ORIGINAL RESEARCH

Evaluation of Serum and Salivary Visfatin Prior to and Post-nonsurgical Periodontal Therapy in Periodontally Healthy and Chronic Periodontitis Patients

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Abstract

Aims: This study aims to evaluate the visfatin levels in periodontally healthy persons and subjects with chronic periodontitis and their change in levels with regard to nonsurgical periodontal therapy (NSPT).

Materials and methods: A total of 30 individuals with healthy periodontium and 30 patients with chronic periodontitis in the age range of 25–65 years and with normal body mass index (BMI) were selected for the study. Scaling and root planing were done for chronic periodontitis patients and were reviewed after 2 months. Periodontal clinical parameters were noted, and salivary and serum samples were collected and stored during the first visit and review. Visfatin levels in the samples were evaluated using enzyme-linked immunosorbent assay (ELISA).

Results: Chronic periodontitis patients had elevated levels of serum (38.1 ng/mL vs 16.42 ng/mL) and salivary (57.86 ng/mL vs 19.94 ng/mL) visfatin in comparison to healthy controls. In periodontitis patients, serum (38.1 ng/mL to 20.32 ng/mL) and salivary (57.86 ng/mL to 19.62 ng/mL) levels of visfatin were reduced in response to NSPT.

Conclusion: The elevation in serum visfatin and salivary visfatin levels in chronic periodontitis patients and its reduction in response to NSPT makes visfatin a probable disease marker and a potential therapeutic target for assessing treatment efficacy.

Clinical significance: Visfatin, being an adipocytokine, is closely related to the process of inflammation cascade. Its association with periodontal inflammation and health, as seen in the present study, shows that visfatin may be utilized as a marker in the diagnosis of periodontitis and in the evaluation of treatment efficacy.

Keywords: Chronic periodontitis, Diagnostic marker, Nonsurgical periodontal therapy, Salivary visfatin, Serum visfatin.

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Introduction

Periodontitis is a multifactorial disease that results in connective tissue destruction and alveolar bone degradation in the periodontium.[1] In response to bacterial infection, locally generated proinflammatory cytokines cause periodontal damage.[2] Proinflammatory cytokines are postulated to be linked to periodontal inflammation.[3] Visfatin is a low-molecular-weight protein that is commonly produced in adipose tissues. It is also produced in a variety of cell types, which include dendritic cells, bone marrow cells, macrophages, lymphocytes, monocytes, hepatic cells, and fetal membranes. Nicotinamide adenine dinucleotide production is also inhibited.

Visfatin is present in white blood cells and macrophages, showing that visfatin is involved in immunological and defense function modulation.[4] Visfatin responds to inflammation and infection and works as an enzyme, biomarker, and growth factor, and generates damaging cytokines like tumor necrosis factor (TNF), interleukin (IL) 1b, and IL-6.[5] Increase in the levels of proinflammatory cytokines like IL-6, IL-1, and TNF may, on the other hand, greatly enhance visfatin expression.[6] Visfatin expression rises in acute and chronic inflammatory situations, and it plays an important role in inflammation being persistent by inhibiting neutrophil death.[7]

As periodontal disease advances, gingival crevicular fluid (GCF) and serum visfatin levels increase, according to Pradeep et al.[8] According to Mamali et al., visfatin functions as a biomarker in saliva and can be utilized to diagnose periodontal disease activity. As a result, visfatin, which has diverse inflammatory actions, is an optimal candidate biomarker for periodontal disease research.[9]

Many researchers have looked at the effects of phase-I therapy, including scaling and root planing on GCF and serum visfatin. However, studies about salivary visfatin levels and their association with periodontal inflammatory diseases have been very less. Moreover, the collection of saliva is simpler compared to the collection of GCF.

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Hence, the present study aimed to determine the visfatin levels in both serum and saliva of persons with healthy periodontium and having chronic periodontitis, as well as the concentration of visfatin in serum and saliva in response to NSPT.

Materials and Methods

The present study was conducted at Vivekananda Dental College for Women, Tiruchengode, Tamil Nadu, India. It is a prospective case-control experimental study involving 60 patients with normal BMI visiting the Vivekananda Dental College for Women, Department of Periodontology for the time period of 1 year (June 2017–June 2018). Ethical committee approval was obtained, and the ethical clearance number assigned to this present study is VDCW/IEC/40/2016.

GPower version 3.1.9.2 was used to calculate the sample size of the present study. The sample size for this study was finalized using the formula $n = [(Z_{\alpha/2} + Z_{\beta})^2 \times \{2(ó)^2\}]/(\mu1-\mu2)^2$. Inclusion criteria included patients aged 25 to 65 years, systemically healthy patients, and patients with evidence of gingival inflammation, probing depth (PD) between 4 and 5 mm, clinical attachment loss (CAL) above 4 mm, and patients with bone loss in radiography. Patients exhibiting aggressive periodontitis, patients with periodontal treatment in the past 12 months, a history of smoking/alcohol, patients with systemic diseases, pregnancy, and any patients on medications were selected for exclusion from the study.

After explaining the study protocol to the subjects, patients provided informed consent, and the examination, collection of data, and sample collection proceeded. Subjects were allotted randomly into two groups. The total sample size was 60. A total of 30 healthy volunteers (group I) and 30 chronic periodontitis patients (group II) were enrolled in the study.

The clinical periodontal parameters like PD, CAL, gingival index (GI) (Loe and Silness), plaque index (PI) (Turesky et al.), gingival bleeding index (GBI) (Ainamo and Bay) were noted in lingual and buccal surfaces at the first visit and during review after 2 months. Group I was the control. They were assessed only at baseline. Group II was the test group which was further divided into (II1—before NSPT) and (II2—after NSPT). They were assessed during their first visit, underwent NSPT, and were reviewed after 2 months. Saliva and serum samples were obtained during the first visit in both groups I and II. Saliva and serum samples were taken 2 months after NSPT during the recall visit in group II alone. 4 mL of whole unstimulated saliva sample was obtained using the modified draining method. The cell debris from the saliva samples was removed by centrifuging the sample at 3000 rpm for 5 minutes. From the remaining fluid, 2 mL was taken and frozen at −80°C till the time of analysis.

A total of 4 mL of blood was obtained by venepuncture from the antecubital region. After the sample remained for 1 hour at room temperature, the resultant clotted sample was then centrifuged for 5 minutes at 3,000 rpm, and serum was extracted. About 2 mL of the serum was stored in 5 mL test tubes at −80°C till the time of further analysis. Phase I therapy was performed, and oral hygiene instructions were provided. Patients were not allowed to use antimicrobials or mouthwashes during the research. Telephonic contact was used to review the patient once every 15 days.

The salivary and serum visfatin concentration was analyzed using a visfatin ELISA kit from Elabscience, Houston, Texas, United States of America. This ELISA kit's minimal detectable dosage was 0.19/ng/mL. The optical density (3.5) of each well was determined at 450 nm. There was no observable significant interference or cross-reactivity between human VF and analogs.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) (IBM SPSS statistics for windows version 23, 2015) was used to analyze the present study's statistical data. Shapiro–Wilks tests and Kolmogorov–Smirnov showed that all variables have a normal distribution. The data was analyzed using parametric approaches. The mean values between groups were compared using the independent samples *t*-test. The mean values between two time points were compared using paired *t*-test. Chi-squared test was utilized to compare the ratios of study and control groups, and Fisher's exact test was used if any anticipated cell frequency was less than five. The linear relationship between variables was examined using Karl Pearson correlations.

Results

When determined by Chi-squared test and *t*-test, control group I with healthy subjects and test group II with chronic periodontitis were found to have no statistically significant difference when compared for gender, age (46.03 ± 9.03 in group I vs 44.87 ± 8.70 in group II), BMI (22.8 ± 1.73 in group I vs 22.65 ± 1.86 in group II), brushing frequency and number of total teeth.

When the clinical periodontal parameters between group I (periodontally healthy subjects) and group II1 (subjects with chronic periodontitis before treatment) were compared, the results showed that group II1 had statistically significant high GI, PI, PD, GBI, CAL, bleeding on probing (BOP) % of sites when compared to group I (Table 1).

Visfatin was found to be present in all serum and salivary samples of both groups. In the chronic periodontitis group (group II1), the mean levels of serum visfatin (38.1 ± 2.89 ng/mL) were substantially higher than group I with healthy persons (16.42 ± 2.11 ng/mL). Similarly, in subjects with the chronic periodontitis group (group II1), the mean levels of salivary visfatin (57.86 ± 3.35 ng/mL) were substantially higher than group I with healthy

Table 1: Comparison of clinical parameters between healthy subjects and chronic periodontitis patients

Clinical parameters	*Group I N = 30*	*Group II1 N = 30*	*Mean difference*	*p-value*
PI	0.40 ± 0.21	2.99 ± 0.59	−2.58	<0.001
GI	0	2.06 ± 0.17	−2.06	<0.001
BOP (%)	0	99.8 ± 0.66	−99.8	<0.001
PD (mm)	2.2 ± 0.53	5.27 ± 0.87	−3.04	<0.001
CAL (mm)	1.05 ± 0.46	6.1 ± 0.88	−5.04	<0.001
PD > 4 mm (%)	0	49.4 ± 10.05	−49.4	<0.001
CAL >5 mm (%)	0	48.0 ± 13.45	−4	<0.001

persons (19.94 ± 2.13 ng/mL). The variation observed in serum (Fig. 1), and salivary levels (Fig. 2) of visfatin from both groups were found to be of statistical significance (Table 2).

Nonsurgical periodontal therapy (NSPT) in chronic periodontitis patients resulted in the reduction of all clinical parameters, which included GBI, PI [2.99 ± 0.59–1.63 ± 0.39], CAL [6.1 ± 0.88–3.09 ± 0.69 mm], GI [2.06 ± 0.17–1.11 ± 0.20], PD [5.27 ± 0.87–2.39 ± 0.67 mm], and the percentage of sites with BOP which were statistically significant as presented in (Table 3).

In chronic periodontitis patients, salivary and serum samples were evaluated for visfatin levels 2 months post-NSPT. Serum [38.1 ± 2.89–20.32 ± 4.84 ng/mL] and salivary [57.86 ± 3.35–19.62 ± 2.61 ng/mL] visfatin levels were found to have gone down posttreatment compared to pretreatment. The reduction in posttreatment visfatin levels in both serum and saliva was found to be statistically significant, which is presented in (Table 4).

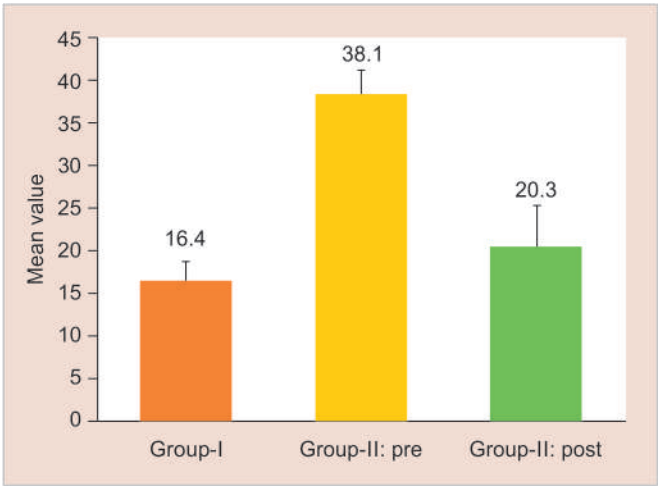


Fig. 1: Mean serum visfatin levels in all the groups

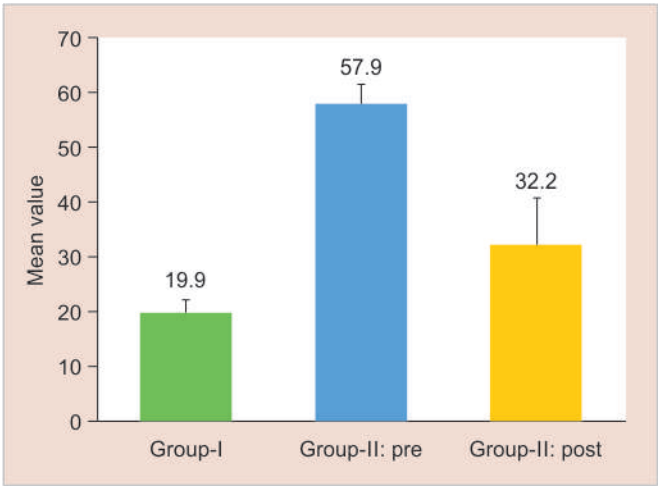


Fig. 2: Mean salivary visfatin levels in all the groups

Serum visfatin, PD, and CAL were found to have a statistically significant positive correlation in all groups. Salivary visfatin was also found to have a positive correlation with regard to PD and CAL (Table 5).

Discussion

The host secretes inflammatory modulating cytokines in reaction to the microorganisms, ultimately leading to periodontal destruction. Previous research has shown a link between adipocytokines such as leptin, resistin, visfatin, and periodontal disease.[10,11] The goal of the current study is to determine the link between salivary and serum visfatin levels in periodontally healthy and diseased patients and to determine the influence of NSPT on salivary and salivary visfatin levels.

Taskesen et al. revealed obesity was associated with elevated serum visfatin. Because obesity could skew the results, obese individuals were excluded, and persons with a normal BMI were included in the present study. Visfatin levels have been linked to a variety of systemic diseases.[12] So, patients with systemic diseases were excluded to prevent the influence of these diseases from affecting the present study results.

Bai et al. found smokers to have elevated serum visfatin levels. Visfatin is secreted in high levels from adipose tissue, the placenta, amnion, fetal membranes, and myometrium. This led us to exclude smokers and pregnant women. In comparison to stimulated saliva, unstimulated whole saliva has a larger protein concentration.[13] Hence the current utilized unstimulated saliva samples.

Salivary visfatin levels of chronic periodontitis subjects were considerably elevated in comparison to healthy persons. The present study findings are similar to those of Tabari et al., who found that visfatin was elevated in chronic periodontitis subjects in comparison to healthy subjects.[14] Patients with periodontitis and gingivitis have elevated salivary visfatin levels in comparison to healthy subjects, according to Ozcan et al.[15]

The current study found elevated serum levels of visfatin in periodontitis subjects in comparison to healthy persons. Turer et al. found that chronic periodontitis patients had elevated levels of serum visfatin in comparison to subjects with gingivitis or periodontally healthy volunteers.[16] This matches the findings of Pradeep et al., who discovered that GCF and serum visfatin concentrations were found to be maximal in periodontitis patients, minimal in healthy controls, and with gingivitis patients in the middle.[8]

In the present research study, NSPT resulted in the reduction of all of the clinical periodontal parameters, which include GI, PI, CAL, and PD. Raghavendra et al. conducted a study in which phase one periodontal therapy resulted in the reduction of all clinical parameters.[17] In comparison to the current study, Tabari et al. found that the reduction in CAL was not significant. This is in contradiction with the results of the current study.[14]

In their research to assess the response of GCF and serum visfatin to NSPT, Raghavendra et al. discovered that the GCF and serum visfatin levels decreased considerably 60 days following NSPT.[17] The current study results also showed that periodontal treatment resulted in a significant statistical reduction of visfatin levels in serum after 60 days.

Table 2: Comparison of serum and saliva visfatin levels between healthy subjects and chronic periodontitis patients

Laboratory parameters	*Group I*	*Group II1*	*Mean difference*	*p-value*
Serum visfatin (ng/mL)	16.42 ± 2.11	38.1 ± 2.89	–21.67	<0.001
Salivary visfatin (ng/mL)	19.94 ± 2.13	57.86 ± 3.35	–37.91	<0.001

Table 3: Comparison of clinical parameters pre-NSPT and post-NSPT in chronic periodontitis patients

Clinical parameters	*Group II1 (Pre-NSPT) N = 30*	*Group II2 (Post-NSPT) N = 30*	*T*	*p-value*
PI	2.99 ± 0.59	1.63 ± 0.39	10.47	<0.001
GI	2.06 ± 0.17	1.11 ± 0.20	23.16	<0.001
BOP (%)	99.8 ± 0.66	19.8 ± 13.42	32.55	<0.001
PD (mm)	5.27 ± 0.87	2.39 ± 0.67	27.48	<0.001
CAL (mm)	6.1 ± 0.88	3.09 ± 0.69	38.6	<0.001
PD > 4 mm (%)	49.43 ± 10.05	29.93 ± 10.35	31.86	<0.001
CAL > 5 mm (%)	48.01 ± 13.45	29.63 ± 7.44	13.80	<0.001

Table 4: Comparison of serum and saliva visfatin levels in chronic periodontitis patients recorded at pre-NSPT and post-NSPT

Laboratory parameters	*Group II1 (Pre-NSPT)*	*Group II2 (Post-NSPT)*	*T*	*p-value*
Serum visfatin (ng/mL)	38.1 ± 2.89	20.32 ± 4.84	17.45	<0.001
Salivary visfatin (ng/mL)	57.860 ± 3.355	19.62 ± 2.61	16.37	<0.001

Table 5: Correlation of serum visfatin and salivary visfatin with PD and CAL

			PD	*CAL*
Group I	Serum visfatin (ng/mL)	r	0.981	0.938
		p	<0.05	<0.05
	Salivary visfatin (ng/mL)	r	0.945	0.981
		p	<0.05	<0.05
Group II1	Serum visfatin (ng/mL)	r	0.874	0.916
		p	<0.05	<0.05
	Salivary visfatin (ng/mL)	r	0.951	0.965
		p	<0.05	<0.05
Group II2	Serum visfatin (ng/mL)	r	0.901	0.839
		p	<0.05	<0.05
	Salivary visfatin (ng/mL)	r	0.884	0.779
		p	<0.05	<0.05

r-value		
0.1–0.3 Weak positive	0.3–0.5 Moderate positive	0.5–0.9 Strong positive

In the current study, NSPT in chronic periodontitis patients led to a significant reduction of visfatin levels in saliva. The current findings matched those of Tabari et al., who found that visfatin levels in saliva dropped considerably after phase-I therapy NSPT.[18] Visfatin levels in blood and saliva were found to be positively linked with clinical indicators, including PD and CAL. Although clinical indicators such as GI, PI, CAL, and PD exhibited an association with visfatin levels in serum and saliva in a study done by Abolfazli et al., the association in the relationship was not statistically significant.[19] The association between salivary visfatin levels and clinical indicators was not significant in Tabari et al. investigation.[18]

Though posttreatment serum visfatin levels were reduced in comparison to pretreatment values, it was found to be high in comparison to healthy controls. However, posttreatment salivary visfatin levels of chronic periodontitis patients were found to be comparable to the healthy group. Tabari et al. found a similar lowering of salivary visfatin levels post-NSPT to that of the control group.[19]

During their investigation on adipokines and inflammatory cytokines in newborn sepsis, Cekmez et al. discovered that visfatin, like C-reactive protein, procalcitonin, and IL-6, might be employed as a marker of diagnosis in neonatal sepsis.[20] In the current study, visfatin was identified in detectable amounts in all serum and saliva samples from both groups. Chronic periodontitis patients had higher levels of visfatin in their serum and saliva. In chronic periodontitis patients, NSPT resulted in a significant decrease in levels of visfatin in serum and saliva. There was a positive correlation with clinical periodontal parameters such as PD and CAL. These findings could suggest that visfatin be used as a potential marker for chronic periodontitis and to assess the response to treatment in periodontal disorders.

Visfatin and its association with regard to various systemic diseases could possibly lead to the identification of a missing link between systemic and periodontal diseases.

Hence, it may be an acceptable option for assessing and evaluating the systemic disorders linked with it. Further follow-up studies involving large patient groups are necessary to validate our study results.

Limitations

The study sample size of the present research was rather small. The duration of the study was also less. Patients with systemic conditions were not included in the present study. Subjects with periodontal conditions like aggressive periodontitis were also not included in the study.

Conclusion

The present study results could lead us to conclude that visfatin could become a suitable marker for detecting periodontal disease progression and a possible target for evaluating the efficacy of treatment because of their rising levels in serum and saliva in chronic periodontitis subjects and their subsequent lowering in response NSPT.

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