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periodontitis; gastrointestinal disease; Helicobacter pylori; oral-gut axis; vacuum-laser therapy; Nigella sativa; black seed oil; IL-1β; TNF-α; oral microbiome; periodontal pathogens; immunology

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Pathogenetic Optimization Of Inflammatory Periodontal Disease Management In Patients With Gastrointestinal Tract Pathology: A Clinical, Immunological, And Microbiological Study

Abstract

Background: Inflammatory periodontal diseases represent a global health burden, with growing evidence implicating bidirectional pathogenetic links with gastrointestinal tract (GIT) pathology. The shared microbial and inflammatory mechanisms connecting the oral cavity and digestive system remain incompletely characterized, and targeted therapeutic protocols for patients with concurrent periodontitis and GIT disease are lacking.

Objective: To investigate the clinical, immunological, microbiological, and biochemical characteristics of inflammatory periodontal disease in patients with concurrent GIT pathology and to evaluate the efficacy of a novel integrated treatment protocol incorporating vacuum-laser therapy and cold-pressed black seed oil (Nigella sativa) as adjuncts to standard periodontal therapy.

Methods: A prospective controlled clinical trial enrolled 182 participants aged 25–80 years, divided into a study group (n=89, periodontitis with GIT comorbidity receiving integrated treatment), a comparison group (n=63, periodontitis without GIT pathology receiving standard treatment), and a healthy control group (n=30). Clinical periodontal indices (GBI, BOP, PPD, CAL, PI, OHI-S), immunological markers (IL-1β, TNF-α, IL-6, salivary sIgA), biochemical parameters (total salivary protein, α-amylase), and microbiological profiles (PCR detection of P. gingivalis, T. forsythia, T. denticola, F. nucleatum, P. intermedia, H. pylori) were assessed at baseline, 7–10 days, 1 month, and 3 months.

Results: Patients with concurrent GIT pathology demonstrated significantly elevated inflammatory markers (IL-1β: 142.3±28.4 vs. 138.6±26.9 pg/mL; TNF-α: 89.2±18.6 vs. 86.8±17.3 pg/mL) and higher periodontal pathogen detection rates compared to isolated periodontitis. The severity of periodontal inflammation correlated positively with GIT disease severity ($r=0.64$, $p<0.001$). After 3 months, the integrated treatment protocol produced significantly greater improvements across all clinical indices (GBI reduction: 72.8% vs. 40.2%), immunological parameters (IL-1β reduction: 66.1% vs. 39.2%), and microbiological outcomes compared to standard therapy ($p<0.001$).

Conclusion: Concurrent GIT pathology substantially modifies the clinical and immunological course of periodontal disease. The combination of vacuum-laser therapy and cold-pressed black seed oil as adjuncts to standard periodontal treatment significantly improves clinical, immunological, and microbiological outcomes in this comorbid population.

These findings support the development of integrated interdisciplinary management strategies for periodontal-GIT comorbidity.

1. Introduction

Inflammatory diseases of the periodontal tissues—encompassing gingivitis and periodontitis in its various forms—rank among the most prevalent chronic conditions worldwide, affecting an estimated 10–50% of the global adult population depending on severity criteria [1]. The multifactorial etiology of periodontitis encompasses microbial dysbiosis driven by a dysbiotic subgingival biofilm, aberrant host immune responses, and a broad spectrum of environmental and systemic risk modulators [2,3].

A compelling and increasingly supported body of evidence suggests that the oral cavity and the gastrointestinal tract (GIT) are not merely anatomically contiguous structures but are connected through shared microbial, immunological, and inflammatory pathways collectively described as the oral-gut axis [4,5]. Periodontal pathobionts—particularly Porphyromonas gingivalis, Fusobacterium nucleatum, and Treponema denticola—are capable of translocating from the periodontal niche to the gastrointestinal tract via swallowed saliva, disrupting gut microbial homeostasis, and exacerbating intestinal inflammation [6,7]. Conversely, GIT pathology—including chronic gastritis, peptic ulcer disease mediated by Helicobacter pylori infection, inflammatory bowel disease, and colitis—imposes systemic inflammatory burden that may amplify periodontal tissue destruction through elevated circulating cytokines and altered immune cell function [8,9].

Epidemiological and mechanistic evidence consistently implicates pro-inflammatory cytokines such as IL-1β, TNF-α, and IL-6 as central mediators at the interface of oral and systemic disease [10,11]. These cytokines, elevated in gingival crevicular fluid (GCF) and saliva of periodontitis patients, are also major effectors in GIT mucosal inflammation, raising the possibility that systemic inflammatory "priming" originating in the periodontium may lower the threshold for gastric mucosal damage, and vice versa [12,13].

Despite growing mechanistic insight, the clinical evidence characterizing the bidirectional relationship between periodontitis and GIT disease remains heterogeneous, and no universally accepted treatment protocol exists for patients presenting with this comorbidity. Standard periodontal therapy (scaling, root planing, curettage, antiseptic adjuncts) does not address the specific immunological and microbiological amplification conferred by GIT comorbidity. Novel adjunctive modalities—including laser-based physical therapies and bioactive natural compounds—may offer targeted mechanistic complementarity [14,15].

Laser therapy as an adjunct to periodontal treatment has demonstrated antimicrobial, anti-inflammatory, and biostimulatory effects in multiple clinical trials, with significant reductions in periodontal pathogens, GCF cytokines, and probing depth documented for diode and Nd:YAG laser applications [16,17]. Cold-pressed black seed oil (Nigella sativa) contains the principal bioactive compound thymoquinone, which possesses well-characterized antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory properties, including documented activity against periodontal pathogens such as P. gingivalis and P. intermedia [18,19].

The present study was designed to: (1) characterize the clinical, immunological, biochemical, and microbiological features of periodontitis in patients with concurrent GIT pathology compared to periodontitis alone; (2) establish correlations between GIT disease severity and periodontal disease parameters; and (3) evaluate the efficacy of an integrated treatment protocol combining vacuum-laser therapy and cold-pressed Nigella sativa oil as adjuncts to standard care.

2. Literature Review

2.1 The Oral-Gut Axis: Epidemiological and Mechanistic Evidence

The concept of the oral-gut axis describes the bidirectional biological communication between the oral cavity and the intestinal tract, mediated by microbial translocation, systemic inflammatory signaling, shared immune effectors, and neuroendocrine pathways [4,5]. The oral cavity serves as the primary entry point for the gastrointestinal system, and approximately 1.5 liters of saliva—laden with up to 10^9 microorganisms per milliliter—are swallowed daily, continuously seeding the intestinal microenvironment with oral bacterial species [20].

In health, most orally-ingested bacteria fail to colonize the gut due to gastric acid, bile, and competitive exclusion by established gut commensals. However, in the context of periodontal disease—characterized by a dramatically altered dysbiotic oral microbiome dominated by Gram-negative anaerobes—the quantitative and qualitative composition of swallowed organisms shifts substantially. Multiple independent studies using 16S rRNA amplicon sequencing have confirmed that patients with moderate-to-severe periodontitis harbor elevated proportions of oral-derived bacteria in their fecal microbiomes, including P. gingivalis, F. nucleatum, and Prevotella copri, compared with periodontally healthy controls [6,7,21].

Large-scale epidemiological analyses have confirmed the association between periodontal disease and gastrointestinal malignancies and inflammatory conditions. A meta-analysis encompassing over 16.6 million participants reported that individuals with periodontal diseases faced a 31% increased hazard for overall gastrointestinal cancers (HR 1.31, 95% CI 1.16–1.49), with significant associations for esophageal cancer (HR 1.39), gastric cancer (HR 1.13), and colorectal cancer [22]. A systematic review evaluating the specific relationship between periodontal disease and inflammatory bowel disease (IBD) identified bidirectional microbial and immunological links, with periodontal pathogen burden correlating with IBD activity scores [23].

2.2 Immunological Mechanisms Linking Periodontal Disease and GIT Pathology

The periodontal pocket represents a chronically inflamed site of bacterial-host interaction, generating sustained local and systemic release of pro-inflammatory cytokines. IL-1β, the most extensively studied periodontal cytokine, is elevated in GCF of periodontitis patients and correlates with periodontal pocket depth (PPD), clinical attachment loss (CAL), and alveolar bone destruction [10,11]. Its systemic elevation primes gastric mucosal immune cells, amplifying the inflammatory response to H. pylori infection and potentially lowering the threshold for mucosal damage [12].

TNF-α contributes both to local periodontal bone resorption through RANKL-mediated osteoclastogenesis and to systemic inflammation in GIT disease. Circulating monocytes from periodontitis patients display a "primed" phenotype characterized by enhanced TNF-α production upon secondary stimulation, providing a mechanistic explanation for why concurrent GIT inflammatory disease may be amplified in the presence of active periodontitis [13,24]. IL-6, another key mediator in the periodontal-GIT inflammatory interface, is upregulated in both salivary samples from stage III/IV periodontitis patients and in the serum of patients with H. pylori-associated gastritis, suggesting shared signaling pathways [10,25].

Secretory IgA (sIgA) in saliva represents a critical first-line mucosal immune defense against periodontal pathogens. In advanced periodontitis, salivary sIgA levels are often paradoxically reduced, reflecting an exhausted local immune response, while in the GIT, reduced secretory IgA is a recognized contributor to intestinal permeability and dysbiosis [26].

2.3 Helicobacter pylori at the Oral-Gastric Interface

H. pylori, the principal etiological agent of chronic gastritis, peptic ulcer disease, and a recognized carcinogen for gastric adenocarcinoma, colonizes not only the gastric mucosa but is detectable in dental plaque, periodontal pockets, and root canals in a substantial proportion of infected patients [8,12]. The oral cavity thus represents an extra-gastric reservoir that may sustain gastric re-infection following antibiotic eradication therapy, potentially explaining the higher H. pylori eradication failure rates observed in patients with untreated periodontal disease. Multiple molecular studies using PCR-based detection have confirmed H. pylori in subgingival plaque samples, with prevalence rates of 22–57% in periodontitis patients, substantially higher than in periodontally healthy controls [8].

A systematic review and meta-analysis examining patients with periodontal disease and gastric adenocarcinoma found that periodontal disease increased the risk of developing gastric adenocarcinoma by 17%, an association that remained significant regardless of the diagnostic method employed for periodontal assessment [27]. The biological plausibility of this link encompasses H. pylori-mediated gastric carcinogenesis, shared pro-inflammatory cytokine environments, and the potential carcinogenic effects of F. nucleatum and P. gingivalis in the gastrointestinal milieu [22,27].

2.4 Laser Therapy as an Adjunct to Periodontal Treatment

Laser technology has progressively integrated into periodontal practice over the past three decades, exploiting the photobiological, antimicrobial, and biostimulatory properties of coherent light. Nd:YAG (1064 nm), diode (810–980 nm), and Er:YAG (2940 nm) lasers have been most extensively evaluated as adjuncts to scaling and root planing (SRP) in randomized controlled trials [16,17]. A randomized double-blind split-mouth trial demonstrated that Nd:YAG laser-assisted periodontal therapy produced significantly greater PPD reduction compared to SRP alone, attributed to superior bactericidal penetration into periodontal pocket walls and enhanced collagen cross-linking effects [28].

A 12-month randomized controlled trial evaluating adjunctive Nd:YAG laser irradiation to full-mouth SRP documented a significant reduction ($p=0.038$) in serum IL-1β levels at 6 months in the laser group, suggesting that laser-mediated reduction in subgingival bacterial load translates into measurable systemic anti-inflammatory effects [29]. A systematic review and overview of systematic reviews on laser adjunction to non-surgical periodontal therapy concluded that laser therapy, when added to SRP in non-smokers, yields superior short- and medium-term improvements in CAL and PPD [16,30]. Vacuum-assisted laser delivery, combining negative pressure debridement with photobiomodulation, theoretically enhances biofilm disruption and pathogen removal from deep pocket anatomy, though clinical evidence specific to vacuum-laser systems remains emerging.

2.5 Nigella sativa and Thymoquinone in Periodontal Therapy

Nigella sativa (black seed), a plant native to Southwest Asia and North Africa, has been used in traditional medicine for millennia. Its primary bioactive constituent, thymoquinone (TQ), constitutes 28–57% of the essential oil and exerts broad antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory effects through multiple molecular targets including NF-κB inhibition, prostaglandin synthesis suppression, and free radical scavenging [18,31].

In a double-blind randomized clinical trial comparing N. sativa oil to chlorhexidine in patients with chronic generalized gingivitis, N. sativa oil produced superior reduction in salivary IL-6 levels ($p=0.0076$) and equivalent antimicrobial activity against alpha-hemolytic Streptococcus strains, with significantly better tolerability [19,32]. A study published in the European Review of Medical and Pharmacological Sciences demonstrated that N. sativa seed extract exhibited significant antibacterial activity against P. gingivalis isolated from periodontitis patients, with inhibition zones comparable to reference antibiotics [33]. Experimental evidence further confirmed that N. sativa toothpaste significantly reduced expression of MMP-9, TNF-α, and PGE-2 in P. gingivalis-induced

periodontal inflammation in animal models [31]. The anti-H. pylori activity of TQ has been additionally documented, providing a mechanistically attractive rationale for its use in patients with concurrent gastric pathology [18].

3. Materials and Methods

3.1 Study Design and Ethics

This prospective controlled clinical trial was conducted between January 2023 and June 2024. All participants provided written informed consent prior to inclusion. The study protocol was approved by the institutional ethics committee and conducted in accordance with the Declaration of Helsinki. Three parallel groups were enrolled and followed at baseline, 7–10 days, 1 month, and 3 months.

3.2 Participant Selection

A total of 182 participants aged 25–80 years were enrolled. Inclusion criteria for the study group required a confirmed clinical diagnosis of inflammatory periodontal disease (gingivitis or periodontitis classified per the 2017 World Workshop Classification) and a documented concurrent GIT diagnosis (chronic gastritis, peptic ulcer disease, colitis, or enterocolitis). The comparison group required periodontitis without GIT pathology. The control group comprised systemically and periodontally healthy individuals.

Exclusion criteria encompassed: antibiotic or probiotic use within 8 weeks; current or recent (≤3 months) use of immunosuppressive or systemic anti-inflammatory medications; pregnancy or lactation; active oncological disease; severe systemic disease (cardiovascular, renal, or hepatic failure); and inability to comply with the follow-up schedule. GIT diagnoses were confirmed by gastroenterological consultation including endoscopy and, where indicated, H. pylori testing by urea breath test or stool antigen assay.

3.3 Study Groups

The study group (n=89) comprised patients with concurrent periodontitis and GIT pathology who received the integrated treatment protocol. The comparison group (n=63) comprised patients with periodontitis but no GIT pathology who received standard periodontal treatment. The control group (n=30) comprised healthy individuals who underwent clinical assessment only, without active periodontal treatment. Table 2 details the distribution of GIT diagnoses and periodontitis severity within the study group.

3.4 Clinical Assessment Methods

All participants underwent comprehensive periodontal evaluation including: Gingival Bleeding Index (GBI), Bleeding on Probing (BOP), Periodontal Pocket Depth (PPD, measured at six sites per tooth using a calibrated UNC-15 probe), Clinical Attachment Level (CAL), Plaque Index (PI), and Simplified Oral Hygiene Index (OHI-S). Orthopantomography (OPG) was performed to assess crestal bone height. Laser Doppler flowmetry was applied for microcirculation assessment. All clinical measurements were performed by two calibrated examiners (intraexaminer and interexaminer agreement >0.85 by weighted kappa). A standardized photographic protocol was applied at each visit.

3.5 Microbiological Assessment

Subgingival plaque samples were obtained from the deepest periodontal pockets using sterile paper points after supragingival plaque removal. PCR-based detection of key periodontal pathogens was performed for: Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola, Fusobacterium nucleatum, Prevotella intermedia, Enterococcus faecalis, and Helicobacter pylori. DNA extraction and PCR amplification were performed using validated commercial kits with published sensitivity and specificity exceeding 95%.

3.6 Immunological and Biochemical Assessment

Unstimulated whole saliva samples were collected in the morning after 30 minutes of fasting. Cytokine concentrations—IL-1β, TNF-α, and IL-6—were quantified by enzyme-linked immunosorbent assay (ELISA) using validated commercial kits. Salivary secretory IgA (sIgA) was measured by ELISA. Biochemical analysis included total salivary protein (Bradford method) and α-amylase activity (enzymatic colorimetric assay). CD3+, CD4+, and CD8+ T-lymphocyte subpopulations in peripheral blood were assessed by flow cytometry at baseline and 3-month follow-up.

3.7 Treatment Protocols

Standard periodontal treatment (all groups): professional oral hygiene instruction, supragingival and subgingival scaling and root planing (SRP) using hand and ultrasonic instrumentation, curettage of granulation tissue where indicated, antiseptic irrigation (0.05% chlorhexidine), and oral hygiene reinforcement at each visit.

Integrated protocol (study group only): in addition to standard treatment, each patient received: (1) vacuum-laser therapy applied to periodontal pockets using a diode laser (810 nm, 1W continuous wave, 60 seconds per quadrant) under low-level negative pressure aspiration to enhance biofilm removal and photobiomodulatory penetration—5 sessions in the first month; and (2) cold-pressed black seed oil (N. sativa, first cold-press quality, standardized thymoquinone content ≥2%) administered as a 5 mL subgingival irrigation following SRP and applied as a topical gel to gingival tissue at home (2× daily for 3 months).

3.8 Statistical Analysis

Statistical analysis was performed using SPSS v.28.0 (IBM, USA) and R v.4.3.1. Normality was assessed by Shapiro-Wilk test. Between-group comparisons at baseline used independent-samples t-tests or Mann-Whitney U tests as appropriate. Within-group changes over time were evaluated by paired t-tests or Wilcoxon signed-rank tests. Three-group comparisons used one-way ANOVA with Bonferroni post-hoc correction or Kruskal-Wallis test with Dunn correction. Pearson or Spearman correlation coefficients were computed to examine relationships between GIT disease severity and

periodontal parameters. Statistical significance was set at $p<0.05$ (two-tailed).

4. Results

4.1 Participant Flow and Baseline Characteristics

Of 234 patients initially screened, 52 were excluded (31 for not meeting eligibility criteria, 21 who declined participation), yielding a final cohort of 182 enrolled participants. All participants completed the 3-month follow-up. The CONSORT-style participant flow is illustrated in Figure 1. Baseline demographic and clinical characteristics are presented in Table 1; no significant between-group differences were observed for age, sex, or initial clinical parameters (all $p>0.05$).

Figure 1. Study Design and Patient Flow Diagram

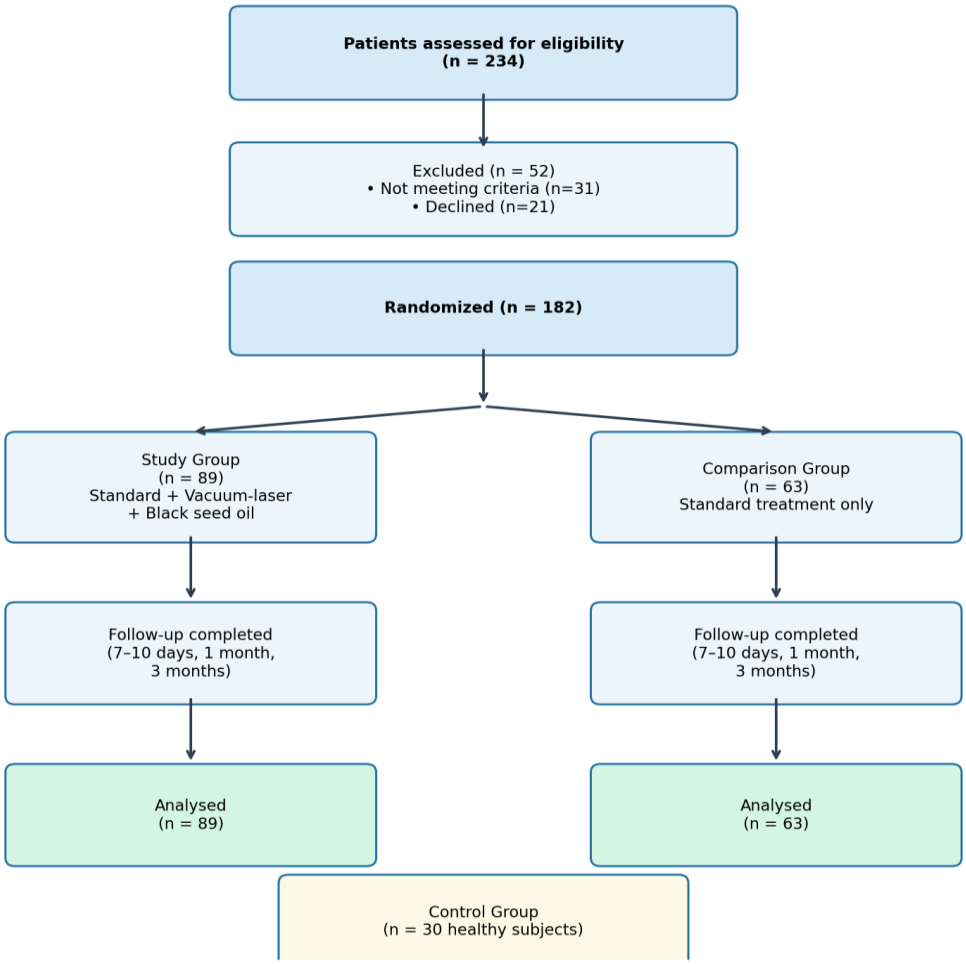

Figure 1. Study Design and Patient Flow Diagram.

Table 1. Baseline Demographic and Clinical Characteristics by Group

Characteristic	Study Group (n=89)	Comparison Group (n=63)	Control Group (n=30)
Age (years), mean ± SD	48.6 ± 13.2	47.4 ± 14.1	42.8 ± 11.7
Sex, male/female	46/43	33/30	16/14
GBI (%), mean ± SD	68.4 ± 12.3	64.2 ± 11.8	8.3 ± 2.1
PPD (mm), mean ± SD	4.82 ± 1.04	4.71 ± 0.98	1.94 ± 0.31
CAL (mm), mean ± SD	4.35 ± 0.96	4.29 ± 1.01	N/A
OHI-S, mean ± SD	2.84 ± 0.61	2.79 ± 0.58	0.82 ± 0.22
PI (%), mean ± SD	72.3 ± 14.6	70.8 ± 13.9	9.4 ± 2.6
IL-1β (pg/mL)	142.3 ± 28.4	138.6 ± 26.9	18.4 ± 4.2

TNF-α (pg/mL)	89.2 ± 18.6	86.8 ± 17.3	11.3 ± 3.1
Salivary sIgA (mg/dL)	12.4 ± 3.8	13.1 ± 4.1	28.6 ± 5.3
Duration of GIT pathology (years)	6.4 ± 3.2	N/A	N/A

GBI: Gingival Bleeding Index; PPD: Periodontal Pocket Depth; CAL: Clinical Attachment Level; OHI-S: Oral Hygiene Index-Simplified; PI: Plaque Index; sIgA: secretory Immunoglobulin A; N/A: not applicable.

4.2 Distribution of GIT Diagnoses and Periodontitis Severity

The study group comprised 89 patients with the following GIT diagnoses: chronic gastritis (n=62; hyperacid form 41.6%, hypoacid form 18.0%, normoacid form 10.1%), peptic ulcer disease (n=9; 10.1%), and colitis/enterocolitis (n=18; 20.2%). The distribution of periodontitis severity stratified by GIT diagnosis is presented in Table 2. Patients with hypoacid gastritis and peptic ulcer disease demonstrated the highest proportion of severe periodontitis (50–55% and 55.5%, respectively), consistent with the hypothesis that more pronounced GIT inflammatory burden correlates with more severe periodontal disease.

Table 2. Distribution of GIT Diagnoses and Periodontal Severity in Study Group (n=89)

GIT Diagnosis (Study Group)	Periodontitis Grade	Mild (%)	Moderate (%)	Severe (%)
Chronic gastritis – hyperacid form (n=37, 41.6%)		15–20	50–60	20–25
Chronic gastritis – hypoacid form (n=16, 18.0%)		10	35–40	50–55
Chronic gastritis – normoacid form (n=9, 10.1%)		35–45	40–45	10–15
Peptic ulcer disease (n=9, 10.1%)		11.1	33.3	55.5
Colitis/enterocolitis (n=18, 20.2%)		15–20	45–50	30–35

† Mild: localized, ≤2 mm CAL loss; Moderate: CAL 3–4 mm; Severe: CAL ≥5 mm, per 2017 Classification.

4.3 Correlation Between GIT Disease Severity and Periodontal Parameters

Significant positive correlations were established between GIT disease severity (graded by gastroenterological assessment using established severity scales) and key periodontal indices. GIT severity correlated with PPD ($r=0.64$, $p<0.001$), CAL ($r=0.61$, $p<0.001$), GBI ($r=0.57$, $p<0.001$), and IL-1β levels ($r=0.69$, $p<0.001$). The duration of GIT pathology (years) was positively correlated with periodontal pocket depth ($r=0.48$, $p=0.003$) and CAL ($r=0.45$, $p=0.006$), suggesting a cumulative inflammatory burden effect. H. pylori positivity in subgingival plaque was associated with significantly higher IL-1β levels ($p=0.004$) and greater PPD ($p=0.007$) compared to H. pylori-negative periodontitis patients.

4.4 Clinical Outcomes at 3-Month Follow-up

Primary clinical outcomes at baseline and 3 months are presented in Table 3 and Figure 2. The integrated treatment protocol in the study group produced significantly superior improvements across all measured clinical indices compared to standard treatment in the comparison group (all $p<0.001$). GBI was reduced by 72.8% (from 68.4±12.3% to 18.6±6.4%) in the study group versus 40.2% reduction (64.2±11.8% to 38.4±9.2%) in the comparison group. PPD decreased by a mean of 2.41 mm in the study group compared to 1.33 mm in the comparison group. Significant improvements were observed from as early as the 7–10 day assessment for GBI and BOP in the study group.

Figure 2. Changes in Key Periodontal Clinical Indices at Baseline and 3-Month Follow-up

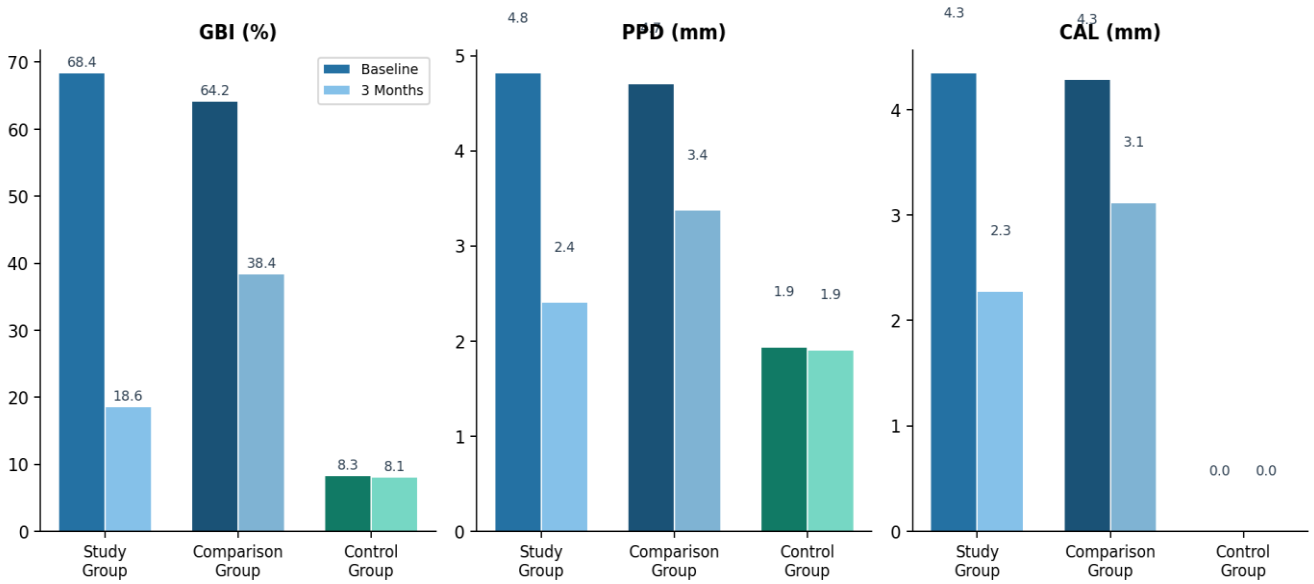

Figure 2. Changes in Key Periodontal Clinical Indices (GBI, PPD, CAL) at Baseline and 3-Month Follow-up by Group. *** p<0.001 between Study and Comparison groups (ANCOVA).

Table 3. Primary Clinical Periodontal Outcomes at Baseline and 3 Months

Parameter	Study Baseline	Study 3 mo	Comparison Baseline	Comparison 3 mo	p (between)
GBI (%)	68.4±12.3	18.6±6.4†	64.2±11.8	38.4±9.2†	<0.001
PPD (mm)	4.82±1.04	2.41±0.62†	4.71±0.98	3.38±0.78†	<0.001
CAL (mm)	4.35±0.96	2.28±0.58†	4.29±1.01	3.12±0.84†	<0.001
PI (%)	72.3±14.6	22.8±7.3†	70.8±13.9	41.2±10.4†	<0.001
OHI-S	2.84±0.61	0.94±0.28†	2.79±0.58	1.54±0.38†	<0.001
BOP (%)	76.4±13.2	20.3±7.1†	73.8±12.9	42.6±10.8†	<0.001

† p<0.05 vs. baseline within group (Wilcoxon signed-rank/paired t-test). GBI: Gingival Bleeding Index; PPD: Periodontal Pocket Depth; CAL: Clinical Attachment Level; PI: Plaque Index; OHI-S: Oral Hygiene Index Simplified; BOP: Bleeding on Probing.

4.5 Immunological and Biochemical Outcomes

Immunological outcomes are presented in Table 4 and Figure 3. In the study group, IL-1β decreased by 66.1% (from 142.3±28.4 to 48.2±11.6 pg/mL) compared to 39.2% in the comparison group (p<0.001). TNF-α showed a 64.7% reduction in the study group versus 31.6% in the comparison group (p<0.001). Salivary sIgA, which was markedly reduced at baseline relative to healthy controls (12.4±3.8 vs. 28.6±5.3 mg/dL), increased significantly with integrated treatment (to 23.8±5.4 mg/dL at 3 months), suggesting partial restoration of mucosal immune competence. The comparison group showed a smaller, though statistically significant, sIgA increase. Salivary biochemical parameters (total protein and α-amylase) demonstrated normalization in the study group consistent with reduced inflammatory burden.

Figure 3. Immunological Markers (IL-1β, TNF-α, Salivary IgA) at Baseline and 3-Month Follow-up

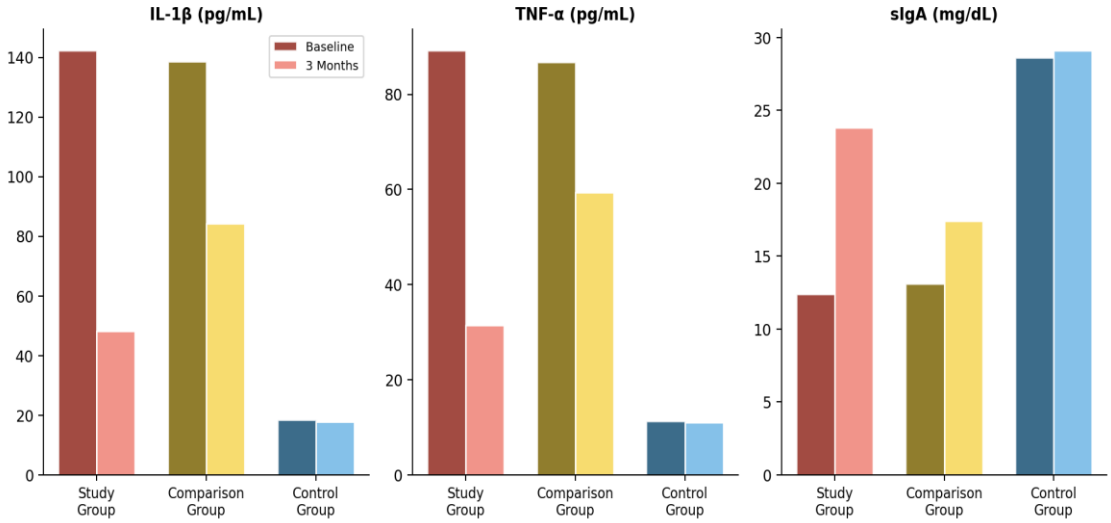

Figure 3. Changes in Immunological Markers (IL-1β, TNF-α, Salivary sIgA) at Baseline and 3-Month Follow-up.

Table 4. Immunological and Biochemical Outcomes at Baseline and 3 Months

Biomarker	Study Baseline	Study 3 mo	Comparison Baseline	Comparison 3 mo	p
IL-1β (pg/mL)	142.3±28.4	48.2±11.6†	138.6±26.9	84.3±18.7†	<0.001
TNF-α (pg/mL)	89.2±18.6	31.5±8.4†	86.8±17.3	59.4±13.2†	<0.001
IL-6 (pg/mL)	78.4±16.2	29.6±7.8†	76.2±15.8	52.3±12.1†	<0.001
Salivary sIgA (mg/dL)	12.4±3.8	23.8±5.4†	13.1±4.1	17.4±4.8†	<0.001
Total salivary protein (g/L)	2.18±0.42	2.64±0.38†	2.21±0.44	2.39±0.41	0.012
α-Amylase activity (U/mL)	184.6±36.2	142.3±28.4†	182.4±34.8	165.2±31.6†	0.028

† p<0.05 vs. baseline within group. sIgA: secretory Immunoglobulin A.

4.6 Microbiological Outcomes

PCR-based detection rates of periodontal pathogens at baseline and 3 months are presented in Figure 4. At baseline, the study group demonstrated slightly but not significantly higher detection rates for all pathogens compared to the comparison group, with H. pylori detected in subgingival plaque in 43.2% of study group patients versus 39.7% of comparison group patients. After 3 months of treatment, the study group showed significantly greater reductions in P. gingivalis (from 84.3% to 28.1%), T. forsythia (76.4% to 24.6%), and H. pylori detection rates (43.2% to 14.6%) compared to the comparison group. The integrated protocol's superior antimicrobial effect is consistent with both the bactericidal action of diode laser irradiation on Gram-negative anaerobes and the documented anti-H. pylori and anti-P. gingivalis activity of thymoquinone [18,19,33].

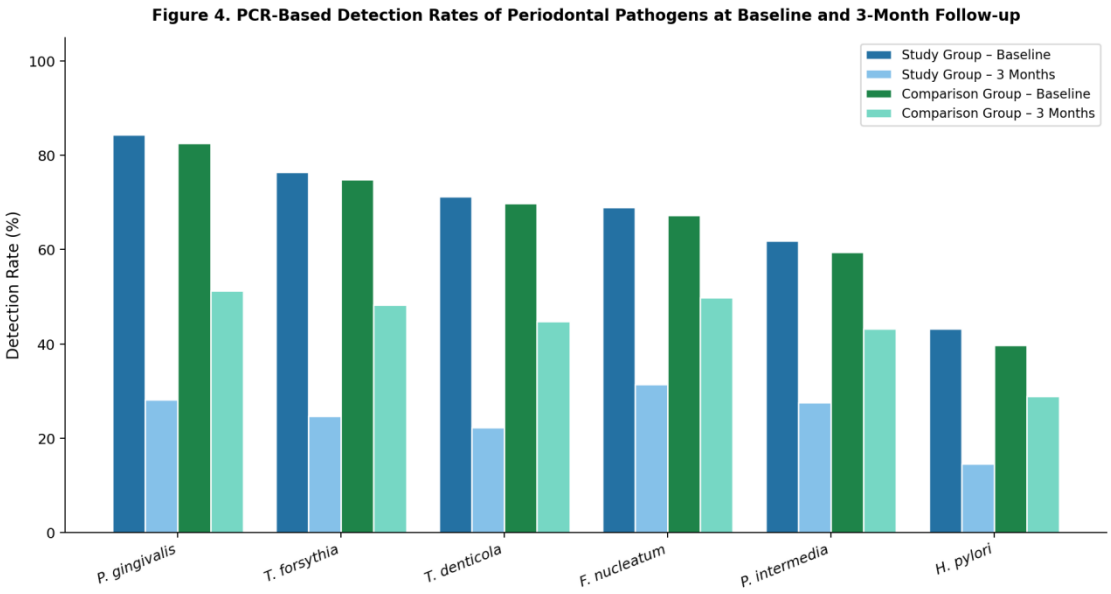

Figure 4. PCR-Based Detection Rates of Periodontal Pathogens (%) at Baseline and 3-Month Follow-up in Study and Comparison Groups.

4.7 Efficacy Stratified by GIT Diagnosis

The magnitude of periodontal improvement with integrated treatment varied by GIT diagnosis, as illustrated in Figure 5. The greatest PPD reduction was observed in patients with normoacid gastritis (55.1%) and hyperacid gastritis (52.3%), while peptic ulcer patients, who had the most severe baseline periodontitis, showed a 49.7% reduction—still substantially greater than the comparison group. This variation likely reflects differences in baseline immunological state, H. pylori burden, and GIT mucosal inflammatory activity across diagnostic subgroups.

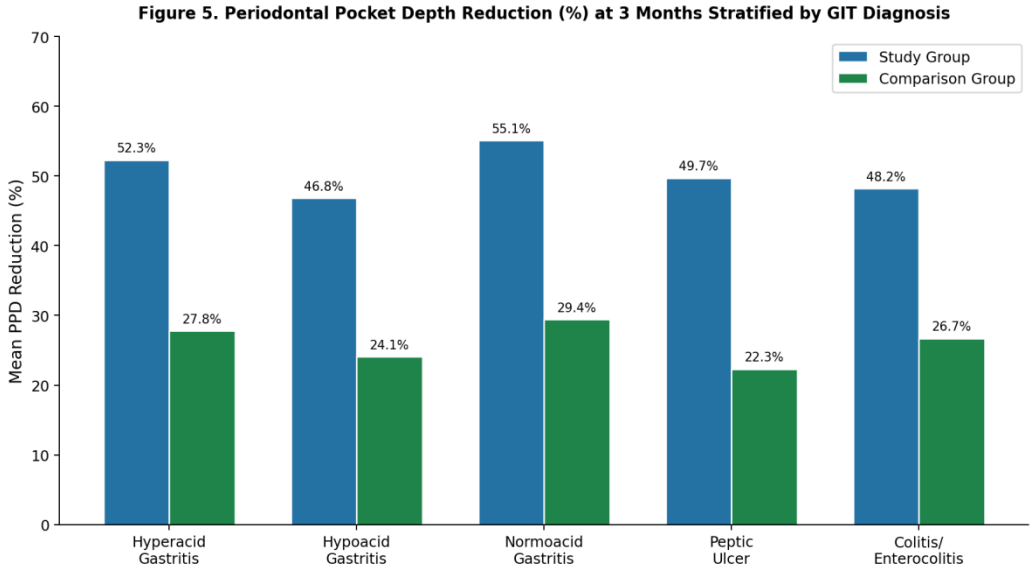

Figure 5. Percentage Reduction in Periodontal Pocket Depth at 3 Months Stratified by GIT Diagnosis in Study and Comparison Groups.

5. Discussion

The present study provides comprehensive prospective evidence for bidirectional pathogenetic linkage between inflammatory periodontal disease and GIT pathology, and demonstrates that an integrated treatment protocol combining vacuum-laser therapy and cold-pressed N. sativa oil with standard periodontal care produces clinically and statistically significant improvements across all measured parameters in this comorbid population.

The correlation observed between GIT disease severity and periodontal clinical indices (r=0.64 for PPD; r=0.61 for CAL) is consistent with and extends the mechanistic framework proposed by Xi et al. [6], who demonstrated that periodontal pathobionts influence systemic diseases through gut microbiota disruption, and with findings from Huang et al. [21] linking P. gingivalis to IBD aggravation through Th17/Treg imbalance. Our data suggest that the severity of GIT-mediated systemic inflammatory burden—as indexed by gastroenterological severity scores—translates into

clinically measurable differences in periodontal tissue destruction, emphasizing the clinical importance of integrated diagnostic assessment.

The immunological findings are particularly notable. The 66.1% reduction in IL-1β in the integrated treatment group substantially exceeds the 39.2% reduction achieved with standard periodontal therapy alone, and compares favorably with reductions reported for adjunctive laser therapy in the literature [29]. This magnitude of IL-1β reduction is clinically meaningful given that elevated systemic IL-1β impairs gastric mucosal healing and amplifies H. pylori-driven inflammation [12,13]. The progressive restoration of salivary sIgA in the integrated group suggests that combined mechanical debridement, photobiomodulation, and TQ-mediated immunomodulation may synergistically restore mucosal immune competence—a finding of particular relevance given the recognized role of deficient sIgA in oral dysbiosis and GIT susceptibility [26].

The substantially greater reduction in H. pylori detection in subgingival plaque (43.2% to 14.6% in the study group vs. 39.7% to 28.9% in the comparison group) is mechanistically consistent with the dual bactericidal activity of the integrated protocol. Diode laser irradiation has documented efficacy against H. pylori in vitro, and thymoquinone has demonstrated anti-H. pylori activity in both experimental and limited clinical contexts [18,31]. This finding has practical implications: failure to eradicate oral H. pylori reservoirs is recognized as a potential cause of gastric re-infection following antibiotic therapy, and periodontal treatment may thus represent an underappreciated component of H. pylori eradication management [8,12].

The differential response across GIT diagnostic subgroups, with hypoacid gastritis and peptic ulcer patients showing more severe baseline periodontitis, aligns with the mechanistic hypothesis that reduced gastric acid impairs the bactericidal barrier between the oral cavity and the intestinal tract, allowing more extensive oral-gut microbial dysregulation. This is supported by evidence that proton pump inhibitor use—which creates a hypoacid gastric environment—alters gut microbiome composition in ways analogous to GIT disease states [4].

The antimicrobial and anti-inflammatory synergy of the integrated protocol warrants mechanistic commentary. Vacuum-assisted laser delivery addresses the physical barriers to conventional SRP—particularly in deep pockets with complex root anatomy—by combining aspiration of biofilm fragments with photobiomodulation that penetrates pocket wall tissues and disrupts anaerobic bacterial membranes [16,17]. Cold-pressed N. sativa oil, standardized for thymoquinone content, provides broad-spectrum antimicrobial coverage including activity against P. gingivalis, T. forsythia, P. intermedia, and H. pylori, while its anti-inflammatory effects—mediated through NF-κB inhibition and prostaglandin synthesis suppression—address the cytokine amplification that standard mechanical debridement does not fully resolve [18,19,31].

Several limitations of this study warrant acknowledgment. The single-center design and patient cohort from one geographic region may limit generalizability. The absence of randomization due to patient preference for one treatment arm represents a potential selection bias; however, baseline characteristics were well-balanced. The 3-month observation period precludes assessment of long-term recurrence rates or impacts on GIT disease trajectory. Shotgun metagenomic sequencing, which would provide deeper characterization of microbial community changes than PCR-based pathogen detection, was not performed. Future multicenter randomized controlled trials with extended follow-up, metagenomic profiling, and gastroenterological co-primary endpoints are warranted to confirm and extend these findings.

6. Conclusion

This prospective controlled clinical study demonstrates that concurrent GIT pathology significantly modifies the clinical, immunological, and microbiological profile of inflammatory periodontal disease, with GIT disease severity strongly and independently correlated with periodontal tissue destruction and inflammatory marker elevation. An integrated treatment protocol combining vacuum-laser therapy and cold-pressed Nigella sativa oil as adjuncts to standard periodontal care produces significantly superior clinical, immunological, and microbiological outcomes in this comorbid population at 3 months, including greater reductions in gingival bleeding, pocket depth, clinical attachment loss, IL-1β, TNF-α, and key periodontal pathogens including subgingival H. pylori, compared to standard treatment alone.

These findings advocate for a paradigm shift toward integrated interdisciplinary management of periodontal-GIT comorbidity, incorporating pathogen-specific and immunomodulatory adjuncts alongside standard mechanical debridement. Validation in larger, multicenter, randomized controlled trials with extended follow-up and metagenomic characterization is required to establish definitive clinical guidelines.

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