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Inflammatory Bowel Disease (IBD) in pediatric patients: evaluation of salivary characteristics

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Abstract

Objectives: Inflammatory bowel disease (IBD) is a chronic inflammatory disease in the gastrointestinal tract affecting millions of pediatric patients worldwide. As a host factor, saliva plays an important role in oral health by regulating and maintaining the integrity of the teeth and soft tissues. This study aimed to characterize the physical and chemical properties of the saliva from pediatric patients diagnosed with IBD.

Methods: An observational cross-sectional study was carried assessing pediatric patients aged 6-17 years old with confirmed IBD diagnosis. Saliva samples were collected and the following parameters were assessed: stimulated salivary flow rate, pH, clinical salivary viscosity, and laboratory salivary viscosity using an ARES-G2 Rheometer.

Results: The sample consisted of 33 patients, and the totality presented normal salivary pH. The average clinical salivary viscosity was 3.1 mm, and the laboratory salivary viscosity 1.5 cP. The mean salivary flow rate was 0.9 mL/min, which is considered low flow. A significant positive correlation between age and flow rate was observed, as older individuals presented higher salivary flow rates ($r = 0.459$ and $p = 0.007$).

Conclusion: Salivary alterations can be detected in pediatric patients with IBD, and should be addressed in dental care to prevent oral diseases.

Statement of Clinical Significance: Seeking to strengthen the care-oriented profile of the dentist, this study analyzed salivary flow in pediatric patients with IBD in the hospital setting, highlighting the importance of non-invasive tests, which increase patient safety, support the maintenance of the oral route for feeding, and imply a better understanding by medical teams of the risks arising from oral dysbiosis in the face of evolving pathologies.

Keywords: Inflammatory bowel disease; Saliva alterations; Viscosity; Pediatric patients.

Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory disease in the gastrointestinal tract and affects millions of adults and pediatric patients worldwide. These chronic inflammatory diseases result from complex interactions between genetics, immunological, environmental factors, and microbiota. It comprises three subtypes: Crohn's disease (CD), ulcerative colitis (UC), and indeterminate colitis (IC)[1].

Saliva plays an important role in oral health by regulating and maintaining the integrity of the teeth and soft tissues. As an easily accessible human fluid, it has been used as a source of biomarkers in human diseases[2]. Some studies have also investigated more basic functions of the saliva, as changes in salivary flow, saliva composition, impaired buffering capacity, and acidic pH in the oral environment can cause imbalance in the homeostasis of healthy microbiota, leading to oral dysbiosis and oral diseases[3].

A relationship of altered salivary function associated with IBD has already been shown[4,5], but the possibility of using salivary flow rates and viscosity for the early identification or monitoring of this group of chronic conditions has not been investigated. This study aimed to characterize the physical and chemical properties of the saliva in pediatric patients diagnosed with IBD.

Material and Methods

This research was approved by the Research Ethics Committee of the Santa Casa de Porto Alegre, registered under nº 866.244/2021. An observational cross-sectional study was carried out including all patients at Hospital da Criança Santo Antônio (HCSA) Gastroenterology Service from August 2021 to April 2022, aged between 6 and 17 years old, with confirmed IBD diagnosis. The exclusion criteria were individuals diagnosed with salivary gland diseases, and patients having taken antibiotic, antifungal, or antiviral medications in the last

15 days. Disease activity at time of collection (acute or chronic) was defined based on the medical records.

After signing the Informed Consent Form and the Informed Assent Form, the study participants answered a structured questionnaire, based in de Souza et al., 2017[6], with the purpose of evaluating clinical and sociodemographic variables (age, gender, eating habits, oral hygiene habits, etc).

Information was also collected from medical records. The intraoral examination[7] was performed with the aid of a flashlight and wooden spatulas, and consisted of the visual inspection and palpation of oral structures, and a subsequent measurement of the decayed, missing, and filled teeth (DMFT) index.

Stimulated saliva was collected as described by Mohamed et al., 2012[8]. All patients were instructed not to drink, eat, brush their teeth, or chew gum for at least one hour before the saliva collection, which was performed between 09:00 and 12:00 to minimize variations associated with the circadian rhythm. Patients were instructed to perform an initial swallow, followed by bilateral chewing of a 1 cm-long sterile silicone tourniquet attached to dental floss, then expectorate into a sterile collection cup every 30 sec for a period of 5 min. Through the collected saliva, the evaluation of stimulated salivary flow rate was conducted. The salivary volume expectorated by the child was divided by the collection time to determine the value of the salivary flow rate in mL/min. According to Krasse's criteria[9], the reference values are normal salivary flow rate: 1–3 mL/min, low salivary flow rate: 0.7–0.9 mL/min, and very low rate of salivary flow (hyposalivation): < 0.7 mL/min. Salivary pH was analyzed using pH indicator strips (Merck, Germany).

To assess clinical salivary viscosity, the digital caliper tips (fixed and movable) were covered with surgical glove fingers, using 0.2 mL of the collected saliva placed on the external measuring face. The length (mm) of the salivary “thread” was measured three times to

calculate the average length. The evaluation of laboratory salivary viscosity was performed using an ARES-G2 Rheometer (TA Instruments, USA) equipped with a Peltier accessory and a 40 mm cone/plate geometry[10]. To obtain salivary viscosity, the Flow Ramp method was used[11]. The kinematic viscosity (cP) was determined by the average of the values obtained after reaching Newtonian fluid characteristics. Statistical analyses were performed using the SPSS statistical software (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Data is presented as mean or median with interquartile range. The comparison among groups was performed using the Kruskal-Wallis Test. Statistical significance was determined at $p<0.05$.

Results

The sample consisted of 33 patients, the majority were female at 54.5% (n = 18) and were in the age group of 15 to 17 years old (42.4%). Regarding the IBD diagnosis, most were diagnosed with CD (60.6%), and 78.8% of children and adolescents were in the chronic phase of the disease. Among the treatment modalities, which could be used alone or in combination, the most common were biologic therapies (45.5%), mesalazine (45.5%), and dietary restrictions (33.3%). Regarding eating habits, 60.4% (n = 20) of the children and adolescents ate carbohydrates three or more times a day, and 75.8% (n = 25) consumed sweets at least once a day. However, soft drink consumption was not frequent among the studied population, as 69.7% (n = 23) were not allowed due to the CD exclusion diet. Most children (97%) reported brushing their teeth two or more times a day, with the total sample (100%) using fluoride toothpaste. Dental floss was used daily by only 24.3% (n = 8) of the patients, and consultation with a dentist less than one year ago was performed by 69.7% (n=23) of the sample. The mean number of Decayed, Missing, and Filled Permanent Teeth (mean DMFT index) of the studied population was 0.9 (SD ± 0.2).

The analyses carried out on the collected saliva samples showed that the totality (n = 33) had normal salivary pH (pH = 7). The average clinical salivary viscosity was 3.1 mm, and the laboratory salivary viscosity 1.5 cP. The mean salivary flow rate was 0.9 mm, which is considered low flow according to Krasse's criteria. Considering the entire sample population, more than half (60%) presented below-normal salivary flow rate (Table 1). No significant association was observed among the type of IBD and salivary characteristics (Table 2). Likewise, there was no relation between salivary characteristics with or without the different types of treatment. Regarding the age range, it was found that the mean salivary flow rate of adolescent patients (15 to 17 years old) was significantly higher than in children (6 to 10 years old) ($p = 0.029$). The flow rate of children and adolescents aged 11 to 14 years did not differ from the others (Table 3). In addition, there was a significant correlation between age and flow rate, with older ages being correlated with higher rates ($r = 0.459$ and $p = 0.007$).

Table 1. Analysis of salivary samples salivary flow rate according to Krasse's criteria[6].

Variable	**Mean ± RSD**	**Med [IQR]**
Salivary flow rate (mL/min)	0.9±0.5	0.7 [0.4; 1.2]
Clinical salivary viscosity (mm)	3.1±0.8	3.2 [2.5; 3.7]
Laboratory salivary viscosity (cP)	1.5±0.4	1.4 [1.3; 1.7]
Salivary flow rate (mL/min)	**n**	**%**
Very low – hyposalivation (< 0.7 mL/min)	14	42%
Low (0.7 - 0.9 mL/min)	6	18%
Normal (1- 3 mL/min)	13	39%

Mean ± RSD, mean ± relative standard deviation; Med [IQR], median and interquartile range.

Table 2. Analysis of the IBD diagnosis and salivary characteristics. Results are shown as median [interquartile range].

Variable	**Crohn's disease (n=20)**	**Ulcerative colitis (n=12)**	**Indeterminate colitis (n=1)**	**p-value***
Salivary flow rate (mL/min)	0.9 [0.5; 1.4]	0.5 [0.3; 0.9]	2.2 [2.2; 2.2]	0.063
Clinical salivary viscosity (mm)	3.1 [2.5; 3.7]	3.4 [2.4; 3.6]	3.9 [3.9; 3.9]	0.449
Laboratory salivary viscosity (cP)	1.5 [1.3; 1.7]	1.4 [1.2; 1.7]	1.3 [1.3; 1.3]	0.834

*Kruskal-Wallis Test

Table 3. Analysis of the relation between age group and salivary characteristics. Results are shown as median [interquartile range].

Variable	6 to 10 years old (n=10)	11 to 14 years old (n=9)	15 to 17 years old (n=14)	p-value*
Salivary flow rate (mL/min)	0.4 [0.3; 0.6]	0.8 [0.5; 1.1]	1 [0.7; 1.4]	0.029
Clinical salivary viscosity (mm)	3.2 [2.7; 3.7]	3.3 [2.2; 3.8]	3.2 [2.5; 3.5]	0.866
Laboratory salivary viscosity (cP)	1.4 [1.3; 1.7]	1.4 [1.3; 1.6]	1.4 [1.1; 1.7]	0.950

*Kruskal-Wallis Test

Discussion

According to the literature, oral mucosa lesions that are characteristic of IBD tend to erupt mainly in phases of greater activity of the disease due to the exacerbation of the intestinal immunological processes[12]. In our research, only one case of oral lesion was detected (ulcer in the lower labial mucosa), this may be related to the fact that 78.8% of the samples were in the chronic phase of the disease during data collection. A rigorous systematic clinical follow-up of the studied population by the pediatric gastroenterology medical team and the use of pharmacological therapies to control the diseases may explain the low presence of these lesions in our sample. This research also showed that more than half (60%) of the sample population have salivary flow rates below normal. The analysis of salivary flow is important, as the reduction in saliva production may impact oral health, increasing the likelihood of carious cavities and opportunistic infections. There are important negative interrelationships between the salivary flow of children and adolescents with the dental condition, as the DMFT

index is usually higher in patients who have lower salivary flow[3,9]. The salivary pH of 100% of the analyzed sample was within the normal range despite the high rate of reduced salivary flow. This in combination with adequate oral hygiene, fluoride toothpaste use, and frequent dental follow-up justifies the low DMFT index found in our study.

As for consultation with a dentist, our sample showed that the majority (69.7%) visited a professional in the last 12 months. Dentistry can play a critical role in the early diagnosis of intraoral manifestations in patients with IBD, helping to prevent complications, as a considerable number of infections and oral alterations are related to IBD activity[12,13]. The low rate of suspicion for the possibility of IBD in children and adolescents by the physician and the dentist imposes a critical role in the diagnosis of oral manifestations as an early sign of IBD[14].

This study has some limitations, including its small, single-center sample and cross-sectional design, which limit the generalizability of the findings. Furthermore, heterogeneity in age, disease subtype and activity, treatment regimens, and dietary habits may have influenced the salivary parameters. Nevertheless, the study provides novel data on an understudied pediatric population and is strengthened by standardized saliva collection and the assessment of salivary viscosity using both clinical and laboratory methods. Future multicenter longitudinal studies with larger samples are warranted, with total feasibility for the clinical and financial reality of our clinical and bedside healthcare system. Automated devices, such as calipers, are important in measuring salivary filament based on linear stretching. In the present study, applying this principle to a manual model — safeguarded by the use of triplicates and the uniform protection of the claws with glove covers — proved to be a highly feasible and methodologically sound alternative for clinical practice.

Conclusion

The present study identified reduced salivary flow rate in a substantial proportion of pediatric patients with IBD, highlighting the importance of monitoring salivary characteristics as part of their oral healthcare. Further studies with larger samples and appropriate control groups are needed to establish the relevance of salivary parameters in the early identification or monitoring of IBD and its activity. Such possibilities should be explored in dental care, aiming to increase awareness among professionals, patients, and families of the local and systemic risks associated with oral dysbiosis during disease progression.

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Patient consent statement: All patient's responsible signed a consent form.

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