ORIGINAL RESEARCH

Effectiveness of Nonsurgical Periodontal Therapy on Salivary Visfatin: A Clinical and Biochemical Analysis

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Abstract

Aim: To assess the effectiveness of nonsurgical periodontal therapy (NSPT) on salivary visfatin (VF) levels in chronic periodontitis patients.

Materials and methods: A total of 40 individuals with body mass index (BMI) of 18.5–24.9, aged between 30 and 50 years (group I—*n* = 20, periodontally healthy and group II1—*n* = 20, generalized chronic periodontitis patients) were enrolled in this experimental study. Clinical parameters such as periodontal probing depth (PPD) and clinical attachment level (CAL) were recorded. Unstimulated salivary samples were collected and assayed for VF using a human VF enzyme-linked immunosorbent assay (ELISA) kit. After clinical examination and saliva collection at baseline, scaling, and root planing (SRP) was done for generalized chronic periodontitis patients, and after 3 months, clinical examination and saliva collection was done (group II2). The results were analyzed using Statistical Package for Social Sciences (SPSS) software, version 23.0. Within-group comparison between different time frames was made by paired *t*-test, and intergroup comparison was made by independent *t*-test. Pearson correlation was done to assess the relationship between variables.

Results: The salivary VF level was higher in group II1 (37.96 ± 1.74 ng/mL) as compared to group I (19.23 ± 1.33 ng/mL). Between groups II1 (before NSPT) and II2 (after NSPT), there was a reduction in PPD from baseline (4.65 ± 0.36) to 3 months (2.73 ± 2.77), and there was a reduction in CAL from baseline (5.04 ± 0.55) to 3 months (2.98 ± 2.22). Also, there was a reduction of VF from baseline (37.96 ± 1.74) to 3 months (19.04 ± 0.34). Pearson correlation in groups II1 and II2 revealed the correlation between VF and clinical parameters (PPD and CAL) was strongly positive and statistically significant.

Conclusion: The present study suggests that there was a significant reduction in salivary VF levels among periodontitis patients after NSPT. Also, there exists a positive correlation between salivary VF and periodontal parameters.

Clinical significance: Salivary VF may be used as a potential diagnostic biomarker in the detection of periodontal diseases. Furthermore, it can be used to monitor the efficacy of the treatment during the course of the management of periodontitis.

Keywords: Adipokines, Biomarker, Periodontitis, Visfatin.

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Introduction

Periodontitis is a chronic inflammatory disease that affects the supporting structures of the teeth.[1] Even though bacterial plaque is the major cause of periodontal disease, the disease process is based on the interaction between bacteria and the host immune system. In response to bacterial plaque, the inflammatory and immune pathways of the host intend to protect, but this results in the production of proinflammatory mediators like interleukin (IL) 1, IL-6, tumor necrosis factor (TNF) α, matrix metalloproteinases, and prostaglandins causing tissue damage.[2] In addition to this, there are a number of risk factors, including age, gender, systemic diseases, smoking, stress, hormonal influences, heredity, malnutrition, certain types of prostheses and their improper loading, and socioeconomic status that might aggravate the condition.[3–6]

Adipose tissue is a complex endocrine organ that secretes a variety of immunomodulatory substances and regulates different inflammatory pathways, including periodontitis.[7] Adipokines are polypeptides that are secreted by adipocytes, preadipocytes, inflammatory cells like macrophages, and other cells which include leptin, VF, adiponectin, retinol-binding protein-4, resistin, TNF-α, IL-6.[8] Adipokines have potent autocrine, paracrine, and endocrine functions. Adipokines function as classic circulating hormones to communicate with other organs, including the brain, liver, muscle, immune system, and adipose tissue itself.[9]

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Literature evidence reveals leptin, resistin, adiponectin, and VF are potent markers of chronic periodontitis.[10-12] VF is also called the pre-B-cell colony-enhancing factor. It is secreted by lymphocytes, macrophages, monocytes, dendritic cells, periodontal ligament cells, bone marrow cells, and liver cells. It acts as a growth factor, cytokine, and proinflammatory mediator and plays a role in the proliferation of cells and angiogenesis.[13] In addition, it modulates

the host response by inhibiting neutrophil apoptosis during inflammation and increases the production of TNF-α, IL-1β, and IL-6. The increase in the expression of these proinflammatory cytokines, in turn, leads to periodontal disease destruction.[14]

There are several studies correlating serum or gingival crevicular fluid (GCF) VF levels with periodontal status.[15–17] Collecting saliva as a diagnostic fluid in analyzing periodontal disease is a convenient and non-invasive technique as compared to serum and GCF. Also, compared to serum and GCF, saliva consists of numerous proteins which maintain the integrity of the oral cavity, and such proteins play a crucial role in periodontal disease initiation and progression. However, a literature search reveals only a few studies correlating salivary VF with periodontal status before and after periodontal therapy.[18,19] Therefore, the present study intended to assess the effectiveness of NSPT on salivary VF levels in chronic periodontitis patients.

Materials and Methods

This case-control, experimental study was conducted among 40 outpatients who reported to the Department of Periodontics, Saveetha Dental College and Hospitals, Chennai, Tamil Nadu, India. The study was performed from September 2021 to June 2022 after getting approval from the Institutional Ethical Committee (IHEC/SDC/FACULTY/21/PERIO/351). The patients explained the whole study protocol and written informed consent was obtained from them.

A total of 40 participants (20 males and 20 females) aged between 30–50 years were enrolled. Out of 40, 20 were periodontally healthy (group I), and 20 were generalized chronic periodontitis patients (group II1) based on the American Academy of Periodontology Criteria 1999. All the subjects enrolled were non-obese with a BMI of 18.5–24.9, based on the definition of obesity using BMI developed by the National Institutes of Health. Using an unpaired *t*-test with a two-sided significance level of 0.05, the sample size was calculated to be 40, with 80% power.

Inclusion criteria for all patients in both groups were aged between 30 and 60 years, BMI of 18.5–24.9, having at least 18 natural teeth excluding third molars, and being systemically healthy. Individuals presented with probing pocket depth (PPD) of 1–3 mm were enrolled in group I, and patients with PPD of 4–5 mm in >30% of the sites were enrolled in group II1. Exclusion criteria considered were—patients with systemic diseases like diabetes mellitus, cardiovascular diseases, hypertension, and rheumatoid arthritis; patients who had undergone periodontal therapy in the last 1 year, pregnant and lactating women, smokers, and patients under long-term medications.

Clinical Examination

Full-mouth PPD and CAL were measured at six sites around the teeth (mesial, mid, and distal on both buccal and lingual surfaces) using a UNC-15 periodontal probe, and the average was recorded.

Saliva Collection

Before saliva collection, participants were requested to fast for at least 2 hours without eating or drinking. The spitting method was used to collect 5 mL of unstimulated whole saliva from each subject between 11:00 am and 12:00 pm. Saliva was collected in sterile tubes and immediately frozen at 80°C until the experiment began. Within 6 months of collection, samples were defrosted and examined.

Each 5 mL saliva sample was pipetted into a clean microcap tube and centrifuged at 10000 rpm for 1 minute to clarify it. The supernatant was immediately transferred to clean microcap tubes and used for an ELISA. Concentrations of VF were determined using Elabscience Human VF ELISA kit, United States of America, according to the manufacturer's instructions. Absorbance of the substrate color reaction was read using 450 nm as the primary wavelength. The results of the VF assay were expressed as ng/mL. The minimum detectable dose of VF using this kit was determined to be 0.19 ng/mL.

Nonsurgical Periodontal Therapy (NSPT)

After clinical examination and saliva collection at SRP was done using hand curettes (Gracey curettes, Hu-Friedy™ Manufacturing Inc., Chicago, Illinois, United States of America) were carried out for generalized chronic periodontitis (groups II1) patients. Oral hygiene instructions were given to all patients, and they were asked to brush twice daily by using the modified bass method; the patients refrained from the use of mouth rinses throughout the study. Following NSPT, at the end of 3 months, clinical examination and saliva collection was repeated (group II2).

Statistical Analysis

The data were analyzed using the SPSS (SPSS Software, Version 23.0; IBM Corp., Armonk, New York, United States of America). The results were evaluated using the Kolmogorov–Smirnov test and the Shapiro–Wilk test of normality. According to the data, the findings followed a parametric distribution. Within-group comparison between different time frames was made by paired *t*-test, and intergroup comparison was made by independent *t*-test. Pearson correlation was done to assess the relationship between variables. The results were considered statistically significant when the *p*-value was <0.05.

Results

Table 1 summarizes the demographic and clinical characteristics and VF levels of both groups. Periodontally healthy individuals (group I) presented with a mean age of 41.20 ± 5.92 years, BMI of 21.93 ± 2.00 kg/m^2, PPD of 1.77 ± 0.74 mm, CAL of 0 mm, and salivary VF of 19.23 ± 1.33 ng/mL. Generalized chronic periodontitis patients (group II1) presented with a mean age of 40.90 ± 6.62 years, BMI of 22.14 ± 1.99 kg/m^2, PPD of 4.65 ± 0.36 mm, CAL of 5.04 ± 0.55 mm, and salivary VF of 37.96 ± 1.74 ng/mL. There was

Table 1: Demographic, clinical characteristics, and salivary VF levels of the study population

Parameter	*Group I (n = 20)*	*Group II1 (n = 20)*	*p-value*
Age (years)	41.20 ± 5.92	40.90 ± 6.62	0.55
BMI (kg/m$^{2)}$	21.93 ± 2.00	22.14 ±1.99	0.98
PPD (mm)	1.77 ± 0.74	4.65 ± 0.36	0.00*
CAL (mm)	0.00	5.04 ± 0.55	0.00*
Salivary VF (ng/mL)	19.23 ± 1.33	37.96 ± 1.74	0.03*

*Statistically significant at p<0.05

no statistically significant difference between group I and II1 in terms of age ($p = 0.55$) and BMI ($p = 0.98$). Clinical parameters like PPD and CAL were significantly higher in group II1 than in group I ($p = 0.00$, $p = 0.00$). Salivary VF levels were detected in both groups, but the levels were significantly higher in group II1 than in group I ($p = 0.03$). Salivary VF level was higher in the periodontally compromised population as compared to the periodontally healthy population.

Table 2 shows a comparison of clinical parameters and salivary VF levels in chronic periodontitis patients before (group II1) and after (group II2) NSPT using paired *t*-test. There was a reduction in PPD from baseline (4.65 ± 0.36) to follow-up after 3 months (2.73 ± 2.77), and the difference was statistically significant ($p = 0.00$). There was a reduction in CAL from baseline (5.04 ± 0.55) to follow-up after 3 months (2.98 ± 2.22), and the difference was statistically significant ($p = 0.00$). Also, when the salivary VF levels were compared before and after NSPT, there was a reduction from baseline (37.96 ± 1.74) to follow-up after 3 months (19.04 ± 0.34), and the difference was statistically significant ($p = 0.00$). A significant reduction in salivary VF level was observed among periodontitis patients after NSPT.

Table 3 shows the Pearson correlation between salivary VF levels with clinical parameters among periodontitis patients before and after NSPT. In group II1, the correlation between VF and PPD was strongly positive and statistically significant (r = 0.957, $p = 0.000$), and the correlation between VF and CAL was strongly positive and statistically significant (r = 0.987, $p = 0.000$). In group II2, the correlation between VF and PPD was strongly positive and statistically significant (r = 0.706, $p = 0.000$), and the correlation between VF and CAL was moderately positive and statistically significant (r = 0.4 83, $p = 0.000$). From the correlation analysis, a positive correlation was observed between salivary VF and periodontal parameters, including PPD and CAL.

Discussion

Our understanding of the pathogenesis of periodontal disease has expanded enormously in light of advances in clinical research. There are numerous diagnostic methods available in addition to clinical measures in predicting periodontal disease. As periodontitis is a disease of bacterial-host interaction, assessing the mediators of host response not only diagnoses the periodontal disease but also helps in predicting the prognosis of periodontal therapy. Assessment of these biomarkers as a part of periodontal therapy has gained importance in recent days.

Visfatin (VF) is an inflammatory mediator which plays a role in periodontal disease progression as it induces the production of proinflammatory mediators, which further worsen the periodontal breakdown. The present study assessed the effectiveness of NSPT on salivary VF levels in chronic periodontitis patients and compared it with the healthy controls.

The results of the present study revealed that the mean salivary VF concentration was higher in chronic periodontitis patients as compared to periodontally healthy individuals. Tabari et al. compared the salivary VF levels in generalized chronic periodontitis patients with periodontally healthy individuals and suggested that the level of VF was higher among patients with periodontitis.[15] Also, VF levels were significantly elevated in chronic periodontitis patients as compared to healthy controls in studies by Abolfazli et al.,[16] and Ozcan et al.,[17] which is consistent with the current study.

This finding is similar to various previous studies, where the VF concentration was high among periodontally compromised patients. When crevicular and serum VF was correlated with periodontally healthy and periodontally compromised individuals, it was observed that VF levels were increased in GCF and serum with the severity of disease from healthy to periodontitis. Also, VF levels in GCF were higher than that of serum.[20] Furthermore, the salivary VF level was positively correlated to periodontal parameters, including plaque index, gingival index, PPD, and CAL.[17] In addition, there exists a correlation between periodontal pathogens and GCF VF concentration. Also, it was suggested that the colonization of *Porphyromonas gingivalis* in pockets could increase the synthesis of VF.[21] The findings of these studies are in agreement with the present study as the VF concentration is higher in the periodontitis group than in healthy controls, suggesting VF as a potential marker in periodontal diseases.

Furthermore, a literature search revealed VF was assessed in comorbid conditions like obesity and systemic diseases.[22,23] Cetiner et al. studied the levels of VF in GCF in obese and non-obese patients with and without periodontitis and found that VF links the pathogenesis of obesity and periodontitis. This is due to the fact that the release of VF in fat cells is linked to obesity, and the abundance of adipose tissue in obese individuals is responsible for elevated levels of VF.[22] Also, when VF was assessed in periodontitis patients with and without type 2 diabetes mellitus patients, it was suggested

Table 2: Comparison of PPD, CAL, and salivary VF before and after NSPT

	Mean ± SD		
Variable	*Group II1*	*Group II2*	*p-value*
PPD	4.65 ± 0.36	2.73 ± 2.77	0.00*
CAL	5.04 ± 0.55	2.98 ± 2.22	0.00*
Salivary VF (ng/mL)	37.96 ± 1.74	19.04 ± 0.34	0.00*

*Statistically significant at $p < 0.05$

Table 3: Correlation of VF with clinical parameters

	Correlation variable	*Correlation coefficient (r)*	*p-value*
Group II 1	VF vs PPD	0.957**	0.000
	VF vs CAL	0.987**	0.000
Group II 2	VF vs PPD	0.706**	0.000
	VF vs CAL	0.483*	0.030

**Strong positive correlation; *moderate positive correlation

that VF concentration in both type 2 diabetes mellitus patients with periodontitis and periodontitis patients without diabetes exhibited a positive correlation with PPD and CAL.[23] These findings suggest the role of VF in modulating inflammatory and immune pathways.

In the present study, it was observed that there was a significant reduction in salivary VF concentration in chronic periodontitis patients after NSPT. And when the clinical parameters, including PPD and CAL, were assessed in chronic periodontitis patients after NSPT, there was a significant reduction. Furthermore, this study highlighted that there exists a positive correlation between VF and clinical parameters (PPD and CAL). Raghavendra et al. suggested that VF in GCF and serum was high among periodontitis patients and decreased after NSPT, and hence a positive correlation was obtained between VF and periodontal parameters.[18] Similarly, when the effect of NSPT on VF among moderate and severe chronic periodontitis patients was assessed, the decrease in VF levels was more prominent after NSPT.[16]

Studies by Mopidevi et al.,[24] Mishra et al.,[25] and Mamali et al.,[26] also highlighted the positive correlation between VF levels and periodontal parameters. Also, when the relationship of VF was investigated in patients with diabetes and periodontitis before and after NSPT, the findings suggested that NSPT was useful for glycemic control and also associated with reduced VF in patients with diabetes and periodontitis.[27] It is evident from the previous studies that periodontal inflammation upregulates the proinflammatory mediators, which in turn causes high expression of VF, and hence the resolution of periodontal inflammation could significantly reduce the VF level.

Since the findings of the current study are similar to those of studies that looked at serum or GCF VF concentrations in periodontitis, it appears that assessing VF concentration in saliva could be an alternative in the diagnosis of periodontitis. Also, the VF concentration in saliva was found to be higher among periodontitis patients and decreased after NSPT. Hence VF could be considered a prognostic biomarker in the management of periodontal diseases. However, prospective multicentre studies with a larger population and long-term follow-up are needed to substantiate the findings of the present study. Also, both the study groups were matched in BMI and age and excluded smokers and patients with systemic diseases to limit the potential effects of confounders. Furthermore, the severity of periodontitis was not taken into account in this investigation. Further studies are warranted to correlate VF with the severity of periodontitis.

Conclusion

The present study suggests that the level of salivary VF was higher in the periodontally compromised population as compared to a periodontally healthy population. There was a significant reduction in salivary VF levels among periodontitis patients after NSPT. Also, there exists a positive correlation between salivary VF and periodontal parameters, including PPD and CAL. This illustrates that salivary VF may be used as a potential prognostic biomarker in the management of periodontal diseases.

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