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Review Article

Susceptibility of periodontitis and its impact on patients with inflammatory bowel disease

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ABSTRACT

Inflammatory bowel disease (IBD) and periodontitis are chronic, progressive, inflammatory diseases with similarly complex pathogeneses that include dysbiotic microbiota and dysregulated immune-inflammatory responses, and both are influenced by genetic and environmental factors. This review aimed to provide an overview of the emerging evidence dealing with the susceptibility of periodontal disease and its impacts on patients with IBD by explaining the risk factors, possible pathogenic interactions, and disease activity by reviewing recent literature from open-source journals on the same topic. There seems to be an increased prevalence of periodontitis in patients with IBD when compared to healthy controls, which was more pronounced in ulcerative colitis (UC) than Crohn's disease (CD). In addition, both greater severity and extent of periodontitis have been found in IBD patients when compared to healthy controls. Age, gender, lifestyle or environmental factors, and smoking history were the associated risk factors. In conclusion, the findings suggest that patients with IBD be kept under close surveillance to prevent periodontitis and/or mitigate its progression. Oral health education and effective treatment are required for IBD patients. However, we still need more data derived from human studies to confirm the results. Thus, mechanistic studies are warranted to clarify this possible bidirectional association.

Keywords: Periodontitis disease, Inflammatory bowel disease, Ulcerative colitis, Crohn's disease

INTRODUCTION

Inflammatory bowel disease (IBD), a chronic relapsing and remitting intestinal inflammatory disease that comprises two forms, ulcerative colitis (UC) and Crohn's disease (CD) is a significant problem across the world, affecting about one in 200 people in developed nations and having a rising incidence and prevalence in developing nations.[1] Crohn's disease affects the whole gastrointestinal tract and entails transmural inflammation, whereas UC primarily affects the colon and rectum with an inflammation limited to the mucosal layer.[2] Both types of IBD occur in genetically susceptible individuals due to the antigenic effect of intestinal microbiota.[3] Numerous debilitating indications, such as anorexia, lethargy, rectal bleeding, and urgent diarrhoea, are associated with IBD and can frequently result in inadequate psychological well-being with serious repercussions.[4]

Many of these IBD-relevant causes and effects also increase the chance of developing periodontitis.[5] Additionally, research has demonstrated that immune inflammatory processes and tissue degradation are features of the disease development in both IBD and periodontitis.[5] Periodontitis is strongly linked to the pathogenesis of IBD, and up to 37% of IBD patients have oral symptoms, including pyostomatitis, cobblestoning, aphthous ulcers, lymphadenopathy, and oral soft-tissue lesions.[6-8] An increased prevalence of periodontal diseases has been reported in IBD patients over the last few decades. Periodontitis is a chronic inflammatory condition that results in irreparable destruction of the periodontium and is brought on by oral dysbiosis. It leads to gingival bleeding and tooth mobility and loss and negatively affects the general health of the patient by altering critical functions such as nutrition, swallowing, and phonation, as well as self-perception.[9]

Even periodontitis is a commonly quoted extraintestinal manifestation of IBD. The susceptibility and its impact on IBD are still inconclusive. In this review, we aimed to evaluate the studies dealing with IBD and the susceptibility of periodontal diseases and their relation, emphasizing the microbiota and cytokine roles and the impacts on IBD activity or severity.

DISCUSSION

Prevalence and risk of periodontal disease in IBD patients

A handful of epidemiological studies have been performed to investigate a possible increase in the prevalence of periodontal disease in patients with IBD, and they have revealed that it is more common in various IBD populations. A hospital-based observational study showed that periodontitis affected more sites per subject in the IBD group in the US population and reported an overall 12% prevalence of periodontal disease.[10] Patients with IBD were found to be more susceptible to mild to moderate periodontitis than people without IBD. This early study's reliance on partial-mouth clinical periodontal data recording raises concerns about underestimating bias in prevalence research. There were no confounding variables like food habits, medications, smoking, or other systemic disorders noted. Therefore, it is important to carefully analyse these conflicting results. In a case-control study, higher prevalence and severity of periodontitis were found in IBD patients than in non-IBD comparisons in Jordanians.[11] Brito et al reported that patients with UC had a greater prevalence of periodontitis (90.0%) and CD (81.8%) than controls (67.6%) in a Brazilian population.[12] According to Yu et al in the Taiwan cohort, the rate of periodontitis was higher in IBD cases than in the control group (risk factor: 1.82 times) after accounting for all possible confounding factors to minimize bias.[13] The large population subset and the longitudinal design of the study—over nine years of follow-up—make it more relevant that the authors conclude by recommending an intensive regular oral check-up for periodontal status IBD patients in Taiwan. A meta-analysis of nine cross-sectional studies (n=1,297) concluded that patients with IBD had a 33.2% higher risk of periodontitis than control groups without IBD.[14] Another recent meta-analysis included six studies comprised of 599 IBD patients and 448 controls and found an OR of 3.17 (95% CI: 2.09–4.8) with 0% heterogeneity, and the pooled OR for the sub categories of CD and UC were 3.64 (95% CI: 2.33–5.67) and 5.37 (95% CI: 3.30–8.74), respectively.[15] Other recent research showed that in the last decade, patients with IBD had a higher chance of developing periodontitis.[16] In accordance with the latest survey report from Sweden, periodontitis is strongly linked to both an increase in IBD disease activity and an increase in IBD-related impairment.[17] Also, IBD patients were found to have deeper periodontal pockets, less clinical attachment, and more severe gingival bleeding compared with those of the healthy controls.[18] In an interesting finding, Prideaux et al investigation of the Asian population revealed a gender preference for the association.[19] They found that among Asian women with IBD, the risk of developing periodontitis was noticeably higher than in the non-IBD group. They concluded that gender differences could be one of the risk factors for developing periodontitis because, in their study of IBD patients, females had a higher risk than males. In a subsequent study, which focused on the epidemiology of IBD in the Asian population, in addition to confirming Prideaux et al's findings regarding gender prediction, it was hypothesized that hormonal influences may be a significant contributor to the phenomenon of higher risk of periodontitis in female patients.[20] Considering all of this together, periodontitis in IBD patients was more prevalent across the world.

Since each form of IBD (UC or CD) involves different pathogens and disease behaviors, each subtype has a unique effect on periodontal health, with UC patients experiencing more severe periodontitis than CD patients.[16,21] However, uncertainty persists regarding the core pathophysiological mechanisms. On the basis of a full-mouth examination, age-matched case-control research in the Brazilian population found that UC patients had a larger percentage of sites with clinical attachment loss of less than 3 mm than CD patients.[21] Additionally, they found that smoking was a major influencing factor in the association between subtypes of IBD and periodontitis. The other contributing or common predisposing factors possessed by IBD, and periodontitis are age and genetic predisposition, as well as environmental or lifestyle factors. The risk and protective parameters for periodontitis varied in subtypes of IBD patients. The two main risk factors for periodontitis in CD patients were a history of smoking and clinical activity. But smoking seems to play a protective role in UC, with a decrease in the expression of pro-inflammatory Th1/Th17 cytokines in the colon.[22] However, aspects like smoking and socioeconomic level can skew this association, and smokers were in fact more severely impacted than non-smokers. In addition, in IBD subgroups compared with

healthy controls, the existence of perianal extraintestinal manifestations in IBD and proctitis in patients with UC were risk factors for periodontitis.[23] The drug species used for the treatment of IBD may cause changes in periodontal tissues due to their direct toxic effects as well as indirect immune depressive effects with the emergence of opportunistic infections. However, in a retrospective cohort study, authors speculated an increased hazard ratio for subsequent periodontitis among CD patients when opposed to matched controls, where management of CD showed protection against periodontitis due to the protective effect of some specific medications.[24]

In a large matched case-control study involving 1108 cases and 3429 matched controls, patients with IBD had higher odds of having worse self-perceived oral health and severe periodontitis compared to controls.[25] Another matched case-control study revealed that significantly more patients with IBD had moderate or severe periodontitis (85.6% versus 65.6%) and severe periodontitis (36.7% versus 25.6%) compared to controls. Differences were more pronounced in the 35- to 50-year-old and 51- to 65-year-old age groups, but there were no significant differences between CD and UC.[26] However, in contrast, a case-control study asserted that IBD was not related to worsening periodontal diseases, indicating that IBD did not necessarily enhance susceptibility to periodontitis.[27] Factors such as the elderly age group, and smoking status, were found to have greater odds of developing periodontitis and its severity in IBD patients.[28] Different IBD subtypes and disease activity/remission stages have different dietary preferences and drug usage. To determine whether or not these characteristics independently relate to periodontitis and IBD subtype, additional research must be conducted.

Biological rationale for the relation between IBD and periodontitis

The reasons why IBD patients present with poorer periodontal health have not been systematically investigated. Since both diseases share pathogenic similarities and their development is related to an aberrant immune response to a dysbiotic microbiota, disturbances of these factors are proposed as the mechanisms responsible for the interaction between the diseases.

IBD and periodontitis are interrelated because of their shared etiologies, which include dysbiotic microbiota, immune response dysregulation, and persistent inflammation in people with genetic susceptibility. In recent decades, the relationship between IBD and periodontitis has been established in two ways: by infectious or microbiota evidence and by inflammatory evidence. The relationship between oral microbiota and a reasonable factor for susceptibility to periodontal disease in IBD patients has been investigated in several studies thus far. Van Dyke et al were the first to report a high prevalence of "unusual bacteria," representing more than 90% of the overall flora and characterised as tiny motile rods that were most consistent with the genus *Wolinella*, in the periodontal pockets of IBD patients relative to those of non-IBD patients.[29]

Docktor et al and Said et al reported the compositional diversity of the gingival or salivary flora among IBD and control patients.[30,31] Certain species, according to Lira-Junior et al may harm host-microbe interactions in those who have IBD and untreated periodontal disease.[32] Strauss et al observed an elevated prevalence (69%) of the subgingival microbiota in IBD patients, which is firmly related to periodontitis. Fusobacterium spp. recovered in colon biopsies of IBD patients and were identified as *F. nucleatum*, a periodontal pathogen. The *F. nucleatum* identified in biopsies of inflamed tissue was more invasive than those isolated from healthy tissue from either IBD or control patients.[33] In a site- and taxa-specific way, the oral microbiome demonstrated IBD-associated dysbiosis in Somineeni et al study.[34] Oral microbiota may identify between patients with inflammatory bowel disease (IBD), with salivary microbiota performing best and closely matching stools and other oral sites. Plaque samples showed a rather high level of dysbiosis, and the bacteria that were most commonly associated with the condition belonging to the phylum Firmicutes.[34] In the latest case-control study, Imai et al stated that in both patients with UC and those with CD, the gut microbiome was significantly more like the oral microbiome than in healthy controls.[35] Research on the subgingival microbiota in patients with untreated periodontal disease and IBD found that, regardless of the level of periodontal destruction, differences in several species, including *Campylobacter gracilis* and *Treponema denticola*, existed between patients with CD, UC, and controls in inflamed sites. These differences were more noticeable in CD patients.[32]

Individuals who are genetically predisposed to dysbiosis and immunological inflammatory reactions caused by pathogenic microbes are more prone to encounter these conditions. By traveling via the bloodstream from one part of the body to another faraway organ, immune cells and inflammatory cytokines might cause later disorders.[36,37]

Limited studies have investigated cytokines in the gums, serums, and intestinal tissue of IBD and non-IBD patients. In the course of IBD, elevated cytokines may be secreted systemically. Increased levels of proinflammatory cytokines have been noticed in the saliva of IBD patients. The cytokine parameter in the crevicular fluid of IBD patients has been found to be very similar to periodontal clinical parameters, except for IL-4 levels. Greater levels of salivary TNF-α, IL-1β, and IL-6 were discovered in patients with active CD, and elevated salivary TNF-α and IL-6 correspond with particular oral lesions.[38] Systemic administration of Anti-TNF has been used to manage IBD.[39] Additionally, studies have indicated that anti-TNF medication has a positive impact on periodontal health.[40] This evidence suggests that the immunological etiologies of periodontitis and IBD are related.

Contrastingly, periodontal flora can impair intestinal function, and the effect of the oral microbiota on gut dysbiosis has also been studied. However, the mechanisms by which oral bacteria may contribute to the advancement of IBD are still evolving. In a cohort study, the risk of UC was also increased in periodontitis subjects in comparison to the control subjects (HR=1.56, 95% CI: 1.13–2.15), indicating a two-way interaction between IBD and periodontitis. A person generates and swallows about 1.5 litres of saliva every day, which contains about one gram of bacteria. This is notable as background information. This oral fluid is the most plausible vehicle for oral microorganisms and their biologically active components to be translocated to other parts of the digestive tract,[41] making it convincible that oral microbiology would affect gastrointestinal microbiology. Mechanistic studies are warranted to unveil the bidirectional association of specific mechanisms of pathogenesis and interactions between the conditions.

CONCLUSION

IBD was related to a higher risk of periodontitis compared to healthy control subjects, which was more pronounced in UC than in CD. The findings suggest that patients with IBD are kept under close surveillance to prevent periodontitis and/or mitigate its progression. 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 check-ups and prophylaxes.

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