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Quality of life (QoI) in pediatric patients with oral lesions secondary to inflammatory bowel diseases (IBDs): a prospective study
by
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THESIS

Submitted in partial satisfaction of the requirements for degree of
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in the

GRADUATE DIVISION

of the

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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Quality of life (QoL) in pediatric patients with oral lesions secondary to inflammatory bowel diseases (IBDs): a prospective study

Abrar Bakhsh

Abstract

Background: Inflammatory bowel diseases (IBDs) are a group of chronic inflammatory conditions that affect the digestive tract. The two primary types of IBD are Crohn's disease (CD) and ulcerative colitis (UC) have been reported in 1.2 million Americans. Oral manifestations of IBD are common and may cause physical and emotional discomfort in affected individuals and can significantly reduce their quality of life (QoL).

Objectives: To examine the QoL in pediatric patients with oral manifestation of IBD.

Methods: This was a single-center, prospective cross-sectional study of pediatric patients (ages 2-18) diagnosed with IBDs and oral manifestations of IBD seen at the University of California San Francisco (UCSF). The study was conducted between September 2021 and April 2023. Eligible patients or their guardians engaged in an online survey that incorporated the modified Chronic Oral Mucosal Diseases Questionnaire-15 (COMDQ-15). This tool was designed to gauge the effects of oral diseases on their quality of life, probing into domains such as physical discomfort, medication, emotional and social repercussions, and patient support. Data were collecting using Redcap. Descriptive analyses were used to summarize the data.

Responses to the COMDQ-15 were scored on a 5-point Likert scale from "not at all" (0) to "extremely" (4). Means and the standard deviations were calculated for each domain.

Results: A total of 193 pediatric patients with oral lesions secondary to IBD were identified. Of these, 30 (15.5%) completed the survey questions. The average age of

participants was 15 years, with the majority (66.7%) diagnosed with Crohn's Disease. The most commonly prescribed systemic medications for IBD were infliximab (63.3%) and adalimumab (16.7%). Oral ulcers were the most prevalent oral condition (93.3%). Questionnaire results highlighted a range of experiences, from physical discomfort to emotional impact, with (46.7%) reporting no discomfort during oral hygiene activities and (46.7%) feeling not at all emotionally impacted. The COMDQ-15 score revealed that sensitivity to spicy and acidic foods had the highest mean score (1.47 SD: \pm 0.97) and patients expressed the most satisfaction with family support, averaging a score of (2.93 SD: \pm 1.16).

Conclusion: Pediatric patients with IBD often present with oral lesions that may significantly compromise their QoL. Timely identification and early intervention for these lesions are paramount to improve patient's overall health and QoL. Clinicians should be cognizant of the profound repercussions of these lesions on pediatric patients' well-being and should advocate for a collaborative, multidisciplinary approach with oral medicine specialists for optimal clinical outcomes.

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List of Abbreviations

ANCA: Anti-neutrophil cytoplasmic antibodies

ASCA: Anti-Saccharomyces cerevisiae antibodies

TNF- α : Anti-tumor necrosis factor

CRP: C-reactive protein

COMDQ-15: Chronic Oral Mucosal Diseases Questionnaire-15

CBC: Complete blood count

CD: Crohn's disease

ESR: Erythrocyte sedimentation rate

HLA: Human leukocyte antigen

IBDs: Inflammatory bowel diseases

OFG: Orofacial granulomatosis

QoL: Quality of life

REDCap: Research Electronic Data Capture

UC: Ulcerative colitis

UCSF: University of California San Francisco

Introduction:

Inflammatory bowel diseases (IBDs), which encompass Crohn's disease (CD) and ulcerative colitis (UC) can develop at any phase of life, although the peak incidence typically falls between the ages of 15 and 30 years.¹ However, it is not uncommon for individuals to be diagnosed with these conditions later in life.² In the United States, approximately 1.2 million individuals are affected by IBDs. Among these, it is estimated that around 565,000 people have CD and about 593,000 have UC. Both males and females are affected by these conditions equally.³

Multiple research studies have extensively investigated the influence of IBD on the quality of life (QoL) of adult patients. A recent systematic review and meta-analysis has shown that individuals with IBD (in both adults and children) had a diminished QoL in comparison to those without the condition.⁴ IBD poses considerable physical and psychological stress on patients because of unforeseen progression and onset in youth.⁵ The findings highlight the significant negative impact of IBD on the overall well-being and QoL of affected individuals.⁶

Crohn's disease

CD has a global distribution, with higher incidence rates in developed countries and urban areas.⁷ The prevalence of CD in pediatric population was 45.9 per 100,000 individuals in 2016.⁸ In 2013, the hospitalization rate was 59.7 per 100,000, and this data was published in 2019.⁹

The exact cause of CD is unknown, but it is believed to result from a complex interplay of genetic, environmental, and immunological factors. Among the genes associated with

CD, NOD2/CARD15 has been strongly linked to an increased risk.¹⁰ Variations in this gene can disrupt the immune response to bacteria in the gut leading to inflammation in the digestive tract¹¹. Another gene, ATG16L1, plays a role in autophagy. When combined with caspase 3 activation, the common risk allele causes a faster breakdown of the ATG16L1 protein. There is a unified pathway linking cellular stress, apoptotic stimulation, and impaired autophagy that contributes to Crohn's disease development.¹² The IL23R gene, involved in regulating immune responses, has also been found to have variations that increase the risk of developing CD.¹³ Additionally, the IRGM gene, which participates in autophagy and pathogen clearance, has been implicated in CD susceptibility.¹⁴ Human leukocyte antigen (HLA) genes, including HLA-DRB1 and HLA-DQB1, are also associated with an increased risk of CD, as they influence immune responses.¹⁵ Dysregulation of the immune system leads to an abnormal inflammatory response in the gastrointestinal tract, involving a combination of innate and adaptive immune mechanisms.¹⁶ Alterations in the gut microbiota, impaired epithelial barrier function, and abnormal immune responses contribute to the chronic inflammation characteristic of Crohn's disease.

A diagnosis of Crohn's disease requires a combination of clinical, endoscopic, radiologic, and histopathologic findings.¹⁷ Common diagnostic tools include patient history, physical examination, blood tests (such as C-reactive protein and fecal calprotectin), endoscopy (e.g., colonoscopy, sigmoidoscopy), imaging studies (e.g., computed tomography, magnetic resonance enterography), and histological examination of biopsy samples.

The presentation of Crohn's disease can vary widely among individuals and depends on the location and extent of gastrointestinal involvement.¹⁸ Common symptoms include abdominal pain, diarrhea, weight loss, fatigue, anemia, and nutritional deficiencies. Extra-intestinal manifestations can also occur, affecting the oral cavity, joints, skin, eyes, liver, and other organs.

The management of Crohn's disease is aimed to induce and maintain remission, alleviate symptoms, and improve patients' QoL.¹⁹ Treatment approaches depend on the severity and location of disease, as well as individual patient factors. Medications commonly used include aminosalicylates, corticosteroids, immunomodulators (such as azathioprine and methotrexate), and biologic agents (such as anti-tumor necrosis factor (TNF- α)), including medications such as infliximab, adalimumab, or certolizumab pegol.²⁰ Surgical interventions may be necessary in cases of complications, strictures, or abscesses.²¹

Ulcerative colitis

UC, similar to Crohn's disease, has a global prevalence, with relatively higher incidence rates in developed regions and urbanized areas. This condition does not exhibit a gender predilection.^{22,23} Between 1999 and 2017 the hospitalization rate was 16.2 per 100,000.²⁴ The prevalence of UC in pediatric population was 21.6 per 100,000 individuals in 2016.²⁵ The precise cause of UC remains an area of ongoing research, but it is believed to arise from a complex interplay of factors including genetics, environmental influences, and immune system responses.²⁶ Genetic factors do play a role, as specific gene variations associated with immune response and gut barrier function have been identified

as potential contributors.²⁷ The specific genetic factors involved in UC are still being investigated, although several genes have been identified as playing a role in the disease. In particular, HLA-DRB1 and HLA-DQB1, have been associated with an increased susceptibility to UC, as these genes are involved in regulating the immune response.²⁸ Variations in the IL-23R gene have also been linked to UC, affecting immune cell signaling and activation.²⁹ The IL-10 gene, which encodes an anti-inflammatory cytokine, has been found to have variations associated with UC.³⁰ Additionally, variations in the SLC22A4 and SLC22A5 genes, involved in nutrient transport, have been implicated in the disease.³¹ Altered expression of mucin genes, such as MUC1 and MUC3A, has also been observed in individuals with UC, impacting the integrity of the intestinal mucosal barrier.³² The development of UC involves immune dysregulation, resulting in abnormal inflammation within the gastrointestinal tract that encompasses both innate and adaptive immune mechanisms.³³ Like Crohn's disease, disturbances in the gut microbiota, impairment of the gut lining, and irregular immune responses contribute to the chronic inflammation that characterizes ulcerative colitis.

Diagnosis of UC entails a comprehensive assessment, involving an analysis of patient history, physical examination, blood tests to evaluate specific markers. Inflammatory markers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), are commonly measured to assess the level of inflammation in the body. Additionally, a complete blood count (CBC) is performed to examine blood cell types, revealing potential anemia and changes in white blood cell counts indicative of UC. Stool tests are also conducted to rule out infections and detect blood or other abnormalities in the stool. Moreover, antibody tests, including anti-Saccharomyces cerevisiae antibodies

(ASCA) and anti-neutrophil cytoplasmic antibodies (ANCA), can be helpful in supporting the diagnosis by detecting specific antibodies associated with UC.³⁴ However, it is important to note that these markers are not definitive on their own, and a combination of other diagnostic methods is necessary to make a comprehensive assessment and establish an accurate diagnosis of UC.

Symptoms of UC can vary among individuals based on the extent and location of the gastrointestinal involvement. Common manifestations include abdominal pain, diarrhea, unintended weight loss, fatigue, anemia, and deficiencies in nutritional status. Additionally, complications outside the intestine may arise, affecting various organs such as the oral cavity, joints, skin, eyes, and liver.³⁵

The treatment plan is usually individualized based on the severity, extent, and complications of the disease. The initial treatment for mild to moderate ulcerative colitis typically involves anti-inflammatory drugs, including 5-ASA agents (mesalamine, sulfasalazine, and balsalazide).²⁶ Corticosteroids, such as prednisone, may also be used to reduce inflammation. For more severe cases of UC, biologic drugs like infliximab, vedolizumab, golimumab, and adalimumab are used. While there are similarities in the treatment approach for UC and CD, there are also some differences due to the varying nature of these conditions.³⁶

A general overview of the clinical differences between UC and CD is presented in Table 1.

Oral manifestations of IBDs

Oral lesions are common in UC and CD and include aphthous like ulcerations, cobblestoning of the oral mucosa, orofacial granulomatosis (OFG), periodontitis,

gingivitis, and *pyostomatitis vegetans*. A thorough examination of the oral cavity is recommended for the early identification of oral signs of IBD.

OFG is a rare inflammatory condition characterized by the presence of non-caseating granulomas in the oral and facial tissues. It primarily affects the lips, but can also involve the cheeks, oral mucosa, tongue, and other parts of the face. It is also characterized by a persistent swelling of the soft tissues in the mouth and lips, with ulceration of the lips, gingiva, mouth, and face, as well as facial nerve paralysis and oroantral fistula formation. OFG is considered a subtype of granulomatous diseases and is often associated with underlying IBDs, though it can occur independently as well.³⁷

Some oral manifestations may be the first sign of IBD disease which may be detected by oral medicine or GI specialist. A systematic review by Vaqués et al. showed that CD can first manifest with oral symptoms and lesions, which may appear prior to intestinal problems.³⁸ Another study concluded that oral manifestations of CD resolve in most children who receive treatment from intestinal Crohn's disease. Interestingly, children with IBD suffer from oral health problems (such as gingival inflammation, carries, etc.) more frequently and severely than children without IBD, despite similar oral hygiene habits.³⁹

While the clinical presentation of oral findings in adult IBD patients is well known, little work has been done amongst pediatric patients. As such, the primary objective of this study was to examine the impact of oral manifestations of IBD on the QoL of pediatric patients. Specifically, the study aimed to assess various dimensions of well-being, including physical, social, and emotional aspects, as well as the influence of medication and treatment on their overall QoL.

Methods:

Study design

This was a single-center, prospective cross-sectional study of pediatric patients diagnosed with IBDs and with oral manifestations of IBD seen at the University of California San Francisco (UCSF). The study was conducted between September 2021 and April 2023.

Pediatric patients with concomitant IBDs and oral diseases were identified from the medical records of the UCSF pediatric gastroenterology clinic, and contacted about the study via phone. Written informed consent was obtained from all the participants, their parents or legal guardians electronically. Data were recorded using the Research Electronic Data Capture (REDCap). Ethical approval for this study was obtained from the UCSF institutional review board (IRB No 20-32667) on November 8, 2021.

Inclusion and exclusion criteria

We included patients aged 2 to 18 years with a history of IBD and concomitant oral lesions (Table 2).

Questionnaire (Measure quality of life):

We used a modified version of the Chronic Oral Mucosal Diseases Questionnaire-15 (COMDQ-15).³⁷ A full version of the modified questionnaire is reported in Appendix 1.

The COMDQ is a validated questionnaire designed to assess the impact of chronic oral mucosal diseases on a patient's quality of life (QoL)⁴¹. It encompasses various domains of the condition, including symptoms, functional limitations, emotional distress, and social consequences. By evaluating these different aspects, the COMDQ provides valuable insights into the overall effect of the disease on the patient's well-being and QoL. The Total COMDQ-15 score is obtained by summing up the responses to all items, with a maximum possible score of 60. The maximum possible subscale and total score of this scale are 34 and 40, respectively. The COMDQ questionnaire consists of 15 items that are divided into four domains:

- Physical discomfort (5 items);
- Medication and Treatment (3 items);
- Social and Emotional (5 items), and
- Patient Support (2 items).

Responses are scored on a 5-point Likert scale from "not at all" (0) to "extremely" (4).

We calculated the mean and the standard deviation for each domain in Table 4

In addition, we collected information on age, gender, medications, and the types of oral lesions from the medical records. Additionally, we received one picture sent by a patient and took another picture during the intraoral examination at the oral medicine clinic.

For the purpose of this study, the questionnaire was translated into Spanish and validated to preserve its integrity and obtain reliable data.

Enrollment

After obtaining consent, pediatric patients diagnosed with IBD and exhibiting oral lesions were recruited for the study. Informed consent or assent was obtained from the participants, depending on their age and legal capacity.

Patients were then instructed to complete an online survey using the RedCap platform. The survey administration took place either in person at the UCSF Oral Medicine Clinic or remotely by sending a survey link through the MyChart portal to eligible patients identified for the research. All patients and their parents or legal guardians received detailed information about the study, including its purpose, procedures, and potential benefits or risks, was provided. To facilitate effective communication with patients and families who spoke languages other than English, a medical translator was utilized whenever necessary.

Data Analysis:

Data was collected using the REDCap and exported into Excel for the statistical analysis. Descriptive statistics were employed to summarize the data. Measures such as the mean, standard deviation, and scores for the COMDQ-15 responses were calculated.

Results

A total of 193 patients were recruited, and 30 (15.6%) completed all survey questions. A total of 29 individuals were recruited over the phone and one patient was referred to the UCSF Oral Medicine Clinic for participation.

Patients' characteristics

A summary of patient demographics is reported in Table 3. The average age (mean) and median of the participants was 15 (SD: 11.22) and 11 years, respectively. Most patients were White (63.3%). 66.7% (n=25) of patients had CD and 16.7% (n=5) had UC. When the drug history was considered, adalimumab was administered to (16.7%) of patients, while a larger portion (63.3%) received infliximab. Methotrexate and vedolizumab were less commonly prescribed at (6.7%) and (10%) respectively, with sulfasalazine accounting for (3.3%) of cases.

A total of 193 patients (30%) had oral lesions secondary to IBD, for which patients were prescribed fluocinonide 0.05% gel (3.3%) and chlorhexidine 0.12% mouth rinse (3.3%), while Magic Mouth Wash, was utilized by 6.7% of patients.

Among the observed oral lesions, mouth ulcers were the most prevalent (93.3%; n=28), followed by “fluctuant induration” and the cobblestone appearance of the oral mucosa, each occurring in 3.3% of cases (n=1).

Questionnaire

Physical discomfort

When physical discomfort was considered a total of 11 patients (36.7%) reported slightly sensitivity to spicy and acidic food, while 14 patients (46.7%) did not experience any discomfort caused by food textures. 14 of the respondents (46.7%) indicated that they did not experience any discomfort related to the temperature of food and drinks.

In terms of daily oral hygiene routine, 14 patients (46.7%) expressed no discomfort during their oral hygiene activities. Among the participants, 6 patients (20%) reported slightly discomfort and 4 patients (13.3%) reported “moderately” and “considerably” experiencing discomfort during their daily oral hygiene routine.

Medication and Treatment

A significant proportion of patients (63.3%; n=19) expressed no reservations about the side effects related to medication use for the management of oral lesions secondary to IBD. This contrasts with 4 patients (13.3%) who indicated minor apprehensions, 5 (16.7%) had “average” concerns, and 2 (6.7%) patients had “substantial worries.” When the frustration with the “lack of standard medication” was considered 6 patients (20.7%) expressed “slight frustration”, 8 patients (27.6%) “moderate frustration”, 2 patients (6.9%) “considerable frustration”, and 3 patients (10.3%) “extreme frustration regarding the absence of standardized medication”. A notable observation was the absence of concerns about “the unavailability of a standardized treatment” among 10 patients (34.5%). Furthermore, in relation to this “lack of uniform medication”, 6 individuals (20.7%) conveyed a minimal level of discontent, 8 (27.6%) showed a “moderate level of unease”, 2 (6.9%) expressed “significant dissatisfaction”, and 3 (10.3%) felt “profound frustration”. Furthermore, “limitations in everyday life due to oral medication use” were experienced by 21 patients (70.0%). Among them, 4 patients (13.3%) reported “slight limitations”, 13.3% moderate limitations, and 3.3% “considerable limitations”.

Social and Emotional

Fourteen patients (46.7%) did not feel emotionally impacted by their oral condition, with 7 patients (23.3%) feeling “slightly affected”, 6 patients (20.0%) experiencing “moderately emotional impact”, and 2 patients (6.7%) reporting “extreme emotional impact”. Additionally, 16 patients (53.3%) did not feel “anxious due to their oral condition”, while 6 patients (20.0%) felt “slightly anxious”, 4 patients (13.3%) experienced “moderate anxiety”, 3 patients (10.0%) experienced “considerable anxiety” and 1 patient (3.3%) reported “extreme anxiety”. Moreover, 50.0% of 14 respondents did not have any concern with “the unpredictability of their oral condition”, 7 patients (23.3%) felt “slightly bothered”, 4 patients (13.3%) experienced “moderate botheration”, 3 patients (10.0%) experienced “considerable botheration”, and 1 patient (3.3%) felt “extremely bothered”. Furthermore, 18 patients (60.0%) expressed “not at all pessimism about their future due to their oral condition”, while 7 participants (23.3%) felt “slightly pessimistic”, 10.0% experienced “considerable pessimism”, and 3.3% reported “extreme pessimism”. Additionally, 19 patients (63.3%) reported “not at all disruption of social activities due to their oral condition”, 6 patients (20.0%) experienced “moderate disruption”, 3 patients (10.0%) felt “slightly disrupted”, and 1 patient (3.3%) reported “extreme disruption”.

Patient Support

When family support regarding the oral lesions secondary to IBD was considered, 3 patients (10.7%) of patients reported “being not at all satisfied”, 2 patients (7.1%) were “slightly satisfied”, 5 patients (17.9%) were “moderately satisfied”, 9 patients (32.1%) were

“considerably satisfied”, and the same percentage, and 9 patients (32.1%) were “extremely satisfied”.

Regarding the support from friends and colleagues, 5 patients (17.2%) were “not satisfied”, 3 patients (10.3%) were “slightly satisfied”, 7 patients (24.1%) were “moderately satisfied”, 5 patients (17.2%) were “considerably satisfied”, and 9 patients (31.0%) were “extremely satisfied”.

COMDQ-15 Score

Study participants reported a mean score of 1.47 (SD: \pm 0.97) for sensitivity to spicy and acidic food. Discomfort caused by food textures yielded an average score of 1.21 (SD: \pm 1.13). Discomfort due to temperature had a mean score of 1.03 (SD: \pm 1.37). In terms of daily oral hygiene routine, respondents indicated an average score of 0.87 (SD: \pm 1.24). The need for medication received an average score of 0.89 (SD: \pm 1.35). Concern about medication side effects had a mean score of 0.53 (SD: \pm 1.13). Frustration with the lack of a standard medication garnered an average score of 1.23 (SD: \pm 1.36). Limitations due to oral medication had a mean score of 0.4 (SD: \pm 0.77). Emotional impact received an average score of 0.87 (SD: \pm 1.26). Anxiety scored an average of 0.97 (SD: \pm 1.20). The unpredictability of the oral condition yielded a mean score of 0.87 (SD: \pm 1.16). Pessimism about the future had a mean score of 0.67 (SD: \pm 1.11). Social disruption mean score of 0.70 (SD: \pm 1.12). Satisfaction with family support had a mean score of 2.93 (SD: \pm 1.16). Lastly, satisfaction with support from friends/colleagues came in at 2.25 (SD: \pm 1.44).

Discussion:

In this study we reported the QoL of pediatric patients with oral manifestations of IBD. Previous research has investigated the effects of IBD on the QoL of adult patients.⁴² To the best of our knowledge this is the first study explored the impact of oral lesions on the QoL of pediatric patients with IBD.

Approximately 46.7% of survey respondents reported no physical discomfort from spicy or acidic foods, while the same percentage reported no discomfort from food temperature. As for social and emotional challenges, 46.7% did not feel impacted emotionally and 53.3% did not feel anxious due to their oral condition. Moreover, 63.3% didn't face any disruption in their social activities. Regarding support, 63.3% were undeterred by medication side effects, while 32.1% were considerably or extremely satisfied with their family support. These findings emphasized the need for comprehensive care and support. Patients with oral lesions experience a range of physical and emotional sensations, varying discomfort levels, and considerations related to medication, emotional well-being, social support, and outlook on the future. The COMDQ-15 scores provided insights with averages ranging from 0.4 (limitations due to oral medication) to 2.9 (satisfaction with family support), all accompanied by their respective standard deviations. This range in scores underlined the diversity in patient experiences, with some areas clearly more impactful than others. The findings highlight the multifaceted nature of living with oral lesions and the importance of addressing both physical and emotional aspects of their care and support.

Comparison with previous studies highlighted negative impact of IBD on QoL, in terms of physical symptoms and psychosocial well-being.⁴³⁻⁴⁴ The current study aligned with these observations, showing that pediatric patients with oral manifestations of IBD experienced varying degrees of discomfort, anxiety, emotional impact, and disruption in their social activities.

In a study conducted by J.L. Howell et al, the majority of patients had oral Crohn's disease at 63%, compared to 66.7% in our study. The average age of patients was 15 in both studies. With regards to medication, 63.3% of our patients used infliximab, in stark contrast to the 75% reported in Howell's study. While most patients in Howell's study expressed satisfaction with their treatment progress 85%, in our research, 63.3% of patients had no concerns about the side effects of their medication. Significantly, both studies exhibited similar percentages across different facets, highlighting the consistent patterns observed in the patient groups studied.⁴⁵ Yu et al. showed that while 61 adults patients with active IBD predominantly faced one psychological challenge, be it anxiety, sleep issues, depression, or a diminished quality of life, a notable 7.44% grappled with a mix of these. On the other hand, in the remission group, a slightly higher 8.46% encountered multiple of these challenges concurrently. While IBD can be linked to oral ulcers, it's crucial to explore alternative causes and undertake a thorough assessment to distinguish them from different types of oral lesions. Oral ulcers can stem from a range of factors, including inflammatory bowel disease (IBD), infections, medication side effects, nutrient deficiencies, and other conditions that affect the oral cavity.⁴⁶ In other terms, in a study undertaken by Laranjeira N et al, it was observed that patients who were undergoing treatment with immunosuppressants and corticosteroids, which are frequently prescribed

for IBD management, reported a higher occurrence of oral symptoms, including aphthous ulcers. However, the study did not find a statistically significant relationship between these oral symptoms and the specific pharmacological therapy used for IBD. Overall, the available evidence indicates an association between aphthous ulcers and IBD, with a greater prevalence of oral mucosal lesions, including aphthous ulcers, in individuals with IBD compared to those without the condition.

Our study reaffirmed the importance of multidisciplinary care in the management of IBD.⁴⁷ Pediatric IBD often presents with recurrent oral manifestations that can significantly affect patients' well-being; in response, pediatric gastroenterologists should proficiently recognize, evaluate, and promptly refer to oral medicine specialists for precise diagnosis and comprehensive treatment strategies aimed at addressing root causes and potential therapies.⁴⁸

Further study revealed that aphthous ulcerations were identified as the predominant oral lesions and accounted for 70.6% of all oral lesions.⁴⁹ In comparison, our study showed a higher prevalence of oral ulcers at 93.3%. In a different study, aphthous stomatitis stands out as the prevailing oral manifestation of IBD.⁵⁰ The presence of mucosal cobblestoning was observed in a low rate 6% of children in the comparison study, whereas our study identified this feature at a comparable rate of 3.3%.⁵¹

Our study had several limitations. The sample size of relatively small (n= 30) and included patients seen at a tertiary institution, and therefore findings may not be generalizable to all pediatric patients with oral lesions secondary to IBD. Future studies should include multiple centers treating pediatric patients with IBD to better understand the impact of oral lesions on the QoL of such a unique group.

To sum it up, the investigation stressed the criticality of identifying oral manifestations of IBD in children, as they notably affected diverse areas of their daily living. The insights gathered underscored the need for comprehensive care methods that catered to both the psychological and emotional challenges posed by the condition. Early detection of IBD through oral lesions might pave the way for more prompt treatments. The results of this study accentuate the indispensable collaboration between pediatric gastroenterologists, and oral medicine specialists in elevating the health of children suffering from IBD and its oral manifestations. The COMDQ-15 was best suited to measure levels of QoL in this population and may be employed in future larger studies.

Conclusion

In conclusion, this study contributes to the growing body of knowledge surrounding the experiences of pediatric patients with IBD-related oral lesions. The findings emphasize the need for personalized and holistic care approaches that address both the physical symptoms and the psychosocial impacts of oral lesions. The relatively moderate concerns about medication side effects and the frustration over the lack of standardized treatment highlight areas for potential improvement in patient care. These insights underscore the importance of patient-centered approaches that consider the individual's unique circumstances, preferences, and challenges. Future research could build upon these findings by conducting longitudinal studies to explore how patients' experiences evolve over time and investigating interventions that could enhance the QoL for individuals dealing with IBD-associated oral lesions.

Table 1. Difference between ulcerative colitis and Crohn’s disease (Obtained from Torres et al, 2011) ⁵²

| Aspect | Ulcerative Colitis | Crohn's Disease |
|-------------------------|--|---|
| Location | Limited to the colon and rectum | Can occur anywhere in the digestive tract |
| Inflammation Pattern | Continuous inflammation in the inner lining of colon | Patchy inflammation throughout the entire digestive tract |
| Depth of Inflammation | Affects the innermost lining (mucosa) | Can involve all layers of the bowel wall |
| Symptoms | Abdominal pain, bloody diarrhea, rectal bleeding | Abdominal pain, diarrhea (may or may not be bloody) |
| Complications | Increased risk of colon cancer | Bowel obstruction, strictures, fistulas |
| Extraintestinal Effects | Joint pain, eye inflammation (uveitis), skin rashes | Joint pain, eye inflammation (uveitis), skin rashes |
| Surgical Treatment | Colectomy (removal of the colon) may provide a cure | Surgery is not curative, as the disease can recur |
| Treatment Approach | Medications can be used to induce and maintain remission | Medications aim to control inflammation and manage symptoms |
| Prevalence | More common in younger age groups | Can affect individuals of any age |

Table 2. Study eligibility criteria

| Inclusion criteria | Exclusion criteria |
|---|---|
| <i>Patients between the age of 2 to 18 years</i> | <i>Patients older than 18 years</i> |
| <i>Pediatric patients with inflammatory bowel disease with a positive history of oral lesions</i> | <i>Patients with primary immunodeficiencies</i> |

Table 3. Patient demographics

| Finding | N | (%) |
|--|----------|------------|
| Age | | |
| Mean (years) | 15 | |
| Median (years) | 11 | |
| Race | | |
| White | 19 | 63.3% |
| Asian | 2 | 6.7% |
| African American | 3 | 10% |
| Others | 6 | 20% |
| Sex at birth | | |
| Male | 14 | 46.6% |
| Female | 16 | 53.3% |
| IBD diagnosis | | |
| Crohn's disease | 25 | 66.7% |
| Ulcerative colitis | 5 | 16.7% |
| Medications for IBD | | |
| Adalimumab | 5 | 16.7% |
| Infliximab | 19 | 63.3% |
| Methotrexate | 2 | 6.7% |
| Sulfasalazine | 1 | 3.3% |
| Vedolizumab | 3 | 10% |
| Medications prescribed for oral lesions | | |
| Fluocinonide 0.05% gel | 1 | 3.3% |
| Chlorhexidine gluconate 0.12 % oral rinse | 1 | 3.3% |
| Magic Mouth Wash (diphenhydramine, hydrochloride/lidocaine/ Aluminum Hydroxide-Magnesium Hydroxide)10 ml | 2 | 6.7% |
| Oral lesions | | |
| Mouth ulcer | 28 | 93.3% |
| Fluctuant induration | 1 | 3.3% |
| Cobblestone appearance of the oral mucosa | 1 | 3.3% |

Table 4. Chronic Oral Mucosal Disease Questionnaire (COMDQ-15) for pediatric patients with oral manifestations of inflammatory bowel disorders

| Aspect | Not at all N (%) | Slightly N (%) | Moderately N (%) | Considerably N (%) | Extremely N (%) | COMDQ-15 Score | |
|---|---------------------|-------------------|---------------------|-----------------------|--------------------|-------------------|------|
| | | | | | | Mean | SD |
| Physical discomfort | | | | | | | |
| Sensitivity to Spicy and Acidic Food | 9 (30.0) | 11 (36.7) | 6 (20.0) | 3 (10.0) | 1 (3.3) | 1.47 | 0.97 |
| Discomfort caused by Food Textures | 14 (46.7) | 6 (20.0) | 6 (20.0) | 3 (10.0) | 1 (3.3) | 1.21 | 1.13 |
| Discomfort caused by the Temperature of Food/Drinks | 14 (46.7) | 6 (20.0) | 6 (20.0) | 2 (6.7) | 2 (6.7) | 1.03 | 1.37 |
| Discomfort during Daily Oral Hygiene Routine | 14 (46.7) | 6 (20.0) | 4 (13.3) | 4 (13.3) | 2 (6.7) | 0.87 | 1.24 |
| Need for Medication for Daily Activities | 14 (50.0) | 5 (17.9) | 4 (14.3) | 3 (10.7) | 2 (7.1) | 0.89 | 1.35 |
| Medication and Treatment | | | | | | | |
| Concern about Side Effects of Medication | 19 (63.3) | 4 (13.3) | 5 (16.7) | 2 (6.7) | 0 (0.0) | 0.53 | 1.13 |
| Frustration with Lack of Standard Medication | 10 (34.5) | 6 (20.7) | 8 (27.6) | 2 (6.9) | 3 (10.3) | 1.23 | 1.36 |
| Limitations in Everyday Life due to Oral Medication | 21 (70.0) | 4 (13.3) | 4 (13.3) | 1 (3.3) | 0 (0.0) | 0.4 | 0.77 |

| Aspect | Not at all N (%) | Slightly N (%) | Moderately N (%) | Consid erably N (%) | Extremely N (%) | COMDQ-15 Score | |
|---|-----------------------------|---------------------------|-----------------------------|------------------------------------|----------------------------|---------------------------|------|
| Social and Emotional | | | | | | | |
| Emotional Impact of Oral Condition | 14 (46.7) | 7 (23.3) | 6 (20.0) | 1 (3.3) | 2 (6.7) | 0.87 | 1.26 |
| Anxiety caused by Oral Condition | 16 (53.3) | 6 (20.0) | 4 (13.3) | 3 (10.0) | 1 (3.3) | 0.97 | 1.20 |
| Botheration with the Unpredictability of Oral Condition | 14 (50.0) | 7 (23.3) | 4 (13.3) | 3 (10.0) | 1 (3.3) | 0.87 | 1.16 |
| Pessimism about the Future due to Oral Condition | 18 (60.0) | 7 (23.3) | 3 (10.0) | 1 (3.3) | 1 (3.3) | 0.67 | 1.11 |
| Disruption of Social Activities due to Oral Condition | 19 (63.3) | 3 (10.0) | 6 (20.0) | 1 (3.3) | 1 (3.3) | 0.70 | 1.12 |
| Patient Support | | | | | | | |
| Satisfaction with Family Support and Understanding | 3 (10.7) | 2 (7.1) | 5 (17.9) | 9 (32.1) | 9 (32.1) | 2.93 | 1.16 |
| Satisfaction with Support from Friends/Coll eagues | 5 (17.2) | 3 (10.3) | 7 (24.1) | 5 (17.2) | 9 (31.0) | 2.25 | 1.44 |



Figure 1. White coated tongue, and an ulcer on the hard palate (red arrow), and a 0.3 x 0.3 cm circular erythema on the right soft palate adjacent to the uvula in an 18-year-old female with Chron's Disease on adalimumab.

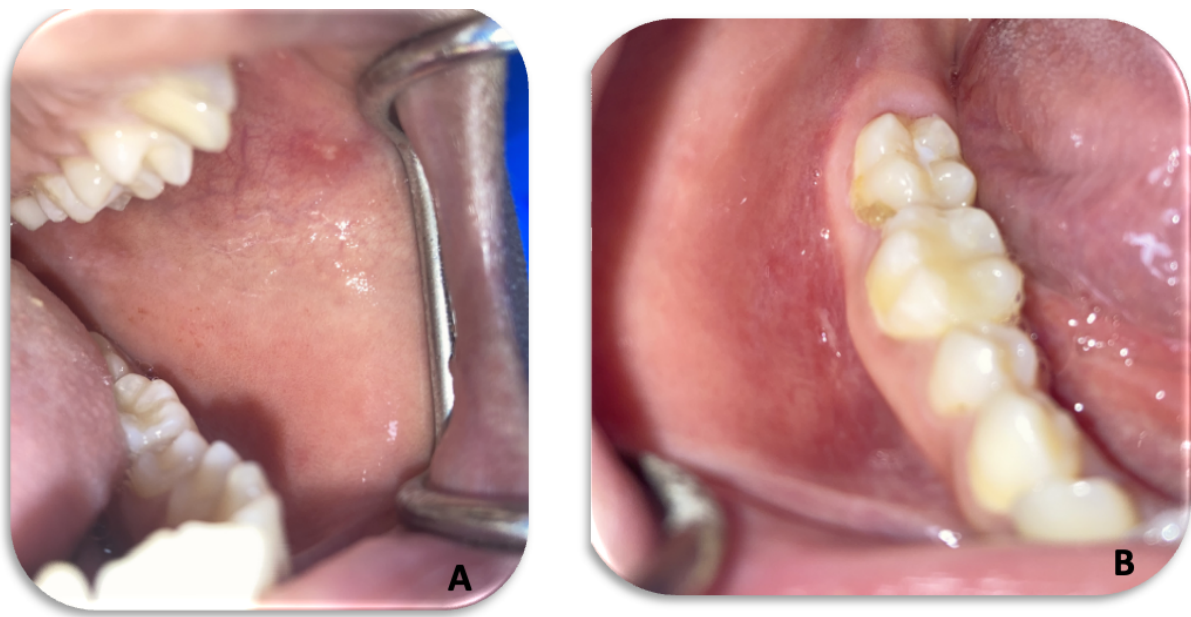


Figure 2. 13-year-old Male with Chron's Disease on vedolizumab. Panel A: 0.2 x 0.2 cm ulcer surrounded by an erythematous halo of the left buccal mucosa. Panel B: linear ulceration measuring 0.1 cm x 0.2 cm of the right buccal vestibule next to tooth number 31.

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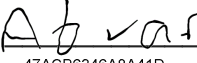
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