ORAL MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASES: THE ROLE OF ORAL HEALTH IN DIAGNOSIS AND CLINICAL MONITORING

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Herick Parente Grangeiro[1], Livya Maria Vasconcelos Lima Sousa[2], Raissa Linhares Ribeiro de Menezes[3], Beatriz Silva de Sousa[4], Isac Tibúrcio de Araújo Silva[5] and Jordan Marques de Oliveira Freire[6]

ABSTRACT

The digestive system is responsible for the ingestion, digestion and absorption of nutrients, in addition to the elimination of unabsorbed substances. Pathological conditions such as gastrointestinal infections, inflammatory bowel diseases (IBD) and neoplasms affect its function, impacting quality of life. Celiac Disease (CD) is an autoimmune disorder triggered by gluten, whose oral manifestations, such as enamel defects and ulcers, are important for early diagnosis. Crohn's Disease (CD) and Ulcerative Colitis (UC) also have oral complications such as stomatitis and periodontitis, which help in the diagnosis and monitoring of the evolution of the diseases. These conditions require a multidisciplinary approach, with emphasis on the role of oral health professionals in the early detection and control of oral complications, improving clinical outcomes and patients' quality of life.

Keywords: Intestinal Inflammation. Oral Manifestation. Dentistry.

[1]Dental Student
Luciano Feijão College
E-mail: herickparente@gmail.com
ORCID: https://orcid.org/0009-0003-8479-5495
LATTES: https://lattes.cnpq.br/7376381092497206
[2]Dental Student
Luciano Feijão College
E-mail: livyamariavasconcelos@hotmail.com
ORCID: https://orcid.org/0009-0002-3994-8774
LATTES: https://lattes.cnpq.br/7126509779398517
[3]Dental Student
Luciano Feijão College
Email: raissalmenezes@outlook.com
ORCID: https://orcid.org/0009-0007-8956-7511
LATTES: http://lattes.cnpq.br/3506483444172272
[4]Dental Student
Luciano Feijão College
E-mail: beatrizsilvasds@outlook.com
ORCID: https://orcid.org/0009-0006-9130-5484
LATTES: https://lattes.cnpq.br/3145698401332429
[5]Dental Student
University of Fortaleza
Email: isacaraujo2003@gmail.com
ORCID: https://orcid.org/0009-0002-9741-4391
LATTES: http://lattes.cnpq.br/3565253776880595
[6]Dr. in Biotechnology
Luciano Feijão College
Email: jordaniafreire25@gmail.com
ORCID: https://orcid.org/0000-0002-3412-8964
LATTES: http://lattes.cnpq.br/9070055317899542

INTRODUCTION

The digestive system comprises the gastrointestinal tract, which includes eight major organs: oral cavity, pharynx, esophagus, stomach, small intestine, large intestine, liver, gallbladder, and pancreas. This anatomically continuous structure performs essential functions, such as the ingestion, digestion and absorption of nutrients from food, as well as the elimination of metabolites and unabsorbed substances. In addition, the gastrointestinal tract acts as a dynamic ecosystem, interacting with thousands of microorganisms that play key roles in immune and metabolic homeostasis (Sommer & Bäckhed, 2013).

However, the digestive system is susceptible to a wide variety of conditions that compromise its functionality and impact the quality of life of individuals. Among these, gastrointestinal infections, inflammatory bowel diseases (IBD) and neoplasms stand out, which are important public health problems due to their high morbidity and mortality (GBD 2019 Inflammatory Bowel Disease Collaborators, 2020). Epidemiological data indicate that the global incidence of IBD has increased significantly over the last decades, from 20,897.4 cases in 1990 to 25,658.6 cases in 2019, representing a growth of 22.78%. Despite this, mortality associated with IBD showed a reduction of 56.17% in the same period, suggesting advances in therapeutic approaches and management of the disease (Zhang et al., 2021). In addition, there is a trend towards diagnosis at increasingly younger ages, which reinforces the need for preventive and therapeutic strategies adapted to different age groups (Khan, Kuenzig & Benchimol, 2021).

In addition to neoplasms and chronic inflammatory diseases, other gastrointestinal pathologies, such as celiac disease, Crohn's disease, and ulcerative colitis, also have a substantial impact on systemic health. These conditions often manifest beyond the digestive tract, and can affect the oral cavity through the development of ulcerations, lesions, and mucosal changes (Aghdassi et al., 2011). These manifestations reinforce the importance of a multidisciplinary approach, considering the interconnection between the digestive system and other aspects of health, such as oral and metabolic health. The growing impact of these diseases reflects not only on digestive health, but also on economic costs and health systems, challenging health professionals to adopt more effective and innovative care models.

In view of the growing prevalence of digestive diseases and their systemic repercussions, it is essential to foster studies and interventions aimed at prevention, early diagnosis, and integrated management of these conditions. Strategies that involve health education, improved access to specialized services, and therapeutic advances are essential for promoting digestive health and the well-being of the population.

METHODOLOGY

This study is a narrative review of the literature, carried out through searches in books and scientific articles that presented content about inflammatory diseases of the gastrointestinal tract in order to gather in a single work general and punctual information on the topic addressed.

It is noteworthy that, considering the intrinsic characteristics of narrative review, the study is not developed based on a specific guiding question, but on a broad theme. In addition, the selection of the source of information was not based on a systematized strategy, but rather on general publications on the subject, providing the reader with a comprehensive and updated view of a specific theme in a short period of time.

RESULTS AND DISCUSSION

ORAL MANIFESTATIONS OF CELIAC DISEASE: DIAGNOSTIC INDICATORS AND CLINICAL IMPLICATIONS

Celiac Disease (CD) is an intestinal autoimmune disorder triggered by exposure to gluten in genetically predisposed individuals, carriers of the HLA-DQ2 or HLA-DQ8 alleles. This chronic immune response results in inflammation of the intestinal mucosa, leading to atrophy of the villi of the small intestine and consequent malabsorption of essential nutrients (Irvine, A.J. et al., 2017). The condition has an estimated global prevalence of between 0.7% and 1.4% of the population (Fasano, A.; Catassi, C., 2012; Singh P. et al., 2018).

Although CD is often associated with gastrointestinal symptoms such as chronic diarrhea, abdominal pain, and weight loss, one study showed that 62% of adults had extraintestinal manifestations. Factors such as circulating autoantibodies, inflammatory cytokines, and nutritional deficiencies are pointed out as determinants of these manifestations (Jericho H. et al., 2017).

Extraintestinal manifestations can be classified into neurological (Hadjivassiliou M. et al., 2019), ocular (Mollazadegan K. et al., 2012), dermatological (Silvester J.A. et al., 2016), musculoskeletal (Heikkila K. et al., 2015) and oral (Rodrigo L. et al., 2018) conditions.

Among the extraintestinal alterations, oral manifestations are of great relevance, since the mouth constitutes the initial part of the digestive system. Thus, alterations in this system can provide diagnostic evidence and markers of CD activity (Ferreira, R.O. et al., 2017; Laurikka, P. et al., 2018). The main oral occurrences in celiac patients include tooth enamel defects, recurrent aphthous ulcer, dry mouth, atrophic glossitis, and burning sensation on the tongue (Nieri M. et al., 2017).

Tooth enamel defects are common changes in patients with CD. (Ahmed et al.,

2021) reported that 66.9% of celiac adults had hypoplasia, discoloration of the grooves on the permanent teeth. The relationship between these changes and CD is often associated with nutrient malabsorption. However, additional factors such as disruption of amelogenesis and autoimmune reactions against amelogenins and ameloblastins also play a significant role in enamel mineralization (Wieser H. et al., 2023). Thus, these alterations can be considered useful markers for the early diagnosis of CD (Simão, T.L.; Ricciardi, F.P.; Braga, T.C.R., 2023).

Recurrent aphthous ulcers are painful oral lesions often observed in patients with CD (Rodrigo L. et al., 2018). Its pathogenesis may be related to the deficiency of micronutrients, such as iron, folic acid, and vitamin B12, due to intestinal malabsorption, or to direct immune reactions to gluten exposure (Rodrigo L. et al., 2018; Oliveira, A.B.; Lopes, L.M.; Mota, R.M., 2022). Patients with recurrent aphthous ulcer have an imbalance in inflammatory cytokines, with upregulation of IL-2 and TNF-alpha and reduction of anti-inflammatory cytokines, such as TGF-b and IL-10, a pattern also observed in celiacs (Alebióda Z. et al., 2014).

Another condition associated with CD is atrophic glossitis, which is characterized by a smooth, reddish tongue. In addition, CD can affect the salivary glands, resulting in xerostomia, which increases the risk of cavities and gum disease. The reduction in salivary flow impairs acid neutralization, compromising oral homeostasis and contributing to a cycle of oral complications (Machado, M.S.; Carvalho, P.V.; Ferreira, J.R., 2021; Rogers et al., 2015).

Other manifestations include increased predisposition to periodontal disease due to chronic inflammation and immune compromise. Erythematous lesions in the oral mucosa have also been reported, possibly associated with direct irritation by gluten-containing foods (Catassi, C.; Fasano, A., 2008).

The diagnosis of CD is based on serological tests, such as anti-tissue transglutaminase (anti-tTG) and antiendomysium (EMA) antibodies, in addition to histological confirmation by means of small bowel biopsy. Dental surgeons play a crucial role in the early recognition of oral signs of CD, especially in patients without classic gastrointestinal symptoms. Detailed clinical evaluation of the oral cavity can aid in diagnostic suspicion, allowing referral for medical investigation and contributing to significant improvements in patients' quality of life (Rubio-Tapia, A.; Murray, J.A., 2010).

CROHN'S DISEASE: MANIFESTATIONS, DIAGNOSIS AND MANAGEMENT

Crohn's Disease (CD) is a chronic inflammatory condition of the gastrointestinal tract,

often associated with genetic factors and triggered by environmental elements (Kong et al., 2021). These factors contribute to an imbalance between luminal antigens and the immune response of the intestinal mucosa, perpetuating the inflammatory process and favoring the appearance of complications, such as intestinal fibrosis, strictures, and fistula formation (Matsuoka et al., 2018; Santos et al., 2021). This inflammatory bowel disease mainly affects the mucous membranes of the small intestine and colon, although it can compromise other organs in specific cases (Matsuoka et al., 2018; Ferreira et al., 2021; Fumery et al., 2018; Thia et al., 2010).

Evidence indicates that genetic predisposition and the interaction between the innate and adaptive immune systems play crucial roles in activating and regulating the immune response, influencing both the progression and the form of manifestation of the disease (Hedin et al., 2019; Barro et al., 2021; Brandão, C. F., et al., 2020). A striking feature of Crohn's Disease is its segmented manifestation, with areas of inflammation separated by stretches of healthy tissue (Venito et al., 2022). In addition, extraintestinal manifestations may be present, amplifying the systemic impact of the disease (Rubin & Palazza, 2006; Kira, 2011; Millan, 2017). These manifestations are more frequent in young patients at the onset of the disease, and may present clinically before or after diagnosis (Jang, Kang, & Choe, 2019).

Crohn's disease can present several extra-intestinal manifestations, including anemia, inflammatory joint changes, hepatobiliary diseases, metabolic osteopathies, ocular complications, nephropathies, mucocutaneous lesions and changes in the oral cavity. The oral cavity, as it is interconnected to the gastrointestinal tract, is a site prone to various manifestations of the disease, reflecting its systemic and inflammatory nature. Oral lesions affect about 0.5% to 20% of patients and can be the first indication of the disease, helping in early diagnosis (Laranjeira et al., 2015). Among the main oral symptoms, aphthous stomatitis, periodontitis, and orofacial granulomatosis stand out (Pecci-Lloret et al., 2023).

Aphthous lesions are among the most common oral manifestations associated with Crohn's disease. This symptom can affect patients of all age groups, being more frequent in the jugal, labial, and oral mucosa (Scheper & Brand, 2002; Fatahzadeh et al., 2009; Boirivant & Cossu, 2012; Lauritano et al., 2019). In severe cases, these lesions can progress to deep ulcers with a granulomatous appearance. However, treatment with topical steroids and local anesthetics generally has good results, promoting symptom relief and effective healing (Estados et al., 2020).

Periodontitis is an inflammatory condition that compromises the gums and teeth, resulting in the destruction of the alveolar bone and supporting soft tissues. This disease is

also associated with the oral manifestations of Crohn's Disease, presenting symptoms such as gingival inflammation, edema, bleeding, and tooth mobility, which can lead to tooth loss if not treated properly (Lamont et al., 2015). Treatment requires regular dental follow-up, with strict plaque control and specific therapeutic interventions (Vavricka et al., 2013).

Orofacial granulomatosis is a chronic inflammatory condition characterized by persistent enlargement of the soft tissues of the orofacial region. It is considered a rare oral manifestation of Crohn's Disease (Sarra et al., 2016). Clinically, it presents in a variety of ways, including diffuse and chronic swelling of the lips, particularly of the upper lip, or the lower half of the face. Other manifestations include recurrent oral ulcerations, cleft lip, and hyperplastic gingivitis (Bogenrieder et al., 2013). The condition is more prevalent in young men, especially in the age group between 14 and 20 years, although it can affect other groups (Lazzerini, Bramuzzo, & Ventura, 2014). Treatment is multidisciplinary and depends on the severity of the manifestations, and may include the use of topical or systemic corticosteroids, immunomodulators, dietary adjustments, and management of the underlying disease (Lofberg et al., 2012).

The presence of these conditions may indicate the severity of the disease and its evolution. Appropriate treatment, which involves both the management of intestinal and oral manifestations, is essential for the control of Crohn's Disease and the improvement of patients' quality of life.

ORAL MANIFESTATIONS IN ULCERATIVE COLITIS: EARLY SIGNS AND CLINICAL IMPLICATIONS

Ulcerative Colitis (UC) is a chronic inflammatory disease of an immune-mediated nature that significantly affects the quality of life of patients. Its etiology involves changes in the epithelial barrier, such as abnormal secretion of antimicrobial peptides or failures in the physical integrity of the mucosa, resulting in exacerbated neutrophil recruitment and dysregulated immune responses (Pabla & Schwartz., 2020).

Inflammation is a marker of disease activity, being influenced by genetic factors, medical history, previous hospitalizations, in addition to impacting quality of life, causing intestinal impairment, and leading to structural damage (Pabla & Schwartz., 2020). UC has different stages of extent, activity, and severity, which results in a wide range of clinical symptoms. The most common signs include progressive or sudden abdominal pain, persistent or recurrent bloody diarrhea, presence of pus in the stool, weight loss, fever, anal lesions, urgency, and fecal incontinence. Bloody diarrhea (>90%) is the most prevalent symptom, often associated with colic abdominal pain and fecal urgency (>70%) (Seyedian

et al., 2019; Nazake et al., 2021).

In severe cases, abdominal tenderness associated with fever and peritoneal signs indicate a poor prognosis, which may progress to fulminant colitis and toxic megacolon (D'Haens et al., 2019; Seyedian et al., 2019; Kucharzik et al., 2020; Saez et al., 2023).

Progressive, ascending inflammation of the large intestine, usually beginning in the rectum, is a hallmark feature of UC. It differs from Crohn's Disease by inflammation restricted to the mucosal layer of the colon, whereas Crohn's Disease affects the entire gastrointestinal tract in a transmural manner. In addition, there is evidence that appendicitis may have a protective effect against UC. However, the disease is clinically heterogeneous, with only 30% of patients presenting extensive colitis and 15% evolving to aggressive forms (D'Haens et al., 2019; Ko et al., 2019; Seyedian et al., 2019; Renuzza et al., 2022).

Most patients present with a mild to moderate clinical picture, with periods of activity and remission. UC is more prevalent in developed countries, but its incidence is increasing in developing countries, predominantly affecting young adults (D'Haens et al., 2019; Ko et al., 2019; Seyedian et al., 2019; Renuzza et al., 2022).

Although UC is predominantly intestinal, extraintestinal manifestations, especially in the oral cavity, are often observed (Muhvić-Urek et al., 2016). These manifestations include aphthous stomatitis, angular cheilitis, and, more rarely, vegetative pyostomatitis, an oral lesion characteristic of UC. Changes in the oral cavity can be caused by malnutrition, anemia, mineral and vitamin deficiency, in addition to the adverse effects of drugs used in the treatment of UC, which can impact immunity and increase the risk of opportunistic infections (Muhvić-Urek et al., 2016).

Patients with UC may present with diffuse pustules and nonspecific gingivitis. Aphthous stomatitis manifests as shallow, round ulcers surrounded by an erythematous halo with a central fibrin membrane (Lankarani et al., 2013).

Oral dysbiosis, characterized by an imbalance in the microbiota, including variations in the presence of Streptococcus, Haemophilus, Prevotella, and Veillonella, may be associated with exacerbated inflammatory response due to decreased salivary lysozyme and increased levels of interleukin (IL)-1β. This picture may reflect gut dysbiosis, suggesting a possible link between oral manifestations and UC (Disse et al., 2014). In addition, gut dysbiosis promotes a chronic inflammatory state and mucosal-associated lymphatic tissue (MALT) activation, which can result in extraintestinal manifestations. It is hypothesized that aphthous ulcers in patients with UC may be triggered by gut dysbiosis and factors such as oral microtraumas (Cappello et al., 2019).

Oral lesions are an early marker of UC and are more accessible to observation and

diagnosis than other manifestations. Some lesions, such as vegetative pyostomatitis, can be easily identified through clinical examination and biopsy (Kamal et al., 2020). Therefore, oral manifestations can serve as indicators of UC severity, allowing an early diagnosis and aiding in the therapeutic approach to intestinal disease (Lourenço et al., 2010).

CONCLUSION

The connection between gastrointestinal diseases and their manifestations in the oral cavity highlights the need for a broad clinical approach that prioritizes early diagnosis and efficient management of these conditions. Celiac Disease, Crohn's Disease and Ulcerative Colitis not only affect the digestive tract, but also present significant extraintestinal manifestations, which can be essential for early identification and the implementation of timely therapeutic interventions. Among these manifestations, changes in the oral cavity play a relevant role, and may serve as initial signs of underlying diseases.

Oral lesions such as dental enamel defects, recurrent aphthous ulcers, atrophic glossitis, xerostomia, and orofacial granulomatosis often do not receive due attention, despite their clinical importance. The presence of these alterations can directly affect the quality of life of patients, interfering with eating, emotional well-being, and social interaction. Thus, early identification and the adoption of appropriate therapeutic strategies are essential to reduce complications and optimize clinical outcomes.

The treatment of these diseases requires a multidisciplinary approach, involving gastroenterologists, immunologists, nutritionists and, especially, dentists. The dental professional plays an essential role in the early detection of these diseases, facilitating referral for definitive diagnosis and allowing timely interventions. In addition, its performance contributes to the control of oral manifestations, promoting the functional and aesthetic rehabilitation of the oral cavity, which has a direct impact on the quality of life of patients.

Collaboration between different medical specialties is essential for effective management of inflammatory bowel diseases, highlighting the importance of continuous training of health professionals on the systemic manifestations of these conditions. Improving access to health services, developing new therapeutic approaches, and raising awareness among the population about the relationship between oral and systemic health are key measures to promote digestive health and the well-being of affected individuals.

Therefore, the relevance of oral manifestations in gastrointestinal diseases highlights the importance of an integrated and multidisciplinary approach. The involvement of the dental surgeon in this context not only favors early diagnosis and appropriate treatment, but

also reinforces the role of dentistry in promoting systemic health and improving the quality of life of patients.

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