | | | | |
| Occasionally | 173 (65.3) | 175 (66.0) | 75 (60.5) | | | | |
| Often | 47 (17.7) | 53 (20.0) | 28 (22.6) | | | | |
| Almost everyday | 12 (4.5) | 20 (7.5) | 7 (5.6) | | | | |
| Frequency of eating dessert and candies ( biscuit, cake, bread) | | | | < 0.001 | 0.001 | < 0.001 | 0.060 |
| Seldom/never | 53 (20.0) | 84 (31.7) | 50 (40.3) | | | | |
| 1–3 times/month | 63 (23.8) | 71 (26.8) | 34 (27.4) | | | | |
| 1 time/week | 53 (20.0) | 42 (15.8) | 21 (16.9) | | | | |
| 2–6 times/week | 63 (23.8) | 46 (17.4) | 16 (12.9) | | | | |
| 1 time/day | 24 (9.1) | 12 (4.5) | 2 (1.6) | | | | |
| ≥ 2 times/day | 9 (3.4) | 10 (3.8) | 1 (0.8) | | | | |
| Frequency of consuming sweetened drinks (syrup, sodas, fruit juice) | | | | < 0.001 | < 0.001 | < 0.001 | 0.158 |
| Seldom/never | 65 (24.5) | 121 (45.7) | 67 (54.0) | | | | |
| 1–3 times/month | 65 (24.5) | 53 (20.0) | 23 (18.5) | | | | |
| 1 time/week | 54 (20.4) | 31 (11.7) | 18 (24.5) | | | | |
| 2–6 times/week | 61 (23.0) | 43 (16.2) | 12 (9.7) | | | | |
| 1 time/day | 14 (5.3) | 13 (4.9) | 4 (3.2) | | | | |
| ≥ 2 times/day | 6 (2.3) | 4 (1.5) | 0 (0.0) | | | | |
| Frequency of consuming sweetened milk, yogurt and coffee | | | | < 0.001 | < 0.001 | < 0.001 | 0.756 |
| Seldom/never | 37 (14.0) | 85 (32.1) | 52 (41.9) | | | | |
| 1–3 times/month | 48 (18.1) | 59 (22.3) | 25 (20.2) | | | | |
| 1 time/week | 52 (19.6) | 33 (12.5) | 9 (7.3) | | | | |
| 2–6 times/week | 94 (35.5) | 68 (25.7) | 24 (19.4) | | | | |
| 1 time/day | 24 (9.1) | 18 (6.8) | 13 (10.5) | | | | |
| ≥ 2 times/day | 10 (3.8) | 2 (0.8) | 1 (0.8) | | | | |
| Frequency of eating fruits | | | | 0.325 | | | |
| Seldom/never | 5 (1.9) | 16 (6.0) | 5 (4.0) | | | | |
| 1–3 times/month | 17 (6.4) | 19 (7.2) | 10 (8.1) | | | | |
| 1 time/week | 38 (14.3) | 36 (13.6) | 17 (13.7) | | | | |
| 2–6 times/week | 121 (45.7) | 112 (42.3) | 46 (37.1) | | | | |
| 1 time/day | 62 (23.4) | 54 (20.4) | 35 (28.2) | | | | |
| ≥ 2 times/day | 22 (8.3) | 28 (10.6) | 11 (8.9) | | | | |
| Frequency of eating cereals and tubers | | | | 0.892 | | | |
| 1 time/day | 3 (1.1) | 2 (0.8) | 1 (0.8) | | | | |
| ≥ 2 times/day | 262 (98.9) | 263 (99.2) | 123 (99.2) | | | | |
| Frequency of eating vegetables | | | | 0.021 | 1.000 | 0.040 | 0.028 |
| Seldom/never | 1 (0.4) | 4 (1.5) | 1 (0.8) | | | | |
| 1–3 times/month | 8 (3.0) | 5 (1.9) | 1 (0.8) | | | | |
| 1 time/week | 12 (4.5) | 9 (3.4) | 2 (1.6) | | | | |
| 2–6 times/week | 54 (20.4) | 44 (16.6) | 16 (12.9) | | | | |
| 1 time/day | 66 (24.9) | 83 (31.3) | 30 (24.2) | | | | |
| ≥ 2 times/day | 124 (46.8) | 120 (45.3) | 74 (59.7) | | | | |
| Frequency of eating beans | | | | 0.009 | 0.020 | 0.044 | 1.000 |
| Seldom/never | 22 (8.3) | 49(18.5) | 23 (18.5) | | | | |
| 1–3 times/month | 56 (21.1) | 56 (21.1) | 27 (21.8) | | | | |
| 1 time/week | 75 (28.3) | 66 (24.9) | 32 (25.8) | | | | |
| 2–6 times/week | 92 (34.7) | 79 (29.8) | 36 (29.0) | | | | |
| 1 time/day | 15 (5.7) | 12 (4.5) | 5 (4.0) | | | | |
| ≥ 2 times/day | 5 (1.9) | 3 (1.1) | 1 (0.8) | | | | |
| Frequency of eating eggs | | | | 0.236 | | | |
| Seldom/never | 1 (0.4) | 0 (0.0) | 0 (0.0) | | | | |
| 1–3 times/month | 8 (3.0) | 8 (3.0) | 6 (4.8) | | | | |
| 1 time/week | 21 (7.9) | 21 (7.9) | 10 (8.1) | | | | |
| 2–6 times/week | 45 (17.0) | 44 (16.6) | 16 (12.9) | | | | |
| 1 time/day | 41 (15.5) | 65 (24.5) | 36 (29.0) | | | | |
| ≥ 2 times/day | 9 (3.4) | 11 (4.2) | 3 (2.4) | | | | |
| Frequency of eating fish | | | | 0.325 | | | |
| Seldom/never | 15 (5.7) | 21 (7.9) | 12 (9.7) | | | | |
| 1–3 times/month | 43 (16.2) | 33 (12.5) | 17 (13.7) | | | | |
| 1 time/week | 58 (21.9) | 58 (21.9) | 29 (23.4) | | | | |

(continued)

**Table 2** continued

| Variables | Controls $n$ (%) | CD $n$ (%) | UC $n$ (%) | $P$ | $P1$ | $P2$ | $P3$ |
|---|---|---|---|---|---|---|---|
| 2–6 times/week | 123 (46.4) | 113 (42.6) | 56 (45.2) | | | | |
| 1 time/day | 16 (6.0) | 25 (9.4) | 8 (6.5) | | | | |
| ≥ 2 times/day | 10 (3.8) | 15 (5.7) | 2 (1.6) | | | | |
| Frequency of eating livestock and poultry meat | | | | | | | |
| Seldom/never | 5 (1.9) | 16 (6.0) | 4 (3.2) | 0.280 | | | |
| 1–3 times/month | 23 (8.7) | 22 (8.3) | 16 (12.9) | | | | |
| 1 time/week | 47 (16.6) | 42 (15.8) | 23 (18.5) | | | | |
| 2–6 times/week | 146 (55.1) | 132 (49.8) | 57 (46.0) | | | | |
| 1 time/day | 35 (13.2) | 35 (13.2) | 17 (13.7) | | | | |
| ≥ 2 times/day | 12 (4.5) | 18 (6.8) | 7 (5.6) | | | | |
| Frequency of eating fried food | | | | | | | |
| Seldom/never | 72 (27.2) | 152 (57.4) | 83 (66.9) | **< 0.001** | **< 0.001** | **< 0.001** | 0.569 |
| 1–3 times/month | 85 (32.1) | 61 (23.0) | 22 (17.7) | | | | |
| 1 time/week | 59 (22.3) | 25 (9.4) | 14 (11.3) | | | | |
| 2–6 times/week | 44 (16.6) | 24 (9.1) | 4 (3.2) | | | | |
| 1 time/day | 4 (1.5) | 1 (0.4) | 1 (0.8) | | | | |
| ≥ 2 times/day | 1 (0.4) | 2 (0.8) | 0 (0.0) | | | | |
| Avoiding some food | 50 (18.9) | 142 (53.6) | 62 (50.0) | **< 0.001** | **< 0.001** | **< 0.001** | 1.000 |
| Kinds of food avoided | | | | | | | |
| High-fibre food | 1 (0.4) | 20 (7.5) | 3 (2.4) | **< 0.001** | **< 0.001** | 0.291 | 0.138 |
| Milk products | 4 (1.5) | 10 (3.8) | 9 (7.3) | **0.016** | 0.312 | **0.018** | 0.411 |
| Greasy food | 5 (1.9) | 22 (8.3) | 9 (7.3) | **0.003** | **0.003** | **0.048** | 1.000 |
| Seafood products | 6 (2.3) | 17 (6.4) | 10 (8.1) | **0.022** | **0.027** | **0.021** | 1.000 |
| Spicy food | 8 (3.0) | 66 (24.9) | 36 (29.0) | **< 0.001** | **< 0.001** | **< 0.001** | 1.000 |
| Cold food | 2 (0.8) | 18 (6.8) | 6 (4.8) | **0.002** | **< 0.001** | **0.045** | 1.000 |

$P$: the significance of differences among the controls and patients with CD and UC was analysed by the Kruskal–Wallis test or the $\chi^2$ test, while pairwise comparisons were performed using Bonferroni correction.
$P1$: the significance of the differences between patients with CD and controls; $P2$: the significance of the differences between patients with UC and controls; $P3$: the significance of the differences between patients with CD and UC.
Significant results ($P < 0.05$) are highlighted in bold.
CD, Crohn's disease; UC, ulcerative colitis.

**Table 3** Tobit regression analyses of the severity and extent of dental caries parameters in groups stratified by disease status

| Variables | CD ($n$ = 265) Median (IQR) | $P1$ | Controls ($n$ = 265) Median (IQR) | $P2$ | UC ($n$ = 124) Median (IQR) | $P3$ |
|---|---|---|---|---|---|---|
| DMFT | 5.00 (2.00–7.00) | **< 0.001** | 2.00 (0.00–3.00) | **< 0.001** | 4.00 (2.00–7.00) | 0.711 |
| DMFS | 7.00 (3.00–16.00) | **< 0.001** | 2.00 (0.00–5.00) | **< 0.001** | 6.00 (2.00–15.00) | 0.154 |
| DT | 3.00 (1.00–6.00) | **< 0.001** | 0.00 (0.00–1.00) | **< 0.001** | 2.00 (1.00–5.00) | 0.330 |
| MT | 0.00 (0.00–1.00) | **< 0.002** | 0.00 (0.00–0.00) | **< 0.002** | 0.00 (0.00–1.00) | 0.300 |
| FT | 0.00 (0.00–2.00) | 0.724 | 0.00 (0.00–1.00) | 1.000 | 0.00 (0.00–1.00) | 0.716 |
| DS | 5.00 (2.00–9.00) | **< 0.001** | 0.00 (0.00–2.00) | **< 0.001** | 4.00 (1.00–8.00) | 0.773 |
| MS | 0.00 (0.00–5.00) | **< 0.001** | 0.00 (0.00–0.00) | 0.061 | 0.00 (0.00–5.00) | 0.280 |
| FS | 0.00 (0.00–3.00) | 0.126 | 0.00 (0.00–2.00) | 1.000 | 0.00 (0.00–2.00) | 0.126 |

After adjusting for age, sex, education level, smoking and the daily frequency of tooth-brushing, $P$-values were obtained from Tobit regression analyses, while pairwise comparisons were performed using Bonferroni correction.
$P1$: significance of the differences between patients with CD and controls; $P2$: significance of the differences between patients with UC and controls; $P3$: significance of the differences between patients with CD and UC.
Significant results ($P < 0.05$) are highlighted in bold.
CD, Crohn's disease; DMFS, decayed, missing and filled surfaces; DMFT, decayed, missing and filled teeth; DS, decayed surfaces; DT, decayed teeth; FS, filled surfaces; FT, filled teeth; IQR, interquartile range; MS, missing surfaces; MT, missing teeth; UC, ulcerative colitis.

believe the possible reasons for the generally higher prevalence of dental caries in IBD patients are changes in saliva and the microbial flora of the oral cavity, dietary habits, and malnutrition caused by deficiencies in iron, zinc, magnesium, folic acid, vitamin $B_{12}$ and vitamin D[28,35,36]. Therefore, the cause of the increased susceptibility to dental caries among Chinese IBD patients require further investigation.

Inflammatory bowel disease was associated with a higher risk of periodontitis in 332 of 1,000 patients compared with healthy patients (OR = 4.55, 95% CI: 3.00–6.91) in a meta-analysis[13]. After adjusting for age and the number of missing teeth, Habashneh *et al.*[15] found 4.9-fold and 7.0-fold higher risks of periodontitis in CD and UC patients than those in controls, respectively, in a case-control study of 160

**Table 4** Multiple linear regression and Tobit regression analyses of the severity and extent of periodontal disease parameters in groups stratified by disease status

| Variables | CD ($n$ = 265) Median (IQR) | $P1$ | Controls ($n$ = 265) Median (IQR) | $P2$ | UC ($n$ = 124) Median (IQR) | $P3$ |
|---|---|---|---|---|---|---|
| Average | | | | | | |
| PD | 1.89 (1.68–2.22) | **< 0.001** | 1.54 (1.37–1.73) | **< 0.001** | 2.10 (1.83–2.40) | 0.902 |
| CAL | 0.01 (0.00–0.17) | **< 0.001** | 0.00 (0.00–0.02) | **< 0.001** | 0.14 (0.01–0.38) | 1.000 |
| GR | 0.00 (0.00–0.01) | **0.007** | 0.00 (0.00–0.00) | 0.173 | 0.00 (0.00–0.09) | 1.000 |
| GI | 0.39 (0.22–0.61) | **< 0.001** | 0.07 (0.02–0.13) | **< 0.001** | 0.47 (0.27–0.72) | 0.183 |
| PLI | 0.68 (0.47–0.94) | **< 0.001** | 0.28 (0.19–0.43) | **< 0.001** | 0.70 (0.54–0.98) | 0.885 |
| Percentage of sites with | | | | | | |
| PD ≥4 mm | 0.00 (0.00–4.86) | **< 0.001** | 0.00 (0.00–0.00) | **< 0.001** | 2.38 (0.00–9.49) | 0.458 |
| PD ≥5 mm | 0.00 (0.00–0.60) | **< 0.001** | 0.00 (0.00–0.00) | **< 0.001** | 0.00 (0.00–2.38) | 1.000 |
| CAL ≥3 mm | 0.00 (0.00–2.38) | **0.001** | 0.00 (0.00–0.00) | **< 0.001** | 1.85 (0.00–6.21) | 1.000 |
| CAL ≥4 mm | 0.00 (0.00–0.00) | **< 0.001** | 0.00 (0.00–0.00) | **< 0.001** | 0.00 (0.00–1.19) | 1.000 |
| GR ≥1 mm | 0.00 (0.00–1.23) | **0.007** | 0.00 (0.00–0.00) | 0.173 | 0.30 (0.00–5.28) | 1.000 |
| GR ≥2 mm | 0.00 (0.00–0.00) | **< 0.001** | 0.00 (0.00–0.00) | **< 0.001** | 0.00 (0.00–2.47) | 1.000 |
| BOP | 14.81 (7.69–28.57) | **< 0.001** | 2.38 (0.00–7.14) | **< 0.001** | 22.77 (10.71–33.33) | 0.279 |
| CI | 53.57 (39.29–63.16) | **< 0.001** | 35.71 (21.43–51.85) | **< 0.001** | 58.01 (44.22–67.86) | 0.847 |

After adjusting for age, sex, education level, smoking, and the daily frequency of tooth-brushing, the mean values for PD, GI, PLI, and the percentages of sites with BOP and CI were logarithmically transformed, and then multiple linear regression analyses were performed to compare differences among the three groups. The remaining parameters were analysed using the Tobit regression model to compare intergroup differences. Pairwise comparisons were performed using Bonferroni correction.
$P1$: significance of the differences between patients with CD and controls; $P2$: significance of the differences between patients with UC and controls; $P3$: significance of the differences between patients with CD and UC.
Significant results ($P < 0.05$) are highlighted in bold.
BOP, bleeding on probing; CAL, clinical attachment loss; CD, Crohn's disease; CI, calculus index; GI, gingival index; GR, gingival recession; IQR, interquartile range; PD, probing pocket depth; PLI, plaque index; UC, ulcerative colitis.

IBD patients and 100 healthy subjects in Jordan. In our study, the prevalence of periodontitis in IBD patients was 37.5%, and the risk of periodontitis in IBD patients was 4.54-times higher than in controls, similar to previous reports[13–15]. However, Grössner-Schreiber *et al.*[16] failed to detect any distinct differences in the prevalence of periodontitis and the mean value of PD between IBD patients and controls in Germany. A potential explanation for these different results is the partial-mouth periodontal examination (PMPE) performed in the study by Grössner-Schreiber, which assessed only four sites of all teeth in two quadrants. PMPE underestimates the prevalence of periodontitis[38], and misjudges (under- or overestimates) the severity and extent of periodontitis[39,40]. In the present study, we used the 'gold-standard' for survey examinations, full-mouth periodontal examinations, to accurately determine the periodontal status of the participants. In addition, the different results between our study and Grössner-Schreiber's study may also be due to differences in ethnicity, education levels, and social and cultural environments.

By evaluating the severity and extent of periodontal disease, we identified significantly higher mean values for PD, CAL, the GI and BOP, as well as higher percentages of sites with a PD ≥ 5 mm, CAL ≥ 4 mm and GR ≥ 2 mm in patients with CD and UC than those in controls. These findings are inconsistent with a report by Flemmig *et al.*[17] in which the mean CAL was lower in patients with IBD than in the general population, although the difference was not statistically significant. The study by Flemmig lacked a control group, and their results were compared with epidemiological data from the Oral Health of United States Adults. In our survey, we established age- and sex-matched controls, and set strict inclusion and exclusion criteria for participants to minimise selection bias. Common confounders, namely, age, sex, education level, smoking, and the daily frequency of tooth-brushing, were controlled for in the multivariate statistical analysis.

Habashneh *et al.*[15] and Brito *et al.*[28] reported a higher prevalence and severity of periodontitis in UC patients than in CD patients. The authors proposed that the differences were related to the different pathophysiological mechanisms of the two diseases, as CD is possibly mediated by Th1 and Th17, whereas UC may be mediated by Th2[41]. In our study, after adjusting for confounding factors, significant differences in the prevalence and severity of periodontal disease were not observed between CD and UC patients. In addition, we reassessed the prevalence of periodontitis in CD and UC patients using the diagnostic criteria for periodontitis described by Habashneh *et al.* and Brito *et al.*, respectively, to analyse whether the use of different diagnostic criteria for periodontitis generated different results. However, we did not detect any difference in the prevalence of periodontitis between CD and UC patients. A retrospective study of 3,100 Chinese UC patients suggested that most UC patients in China had mild to moderate disease. Additionally, extraintestinal manifestations,

**Table 5** Binary logistic regression analyses of the differences in the prevalence of dental caries and periodontitis among the disease groups

| Variables | Dental caries | | Periodontitis | |
|---|---|---|---|---|
| | OR (95% CI) | *P*1 | OR (95% CI) | *P*2 |
| Group | | | | |
| CD | 4.27 (2.63–6.95) | **< 0.001** | 4.46 (2.50–7.95) | **< 0.001** |
| UC | 2.21 (1.24–3.94) | **0.007** | 4.66 (2.49–8.71) | **< 0.001** |
| Controls | 1 (reference) | | 1 (reference) | |
| Age (years) | 1.02 (0.99–1.04) | 0.174 | 1.12 (1.10–1.15) | **< 0.001** |
| Gender | | | | |
| Female | 1.97 (1.26–3.08) | **0.009** | 0.83 (0.51–1.35) | 1.000 |
| Male | 1 (reference) | | 1 (reference) | |
| Education | | | | |
| Less than junior college | 1.12 (0.70–1.78) | 0.642 | 0.80 (0.51–1.27) | 0.344 |
| Junior college or more | 1 (reference) | | 1 (reference) | |
| Smoking | | | | |
| Current smoker | 1.89 (0.86–2.15) | 0.113 | 1.65 (0.80–3.38) | 0.174 |
| Ex-smoker | 1.07 (0.55–2.11) | 0.836 | 1.11 (0.57–2.15) | 0.764 |
| Non-smoker | 1 (reference) | | 1 (reference) | |
| Frequency of tooth-brushing per day | | | | |
| < 2 times | 1.64 (1.07–2.52) | **0.024** | 1.03 (0.66–1.63) | 0.890 |
| ≥ 2 times | 1 (reference) | | 1 (reference) | |

Binary logistic regression analyses were used to determine the associations of CD and UC (independent variable) with dental caries or periodontal disease (dependent variable) after adjusting for age, sex, education level, smoking, and the daily frequency of tooth-brushing.
Significant results ($P < 0.05$) are highlighted in bold.
CD, Crohn's disease; CI, confidence interval; OR, odds ratio; UC, ulcerative colitis.

complications, operative rates, mortality and the rate of cancer development were all lower in Chinese UC patients than those reported in studies performed in other countries[42]. Therefore, we speculate that the lack of difference in the prevalence of periodontal disease between patients with CD and UC observed in our study may be due to the fact that UC patients in China typically have a milder form of disease than patients in Western countries. However, the exact cause is still unclear, and further studies are warranted to confirm this hypothesis.

Periodontal disease and IBD have been shown to share common pathogenic mechanisms and risk factors as both involve complex interactions between microorganisms and the host immune system[43]. On the one hand, IBD can alter the periodontal flora. Brito *et al.*[44] found that IBD patients harbour higher levels of bacteria in inflamed subgingival sites compared with non-IBD patients. On the other hand, the periodontal flora can disrupt intestinal function. Oral administration of *Porphyromonas gingivalis* (strain W83) in C57BL/6 mice had significant effects on the composition of gut microbes and on the barrier function of the intestines, and led to the spread of intestinal bacteria to the liver[45]. Recently, two cohort studies conducted in Taiwan revealed an increased risk of periodontitis in CD patients compared with that in non-CD subjects [hazard ratio (HR) = 1.36, 95% CI: 1.25–1.48], and the risk of UC was also increased in patients with periodontitis compared with that in controls (HR = 1.56, 95% CI: 1.13–2.15), indicating a two-way interaction between IBD and periodontitis[20,46]. However, the specific mechanisms of pathogenesis and interactions between the conditions remain unclear. To date, no cohort studies on IBD and periodontal disease have been conducted in mainland China.

According to the questionnaire survey, although the subjects had oral self-care awareness, most did not properly perform oral hygiene behaviours, and < 15% of the subjects used dental floss, interdental brushes or oral irrigators. Additionally, more than half of the participants had never seen a dentist, and only approximately 10% of the subjects had their teeth cleaned in the past year. IBD patients had higher mean values of PLI and dental CI than controls. These results suggest that oral health education and effective treatment are required for IBD patients, including the use of fluoride toothpaste, brushing the teeth more often, and regular dental checkups and prophylaxes.

## Strengths and limitations

To our knowledge, this is the first large-scale clinical study to reveal an association between oral diseases and IBD in mainland China. The First Affiliated Hospital of Sun Yat-sen University initially established the Center for Inflammatory Bowel Disease in China, which manages a large number of IBD patients. According to the established criteria of the World Health Organization and the Fourth Oral Health Survey in China, we designed a questionnaire and conducted a comprehensive oral examination of each participant. In addition, we used several methods to control confounders, including setting strict inclusion and exclusion criteria, using a matching design, and performing multivariate statistical analysis. This study also has some limitations. First, the findings cannot explain any causal relationship between oral diseases and IBD because the cross-sectional study only provides a "single assessment" of the investigated diseases without determining the temporal relationship between exposure and outcomes. Second, participants were recruited from two hospitals within the same area. Therefore, the results may not be representative of the general population, and selection bias may exist. Well-designed, prospective controlled longitudinal studies of patients with/without IBD and oral diseases are needed to further clarify the interrelations between IBD and oral diseases, as well as their common mechanisms of pathogenesis.

## CONCLUSIONS

In conclusion, Chinese patients with IBD had an increased risk of dental caries and periodontal disease and worse oral health, suggesting that monitoring the oral health of IBD patients is particularly important. Dentists and gastroenterologists should understand the potential relationship among dental caries, periodontal disease and IBD, and strengthen oral health education and multidisciplinary treatment for IBD patients to prevent the occurrence and development of oral diseases and improve patients' quality of life.

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### Conflict of interest

None.

### Author contributions

Limin Zhang designed the study, examined participants' oral and teeth, analysed and interpreted data, and wrote the manuscript. Jiamin Zhou, Shan Chen and Yingfan Zhang designed the study, collected, analysed and interpreted data. Xiang Gao and Jinxin Zhang designed the study, analysed and interpreted data, and provided conceptual advice. Baili Chen and Junying Yang designed and conducted the study, analysed and interpreted data, and revised the manuscript for intellectual content. All authors read and approved the final version of the manuscript.

## REFERENCES

1. Bui FQ, Almeida-da-Silva C, Huynh B *et al*. Association between periodontal pathogens and systemic disease. *Biomed J* 2019 42: 27–35.
2. Zhou Y, Jiang S, Li KY *et al*. Association between oral health and upper respiratory tract infection among children. *Int Dent J* 2018 68: 122–128.
3. Yuksel SS, Ozturk A, Bektas A *et al*. Periodontal treatment is more effective in gastric *Helicobacter pylori* eradication in those patients who maintain good oral hygiene. *Int Dent J* 2019 69: 392–399.
4. Lauritano D, Boccalari E, Stasio DD *et al*. Prevalence of oral lesions and correlation with intestinal symptoms of inflammatory bowel disease: a systematic review. *Diagnostics (Basel)* 2019 9: 77–92.
5. Mortada I, Leone A, Gerges GA *et al*. Oral manifestations of inflammatory bowel disease. *J Biol Regul Homeost Agents* 2017 31: 817–821.
6. Zhang YZ, Li YY. Inflammatory bowel disease: pathogenesis. *World J Gastroenterol* 2014 20: 91–99.
7. Vegh Z, Kurti Z, Lakatos PL. Epidemiology of inflammatory bowel diseases from west to east. *J Dig Dis* 2017 18: 92–98.
8. Ng SC, Shi HY, Hamidi N *et al*. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet* 2018 390: 2769–2778.
9. Li X, Song P, Li J *et al*. The disease burden and clinical characteristics of inflammatory bowel disease in the Chinese population: a systematic review and meta-analysis. *Int J Environ Res Public Health* 2017 14: 238–249.
10. Wehkamp J, Gotz M, Herrlinger K *et al*. Inflammatory bowel disease. *Dtsch Arztebl Int* 2016 113: 72–82.
11. Aloi M, Carloni E, Palmacci F *et al*. Quality of life and disease activity in children and adolescents with inflammatory bowel disease. *J Crohn's Colitis* 2019 13: S485.
12. Dudeney TP. Crohn's disease of the mouth. *Proc R Soc Med* 1969 62: 1237.
13. Papageorgiou SN, Hagner M, Nogueira AV *et al*. Inflammatory bowel disease and oral health: systematic review and a meta-analysis. *J Clin Periodontol* 2017 44: 382–393.
14. Vavricka SR, Manser CN, Hediger S *et al*. Periodontitis and gingivitis in inflammatory bowel disease: a case-control study. *Inflamm Bowel Dis* 2013 19: 2768–2777.
15. Habashneh RA, Khader YS, Alhumouz MK *et al*. The association between inflammatory bowel disease and periodontitis among Jordanians: a case-control study. *J Periodontal Res* 2012 47: 293–298.
16. Grössner-Schreiber B, Fetter T, Hedderich J *et al*. Prevalence of dental caries and periodontal disease in patients with inflammatory bowel disease: a case-control study. *J Clin Periodontol* 2006 33: 478–484.
17. Flemmig TF, Shanahan F, Miyasaki KT. Prevalence and severity of periodontal disease in patients with inflammatory bowel disease. *J Clin Periodontol* 1991 18: 690–697.

18. Tan CX, Brand HS, de Boer NK *et al*. Gastrointestinal diseases and their oro-dental manifestations: Part 2: ulcerative colitis. *Br Dent J* 2017 222: 53–57.

19. Tan CX, Brand HS, de Boer NK *et al*. Gastrointestinal diseases and their oro-dental manifestations: Part 1: Crohn's disease. *Br Dent J* 2016 221: 794–799.

20. Chi YC, Chen JL, Wang LH *et al*. Increased risk of periodontitis among patients with Crohn's disease: a population-based matched-cohort study. *Int J Colorectal Dis* 2018 33: 1437–1444.

21. Wang HM, Qu YZ, Li T *et al*. The characteristics of oral mucosal in patients with Crohn's disease. *J Clin Stomatol* 2014 30: 735–737.

22. Magro F, Gionchetti P, Eliakim R *et al*. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 1: definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders. *J Crohns Colitis* 2017 11: 649–670.

23. Gomollón F, Dignass A, Annese V *et al*. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's disease 2016. Part 1: Diagnosis and Medical Management. *J Crohns Colitis* 2017 11: 3–25.

24. Yeung CA. *Oral Health Surveys: Basic Methods*, 5th ed. London: British Dental Journal; 2014. p. 42-56; 111-114.

25. Wang X. *Report of the Fourth National Oral Health Epidemiological Survey*, 4th ed. Beijing: People's Medical Publishing House; 2018. p. 149–171; 188–191.

26. Eke PI, Page RC, Wei L *et al*. Update of the case definitions for population-based surveillance of periodontitis. *J Periodontol* 2012 83: 1449–1454.

27. Rooney TP. Dental caries prevalence in patients with Crohn's disease. *Oral Surg Oral Med Oral Pathol* 1984 57: 623–624.

28. Brito F, de Barros FC, Zaltman C *et al*. Prevalence of periodontitis and DMFT index in patients with Crohn's disease and ulcerative colitis. *J Clin Periodontol* 2008 35: 555–560.

29. Szymanska S, Lördal M, Rathnayake N *et al*. Dental caries, prevalence and risk factors in patients with Crohn's disease. *PLoS ONE* 2014 9: e91059.

30. Yang X, Zhang JC, Li M *et al*. Food intolerance and inflammatory bowel disease. *Shi Jie Hua Ren Xiao Hua Za Zhi* 2011 19: 3182–3185.

31. Lim HS, Kim SK, Hong SJ. Food elimination diet and nutritional deficiency in patients with inflammatory bowel disease. *Clin Nutr Res* 2018 7: 48–55.

32. Casanova MJ, Chaparro M, Molina B *et al*. Prevalence of malnutrition and nutritional characteristics of patients with inflammatory bowel disease. *J Crohns Colitis* 2017 11: 1430–1439.

33. Uranga JA, López-Miranda V, Lombó F *et al*. Food, nutrients and nutraceuticals affecting the course of inflammatory bowel disease. *Pharmacol Rep* 2016 68: 816–826.

34. Schütz T, Drude C, Paulisch E *et al*. Sugar intake, taste changes and dental health in Crohn's disease. *Dig Dis* 2003 21: 252–257.

35. Sundh B, Emilson CG. Salivary and microbial conditions and dental health in patients with Crohn's disease: a 3-year study. *Oral Surg Oral Med Oral Pathol* 1989 67: 286–290.

36. Said HS, Suda W, Nakagome S *et al*. Dysbiosis of salivary microbiota in inflammatory bowel disease and its association with oral immunological biomarkers. *DNA Res* 2014 21: 15–25.

37. Koutsochristou V, Zellos A, Dimakou K *et al*. Dental caries and periodontal disease in children and adolescents with inflammatory bowel disease: a case-control study. *Inflamm Bowel Dis* 2015 21: 1839–1846.

38. Kingman A, Albandar JM. Methodological aspects of epidemiological studies of periodontal diseases. *Periodontol 2000* 2002 29: 11–30.

39. Tran DT, Gay I, Du XL *et al*. Assessing periodontitis in populations: a systematic review of the validity of partial-mouth examination protocols. *J Clin Periodontol* 2013 40: 1064–1071.

40. Chu Y, Ouyang X. Accuracy of partial-mouth examination protocols in periodontal epidemiological surveys: a systemic review. *Zhonghua Kou Qiang Yi Xue Za Zhi* 2014 49: 549–553.

41. Indriolo A, Greco S, Ravelli P *et al*. What can we learn about biofilm/host interactions from the study of inflammatory bowel disease. *J Clin Periodontol* 2011 38(Suppl 11): 36–43.

42. Infections Bursal Disease Cooperation Group of China, Wang YF, Ouyang Q. A retrospective study of 3100 inpatients with ulcerative colitis in China. *Chin J Dig* 2006 26: 368–372.

43. Lira-Junior R, Figueredo CM. Periodontal and inflammatory bowel diseases: Is there evidence of complex pathogenic interactions? *World J Gastroenterol* 2016 22: 7963–7972.

44. Brito F, Zaltman C, Carvalho AT *et al*. Subgingival microflora in inflammatory bowel disease patients with untreated periodontitis. *Eur J Gastroenterol Hepatol* 2013 25: 239–245.

45. Nakajima M, Arimatsu K, Kato T *et al*. Oral administration of *P. gingivalis* induces dysbiosis of gut microbiota and impaired barrier function leading to dissemination of enterobacteria to the liver. *PLoS ONE* 2015 10: e134234.

46. Lin CY, Tseng KS, Liu JM *et al*. Increased risk of ulcerative colitis in patients with periodontal disease: a nationwide population-based cohort study. *Int J Environ Res Public Health* 2018 15: 2602–2613.

*Correspondence to:*
*Dr Baili Chen,*
*Department of Gastroenterology,*
*The Center for Inflammatory Bowel Disease,*
*The First Affiliated Hospital,*
*Sun Yat-sen University,*
*Guangzhou 510080,*
*Guangdong*
*China,*
*Email: chenbaili05@163.com*
*and*
*Dr Junying Yang,*
*Department of Stomatology,*
*The First Affiliated Hospital,*
*Sun Yat-sen University,*
*Guangzhou 510080,*
*Guangdong,*
*China,*
*Email: aliceyang2006@126.com*

 