

## SALIVARY OXIDATIVE STRESS BIOMARKERS AND ORAL HEALTH IN PATIENTS WITH ACTIVE INFLAMMATORY BOWEL DISEASE: PRELIMINARY RESULTS

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SALIVARY OXIDATIVE STRESS BIOMARKERS AND ORAL HEALTH IN PATIENTS WITH ACTIVE INFLAMMATORY BOWEL DISEASE: PRELIMINARY RESULTS (Abstract): The oral cavity and the intestine are interconnected through shared microbial and immunological pathways, supporting a bidirectional relationship between oral health and inflammatory bowel disease (IBD). Oral pathological conditions are more prevalent and severe in IBD, while oxidative stress represents a key mechanistic link between oral and intestinal inflammation. However, salivary oxidative stress biomarkers remain insufficiently characterized in IBD, and comparative data with healthy controls are limited. **Materials and methods:** This cross-sectional study evaluated adult participants at a single time point, who underwent standardized oral examinations and unstimulated saliva collection. Salivary oxidative stress biomarkers, including superoxide dismutase (SOD), glutathione peroxidase (GPx), malondialdehyde (MDA), and total protein levels, were assessed using validated biochemical methods. Correlation and linear regression analyses were performed to examine associations between salivary biomarkers and clinical dental indices in patients with clinically active IBD, compared with a healthy control group. **Results:** In patients with active IBD, salivary oxidative stress biomarkers (SOD, GPx, MDA) and total protein levels showed weak, non-significant associations with oral health indices. MDA demonstrated modest positive trends with caries experience (DMFT;  $r \approx 0.45$ ) and periodontal status (PDI;  $r \approx 0.54$ ), while SOD and GPx showed minimal correlations across oral parameters (all  $p > 0.05$ ). Compared with controls, patients with IBD showed lower mean salivary SOD and GPx activities and higher MDA levels; however, these intergroup differences did not reach statistical significance. **Conclusions:** Salivary oxidative stress biomarkers were not significantly correlated with dental indices in patients with active IBD. Nevertheless, the observed trends for MDA suggest that lipid peroxidation may more closely reflect the shared chronic inflammatory burden affecting oral and intestinal tissues, warranting further investigation in larger, adequately powered studies. **Keywords:** ORAL HEALTH, PERIODONTAL DISEASE, INFLAMMATORY BOWEL DISEASE, OXIDATIVE STRESS, SALIVARY BIOMARKERS.

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### INTRODUCTION

The oral cavity and the intestine are distinct yet interconnected components of the orodigestive tract, linked through shared anatomical, microbial, and immunological pathways that generate bidirectional influences on host health. Increasing evidence indicates that oral diseases and inflammatory bowel diseases (IBD) should not be regarded as isolated conditions, but rather as components of a complex and interdependent pathogenic network (1).

Inflammatory bowel diseases, comprising ulcerative colitis and Crohn's disease, are characterized by chronic inflammation of the gastrointestinal tract. Its etiology is multifactorial, involving genetic predisposition, disruption of the intestinal epithelial barrier, and a dysregulated immune response to luminal contents, alongside influences from lifestyle, diet, microbiota composition, and environmental exposures. Certain factors, such as smoking, increase the risk of Crohn's disease, whereas a Western-style diet rich in animal proteins and fats, the frequent use of antibiotics or nonsteroidal anti-inflammatory drugs, and psychosocial stress can trigger or exacerbate IBD (2) (3). Modern dietary patterns, through their profound influence on both the oral and intestinal microbiome, contribute to the increasing susceptibility to IBD and other chronic metabolic disorders (1).

Periodontitis is a chronic inflammatory disease of the tooth-supporting structures, arising from the complex interplay between microbial dysbiosis and the host immune response. This microbial imbalance is characterized by the proliferation of pathogenic oral bacteria and the reduction of protective commensal species, while disease initiation is linked to the accumulation of dental plaque and the subsequent activation of

inflammatory pathways that progressively destroy periodontal tissues. In this context, periodontitis is not merely a localized condition but a disorder with significant systemic implications (4).

The relevance of the oral cavity in IBD extends beyond extraintestinal manifestations and reflects a complex interplay between local and systemic inflammatory processes. Crohn's disease may involve oral mucosa, lips, tongue, teeth, and periodontium, with oral involvement reported in approximately 0.5% to 20% of cases (5). Moreover, an increased burden of periodontitis has been documented in patients with IBD compared with the general population, underscoring the bidirectional relationship between these two conditions (6, 7, 8). Additionally, a higher prevalence and severity of periodontitis has been consistently reported among individuals with IBD compared with healthy cohorts, highlighting the influence of intestinal health on the oral cavity (9).

Through the dissemination of oral pathogens and the promotion of low-grade systemic inflammation, periodontitis may contribute to the development or exacerbation of systemic conditions such as IBD, cardiovascular disease, diabetes, and other metabolic or inflammatory complications (10).

The primary aim of our study was to evaluate the relationship between salivary oxidative stress biomarkers, specifically the salivary antioxidant enzymes superoxide dismutase and glutathione peroxidase, as well as malondialdehyde, as a marker of lipid peroxidation, and clinical oral parameters in patients with active IBD, in order to explore their potential relevance as non-invasive indicators of systemic inflammatory burden. A secondary aim was to assess

the associations between these salivary biomarkers and established oral health Periodontal Disease Index (PDI) (11), the Simplified Oral Hygiene Index (OHI-S) (12), and the Decayed, Missing, and Filled Teeth (DMFT) (13) with the objective of determining the extent to which salivary oxidative stress reflects oral health status in the context of IBD.

## MATERIALS AND METHODS

**Patients and study design.** A cross-sectional study was conducted, including 30 patients with IBD and a control group of 5 healthy subjects, who were clinically and biologically evaluated at the time of inclusion. Patients with confirmed IBD were recruited from the Institute of Gastroenterology and Hepatology, “Sf. Spiridon” County Clinical Emergency Hospital, Iași. Nineteen patients were diagnosed with ulcerative colitis (UC) and eleven with Crohn’s disease (CD). The diagnosis of IBD was established based on clinical, biological, imaging, and endoscopic criteria.

The inclusion criteria comprised adult patients ( $\geq 18$  years) with a confirmed diagnosis of active IBD (ulcerative colitis or Crohn’s disease), without recent major surgical interventions and with no use of antioxidant supplements during the preceding four weeks. The control group included healthy subjects of comparable age, with no systemic inflammatory or autoimmune diseases and a healthy oral status, defined by periodontal indices PDI, oral hygiene OHI-S, and dental caries DMFT within normal ranges, with no evidence of active periodontitis or active carious lesions. The exclusion criteria included patients with diabetes mellitus, advanced cardiovascular or renal diseases, acute oral conditions,

recent use of antibiotics or anti-inflammatory drugs, heavy smoking, chronic alcohol consumption, a history of recent dental interventions ( $< 3$  months), as well as pregnant or breastfeeding women.

The study protocol was reviewed and approved by the local Ethics Committee, and all procedures were conducted in accordance with the principles of the Declaration of Helsinki. Prior to participation, all subjects received detailed information regarding the study objectives and procedures and provided written informed consent.

Demographic and clinical characteristics were compared between the control group and patients with active IBD. For each participant, age, sex, smoking status, and body mass index (BMI) were recorded. The distribution of categorical variables (sex and active smoking status) was analyzed using Fisher’s exact test, while continuous variables (age and BMI) were compared using independent-samples *t*-tests, with corresponding *p*-values reported. The study enrolled patients with clinically active IBD, as defined by disease-specific activity scores (Mayo score for UC, Crohn’s Disease Activity Index) and elevated inflammatory markers, treated with conventional therapy (5-aminosalicylates and/or immunomodulators) or advanced biologic therapies.

All study patients and subjects underwent oral clinical evaluation as well as biological evaluation of unstimulated saliva samples. Associations between salivary oxidative stress biomarkers (SOD, GPx, MDA, and total proteins) and dental clinical indices were assessed.

**Oral Clinical Evaluation.** All participants underwent a comprehensive intraoral examination performed by an experienced

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dentist. Oral hygiene status was assessed using the Oral Hygiene Index-Simplified (OHI-S), according to standardized methodology. The index was determined by examining six representative dental surfaces (upper right molar, upper left molar, lower right molar, lower left molar, and two central incisors), each evaluated for dental plaque and calculus accumulation. The individual scores were subsequently averaged to obtain the final OHI-S value.

Periodontal status was evaluated using the Periodontal Disease Index (PDI), which includes the examination of the six Ramfjord teeth. For each tooth, gingival inflammation and periodontal attachment loss were assessed, with the final score representing the mean of the recorded values. Higher scores indicate increased periodontal disease severity.

Gingival inflammation was additionally assessed using the Gingival Index (GI), which classifies the severity of gingival inflammation on a scale from 0 (healthy gingiva) to 3 (severe inflammation with bleeding and edema).

Caries experience was evaluated using the DMFT index (Decayed, Missing, Filled Teeth), determined by examining all permanent teeth and recording the number of decayed teeth, teeth missing due to caries, and filled teeth. The total DMFT score reflects cumulative caries experience and overall oral health status.

**Biological Evaluation.** Following the selection interview and clinical examination, unstimulated saliva samples were collected from all participants included in the study. Unstimulated whole saliva was collected by passive drooling into sterile tubes and transferred using a pipette. Approximately 0.5-1 mL of saliva was collected into sterile Eppendorf tubes. Sam-

ples were immediately frozen at  $-50^{\circ}\text{C}$  to prevent biomolecule degradation and to avoid repeated freeze-thaw cycles. For biochemical analyses, samples were gradually thawed from  $-50^{\circ}\text{C}$  to  $4^{\circ}\text{C}$ , then diluted in cold phosphate-buffered saline (PBS) and homogenized. Superoxide dismutase (SOD) activity was determined using a commercial colorimetric assay kit (SOD Assay Kit, Sigma-Aldrich), based on the competition between xanthine oxidase and SOD for superoxide radical generation. Quantification was performed by measuring absorbance changes at 450 nm. Enzymatic activity was expressed as percentage inhibition of the reaction, according to the manufacturer's instructions.

Glutathione peroxidase (GPx) activity was measured using a commercial enzymatic assay (Glutathione Peroxidase Cellular Activity Assay Kit, Sigma-Aldrich), which quantifies NADPH consumption during the GPx-catalyzed reaction. The decrease in absorbance at 340 nm was recorded kinetically, and GPx activity was calculated in enzymatic units normalized to sample volume and dilution factor.

Malondialdehyde (MDA) concentrations, as a marker of lipid peroxidation, were determined using the thiobarbituric acid (TBA) reaction method, considered a standard approach for quantifying end products of lipid peroxide degradation. The MDA-TBA complexes formed were measured spectrophotometrically at 532 nm, and concentrations were calculated based on a standard calibration curve generated with MDA bis(diethyl acetal). Results were expressed as nmol MDA/mL supernatant.

Total soluble protein levels were determined using the Bradford method with a commercial kit (Rapid Protein Quantification Kit, Sigma-Aldrich). Absorbance was

measured at 595 nm, and protein concentrations were calculated using a bovine serum albumin standard curve. TSP concentrations were used to normalize enzymatic activities (SOD U/mg TSP, GPx U/mL TSP) and, optionally, MDA levels expressed relative to protein content (nmol MDA/mg TSP). Routine hematological and biochemical analyses were performed in patients with active IBD, including C-reactive protein (CRP), fecal calprotectin, fibrinogen, hemoglobin, ferritin, total proteins, and electrolytes. These parameters were interpreted according to the standardized recommendations of the CALM study and were used to confirm disease activity at the time of inclusion.

**Statistical Analysis.** Clinical and demographic variables are presented as mean  $\pm$  standard deviation (SD), whereas salivary biomarker data are expressed as mean  $\pm$  standard error of the mean (SEM). To assess the associations between salivary oxidative stress biomarkers (SOD, GPx, MDA, and total proteins) and dental clinical indices, correlation and regression analyses were performed. For each biomarker-parameter pair, scatter plots were generated to visualize the distribution of individual values. Linear regression models were applied using ordinary least squares (OLS) fitting

to estimate the direction and magnitude of the relationships.

The strength of the associations was quantified using Pearson's correlation coefficient ( $r$ ), while statistical significance was evaluated using two-tailed Pearson correlation tests, with corresponding  $p$ -values displayed on each plot. This combined graphical and analytical approach enabled an integrated assessment of both linear trends and the statistical robustness of the observed associations.

## RESULTS

Clinical characteristics of study patients and subjects are presented in first table, with no significant differences between groups.

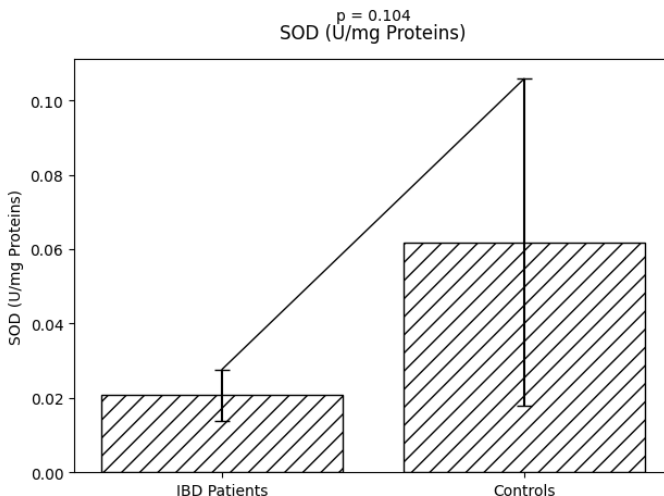
Regarding the specific activity of SOD, a key first-line antioxidant enzyme involved in the defense against oxidative stress development, patients diagnosed with IBD exhibited lower mean SOD activity (0.0207 U/mg protein) compared with the control group (0.0618 U/mg protein) (fig. 1). This difference did not reach statistical significance ( $p > 0.05$ ). The error bars illustrate the within-group variability, indicating a more homogeneous distribution of values among patients and greater dispersion in the control group.

TABLE I.  
Clinical characteristics of the control group and patients with IBD

	Controls (n=5)	IBD patients (n = 30)	p- value
Age (years), Mean $\pm$ SD	45 $\pm$ 5.7	48.8 $\pm$ 16.3	0.35
Sex, n (Male/Female)	1/4	20/10	0.14
Active smokers, n (%)	1 (20%)	4 (13.3%)	0.56
BMI, kg/m <sup>2</sup> Mean $\pm$ SD	20.26 $\pm$ 5.48	23.84 $\pm$ 3.04	0.22
Disease duration (years), Mean $\pm$ SD	-	7.07 $\pm$ 6.77	

BMI: Body-Mass Index

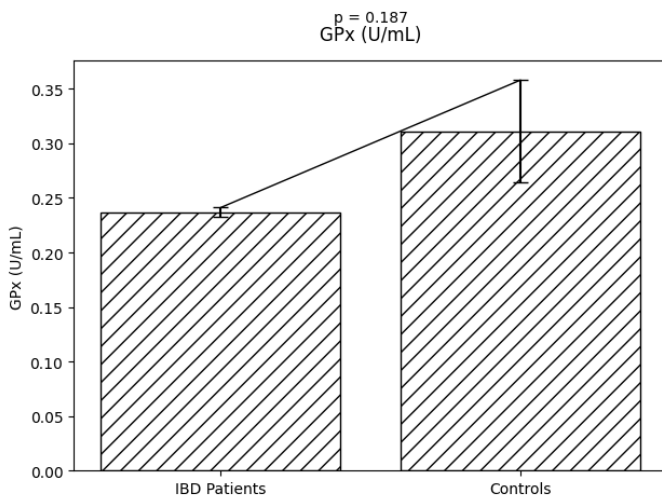
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**Fig. 1.** Specific activity of superoxide dismutase (U/mg protein) in patients with IBD compared with the control group. Values are presented as mean  $\pm$  SEM.

Regarding the second antioxidant enzyme, the mean GPx activity was  $0.2367 \pm 0.0044$  U/mL in the IBD group, compared with  $0.3112 \pm 0.0468$  U/mL in healthy controls (fig. 2). This difference did not reach statistical significance ( $p = 0.187$ ).

Nevertheless, the observed distribution suggests a tendency toward reduced GPx activity in IBD patients relative to controls, possibly reflecting increased enzymatic consumption under conditions of chronic inflammation and oxidative stress.

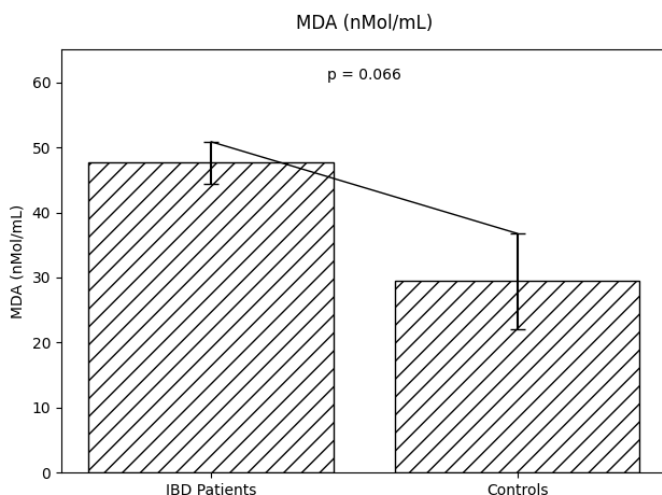


**Fig. 2.** Glutathione peroxidase (U/mL) activity in patients with IBD compared with the control group. Values are expressed as mean  $\pm$  SEM. The statistical comparison yielded  $p = 0.187$

Compared to healthy controls, patients with IBD exhibited higher mean salivary MDA concentrations ( $47.64 \pm 3.22$  nMol/mL versus  $29.43 \pm 7.34$  nMol/mL) (fig. 3). The error bars reflect within-group variability, showing greater dispersion among controls and a more consistent pattern within the IBD group. A borderline trend toward increased MDA levels in IBD patients relative to controls was observed ( $p = 0.066$ ).

To complement the descriptive analysis of salivary oxidative stress biomarker levels, regression-based graphical evaluations

were performed to explore whether these biochemical changes were reflected in oral health status. While the group comparisons illustrated the overall patterns of MDA, SOD, GPx, and total protein concentrations, the scatter plots with linear regression lines provided a detailed view of how these markers aligned with individual dental indices. Together, these two approaches allowed us to assess not only the magnitude of biomarker alterations but also their potential associations with caries experience, periodontal indicators, and cumulative dental disease.



**Fig. 3.** Mean salivary concentration of MDA (nMol/mL) in patients with IBD compared with the control group.

Values are expressed as mean  $\pm$  SEM. A non-significant trend was observed ( $p = 0.066$ )

Correlation analysis revealed no statistically significant relationships between SOD activity (fig. 4) and the assessed clinical oral parameters. Only weak positive trends were observed between SOD activity and the filling score ( $r = 0.21$ ;  $p = 0.55$ ) as well as the DMFT index ( $r = 0.21$ ;  $p = 0.55$ ), suggesting that antioxidant activity does not increase proportionally with den-

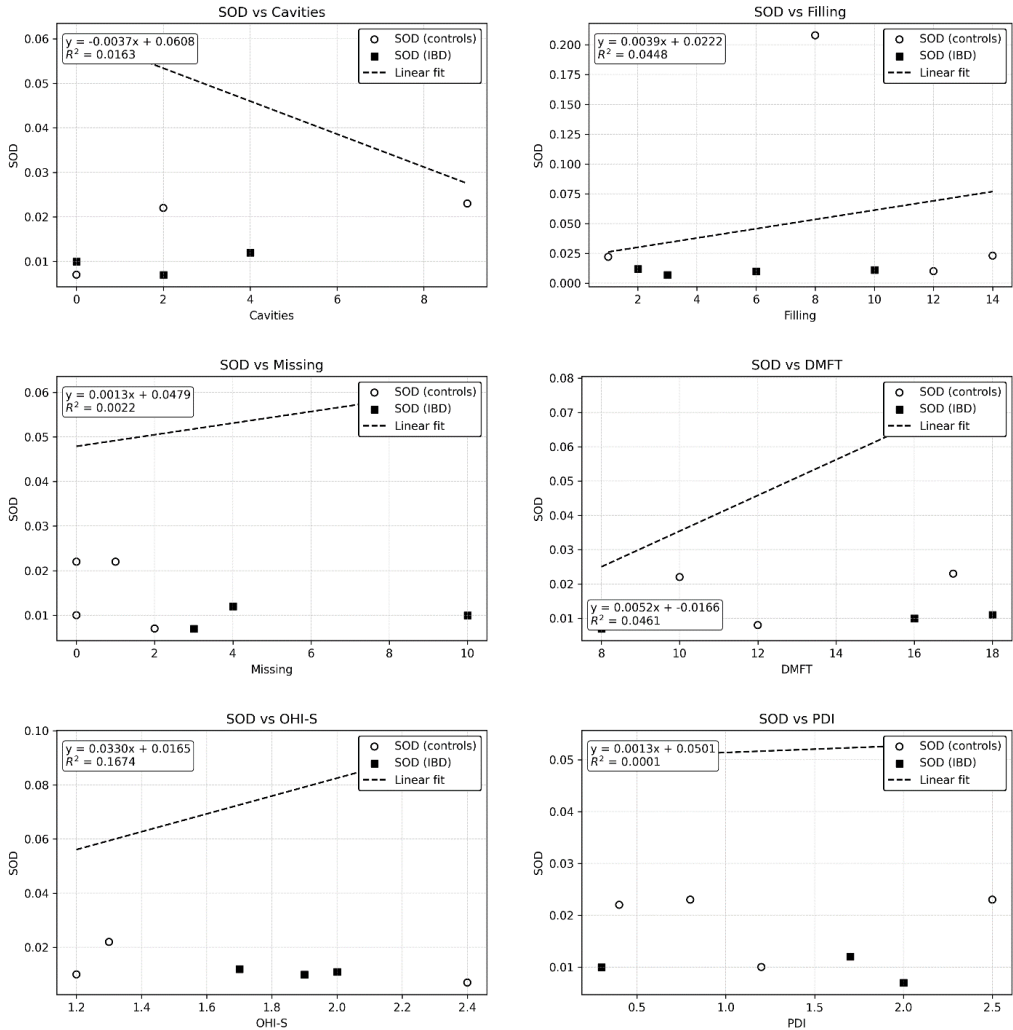
tal caries severity. The strongest association was identified between SOD activity and the oral hygiene index (OHI-S) ( $r = 0.40$ ;  $p = 0.25$ ); however, this correlation did not reach statistical significance.

Regarding the second antioxidant enzyme, GPx (fig. 5) its activity showed no statistically significant associations with any of the oral clinical parameters evaluat-

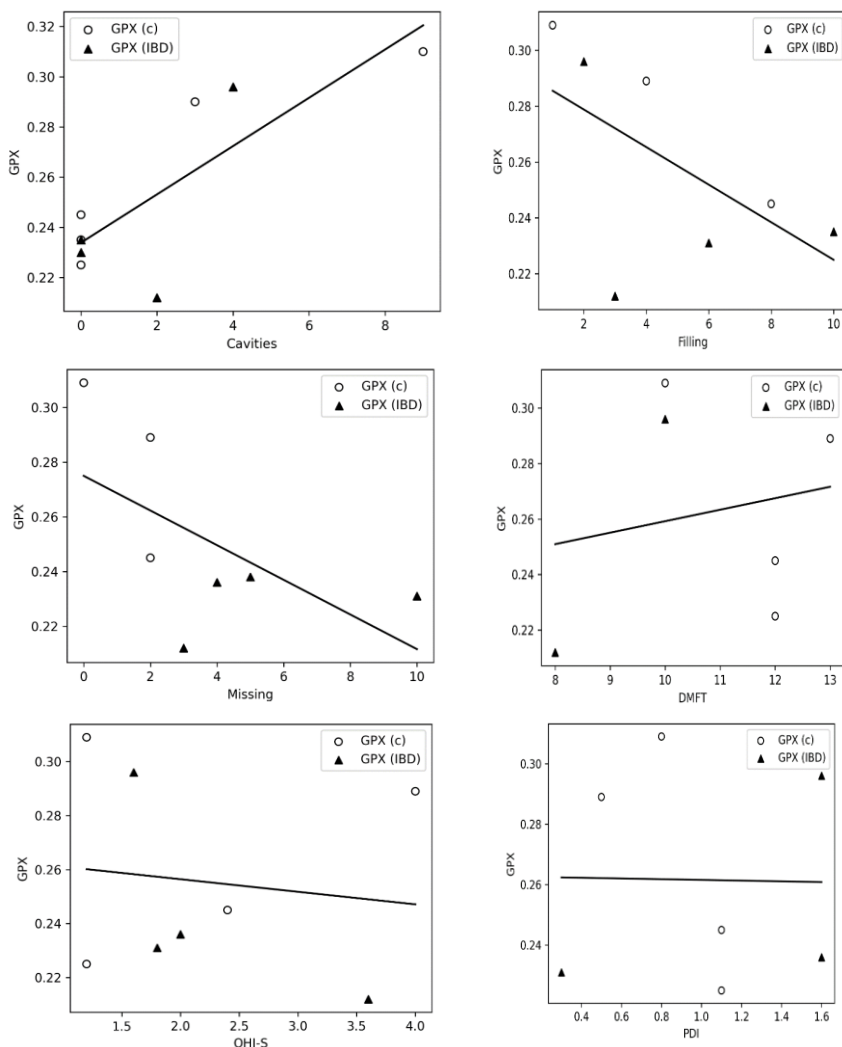
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ed. Scatterplot analyses revealed only weak and nonsignificant correlations between GPx and the number of cavities, filled teeth, missing teeth, and the overall DMFT index, as well as with PDI and OHI-S. Nevertheless, several upward or downward tendencies could be observed: GPx displayed mild positive associations with cavities ( $r = 0.26$ ), filled teeth ( $r = 0.27$ ),

DMFT ( $r = 0.26$ ), and PDI ( $r = 0.35$ ), suggesting a possible compensatory antioxidant response in individuals with greater caries or periodontal involvement. Conversely, negative trends were noted for missing teeth ( $r = -0.35$ ) and OHI-S ( $r = -0.33$ ), indicating that higher tooth loss or poorer oral hygiene may relate to lower GPx activity.



**Fig. 4.** Scatter plots with linear regression lines illustrating the relationships between salivary SOD and dental clinical indices in controls and patients with IBD.



**Fig. 5.** Scatter plots with regression lines showing the relationship between salivary GPx and dental indices in controls and patients with IBD.

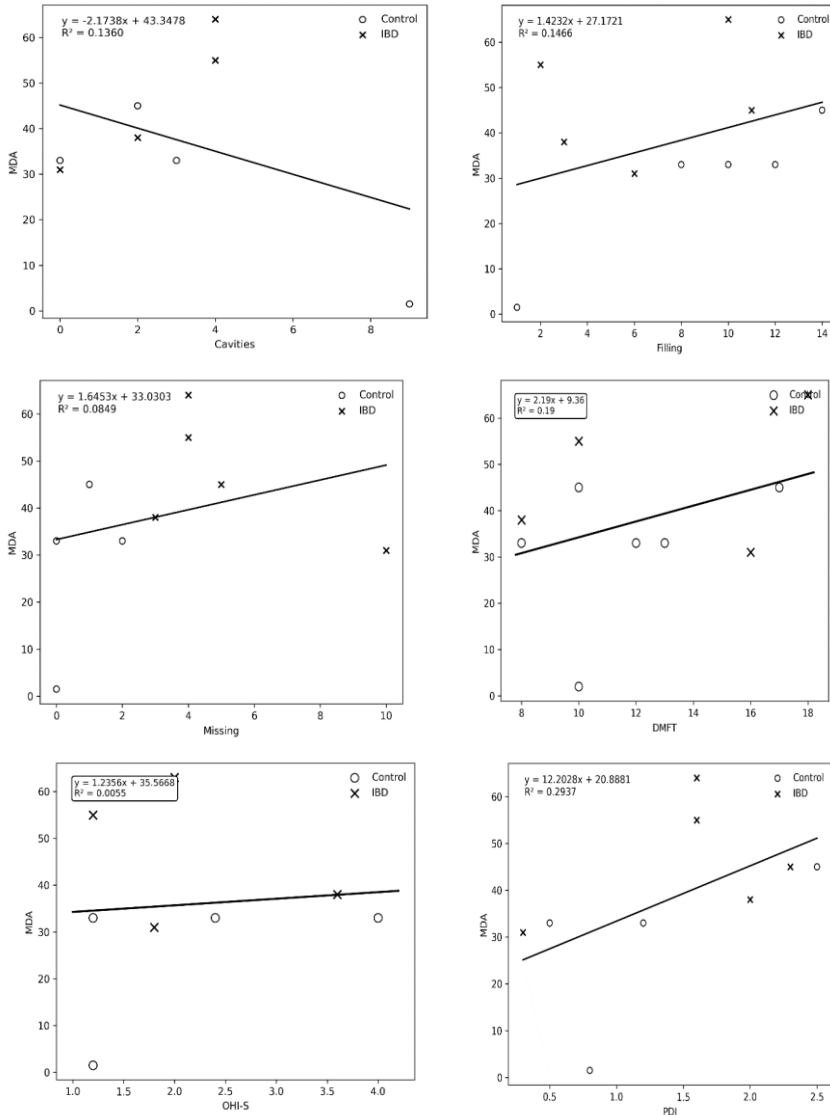
In the case of MDA, an important marker of lipid peroxidation, correlation analyses revealed only weak to moderate, non-significant associations with the evaluated clinical oral parameters (fig. 6). Scatterplot analyses demonstrated a slightly negative trend between MDA levels and the number of carious lesions ( $r = -0.37$ ), suggesting that higher oxidative stress was not accom-

panied by an increase in active caries within this cohort. In contrast, weak positive correlations were observed with the filling index ( $r = 0.38$ ) and the number of missing teeth ( $r = 0.29$ ), indicating that MDA levels tended to be higher in individuals with a history of dental restorations or tooth loss, although these associations did not reach statistical significance. A moderate positive associa-

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tion was also detected with the total DMFT score ( $r = 0.45$ ) and the periodontal disease index (PDI) ( $r = 0.54$ ), potentially reflecting a link between cumulative oral disease burden and increased oxidative stress. The weakest relationship was observed with the OHI-S ( $r = 0.07$ ), suggesting that current

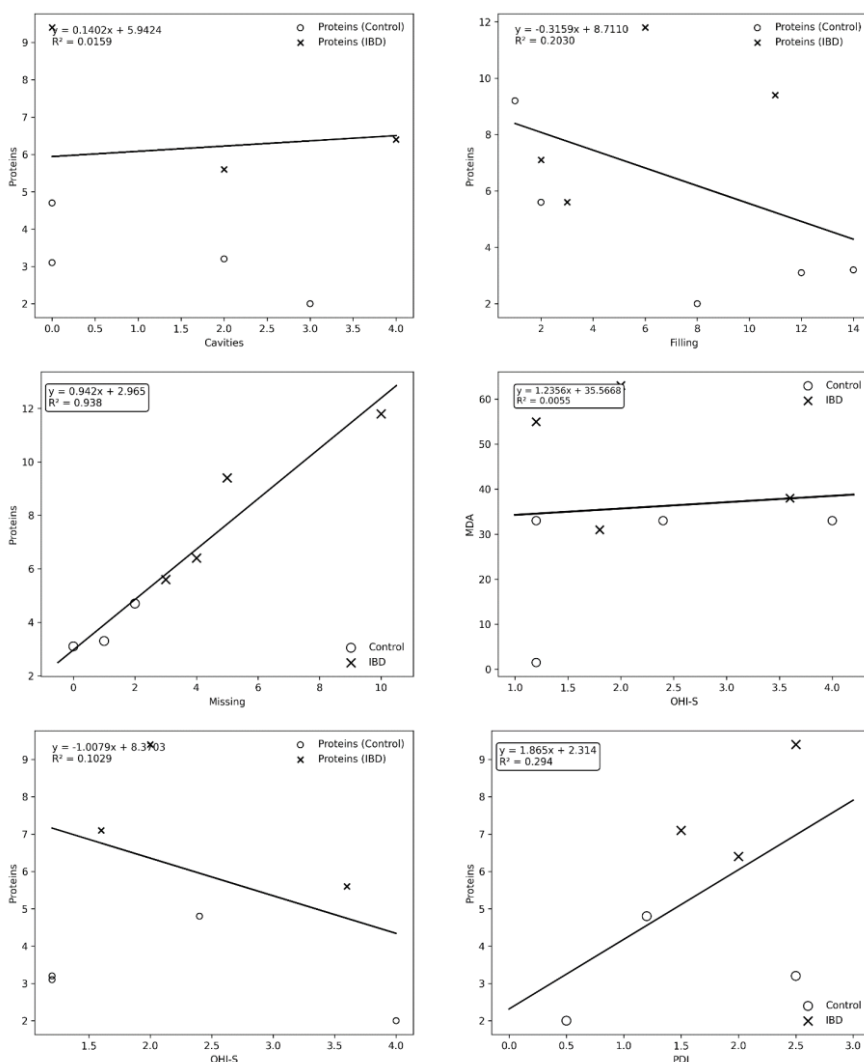
oral hygiene status exerted minimal influence on salivary MDA levels. Overall, none of the correlations reached statistical significance; however, several biologically plausible trends point toward a potential cumulative effect of chronic oral pathology on oxidative stress.



**Fig. 6.** Scatter plots with linear regression lines illustrating the relationships between salivary MDA and dental clinical indices in controls and patients with IBD

The analysis of total salivary protein levels revealed no statistically significant

correlations with the evaluated oral clinical parameters (fig. 7).



**Fig. 7.** Scatter plots with linear regression lines illustrating the relationships between salivary protein levels and dental clinical indices in controls and patients with IBD

Scatterplot assessment indicated that protein concentrations exhibited mild positive but nonsignificant trends in relation to the number of filled teeth ( $r = 0.18$ ,  $p > 0.05$ ), missing teeth ( $r = 0.22$ ,  $p > 0.05$ ), and the overall DMFT score ( $r = 0.24$ ,  $p >$

$0.05$ ), suggesting that individuals with greater cumulative caries experience may present slightly elevated salivary protein levels. In contrast, negative or near-flat associations were observed between protein levels and the number of decayed teeth ( $r =$

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-0.09,  $p > 0.05$ ), indicating that active carious lesions were not accompanied by increases in salivary protein content. PDI and OHI-S also demonstrated weak and nonsignificant relationships with protein concentrations (PDI:  $r = 0.17$ ,  $p > 0.05$ ; OHI-S:  $r = -0.11$ ,  $p > 0.05$ ), with minimal inter-individual variability. Overall, these findings indicate that salivary protein levels remained relatively stable in both the control and IBD groups, with no significant correlations with caries activity or periodontal status in the present sample.

### DISCUSSION

Salivary oxidative stress markers showed biomarker-specific patterns, with MDA levels consistently higher in IBD patients than in controls. Although correlations between MDA and dental indices were weak or borderline significant, their direction suggested an association between greater cumulative dental disease experience and increased lipid peroxidation, with the strongest positive-moderate but nonsignificant-associations observed for DMFT ( $r \approx 0.45$ ) and PDI ( $r \approx 0.54$ ). In contrast, SOD and GPx exhibited low values and minimal variability, resulting in very weak and nonsignificant correlations with clinical oral parameters, indicating limited sensitivity in this small pilot cohort.

In light of our pilot data and previous work from our group, oxidative stress alterations in IBD may reflect not only intestinal inflammation but also associated systemic comorbidities. Our prior studies on chronic inflammatory and hepatobiliary disorders support a broader, multisystem involvement affecting metabolic and oxidative pathways. For example, patients with extrahepatic cholestasis caused by choledocholithiasis were reported to exhibit increased liver stiffness values (6.2-18.4 kPa), which normalized after biliary drainage, with this

improvement correlating significantly with reductions in serum bilirubin (14). Furthermore, Trifan *et al.* demonstrated that a 12-week regimen of paritaprevir/ritonavir, ombitasvir and dasabuvir plus ribavirin was safe and achieved nearly 100% sustained virologic response in elderly patients ( $\geq 70$  years) with HCV genotype 1b compensated cirrhosis (15).

Periodontitis progression has been linked to local oxidative stress, with affected patients showing elevated MDA, hydrogen peroxide, and oxidative DNA damage levels (16). Periodontitis has been associated with reduced SOD and catalase activity and altered oxidative stress biomarkers, including total antioxidant capacity, MDA, and 8-hydroxydeoxyguanosine, compared with healthy controls (17). The pathogenesis of periodontal tissue destruction involves oxidative stress as a central mechanism (16). In a large study, Almerich-Silla *et al.* (17) emphasized that oxidative stress levels in the periodontium are significantly higher in periodontal disease compared with gingivitis or health, displaying a linear trend that parallels disease severity and bleeding on probing (BOP). Patients with periodontitis show increased biomarkers of ROS-mediated tissue damage as well as compensatory increases in antioxidant enzymes within inflamed periodontal tissues and gingival crevicular fluid.

In our study, the MDA-PDI scatterplot showed an upward trend with a steep regression slope, indicating higher MDA levels with increasing periodontal inflammation. Patients with more severe PDI scores exhibited elevated salivary lipid peroxidation, suggesting a relevant association between periodontal severity and oxidative damage. In contrast, GPx and SOD activity showed minimal variation across PDI levels (tab. II), indicating limited antioxidant compensatory responses.

TABLE II.

**Summary of the direction and strength of associations  
between salivary oxidative stress biomarkers and periodontal disease index**

Salivary biomarker	Direction of association with PDI	Correlation strength
MDA	Positive (↑)	Moderate
SOD	Very Weak ( $\approx 0$ )	Very Weak
GPx	Weak Positive (↑)	Weak

Regarding dental caries, current evidence indicates that carious lesions are associated with an altered redox response, characterized by increased lipid peroxidation and a reduction in antioxidant capacity during the progression of the disease (18). The direction of these correlations suggests that a greater cumulative dental disease burden may be accompanied by higher salivary lipid peroxidation. Studies on dental caries in children further report that total antioxidant capacity (TAC) decreases in the presence of carious lesions, whereas higher levels of gingival inflammation are paradoxically associated with increased TAC (19). Some studies have reported higher SOD levels in caries-free dentition (18), although these findings remain inconsistent across cohorts. In our study, both SOD and GPx exhibited generally low values and showed very weak correlations with DMFT or the number of carious lesions, suggesting limited sensitivity in detecting oral redox imbalances.

A major limitation of this study is the relatively small sample size, which reduces statistical power and limits the ability to identify robust associations between salivary oxidative stress biomarkers and clinical oral parameters. The substantial biological variability of salivary markers-shaped by disease activity, oral microbiome composition, behavioral factors, and treatment status-may introduce measurement noise that obscures true biological relationships. Particularly relevant is the potential confounding effect

of biological therapies used in IBD: anti-TNF agents (infliximab, adalimumab) can suppress systemic inflammation and reactive oxygen species production, potentially lowering MDA levels and increasing antioxidant activity (SOD, GPx). Likewise, IL-12/23 blockade (ustekinumab) and JAK1 inhibition (upadacitinib) may significantly modulate oxidative pathways, while vedolizumab, despite its gut-selective action, may indirectly influence periodontal inflammation through improved intestinal disease control. Consequently, the salivary oxidative stress profile observed in this cohort may reflect both disease-related alterations and treatment-related modulation, making it difficult to attribute changes solely to oral or intestinal pathology. The limited sample size also restricts the generalizability of the findings, underscoring the preliminary nature of these results and the need for larger, longitudinal studies to validate these observations.

## CONCLUSIONS

This pilot study suggests that salivary oxidative stress markers, especially MDA, may provide complementary insight into the oral-intestinal inflammatory axis in patients with IBD, although their diagnostic utility appears limited in small, heterogeneous samples. The absence of strong associations for SOD and GPx likely reflects substantial inter-individual variability, disease-related heterogeneity, and the modulatory effects of biological therapies. Larger, longitudinal studies

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integrating salivary biomarkers, microbiome profiling, and disease activity indices are required to clarify the role of salivary oxidative stress as a non-invasive marker of systemic and oral inflammation in IBD.

### CONFLICT OF INTERESTS AND FUNDING

The authors declare no conflict of interests. No financial support was received for perfecting this article.

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