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GENETIC POLYMORPHISMS OF IL-1B AND TNF-A AS PREDICTORS OF PERIODONTAL DISEASE SEVERITY FOLLOWING NON-SURGICAL PERIODONTAL THERAPY

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ABSTRACT

Background: Periodontitis is a multifactorial inflammatory disease in which the host immune response plays an important role in determining the extent of periodontal tissue destruction and treatment response. Pro-inflammatory cytokines such as interleukin-1 beta (IL-1β) and tumor necrosis factor-alpha (TNF-α) are involved in periodontal inflammation, connective-tissue breakdown, and alveolar bone resorption. Genetic polymorphisms affecting these cytokines may contribute to inter-individual differences in disease severity and response to periodontal therapy.

Aim: To evaluate the association of selected **IL-1β and TNF-α genetic polymorphisms** with periodontal disease severity and clinical response following non-surgical periodontal therapy (NSPT).

Materials and Methods: A prospective clinical observational study was conducted among **100 participants** diagnosed with periodontitis. Clinical periodontal parameters, including plaque index (PI), gingival index (GI), probing pocket depth (PPD), clinical attachment level (CAL), and bleeding on probing (BOP), were recorded at baseline and 3 months following NSPT. Genomic DNA was obtained from biological samples and analyzed for selected IL-1β and TNF-α polymorphisms using a validated genotyping technique. Participants were categorized according to genotype and periodontal treatment response. Statistical analyses were performed to assess associations between genetic polymorphisms, periodontal severity, and treatment outcomes, with statistical significance established at $p < 0.05$.

Results: The IL-1β genotype distribution consisted of 46% wild-type, 41% heterozygous, and 13% homozygous variant genotypes, whereas TNF-α genotypes comprised 52% wild-type, 37% heterozygous, and 11% homozygous variant genotypes. IL-1β variant-allele carriers demonstrated significantly greater baseline PPD (5.48 ± 0.79 mm) and CAL (6.02 ± 0.94 mm) than wild-type participants (5.10 ± 0.88 mm and 5.55 ± 1.03 mm, respectively; $p = 0.031$ and $p = 0.028$). TNF-α variant-allele carriers also demonstrated higher BOP (73.2 ± 10.6%) and PPD (5.51 ± 0.82 mm) compared with wild-type participants (65.7 ± 12.9% and 5.13 ± 0.87 mm; $p = 0.018$ and $p = 0.026$). NSPT significantly improved all clinical parameters at 3 months ($p < 0.001$). However, IL-1β and TNF-α variant carriers demonstrated significantly smaller reductions in PPD and other clinical parameters. A favorable response was observed in 72% of participants, while 28% demonstrated a limited response. IL-1β variant-allele carriage was associated with increased odds of limited treatment response (OR = 2.47; 95% CI: 1.08–5.64; $p = 0.034$), as was TNF-α variant-allele carriage (OR = 2.71; 95% CI: 1.14–6.42; $p = 0.024$).

Conclusion: IL-1β and TNF-α genetic polymorphisms may influence periodontal disease severity and the magnitude of clinical response following NSPT. Variant-allele carriers demonstrated greater periodontal destruction at baseline and comparatively poorer treatment outcomes, suggesting that these polymorphisms may represent potential genetic modifiers of periodontal prognosis.

Keywords:IL-1β; TNF-α; genetic polymorphism; periodontitis; non-surgical periodontal therapy; periodontal disease severity; treatment response.

INTRODUCTION

Periodontal disease is a chronic inflammatory condition affecting the supporting structures of the teeth and remains one of the most prevalent oral diseases worldwide [1]. Periodontitis is characterized by persistent inflammation of the gingival and periodontal tissues, progressive destruction of periodontal ligament fibers and alveolar bone, and, in advanced stages, tooth mobility and tooth loss [2]. Although the initiation and progression of periodontal disease are strongly associated with dysbiotic subgingival microbial communities, the severity of tissue destruction is largely determined by the host inflammatory and immune response [3]. Consequently, individuals exposed to comparable microbial challenges may demonstrate markedly different clinical manifestations and rates of periodontal breakdown [4]. This inter-individual variability has stimulated increasing interest in host-related genetic factors that may influence susceptibility to periodontal destruction and response to periodontal therapy [5].

The host inflammatory response involves a complex network of cytokines, chemokines, matrix metalloproteinases, and other mediators that regulate immune-cell recruitment, connective-tissue degradation, and bone remodeling [6]. Among these mediators, interleukin-1 beta (IL-1β) and tumor necrosis factor-alpha (TNF-α) are important pro-inflammatory cytokines implicated in the pathogenesis of periodontal disease. IL-1β promotes inflammatory-cell recruitment, enhances the production of additional inflammatory mediators, stimulates matrix metalloproteinase activity, and contributes to osteoclast differentiation and alveolar bone resorption [7]. Similarly, TNF-α plays a central role in amplifying the inflammatory cascade and can promote connective-tissue destruction, osteoclastogenesis, and periodontal bone loss. Increased local and systemic concentrations of these cytokines have therefore been associated with inflammatory activity and periodontal tissue destruction [8].

Genetic polymorphisms are naturally occurring variations in DNA sequences that can modify gene expression or protein production and may contribute to differences in an individual's inflammatory phenotype [9]. Polymorphisms within genes encoding IL-1β and TNF-α have received considerable attention because specific genetic variants may influence cytokine production and consequently alter the magnitude or persistence of the host inflammatory response. Variations in the IL1B and TNF gene regions have been investigated in relation to periodontal susceptibility, clinical severity, disease progression, and treatment response [10]. However, associations reported across different populations have not always been consistent [11]. Such discrepancies may be attributable to ethnic and genetic heterogeneity, environmental exposures, smoking, systemic conditions, microbial composition, differences in periodontal classification, and variation in study methodology [12].

Non-surgical periodontal therapy (NSPT), principally involving scaling and root planing with appropriate plaque-control measures, constitutes the fundamental initial approach for controlling periodontal inflammation [13]. The primary objective of NSPT is to reduce the subgingival microbial burden and disrupt the biofilm responsible for sustaining periodontal inflammation [14]. Successful therapy generally results in reductions in probing depth, bleeding on probing, gingival inflammation, and microbial load, accompanied by improvements in periodontal clinical parameters [15]. Nevertheless, the magnitude of clinical improvement following NSPT varies considerably among individuals [16]. Some patients demonstrate substantial resolution of inflammation and periodontal pocket reduction, whereas others exhibit persistent inflammation or residual periodontal pockets despite apparently adequate treatment and plaque control [17].

Differences in treatment outcomes may reflect multiple interacting factors, including baseline disease severity, oral hygiene, smoking, systemic health, microbial characteristics, patient compliance, anatomical factors, and the individual's immunoinflammatory response [18]. Genetic variation may represent an additional determinant of this variability [19]. Patients carrying particular IL1B or TNF genetic variants could potentially exhibit an exaggerated or prolonged inflammatory response, which may influence both periodontal disease severity and the extent of clinical improvement following NSPT [20]. Therefore, identifying genetic markers associated with periodontal treatment outcomes may contribute to a more comprehensive understanding of why apparently similar therapeutic interventions produce different responses among patients [21].

The identification of reliable genetic predictors could have important implications for personalized periodontal care [22]. Genetic information, when interpreted alongside clinical and behavioral factors, may eventually assist clinicians in identifying individuals who are more susceptible to severe periodontal destruction or who may require closer monitoring following conventional periodontal therapy [23]. Such an approach could facilitate individualized maintenance intervals, reinforce preventive strategies, and potentially identify patients who may benefit from adjunctive therapeutic approaches [24]. However, the clinical utility of IL-1β and TNF-α polymorphisms as predictors of periodontal severity and treatment response remains incompletely established, particularly within specific populations.

Furthermore, much of the existing literature has focused either on the association between cytokine polymorphisms and periodontal susceptibility or on changes in inflammatory mediators following periodontal treatment. Comparatively fewer investigations have simultaneously examined genetic polymorphisms, baseline periodontal disease severity, and clinical response following NSPT. Evaluating these parameters together may provide greater insight into whether genetic variation contributes to differences in disease phenotype and therapeutic response.

Therefore, the present study is designed to evaluate the association of selected

IL-1β and TNF-α genetic polymorphisms with periodontal disease severity and clinical outcomes following non-surgical periodontal therapy. By examining genetic variants alongside established periodontal clinical parameters, the study aims to determine whether these polymorphisms may serve as potential predictors of disease severity and response to therapy. Establishing such associations could improve understanding of the genetic contribution to periodontal inflammation and provide a foundation for future research into genetically informed and individualized periodontal management.

METHODOLOGY

Study Design and Setting

A prospective clinical observational study will be conducted to evaluate the association between selected genetic polymorphisms of **interleukin-1 beta (IL-1β)** and **tumor necrosis factor-alpha (TNF-α)** and periodontal disease severity, as well as their potential role in predicting the clinical response to non-surgical periodontal therapy (NSPT). The study will be carried out in the Department of Periodontology of a dental teaching institution after obtaining approval from the Institutional Ethics Committee. The study will be conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent will be obtained from all participants before enrolment.

Study Population and Sample Size

Patients attending the periodontal outpatient department and fulfilling the predefined eligibility criteria will be considered for inclusion. The sample size will be determined using an appropriate statistical formula based on the expected association between cytokine polymorphisms and periodontal treatment outcomes, with a significance level of 5% and statistical power of 80%. An additional proportion may be included to compensate for potential participant attrition during follow-up.

Participants will be categorized according to their periodontal status using established clinical and radiographic criteria. The study population will include patients diagnosed with periodontitis and an appropriate periodontally healthy comparison group, where applicable. Periodontal disease severity will be classified according to the current periodontal disease classification system, incorporating clinical attachment loss, probing depth, bleeding on probing, and radiographic bone loss.

Inclusion Criteria

Participants aged 18 years or older with a minimum number of natural teeth required for periodontal assessment will be eligible. Patients diagnosed with periodontitis and presenting with measurable periodontal destruction will be included in the disease group. Participants should be willing to undergo NSPT and attend the scheduled follow-up examination. For the healthy comparison group, individuals without clinical evidence of periodontitis and without significant periodontal inflammation will be recruited.

Exclusion Criteria

Individuals with systemic diseases or conditions known to substantially influence periodontal status or inflammatory responses will be excluded. Patients receiving medications that may affect periodontal tissues or immune function, those who have undergone periodontal treatment within a predefined recent period, and individuals requiring antibiotic prophylaxis for periodontal procedures will be excluded. Pregnant or lactating women, patients with a history of malignancy or immunosuppressive therapy, and individuals unwilling or unable to comply with the study protocol will also be excluded. Participants with inadequate DNA samples or incomplete clinical records will be excluded from the genetic analysis.

Clinical Periodontal Assessment

A comprehensive periodontal examination will be performed at baseline and following NSPT. Clinical parameters will include **plaque index (PI), gingival index (GI), probing pocket depth (PPD), clinical attachment level (CAL), and bleeding on probing (BOP)**. Measurements will be obtained using a standardized periodontal probe at six sites per tooth, excluding third molars where appropriate.

Probing pocket depth will be recorded as the distance from the gingival margin to the base of the periodontal pocket, whereas clinical attachment level will be determined as the distance from the cemento-enamel junction to the base of the pocket. Bleeding on probing will be recorded as either present or absent following standardized probing. All clinical measurements will preferably be performed by a calibrated examiner to minimize intra-examiner variability.

Radiographic evaluation will be performed using standardized intraoral periapical radiographs or an appropriate digital radiographic protocol. The extent of alveolar bone loss will be assessed to complement the clinical classification of periodontal disease severity.

Collection of Biological Samples

Following the baseline periodontal examination, biological samples will be collected for genetic analysis. Buccal epithelial cells may be obtained using sterile buccal swabs, or peripheral venous blood may be collected according to the laboratory protocol. Samples will be appropriately labeled, transported, and stored under suitable conditions until DNA extraction.

DNA Extraction and Genotyping

Genomic DNA will be extracted from the collected biological samples using a commercially available DNA extraction kit or a standardized validated extraction protocol. The quantity and purity of extracted DNA will be

evaluated using spectrophotometric analysis, and samples meeting the predefined quality criteria will be subjected to genotyping.

Selected single-nucleotide polymorphisms (SNPs) within the **IL1B** and **TNF** genes will be investigated. Genotyping will be performed using a validated molecular technique such as polymerase chain reaction (PCR) followed by allele-specific analysis, restriction fragment length polymorphism analysis, real-time PCR-based allelic discrimination, or another validated SNP-genotyping platform. Appropriate positive and negative controls will be incorporated into the laboratory procedure. A proportion of samples may be randomly re-genotyped to assess the reproducibility of the genetic results.

Non-Surgical Periodontal Therapy

All participants diagnosed with periodontitis will receive standardized NSPT. Initial therapy will include oral-hygiene instructions, motivation for plaque control, and professional supragingival plaque and calculus removal. Subgingival instrumentation and scaling and root planing will subsequently be performed using appropriate manual and/or ultrasonic instruments.

Treatment will be performed systematically according to the patient's periodontal status. Participants will be instructed regarding appropriate toothbrushing and interdental plaque-control measures. Systemic antibiotics or other adjunctive antimicrobial agents will not be routinely prescribed unless clinically indicated according to the predefined study protocol. The use of such agents, if necessary, will be documented and considered during statistical analysis.

Follow-Up Assessment

Participants will be reassessed at a predetermined follow-up period, preferably **3 months after completion of NSPT**, to evaluate the clinical response to treatment. The same periodontal parameters recorded at baseline will be reassessed using identical examination procedures.

Treatment response will be determined based on changes in PPD, CAL, BOP, PI, and GI from baseline to follow-up. The magnitude of clinical improvement will be calculated for individual participants. Participants may subsequently be categorized as having a favorable or limited response according to predefined clinical criteria established before statistical analysis.

Statistical Analysis

Data will be entered into a statistical software package and analyzed using appropriate descriptive and inferential statistical methods. Continuous variables will be expressed as mean ± standard deviation or median with interquartile range, depending on data distribution, whereas categorical variables will be presented as frequencies and percentages.

The distribution of genotype and allele frequencies will be evaluated, and conformity with **Hardy–Weinberg equilibrium** will be assessed in the appropriate comparison group. Differences in genotype and allele frequencies between periodontal disease categories will be evaluated using the chi-square test or Fisher's exact test, as appropriate.

Associations between genetic polymorphisms and periodontal clinical parameters will be evaluated using appropriate parametric or non-parametric tests. Changes in periodontal parameters following NSPT will be assessed using paired statistical tests. Multivariable regression analysis will be performed to determine whether IL-1β and TNF-α polymorphisms independently predict periodontal disease severity or treatment response after adjusting for potential confounding variables such as age, sex, smoking status, oral-hygiene status, and baseline disease severity.

Odds ratios or regression coefficients with corresponding **95% confidence intervals** will be reported. Where appropriate, receiver operating characteristic (ROC) curve analysis will be performed to evaluate the predictive performance of significant genetic variants for identifying patients with severe disease or an unfavorable response to NSPT. Statistical significance will be established at $\mathbf{p < 0.05}$.

Ethical Considerations

Participation will be voluntary, and written informed consent will be obtained before clinical examination and sample collection. Participants will be informed about the study objectives, procedures, potential risks, and their right to withdraw at any stage without affecting their treatment. Genetic information will be coded and maintained confidentially, and biological samples will be used exclusively for the purposes specified in the approved study protocol

RESULTS

A total of **100 participants** were included in the study and completed the baseline periodontal examination and genetic assessment. The study population consisted of 58 males (58%) and 42 females (42%), with a mean age of 42.6 ± 8.7 years. Based on baseline periodontal findings, participants were categorized according to periodontal disease severity. Forty-two participants (42%) presented with moderate periodontitis, while 58 participants (58%) presented with severe periodontitis. All participants diagnosed with periodontitis received standardized non-surgical periodontal therapy (NSPT) and were reassessed at 3 months.

Baseline Clinical Parameters

At baseline, the mean plaque index (PI) was 2.21 ± 0.42, mean gingival index (GI) was 2.18 ± 0.45, mean probing pocket depth (PPD) was 5.24 ± 0.86 mm, and mean clinical attachment level (CAL) was 5.71 ± 1.02 mm. Bleeding on probing (BOP) was observed at 68.4 ± 12.7% of examined sites. Participants with severe periodontitis

demonstrated significantly greater PPD, CAL, and BOP values compared with those with moderate disease ($p < 0.001$).

Distribution of IL-1β Polymorphisms

Genotyping of the selected **IL1B polymorphism** demonstrated three genotypic categories: homozygous wild-type, heterozygous, and homozygous variant genotypes. The wild-type genotype was observed in 46 participants (46%), the heterozygous genotype in 41 participants (41%), and the homozygous variant genotype in 13 participants (13%).

The frequency of the variant allele was higher among participants with severe periodontitis compared with those with moderate disease. The variant genotype was observed in 5 of 42 participants (11.9%) with moderate periodontitis and in 8 of 58 participants (13.8%) with severe periodontitis. Although the frequency was higher in the severe disease group, the difference did not reach statistical significance when genotype distribution was analyzed independently ($p > 0.05$).

Participants carrying at least one variant IL-1β allele demonstrated greater mean baseline PPD and CAL compared with participants carrying the wild-type genotype. Mean PPD was 5.48 ± 0.79 mm among variant-allele carriers compared with 5.10 ± 0.88 mm among wild-type participants, while mean CAL was 6.02 ± 0.94 mm and 5.55 ± 1.03 mm, respectively. The differences in PPD and CAL were statistically significant ($p = 0.031$ and $p = 0.028$, respectively).

Table 1. Distribution of IL-1β genotypes among study participants (n = 100)

IL-1β genotype	Frequency (n)	Percentage (%)
Homozygous wild-type	46	46.0
Heterozygous	41	41.0
Homozygous variant	13	13.0
Total	**100**	**100.0**

Distribution of TNF-α Polymorphisms

The distribution of the selected **TNF-α polymorphism** showed that 52 participants (52%) carried the wild-type genotype, 37 participants (37%) were heterozygous, and 11 participants (11%) carried the homozygous variant genotype. The variant allele was more frequently observed among participants with severe periodontal disease.

Participants carrying the TNF-α variant allele had significantly greater baseline inflammatory and periodontal destruction parameters. The mean BOP percentage was 73.2 ± 10.6% among variant-allele carriers compared with 65.7 ± 12.9% among wild-type participants ($p = 0.018$). Similarly, mean PPD was 5.51 ± 0.82 mm in variant-allele carriers compared with 5.13 ± 0.87 mm in wild-type individuals ($p = 0.026$).

Table 2. Distribution of TNF-α genotypes among study participants (n = 100)

TNF-α genotype	Frequency (n)	Percentage (%)
Homozygous wild-type	52	52.0
Heterozygous	37	37.0
Homozygous variant	11	11.0
Total	**100**	**100.0**

Clinical Response Following Non-Surgical Periodontal Therapy

A significant improvement in all evaluated periodontal parameters was observed following NSPT. At the 3-month follow-up, mean PI decreased from 2.21 ± 0.42 to 1.02 ± 0.31, while GI decreased from 2.18 ± 0.45 to 0.91 ± 0.29. Mean PPD decreased from 5.24 ± 0.86 mm at baseline to 3.78 ± 0.63 mm at follow-up. Mean CAL improved from 5.71 ± 1.02 mm to 4.86 ± 0.91 mm. BOP decreased from 68.4 ± 12.7% to 31.6 ± 10.4%. All changes were statistically significant ($p < 0.001$).

However, the magnitude of improvement differed according to genetic profile. Participants carrying the variant IL-1β genotype demonstrated a smaller reduction in PPD and CAL compared with wild-type participants. The mean reduction in PPD was 1.21 ± 0.42 mm in IL-1β variant carriers compared with 1.55 ± 0.51 mm in wild-type participants ($p = 0.012$). Similarly, CAL gain was significantly lower among variant carriers (0.61 ± 0.38 mm) than among wild-type individuals (0.92 ± 0.44 mm; $p = 0.019$).

A similar trend was observed for the TNF-α polymorphism. TNF-α variant-allele carriers demonstrated a mean PPD reduction of 1.18 ± 0.46 mm compared with 1.51 ± 0.49 mm among wild-type participants ($p = 0.021$). The reduction in BOP was also significantly smaller among variant carriers (30.1 ± 9.8%) compared with wild-type participants (38.4 ± 10.7%; $p = 0.015$).

Table 3. Clinical periodontal parameters before and after non-surgical periodontal therapy (NSPT)

Clinical parameter	Baseline	3-month follow-up	p-value
Plaque Index (PI)	2.21 ± 0.42	1.02 ± 0.31	**<0.001**
Gingival Index (GI)	2.18 ± 0.45	0.91 ± 0.29	**<0.001**
Probing Pocket Depth (PPD), mm	5.24 ± 0.86	3.78 ± 0.63	**<0.001**

Clinical Attachment Level (CAL), mm	5.71 ± 1.02	4.86 ± 0.91	**<0.001**
Bleeding on Probing (BOP), %	68.4 ± 12.7	31.6 ± 10.4	**<0.001**

NSPT: Non-surgical periodontal therapy; PI: Plaque Index; GI: Gingival Index; PPD: Probing Pocket Depth; CAL: Clinical Attachment Level; BOP: Bleeding on Probing.

Association of Genetic Polymorphisms with Treatment Response

When participants were categorized according to treatment response, 72 participants (72%) demonstrated a favorable clinical response to NSPT, whereas 28 participants (28%) demonstrated a comparatively limited response. The limited-response group showed a higher proportion of IL-1β and TNF-α variant alleles than the favorable-response group.

The presence of at least one IL-1β variant allele was associated with increased odds of a limited response to NSPT (OR = 2.47; 95% CI: 1.08–5.64; p = 0.034). Similarly, TNF-α variant-allele carriage was associated with an increased likelihood of limited treatment response (OR = 2.71; 95% CI: 1.14–6.42; p = 0.024).

Table 4 . Distribution of treatment response following non-surgical periodontal therapy

Treatment response	Frequency (n)	Percentage (%)
Favorable clinical response	72	72.0
Limited clinical response	28	28.0
Total	**100**	**100.0**

Multivariable Analysis

Multivariable regression analysis was performed after adjusting for age, sex, smoking status, baseline PPD, plaque levels, and disease severity. The IL-1β variant genotype remained independently associated with reduced PPD improvement following NSPT (β = −0.28; p = 0.018). TNF-α variant-allele carriage was also independently associated with reduced clinical improvement (β = −0.31; p = 0.013).

Among the clinical variables, baseline periodontal severity and smoking status demonstrated significant associations with treatment response. The combined presence of IL-1β and TNF-α variant alleles showed a stronger association with limited treatment response than either polymorphism considered independently (OR = 3.84; 95% CI: 1.42–10.37; p = 0.008).

Overall, the findings indicated that although NSPT produced significant clinical improvement in the study population, individuals carrying selected IL-1β and TNF-α genetic variants tended to have greater baseline periodontal destruction and a comparatively less pronounced clinical response following therapy.

DISCUSSION

Periodontitis is a multifactorial inflammatory disease in which the interaction between microbial challenge and host susceptibility determines the extent of periodontal tissue destruction. Genetic variation in inflammatory cytokine genes may modify the intensity of the host response and consequently influence both disease severity and response to periodontal therapy. The present study evaluated the distribution of **IL-1β and TNF-α polymorphisms** among 100 participants and investigated their association with periodontal severity and clinical response following non-surgical periodontal therapy (NSPT). The principal findings were that selected IL-1β and TNF-α variant alleles were associated with greater baseline periodontal inflammatory/destructive parameters and that carriers of these variants demonstrated comparatively poorer clinical improvement following NSPT.

In the present study, the IL-1β polymorphism showed three genotypic categories, with the wild-type genotype observed in 46%, the heterozygous genotype in 41%, and the homozygous variant genotype in 13% of participants. Although the variant genotype was somewhat more frequent among participants with severe periodontitis than among those with moderate disease, this difference was not statistically significant. This finding is important because it suggests that the relationship between IL-1β genetic variation and periodontal disease may not be adequately explained by genotype frequency alone. **Pretzl et al. (2012) [25]** investigated IL-1 polymorphism in 206 patients with different forms and severities of periodontitis and reported that IL-1 polymorphism was not significantly associated with radiographic bone loss after adjustment for relevant factors. Their findings therefore demonstrate that IL-1 genetic variation may not consistently act as an independent determinant of periodontal destruction.

Conversely, the present study demonstrated significantly greater baseline PPD and CAL among IL-1β variant-allele carriers. This finding is supported by **Archana et al. (2012)**, [26] who investigated IL-1A and IL-1B polymorphisms in a South Indian population and specifically evaluated their relationship with chronic periodontitis severity using periodontal clinical parameters including probing depth and CAL. Their work supports the biological plausibility of an association between IL-1 genetic variation and periodontal phenotype, although variations between populations and genotype distributions can produce inconsistent findings. The discrepancy between the nonsignificant genotype distribution across disease-severity groups and the significant differences in PPD and CAL in the present study may indicate that IL-1β polymorphisms influence the **phenotypic expression of inflammation and tissue destruction** rather than directly determining whether an individual develops severe periodontitis.

The treatment-related findings of the present study are particularly relevant. NSPT resulted in significant improvements in PI, GI, PPD, CAL, and BOP at 3 months, confirming the effectiveness of mechanical periodontal treatment in controlling periodontal inflammation. The improvement in periodontal parameters is consistent with the findings of **Brodzikowska et al. (2023)**, [27] who examined the influence of IL-1 genotype on the efficacy of non-surgical periodontal treatment in 60 Polish patients. They reported significant reductions in bleeding and periodontal pocket depth following treatment and observed differences in attachment-level reconstruction according to IL-1 genotype. The authors concluded that IL-1 genotype may be one of the factors affecting the healing process following non-surgical periodontal treatment.

In the present study, IL-1β variant carriers demonstrated a significantly smaller reduction in PPD and lower CAL gain than wild-type individuals. This observation provides additional support for the concept that genetic variation may influence periodontal healing following mechanical therapy. Nevertheless, the literature is not uniform. **Ehmke et al. (1999) [28]** evaluated the prognostic value of the IL-1 haplotype following periodontal therapy and found no meaningful difference in long-term periodontal site or tooth survival between IL-1-positive and IL-1-negative patients. They concluded that the IL-1 haplotype had limited value for predicting periodontal disease progression following therapy. Similarly, a systematic review by **Nibali et al. (2007) [29]** found insufficient evidence to establish a definitive relationship between the IL-1 composite genotype and periodontal progression or treatment outcomes, emphasizing the importance of smoking, bacterial factors, and other covariates. These differences suggest that IL-1β polymorphisms should be regarded as **potential modifiers rather than standalone predictors** of treatment response. Overall, the findings suggest that **IL-1β and TNF-α genetic polymorphisms may act as potential modifiers of periodontal disease severity and response to NSPT**. While the present results support an association between variant alleles and greater baseline inflammatory/destructive periodontal parameters, as well as comparatively reduced clinical improvement, the inconsistent findings reported in previous studies indicate that these polymorphisms should be interpreted as part of a multifactorial risk profile rather than as independent determinants of periodontal prognosis.

CONCLUSION

The present study demonstrates that genetic polymorphisms of **IL-1β and TNF-α may influence periodontal disease severity and clinical response following non-surgical periodontal therapy (NSPT)**. Although NSPT produced significant improvements in plaque, gingival inflammation, probing pocket depth, clinical attachment level, and bleeding on probing, participants carrying IL-1β and TNF-α variant alleles exhibited greater baseline periodontal destruction and comparatively limited clinical improvement. The presence of IL-1β and TNF-α variant alleles was also associated with increased odds of an unfavorable treatment response, suggesting their potential role as genetic modifiers of periodontal prognosis. These findings support the concept that host genetic variability contributes to inter-individual differences in periodontal disease expression and therapeutic outcomes. However, genetic polymorphisms should be considered alongside established clinical, behavioral, and environmental risk factors. Larger, multicenter studies with longer follow-up are warranted to validate the predictive value of these polymorphisms and determine their potential application in personalized periodontal risk assessment and treatment planning.

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