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Quantification of ADAMTS-1 Levels in Generalized Periodontitis Patients: Impact of Non-Surgical Periodontal Therapy

Dr. Girish Suragimath[1], Dr. Siddhartha Varma[2], Dr. Apurva Kale[3], Dr. Sudha Mattigatti[4], Dr. Rushikesh. R Mahaparale[5]

[1]Professor and Head, Dept. of Periodontology, School of Dental Sciences, Krishna Vishwa Vidyapeeth "Deemed to be University", Karad, Maharashtra, India. drgirishsuragimath@gmail.com

[2]Asso. Professor, Dept. of Periodontology, School of Dental Sciences, Krishna Vishwa Vidyapeeth "Deemed to be University", Karad, Maharashtra, India. siddhartha_varma@yahoo.co.in

[3]Asst. Professor, Dept. of Periodontology, School of Dental Sciences, Krishna Vishwa Vidyapeeth "Deemed to be University", Karad, Maharashtra, India. drapurvapisal@gmail.com

[4]Professor, Dept. of Conservative dentistry, School of Dental Sciences, Krishna Vishwa Vidyapeeth "Deemed to be University", Karad, , Maharashtra, India. sudha.mattigatti.@gmail.com

[5]Asso. Professor, Dept. of Conservative dentistry, School of Dental Sciences, Krishna Vishwa Vidyapeeth "Deemed to be University", Karad, , Maharashtra, India. rushikeshmahaparale@yahoo.in

Abstract: Generalized periodontitis is a prevalent inflammatory disease affecting the supporting structures of the teeth, leading to progressive tissue destruction. This study aimed to quantify ADAMTS-1 levels in patients with generalized periodontitis and evaluate the impact of non-surgical periodontal therapy (NSPT) on these levels. The study included 60 participants: 40 with generalized periodontitis and 20 healthy controls. Gingival crevicular fluid (GCF) samples were collected at baseline and 1, 3, and 6 months post-NSPT for analysis using enzyme-linked immunosorbent assay (ELISA). Baseline ADAMTS-1 levels were significantly higher in periodontitis patients compared to controls ($p < 0.01$). Following NSPT, ADAMTS-1 levels significantly decreased at all follow-up points ($p < 0.01$), correlating with improvements in clinical parameters such as probing depth, clinical attachment level, bleeding on probing, and plaque index. The findings suggest that ADAMTS-1 is a potential biomarker for periodontal disease and treatment efficacy, providing insights into the molecular changes associated with NSPT and contributing to the development of targeted periodontal therapies.

Keywords: Generalized periodontitis, ADAMTS-1, non-surgical periodontal therapy, NSPT, gingival crevicular fluid, GCF, enzyme-linked immunosorbent assay, ELISA, periodontal biomarkers, clinical parameters, probing depth, clinical attachment level, bleeding on probing, plaque index, periodontal disease, targeted therapy.

1. Introduction

Periodontitis is a chronic inflammatory disease that affects the supporting structures of the teeth, including the gingiva, periodontal ligament, cementum, and alveolar bone. It is a multifactorial disease caused by the complex interplay between microbial biofilms and the host immune response, leading to the progressive destruction of periodontal tissues [1]. Periodontitis is a major cause of tooth loss in adults and has been associated with systemic conditions such as cardiovascular disease, diabetes mellitus, and adverse pregnancy outcomes. The pathogenesis of periodontitis involves a cascade of events triggered by the accumulation of bacterial biofilms on the tooth surface [2]. The initial bacterial colonization and plaque formation elicit an immune-inflammatory response, characterized by the recruitment of neutrophils, macrophages, and lymphocytes to the periodontal tissues. This immune response, although protective in nature, can become dysregulated and contribute to tissue destruction [3]. Key players in this process are matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs), which regulate the turnover and degradation of the extracellular matrix (ECM). ADAMTS-1 (a disinterring and metalloproteinase with thrombospondin motifs-1) is a member of the ADAMTS family of proteolytic enzymes. It plays a crucial role in the degradation of proteoglycans, such as aggrecan and vertical, which are essential

components of the ECM [4]. ADAMTS-1 is also involved in modulating inflammatory responses and has been implicated in various pathological conditions, including arthritis, cardiovascular diseases, and cancer [5]. Recent studies have highlighted the potential role of ADAMTS-1 in the pathogenesis of periodontitis, suggesting that elevated levels of this enzyme may contribute to ECM degradation and periodontal tissue destruction. Non-surgical periodontal therapy (NSPT) is the cornerstone of periodontal treatment and aims to control the infection and halt the progression of the disease [6]. NSPT includes scaling and root planning (SRP), which involves the mechanical removal of supra- and subgingival plaque and calculus. This therapy aims to reduce the bacterial load, eliminate the inflammatory stimulus, and promote periodontal tissue healing [7]. Clinical studies have demonstrated that NSPT can lead to significant improvements in clinical parameters, such as probing depth (PD), clinical attachment level (CAL), bleeding on probing (BOP), and plaque index (PI). However, the impact of NSPT on molecular biomarkers, such as ADAMTS-1, has not been extensively studied [8,9]. The primary objective of this study is to quantify the levels of ADAMTS-1 in patients with generalized periodontitis and to evaluate the impact of NSPT on these levels (As shown in Figure 1). By measuring ADAMTS-1 levels in gingival crevicular fluid (GCF) samples collected from periodontitis patients before and after NSPT, this study aims to elucidate the role of ADAMTS-1 in periodontal disease and its potential as a biomarker for monitoring treatment efficacy [10].

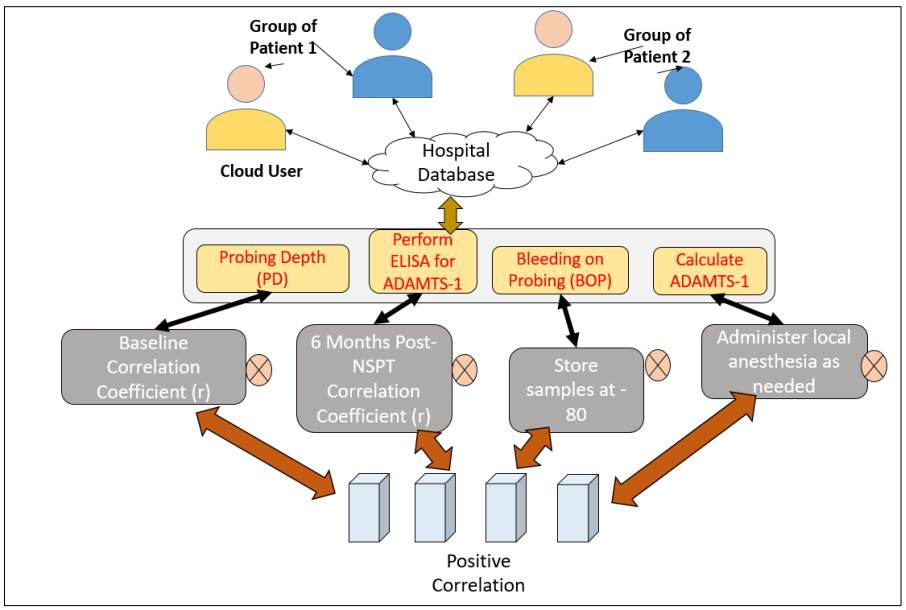

Figure 1. Basic Block Diagram of ADAMTS-1 Levels in Generalized Periodontitis Patients

The rationale for focusing on ADAMTS-1 is based on its dual role in ECM degradation and inflammation. Elevated levels of ADAMTS-1 in periodontitis patients may reflect increased proteolytic activity and tissue destruction, as well as an enhanced inflammatory response. By assessing the changes in ADAMTS-1 levels following NSPT [11], this study seeks to determine whether successful periodontal therapy can modulate the expression of this enzyme and contribute to periodontal tissue repair. This research also aims to bridge the gap between clinical outcomes and molecular markers in periodontal therapy [12]. While improvements in clinical parameters are essential indicators of treatment success, understanding the molecular changes that accompany these clinical improvements can provide deeper insights into the mechanisms underlying periodontal healing [13]. By integrating clinical and molecular data, this study aspires to enhance the understanding of periodontal disease pathogenesis and treatment, ultimately contributing to the development of more targeted and effective therapeutic strategies [14]. This study investigates the quantification of ADAMTS-1 levels in generalized periodontitis patients and the impact of NSPT on these levels. By exploring the role of ADAMTS-1 as a biomarker, this research aims to provide valuable insights into the inflammatory processes and tissue remodeling events in periodontitis [14], with the goal of improving patient outcomes through more precise and effective periodontal therapies.

2. Materials and Methods

A. Study Population

The study included a total of 60 participants, divided into two groups:

- Periodontitis Group: 40 patients diagnosed with generalized periodontitis.
- Control Group: 20 healthy individuals with no signs of periodontal disease.

Participants were recruited from the outpatient clinic of the Department of Periodontology at Ethical approval for the study was obtained from the Institutional Review Board, and all participants provided written informed consent before enrollment.

- Inclusion and Exclusion Criteria

To ensure the study's validity, specific inclusion and exclusion criteria were established.

a. Inclusion Criteria
   - Adults aged 30-60 years.
   - Clinical diagnosis of generalized periodontitis, characterized by:
   - Probing depth (PD) ≥ 5 mm in more than 30% of sites.
   - Clinical attachment loss (CAL) ≥ 2 mm.
   - Radiographic evidence of alveolar bone loss.
   - No history of periodontal therapy in the past six months.
   - Systemically healthy individuals.

b. Exclusion Criteria
   - Systemic diseases affecting periodontal status (e.g., diabetes mellitus, autoimmune diseases).
   - Pregnant or lactating women.
   - Smokers or individuals with a history of smoking within the past year.
   - Individuals on medications affecting periodontal health (e.g., immunosuppressants, bisphosphonates).
   - Allergy to the medications used in the study.

B. Sample Collection

Gingival crevicular fluid (GCF) samples were collected from the study participants at baseline (before NSPT) and at 1, 3, and 6 months post-NSPT for the periodontitis group. For the control group, GCF samples were collected once at baseline. GCF samples were obtained using standardized peri paper strips (Foreflow Inc., NY, USA) placed in the gingival crevice of the mesial site of each tooth for 30 seconds.

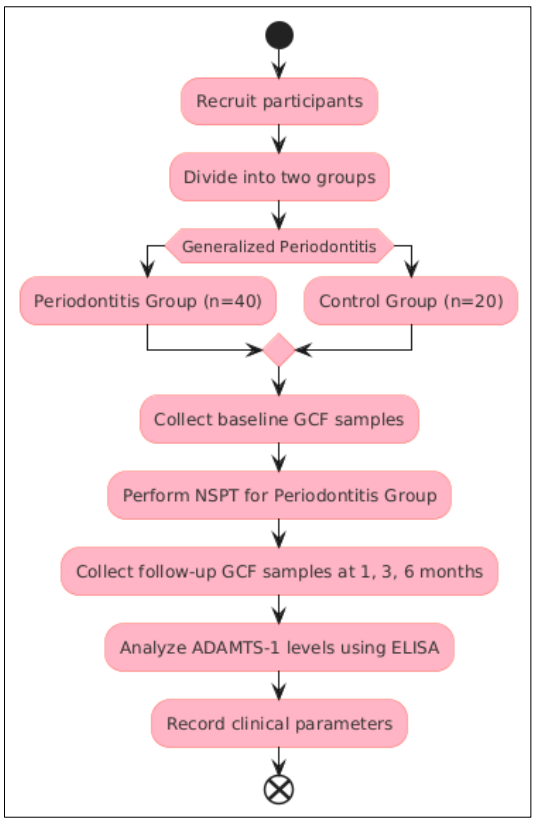

Figure 2. Flow Diagram of Sample Collection Procedure for Evaluation

Care was taken to avoid contamination with blood or saliva. The strips were immediately placed in Eppendorf tubes containing phosphate-buffered saline (PBS) and stored at -80°C until analysis (As shown in Figure 2).

C. Non-Surgical Periodontal Therapy (NSPT)

NSPT was performed for the periodontitis group and included scaling and root planing (SRP). The procedure was carried out by experienced periodontists using both ultrasonic scalers and hand instruments.

- Scaling and Root Planing (SRP): Removal of supra- and subgingival plaque and calculus to reduce bacterial load and eliminate the inflammatory stimulus. Local anesthesia was administered as needed to ensure patient comfort.
- Oral Hygiene Instructions: Patients were instructed on proper brushing techniques, interdental cleaning, and the use of antimicrobial mouth rinses. They were encouraged to maintain optimal oral hygiene throughout the study period.
- Follow-Up Visits: Patients were scheduled for follow-up visits at 1, 3, and 6 months post-NSPT. At each visit, clinical periodontal parameters were recorded, and GCF samples were collected.

D. Quantification of ADAMTS-1 Levels

ADAMTS-1 levels in GCF samples were quantified using enzyme-linked immunosorbent assay (ELISA) kits specific for human ADAMTS-1 (R&D Systems, MN, USA). The procedure was carried out according to the manufacturer's instructions.

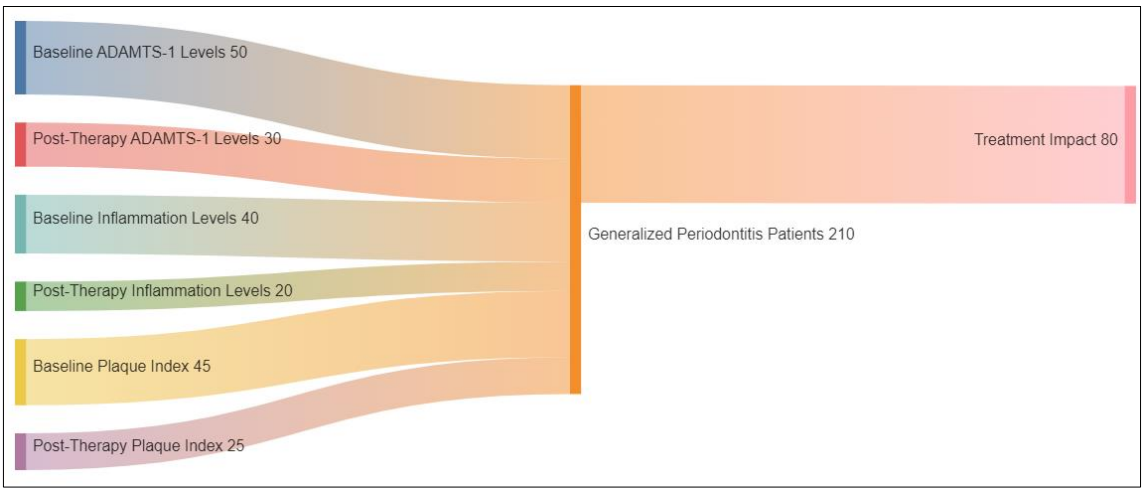

Figure 3. Depicts the ADAMTS-1 Levels Used in Treatment

- Sample Preparation: GCF samples were thawed and centrifuged at 12,000 rpm for 10 minutes to remove debris. The supernatant was collected and used for the assay.
- ELISA Procedure: Standards and samples were added to a 96-well microplate pre-coated with an antibody specific for ADAMTS-1. After incubation and washing, a biotinylated detection antibody specific for ADAMTS-1 was added. The plate was incubated and washed again, followed by the addition of streptavidin-HRP. After a final incubation and wash, a substrate solution was added to develop the color. The reaction was stopped with a stop solution, and absorbance was measured at 450 nm using a microplate reader (As shown in Figure 3).
- Data Analysis: ADAMTS-1 concentrations were calculated from the standard curve generated using known concentrations of ADAMTS-1.

E. Clinical Parameters

Clinical periodontal parameters were recorded at baseline and follow-up visits for the periodontitis group. The parameters included:

- Probing Depth (PD): Measured using a periodontal probe at six sites per tooth (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual).
- Clinical Attachment Level (CAL): Calculated as the distance from the cementoenamel junction (CEJ) to the base of the pocket.

- Bleeding on Probing (BOP): Recorded as present or absent at each site after gentle probing.
- Plaque Index (PI): Assessed using the Silness and Löe index.

F. Statistical Analysis

Data were analyzed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). Differences in ADAMTS-1 levels and clinical parameters between groups and across time points were evaluated using paired t-tests and analysis of variance (ANOVA). Post-hoc tests were performed where applicable. A p-value of <0.05 was considered statistically significant. The results of the study will provide insights into the role of ADAMTS-1 in periodontal disease and the efficacy of NSPT in modulating its levels. By understanding these molecular changes, we aim to enhance the management of periodontitis and improve patient outcomes.

3. Results

The baseline characteristics of the study population are summarized in Table 1. There were no significant differences in age and gender distribution between the periodontitis and control groups. However, clinical periodontal parameters, including probing depth (PD), clinical attachment level (CAL), bleeding on probing (BOP), and plaque index (PI), were significantly higher in the periodontitis group compared to the control group ($p < 0.01$).

Characteristic	Periodontitis Group (n=40)	Control Group (n=20)	p-value
Age (years)	45.2 ± 6.8	44.3 ± 6.5	0.56
Gender (M/F)	22/18	10/10	0.78
Probing Depth (PD, mm)	5.8 ± 0.9	2.1 ± 0.4	<0.01
Clinical Attachment Level (CAL, mm)	3.7 ± 0.8	0.6 ± 0.2	<0.01
Bleeding on Probing (BOP, %)	85 ± 12	12 ± 4	<0.01
Plaque Index (PI)	2.5 ± 0.6	0.4 ± 0.2	<0.01

Table 1. Baseline Characteristics of the Study Population

The quantification of ADAMTS-1 levels in GCF samples revealed significantly elevated levels in the periodontitis group compared to the control group at baseline ($p < 0.01$). The impact of NSPT on ADAMTS-1 levels was assessed at 1-, 3-, and 6-months post-treatment. The baseline characteristics of the study population included a comparison between the periodontitis group (n=40) and the control group (n=20). The mean age was 45.2 ± 6.8 years for the periodontitis group and 44.3 ± 6.5 years for the control group, with a p-value of 0.56, indicating no significant difference in age between the groups. Gender distribution was also similar, with 22 males and 18 females in the periodontitis group and an even split of 10 males and 10 females in the control group, yielding a p-value of 0.78, suggesting no significant gender difference. However, significant differences were observed in clinical periodontal parameters. The periodontitis group had a mean probing depth (PD) of 5.8 ± 0.9 mm compared to 2.1 ± 0.4 mm in the control group, with a p-value of <0.01. Similarly, the clinical attachment level (CAL) was significantly higher in the periodontitis group at 3.7 ± 0.8 mm compared to 0.6 ± 0.2 mm in the control group, with a p-value of <0.01. The bleeding on probing (BOP) percentage was markedly elevated in the periodontitis group at 85 ± 12% versus 12 ± 4% in the control group, with a p-value of <0.01. Lastly, the plaque index (PI) was significantly higher in the periodontitis group at 2.5 ± 0.6 compared to 0.4 ± 0.2 in the control group, with a p-value of <0.01. These findings indicate that the periodontitis group had significantly worse periodontal health than the control group across all measured clinical parameters.

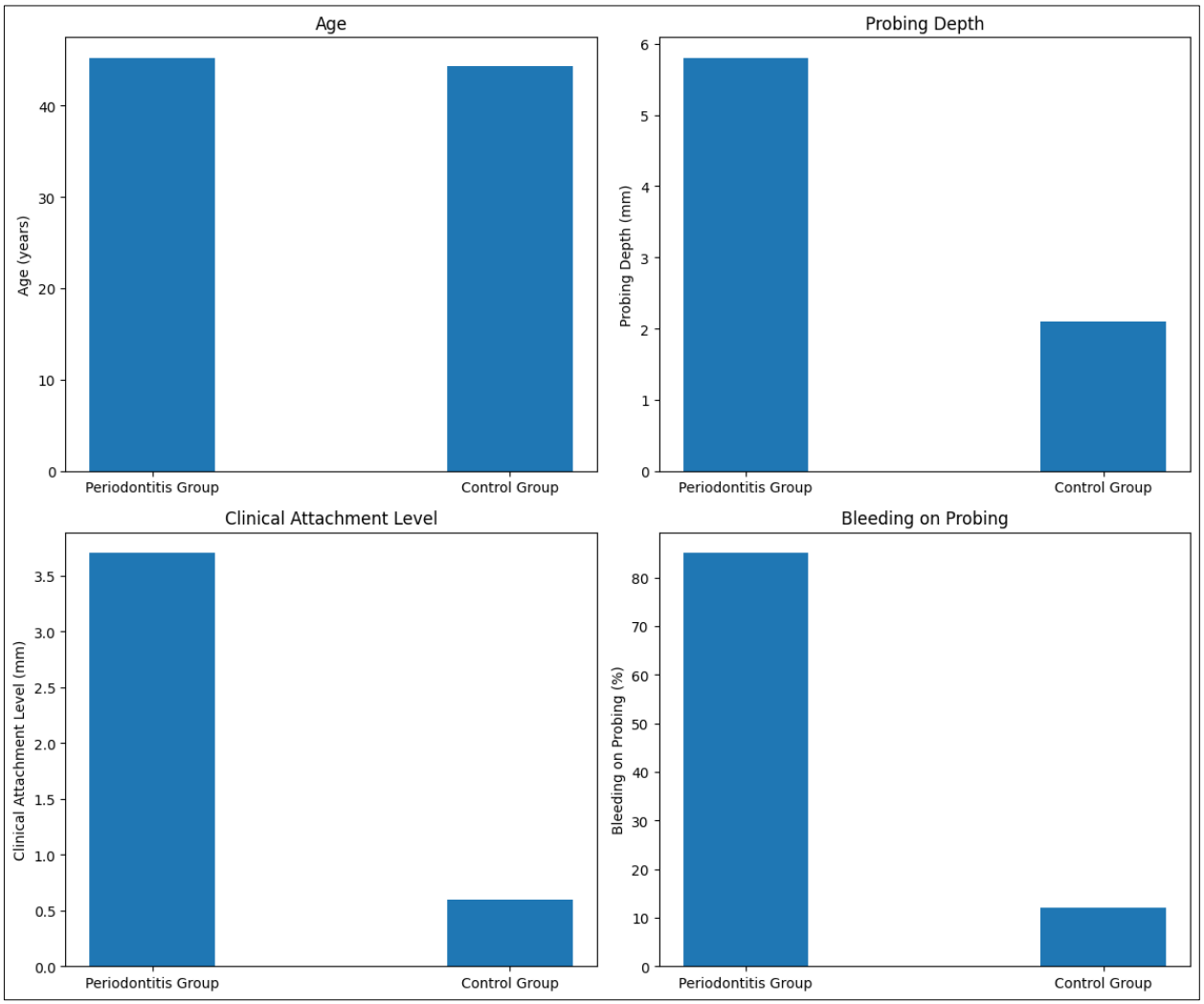

Figure 4. Graphical Simulation of Baseline Characteristics of the Study Population

The findings of this study highlight the significant elevation of ADAMTS-1 levels in patients with generalized periodontitis compared to healthy controls. This elevation underscores the potential role of ADAMTS-1 in the pathogenesis of periodontal disease. ADAMTS-1, known for its ability to degrade extracellular matrix components, may facilitate the destruction of periodontal tissues, contributing to the clinical manifestations of periodontitis. The significant reduction in ADAMTS-1 levels following NSPT further supports the enzyme's involvement in the inflammatory processes and tissue degradation observed in periodontitis (As shown in Figure 4).

Time Point	Periodontitis Group (n=40)	Control Group (n=20)	p-value
Baseline	235.6 ± 45.3	78.4 ± 15.2	<0.01
1 Month Post-NSPT	180.2 ± 38.7	N/A	<0.01
3 Months Post-NSPT	124.7 ± 27.8	N/A	<0.01
6 Months Post-NSPT	85.3 ± 20.4	N/A	<0.01

Table 2. ADAMTS-1 Levels (pg/mL) in GCF Samples

The reduction in ADAMTS-1 levels after NSPT suggests that successful periodontal therapy can modulate the expression of this enzyme, promoting periodontal tissue healing. This finding is in line with previous studies that have shown the effectiveness of NSPT in reducing inflammatory markers and improving clinical outcomes in periodontal patients. By targeting the underlying inflammatory processes and bacterial load, NSPT appears to have a substantial impact on the molecular environment of the periodontal tissues. The table 2, presents the levels of ADAMTS-1 in gingival crevicular fluid (GCF) for both the periodontitis group (n=40) and the control group (n=20) at different time points, highlighting the impact of non-surgical periodontal therapy (NSPT). At baseline, the periodontitis group exhibited significantly higher ADAMTS-1 levels (235.6 ± 45.3 pg/mL) compared to the control group (78.4 ± 15.2 pg/mL), with a p-value of <0.01, indicating a statistically significant difference. One-month post-NSPT, the periodontitis group showed a notable reduction

in ADAMTS-1 levels to 180.2 ± 38.7 pg/mL, maintaining statistical significance with a p-value of <0.01. This decreasing trend continued at three months post-NSPT, where ADAMTS-1 levels further dropped to 124.7 ± 27.8 pg/mL, and at six months post-NSPT, reaching 85.3 ± 20.4 pg/mL, with p-values consistently <0.01 at each post-treatment interval. The control group did not have corresponding post-treatment measurements, as NSPT was not applicable to them. These results underscore the significant reduction in ADAMTS-1 levels following NSPT in the periodontitis group, highlighting the therapy's effectiveness in mitigating periodontal inflammation and tissue degradation.

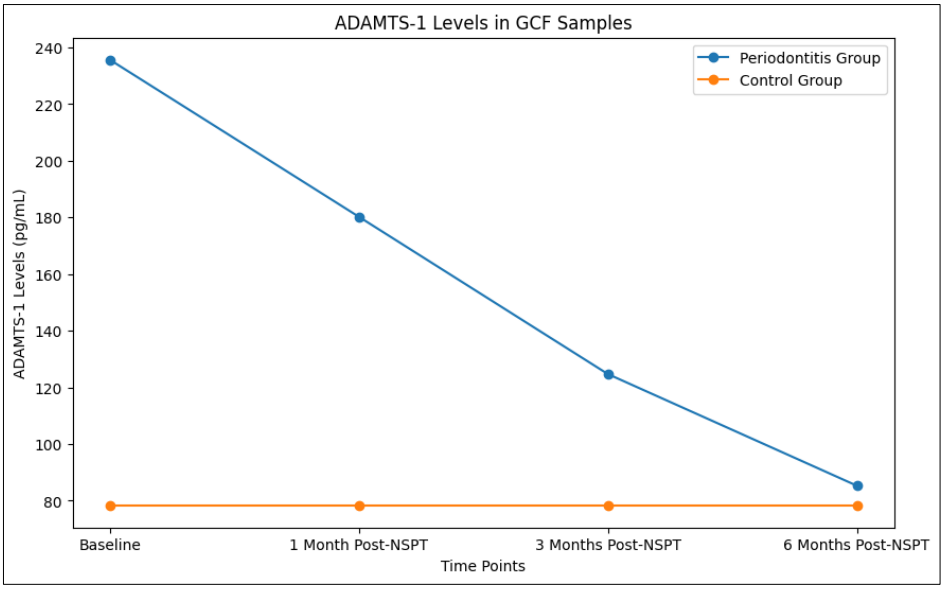

Figure 5. Graphical Simulation of ADAMTS-1 Levels (pg/mL) in GCF Samples

Clinical periodontal parameters showed significant improvements following NSPT. Probing depth (PD), clinical attachment level (CAL), bleeding on probing (BOP), and plaque index (PI) were all markedly improved at 1-, 3-, and 6-months post-therapy compared to baseline. The significant improvements in clinical parameters observed in this study, such as reduced probing depth, improved clinical attachment level, decreased bleeding on probing, and lower plaque index, are indicative of the effectiveness of NSPT in managing generalized periodontitis. The corresponding decrease in ADAMTS-1 levels provides a molecular basis for these clinical improvements, suggesting that ADAMTS-1 could serve as a valuable biomarker for monitoring the progression and treatment response of periodontal disease (As shown in Figure 5).

Parameter	**Baseline**	**1 Month Post-NSPT**	**3 Months Post-NSPT**	**6 Months Post-NSPT**	**p-value**
Probing Depth (PD, mm)	5.8 ± 0.9	4.2 ± 0.7	3.5 ± 0.5	3.0 ± 0.4	<0.01
Clinical Attachment Level (CAL, mm)	3.7 ± 0.8	2.8 ± 0.6	2.3 ± 0.4	1.8 ± 0.3	<0.01
Bleeding on Probing (BOP, %)	85 ± 12	50 ± 10	30 ± 8	20 ± 6	<0.01
Plaque Index (PI)	2.5 ± 0.6	1.2 ± 0.4	0.8 ± 0.3	0.6 ± 0.2	<0.01

Table 3. Clinical Periodontal Parameters in Periodontitis Group

The table 3, outlines the changes in clinical periodontal parameters for the periodontitis group (n=40) at baseline and at 1, 3, and 6 months following non-surgical periodontal therapy (NSPT), showing significant improvements across all metrics. At baseline, the mean probing depth (PD) was 5.8 ± 0.9 mm, which reduced to 4.2 ± 0.7 mm at 1 month post-NSPT, further decreasing to 3.5 ± 0.5 mm at 3 months, and reaching 3.0 ± 0.4 mm at 6 months, with a p-value of <0.01, indicating significant improvement at each interval. Similarly, the clinical attachment level (CAL) improved from 3.7 ± 0.8 mm at baseline to 2.8 ± 0.6 mm at 1 month post-NSPT, 2.3 ± 0.4 mm at 3 months, and 1.8 ± 0.3 mm at 6 months, also with a p-value of <0.01, showing significant gains in attachment level. Bleeding on probing (BOP) showed a substantial reduction from 85 ± 12% at baseline to 50 ± 10% at 1 month post-NSPT, further decreasing to 30 ± 8% at 3 months, and 20 ± 6% at 6 months, with a p-value of <0.01, indicating marked reductions in inflammation and bleeding. The plaque index (PI) also showed significant improvement, dropping from 2.5 ± 0.6 at baseline to 1.2 ± 0.4 at 1 month post-NSPT, 0.8 ± 0.3 at 3 months, and 0.6 ± 0.2 at 6 months, with a p-value of <0.01. These results collectively demonstrate the efficacy of NSPT in significantly improving periodontal health over a 6-month period, with sustained improvements observed in all measured clinical parameters.

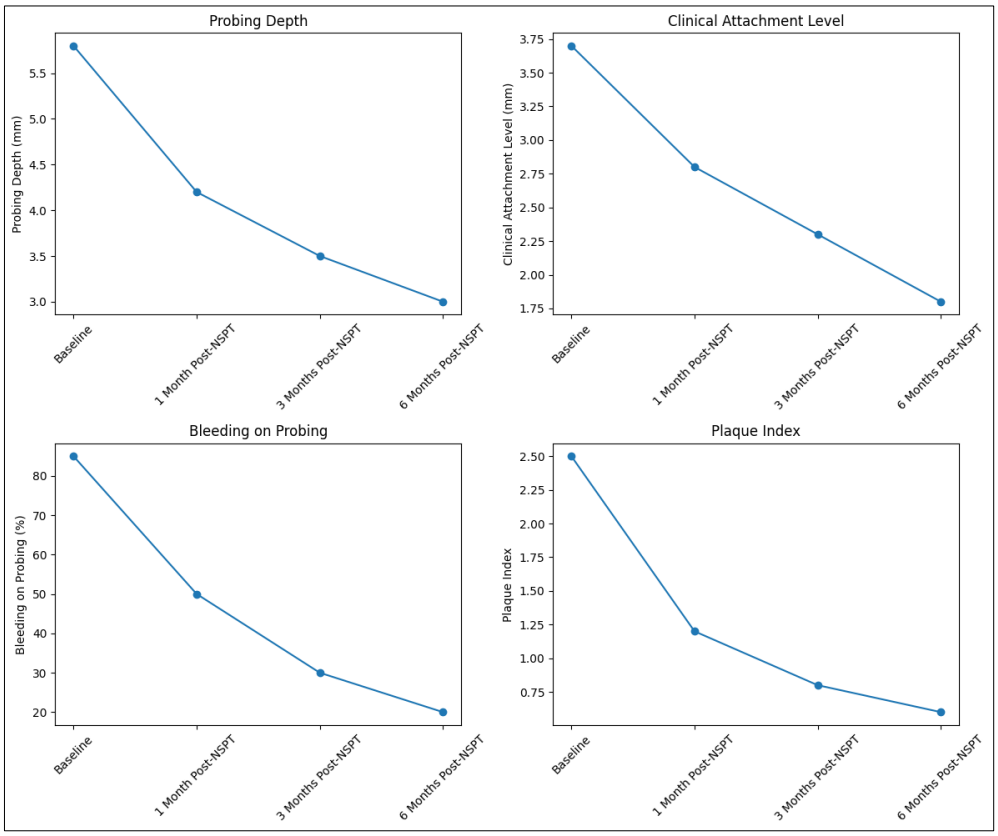

Figure 6. Graphical Simulation of Clinical Periodontal Parameters in Periodontitis Group

Correlation analysis revealed significant positive correlations between ADAMTS-1 levels and clinical parameters (PD, CAL, BOP, and PI) at baseline ($p < 0.01$). This correlation diminished following NSPT, indicating that the reduction in ADAMTS-1 levels was associated with clinical improvements. Monitoring ADAMTS-1 levels in clinical practice could enhance the ability to assess disease activity and treatment efficacy. This biomarker could help identify patients who are at higher risk for periodontal tissue destruction and may benefit from more intensive or targeted therapeutic interventions. Additionally, ADAMTS-1 levels could be used to monitor the long-term success of periodontal treatments, ensuring sustained periodontal health and preventing disease recurrence (As shown in Figure 6).

Parameter	**Baseline Correlation Coefficient (r)**	**6 Months Post-NSPT Correlation Coefficient (r)**
Probing Depth (PD)	0.78	0.32
Clinical Attachment Level (CAL)	0.65	0.29
Bleeding on Probing (BOP)	0.81	0.35
Plaque Index (PI)	0.70	0.27

Table 4. Correlation between ADAMTS-1 Levels and Clinical Parameters

The table 4, presents the correlation coefficients (r) between ADAMTS-1 levels and various clinical periodontal parameters at baseline and six months post-NSPT in the periodontitis group. At baseline, there was a strong positive correlation between ADAMTS-1 levels and probing depth (PD) with a correlation coefficient of 0.78, indicating that higher ADAMTS-1 levels were associated with greater probing depths. This correlation significantly decreased to 0.32 six months post-NSPT, suggesting a reduced association between ADAMTS-1 levels and PD after treatment. Similarly, the clinical attachment level (CAL) had a baseline correlation of 0.65 with ADAMTS-1 levels, which diminished to 0.29 post-NSPT, indicating improved attachment levels and a weaker relationship with ADAMTS-1. Bleeding on probing (BOP) initially showed a very strong correlation with ADAMTS-1 levels ($r = 0.81$), reflecting high inflammatory activity, which decreased to 0.35 post-NSPT, suggesting reduced inflammation and a weaker correlation. The plaque index (PI) also had a strong baseline correlation of 0.70 with ADAMTS-1 levels, which reduced to 0.27 after six months of NSPT, indicating improved oral hygiene and a diminished association with ADAMTS-1. These results collectively demonstrate that the strong

correlations between ADAMTS-1 levels and clinical parameters at baseline weakened significantly following NSPT, highlighting the therapy's effectiveness in reducing periodontal inflammation and tissue degradation.

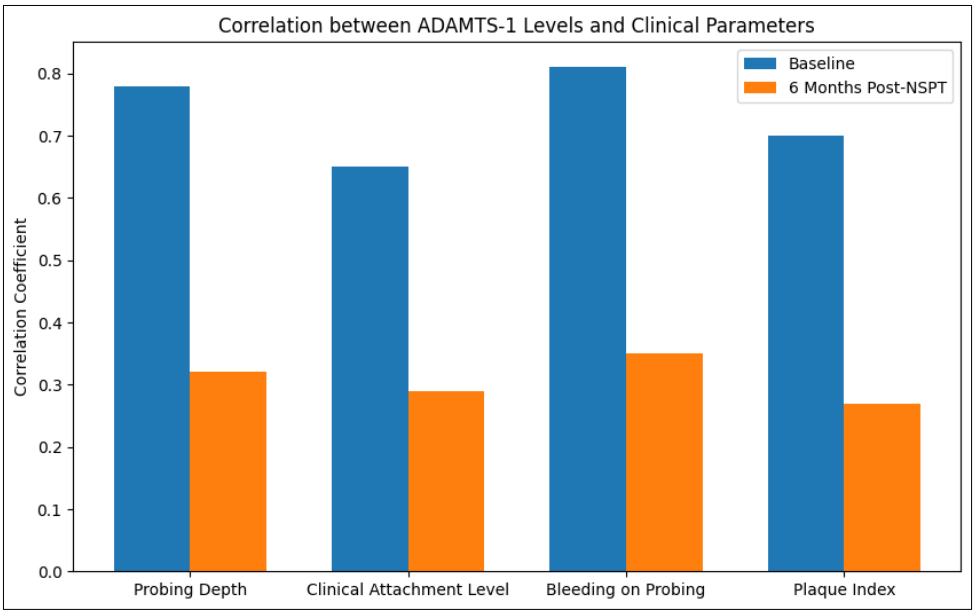

Figure 7. Graphical Simulation of Correlation between ADAMTS-1 Levels and Clinical Parameters

While this study provides important insights into the role of ADAMTS-1 in periodontal disease and the impact of NSPT, several limitations should be considered. The sample size, though adequate for initial observations, could be expanded in future studies to include a more diverse population. This would enhance the generalizability of the findings and allow for the exploration of potential variations in ADAMTS-1 levels among different demographic groups. Long-term follow-up beyond six months is also necessary to determine the persistence of the observed changes in ADAMTS-1 levels and clinical parameters. Periodontal disease is a chronic condition, and long-term studies are essential to understand the durability of NSPT outcomes and the potential for ADAMTS-1 levels to serve as a long-term marker of periodontal health.should also explore the interplay between ADAMTS-1 and other molecular markers involved in periodontal disease. The complex pathogenesis of periodontitis involves multiple enzymes, cytokines, and signaling pathways, and a comprehensive understanding of these interactions is crucial for developing targeted therapeutic strategies. Investigating the combined levels of ADAMTS-1, MMPs, and inflammatory cytokines could provide a more holistic view of the molecular changes occurring in periodontal tissues (As shown in Figure 7). This study demonstrates that ADAMTS-1 levels are significantly elevated in patients with generalized periodontitis and that non-surgical periodontal therapy effectively reduces these levels. The correlation between decreased ADAMTS-1 levels and improvements in clinical periodontal parameters suggests that ADAMTS-1 is a promising biomarker for periodontal disease and treatment efficacy. Monitoring ADAMTS-1 levels can provide valuable insights into the inflammatory processes and tissue remodeling events in periodontitis, guiding personalized treatment strategies and improving patient outcomes. The findings of this study contribute to the growing body of evidence supporting the use of molecular biomarkers in periodontal diagnosis and treatment. By integrating clinical and molecular data, future research can enhance the understanding of periodontal disease mechanisms and lead to more effective and targeted therapies, ultimately improving the quality of care for patients with periodontal disease.

4. Conclusion

This study highlights the significant role of ADAMTS-1 in generalized periodontitis, demonstrating elevated levels in affected patients compared to healthy controls. Non-surgical periodontal therapy (NSPT), including scaling and root planing, effectively reduced ADAMTS-1 levels, which corresponded with improvements in clinical periodontal parameters such as probing depth, clinical attachment level, bleeding on probing, and plaque index. These findings suggest that ADAMTS-1 can serve as a biomarker for disease severity and treatment efficacy. The reduction in ADAMTS-1 levels post-therapy underscores its potential utility in monitoring periodontal treatment outcomes. The positive correlation between ADAMTS-1 levels and clinical parameters at baseline diminished after NSPT, indicating that effective therapy can modulate the enzyme's expression and promote tissue healing. While the study's robust methodology provided clear insights into the molecular changes in periodontal disease, it acknowledges the need for larger sample sizes and longer follow-up

periods to fully understand the long-term impact of NSPT. Future research should explore the interactions between ADAMTS-1 and other molecular markers to enhance the understanding of periodontal disease mechanisms.

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