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Cytokine profile of Inflammatory Bowel Diseases Patients

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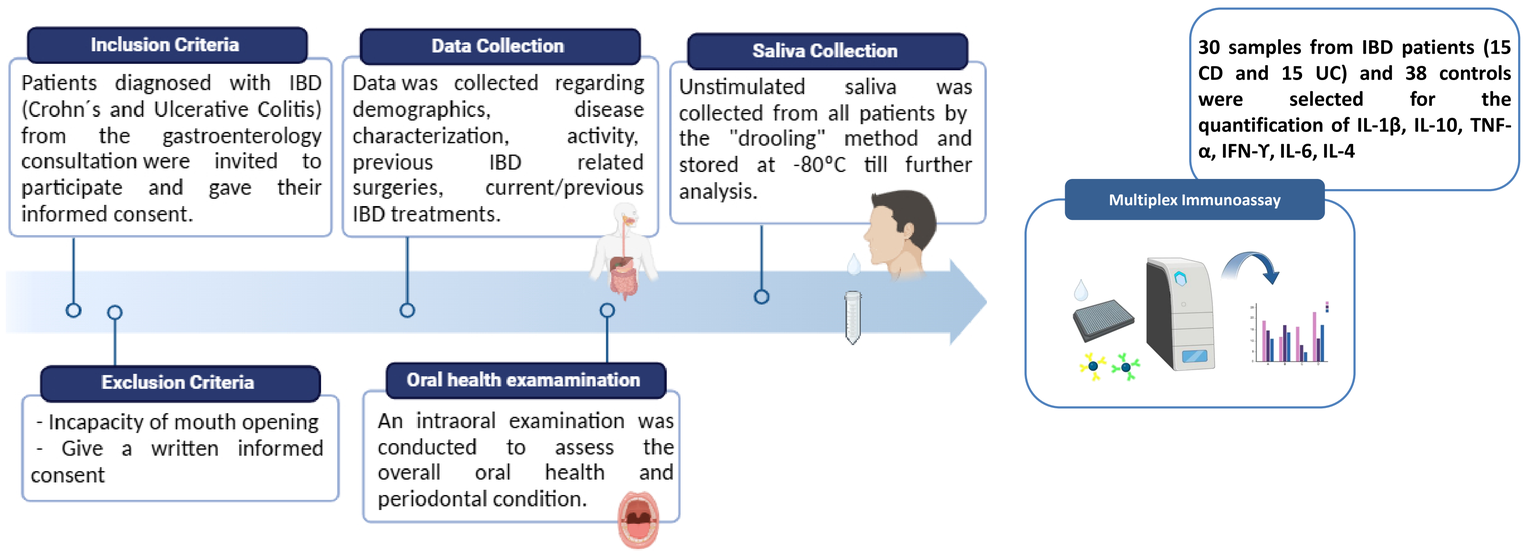
Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of the gastrointestinal tract that comprises Crohn´s disease (CD) and Ulcerative colitis (UC). IBD etiopathogenesis is partly understood and includes both genetic and environmental factors, inducing an abnormal immune response[1]. However, risk factors associated with these pathologies point to a combination of environmental and genetic components. The IBD pathophysiology is understood as a cytokine-induced inflammatory response. Several data referred that there is a significant association of IBD and oral conditions, namely tooth decay and periodontal disease.[2] Medications such as anti-inflammatories, corticosteroids and biological therapies are the treatment of choice for these chronic conditions, depending on the etiology. Thus, understanding immune dysregulation, exploring novel biomarkers, and advancing therapeutic strategies contribute to better managing IBD and improving patient outcome. The identification, quantification and/or validation of biomarkers is primarily performed in tissue, blood and fecal samples but only few studies have been done with saliva[3], which reflects the same type of biomarkers, allowing noninvasive sample collection. This work aims to study the inflammatory profile of IBD patients, exploring new salivary biomarkers for monitoring diseases status, identifying high-risk patients allowing target interventions.

Methods

This was a collaborative transversal cohort study between an IBD consultation in a tertiary hospital and a dental medicine faculty.



Results

Table 1. Demographics and clinical characteristics of patients

		IBD (N=92)	CD (N= 56)	UC (N=36)
Age (y)		45 (24)	42 (29)	49 (±15)
Gender (F/M)		41/ 51	21/35	20/16
Disease duration (y)		8.5 (10)	6 (8.5)	12 (9.75)
Smoking, n (%)	Yes	9 (9.8)	8 (14.3)	2 (5.6)
	No	83 (90.2)	48 (85.7)	34 (94.4)
Current therapy, N (%)	5-ASA	21 (22.8)	5 (8.9)	16 (44.4)
	Immunomodulators	9 (9.8)	7 (12.5)	2(5.6)
	Immunomodulators + biologics	10 (10.9)	7 (12.5)	3 (8.3)
	1 biologic	40 (43.5)	25 (44.6)	15 (41.7)
	Without treatment	12 (13.0)	12 (21.4)	0 (0)
CRP (mg/dL)		0.115 (0.318)	0.115 (0.49)	0.11 (0.313)
Ferritin (ng/mL)		75.5 (464)	76 (92.5)	75.5 (99)
ESR (mm/hr)		2.5 (3)	2 (4)	3 (3)
Hemoglobin (g/dL)		14.35 (2.1)	14.614 (±1.3611)	13.8 (2.3)

Table 2. Oral Health Status of the patients

		IBD (N=92)	CD (N= 56)	UC (N=36)	Control (N =15) *
DFMT		7.89 (± 7.92)	8.60 (±8.24)	7.89 (±7.92)	10 (±6.49)
Periodontal Diagnosis	Periodontal Heath	21 (22.8%)	14 (25.0%)	7 (19.4%)	5 (35.7%)
	Gingivitis	11 (11.9%)	9 (16.1%)	2 (5.5%)	4 (28.5%)
	No teething	4 (4.34%)	2 (3.6%)	2 (5.5 %)	0
	Periodontal disease	56 (60.8%)	31(55.3%)**	25 (69.4%)**	4 (28.6%)
	- SI/GB	10 (17.8%)	7 (33.3%)	3 (12.0 %)	0
	- SII/GB	15 (26.8%)	4 (12.9%)	11 (44.0%)	3 (75.0%)
	- SIII/GB	22 (39.2%)	14 (45.2%)	8 (32.0%)	1 (25.0)
	- SIV/GB	9 (16.1%)	6 (19.4%)	3 (12.0%)	0
Need for dental treatment	Yes	81 (88.1%)	52 (92.8%)***	29 (80.6%)***	8 (57.1%)
	No	11 (11.9%)	4 (7.2%)	7 (19.4%)	6 (42.8%)
Need for prosthetic rehabilitation	Yes	35 (38.1%)	21 (37.5%)	14 (38.9%)	3 (21.4%)
	No	57 (61.9%)	35 (62.5%)	22 (61.1%)	11 (78.6%)

*Due to the high incidence of oral pathologies in IBD, namely periodontal disease (PD), oral health status of the patients and the control group were also assessed. Control group. Age (y): 48.1 (±12.7); Gender: F- 8 participants (47.3%), M- 6 participants (47.4 %). All no-smokers. ** Significantly different from control group (Mann-Whitney U test: p=0.041). *** Significantly different from control group (Fisher-Freeman-Hanton exact test: p = 0.008)

Cytokine profile of IBD patients

- IBD patients have increased levels of IL-10, IL-1β and IL-4.
- Ulcerative colitis patients presented high levels of the anti-inflammatory IL-4.

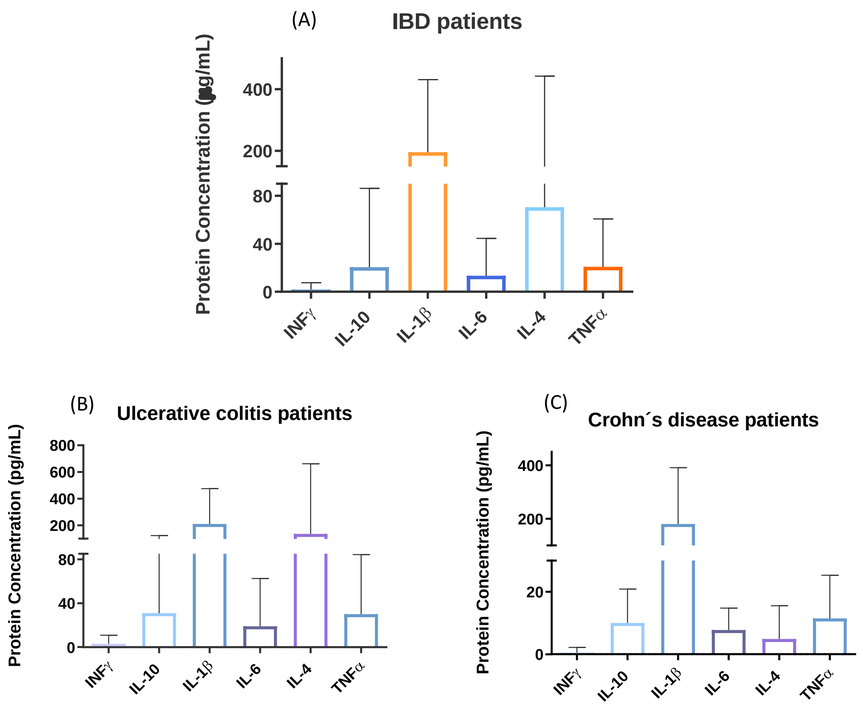


Figure 1 – (A) Inflammatory profile of patients with IBD. (B) Inflammatory profile of patients with ulcerative colitis. (C) Inflammatory profile of patients with Crohn´s disease.

Cytokine profile of Control group

Inflammatory profile of control group has a different profile

- Control group presented high levels of IL-1β, which can be attributed to PD.
- Participants without PD showed basal levels of pro-inflammatory cytokines IL-1β, IL-6 and TNFα below 50 pg/mL.
- No IL-4 was detected in control group.

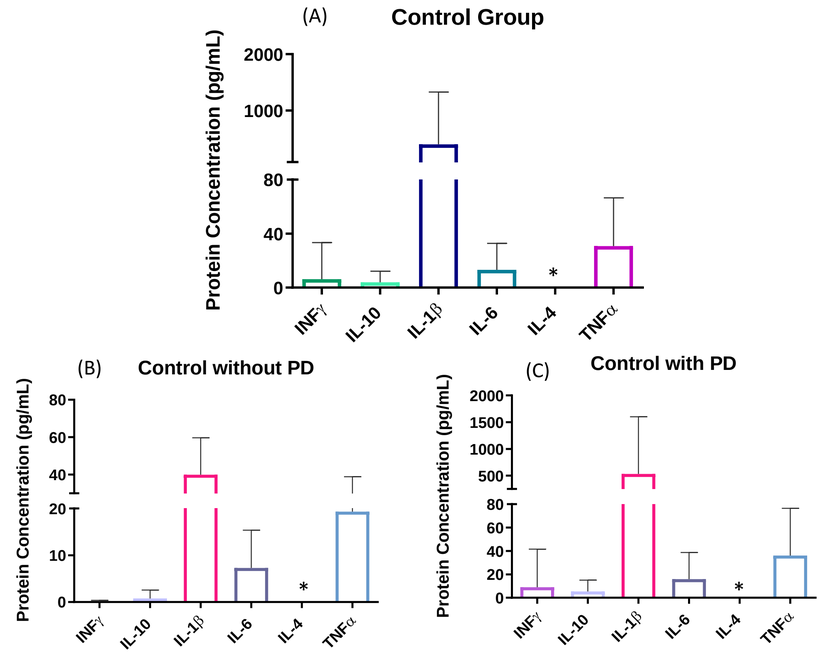


Figure 2 – (A) Inflammatory profile of control group. (B) Inflammatory profile of participant of the control group without periodontal disease (PD). (C) Inflammatory profile of participants of control group with periodontal disease (PD). * IL-4 not detected.

Conclusion

The results showed that salivary inflammatory profile of IBD patients is different from patients without IBD (with and without PD). All IBD patients presented increased levels of IL-1β in both diseases' forms, being the PD, probably, the main contributor for this elevated state. UC patients presented high levels of the anti-inflammatory IL-4. UC is often associated with a Th2 response, leading to increased IL-4 levels, one of the main cytokines produced in UC immune response. Thus, salivary IL-4 could be considered a possible biomarker for this form of the disease. This study generates new insights on IBD, opening new perspectives for future works aiming to develop adequate therapeutic protocols for each patient, towards a precision medicine.

References

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Ethical declaration

The ethical aspects of the present study were reviewed and approved by the Ethics Committee for Health of Universidade Católica Portuguesa (project number 225).

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