



## Evaluation of Salivary Chemerin and Visfatin in Relation to Periodontitis and Obesity

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### Abstract

Periodontitis is a common disorder caused by imbalanced plaque biofilms and associated with gradual deterioration of the teeth supporting apparatus. Obesity is documented as a significant health concern and considered a primary risk factor for the progression of many diseases, such as hypertension, diabetes, malignancies, and periodontitis. Proinflammatory cytokines released in response to these health conditions are of great importance and establish the link between diagnosis and treatment. The present study was conducted to assess levels of chemerin and visfatin in saliva and to evaluate the impact of obesity on periodontitis. Ninety participants were included in the study and divided into three groups: (Group I: obese and periodontitis patients, n = 30), (Group II: periodontitis patients, n = 30) and (Group III: healthy controls, n = 30). We selected all participants based on their BMI measurement and examination of periodontal parameters. Unstimulated saliva was the obtained sample for evaluation of chemerin and visfatin using the ELISA technique. The study results found that chemerin and visfatin levels were different among study groups, but group I members have the highest levels, followed by group II and group III. In conclusion, obesity has a high impact on periodontitis through the expression of proinflammatory biomarkers in saliva like adipokines (cytokines produced by adipose tissue).

**Keywords:** Chemerin, Visfatin, Obesity, Periodontitis.

### 1. Introduction

Periodontitis is a major public health problem due to its widespread incidence and prevalence globally (1). It is generally initiated by dental plaque bacteria that later on interact with the host, resulting in a dysbiotic microbiome and dysregulated production of inflammatory substances that exacerbate inflammation and lead to periodontal tissue destruction and tooth loss (2). Obesity, on the other hand, is a medical condition characterized by excessive body fat that may lead to various complications (3). Adipose tissues are mainly infiltrated by macrophages that, together with adipocytes, can adversely affect the health of periodontium owing to increased levels of



proinflammatory cytokines in obese individuals in comparison with individuals of normal weight, with a hyperinflammatory reaction being observed in the periodontal tissue (4). In addition, obesity affects the oral microbiota through interference with the response of the immune system to periodontal pathogens, including *Porphyromonas gingivalis*, *Tannerella forsythia*, *Aggregatibacter actinomycetemcomitans*, and *Eubacterium nodatum* in subgingival biofilm (5). Host immune response to these pathogens could be a crucial part in the pathogenesis of periodontal disease. Chemerin and visfatin are two adipokines produced by the host that have been implicated in the pathogenesis of periodontal disease. Adipokines are cytokines produced by adipose tissue that regulate metabolism, inflammation, and immunity (6).

Chemerin is produced by adipose tissue, epithelial cells, and immune cells and is involved in the regulation of inflammation and immune cell recruitment. Elevated salivary levels have been recorded in patients with periodontal disease compared to healthy individuals and therefore could be used as an indicator for periodontitis. It also induces the synthesis of several cytokines, especially the pro-inflammatory ones, such as IL-1 $\beta$ , IL-6, and TNF- $\alpha$ , by immune cells and epithelial cells in the gingival tissues (7).

Visfatin is a discovered adipokine in the last decade that is not merely produced by immune cells but also by other inflammatory cells infiltrated in the adipose tissue, such as macrophages and leukocytes. It has immunoregulatory and proinflammatory properties, including leukocyte activation, production of adhesion molecules, and other cytokines. Increased levels of visfatin have been reported in obesity and other diseases (8).

## 2. Materials and Methods

This case control study was conducted from December 2021 to April 2022. Ninety subjects aged (30-40) years were enrolled in this study; all have been selected from Periodontics Clinic/ College of Dentistry/ University of Baghdad.

The following inclusion criteria were set in order to include subjects under this study (9):

1. Individuals with good general health with no history of any systemic diseases.
2. The presence of at least twenty or more natural teeth.

While the exclusion criteria were:

3. Individuals with any systemic diseases.
4. Use of antibiotics and anti-inflammatory drugs during the last month before examination.
5. History of smoking and hormonal disturbances.
6. Individuals under orthodontic treatment or others wearing prosthodontic appliances.
7. Pregnant women.

### 2.1. Groups of analysis included

- Group I: Thirty subjects with periodontitis and obesity (BMI ranged from 30-38).
- Group II: Thirty subjects with periodontitis and normal weight (BMI ranged from 20-24.9).
- Group III: Thirty subjects with healthy periodontium and normal weight (BMI ranged from 20-24.9).

## 2.2. BMI Measurement

The study assessed the body mass index (BMI) of each participant by dividing their weight in kilograms by the square of their height in meters ( $\text{Kg/m}^2$ ). BMI values falling between 25 and 29.9 indicate overweight, while values ranging from 30 to 34.9, 35 to 39.9, and above 40 signify mild or first-degree obesity, moderate or second-degree obesity, and severe or third-degree obesity, respectively (10).

## 2.3. Oral Examination

A clinical examination by a specialist dentist was performed for all study groups using a periodontal probe of William's graduation in order to record the following periodontal parameters: plaque index (PLI), bleeding on probing (BOP), probing pocket depth (PPD), and clinical attachment level (CAL) (11).

## 2.4. Sample Collection

Saliva was collected from patients and the control group between 9 and 12 am to evaluate the concentrations of levels of chemerin and visfatin in saliva. After the oral examination, ensure participants did not eat or drink for at least one hour before starting saliva collection. Each study participant provided four milliliters of unstimulated saliva by the drooling method, which is done by tilting the head and putting the plane tube close to the lips to allow the saliva to drool easily in a sterile tube. Then, each participant's saliva-collecting tubes were numbered and transported in an ice box to the laboratory. The collected saliva samples were then subjected to centrifugation at 3000 rpm for 10 minutes. After centrifugation, the supernatant was carefully collected and subsequently stored at  $-20^{\circ}\text{C}$  until it was ready for analysis (12).

## 2.5. Laboratory analysis of the study sample

Laboratory procedures were followed according to the manufacturer's instructions for Human-specific Enzyme-Linked Immunosorbent Assay (ELISA) kits (Chemerin: My BioSource, America) and (Visfatin: My BioSource, America).

## 2.6. Statistical analysis

The data obtained from the study were collected and analyzed using SPSS (statistical package of social science) software version 25 (Chicago, USA). The following tests were employed:

- One-way analysis of variance (ANOVA).
- Kruskal-Wallis test.
- Pearson correlation coefficient.
- Spearman's correlation coefficient

## 3. Results

According to the findings presented in **Tables 1** and **2**, the average levels of salivary Chemerin and Visfatin were observed to be highest in Group I, Group II, and finally Group III in sequence. A significant difference ( $P < 0.001$ ) was observed among the study groups in terms of these values. Additionally, **Tables 3** and **4** showed another statistical analysis to evaluate the correlation between both Chemerin and Visfatin and each of the evaluated periodontal parameters and BMI. The results were as follows:

For Group I, Chemerin and Visfatin had a significant correlation with each of PI, BOP, PPD, CAL, and BMI. While for Group II, Chemerin and Visfatin had a significant correlation with PI only, and a nonsignificant correlation was revealed with BOP, PPD, CAL, and BMI.

**Table 1.** The difference in mean rank values of chemerin among study three groups.

Chemerin	Study groups			Kruskal-Wallis test ( <i>P</i> -value)
	Group I periodontitis and obesity n=30	Group II periodontitis and normal weight n=30	Group III healthy periodontium and normal weight n=30	
Minimum	0.009	0.008	0.021	0.000**
Maximum	2.386	1.220	0.612	
Median	0.558	0.251	0.139	
Mean	36.30	24.70	15.54	
Rank				

**Table 2.** The difference in mean values of visfatin among study groups.

Visfatin	Study groups			ANOVA ( <i>P</i> -value)
	Group I periodontitis and obesity n=30	Group II periodontitis and normal weight n=30	Group III periodontitis and normal weight n=30	
Minimum	6.96	6.88	4.45	0.000**
Maximum	18.43	13.88	9.81	
Mean± SD	11.83±3.80	9.24±1.64	6.68±1.33	

**Table 3.** Spearman's correlation between chemerin and (clinical parameters and BMI) in Group I and Group II.

Group I periodontitis and obesity		
Chemerin	R-value	<i>P</i> -value
PI	0.595	0.001**
BOP	0.573	0.001**
PPD	0.509	0.004**
CAL	0.495	0.004**
BMI	0.656	0.000**
Group II periodontitis and normal weight		
Chemerin	R-value	<i>P</i> -value
PI	0.413	0.023*
BOP	0.238	0.205 <sup>NS</sup>
PPD	0.104	0.584 <sup>NS</sup>
CAL	0.061	0.749 <sup>NS</sup>
BMI	0.093	0.626 <sup>NS</sup>

**Table 4.** Pearson's correlation between Visfatin and (clinical parameters and BMI) in Group I and Group II.

<b>Group I</b>		
<b>periodontitis and obesity</b>		
<b>Visfatin</b>	<b>R-value</b>	<b>P-value</b>
PI	0.785	0.000**
BOP	0.760	0.000**
PPD	0.751	0.000**
CAL	0.676	0.000**
BMI	0.749	0.000**
<b>Group II</b>		
<b>periodontitis and normal weight</b>		
<b>Visfatin</b>	<b>R-value</b>	<b>P-value</b>
PI	0.421	0.020**
BOP	0.189	0.318 <sup>NS</sup>
PPD	0.229	0.230 <sup>NS</sup>
CAL	0.259	0.167 <sup>NS</sup>
BMI	0.188	0.320 <sup>NS</sup>

#### 4. Discussion

Obesity is associated with a low-grade inflammatory state that is characterized by uncontrolled fat deposition in the adipose tissue. As a consequence, a variety of cytokines are released from adipose tissue into oral fluids, participating in the pathogenesis of periodontitis (13). Many studies investigated salivary biomarkers as potential candidates of periodontal disease initiation and progression. Salivary samples are proven measures that are collected and analyzed easily for diagnostic purposes (14–18). For that reason, the current study was conducted to evaluate the impact of obesity on periodontitis and to determine the levels of salivary chemerin and visfatin on periodontitis patients in relation to obesity. The results of the present study revealed that Group I has higher salivary levels of Chemerin and Visfatin as compared to other study groups. Subjects within this group were obese with periodontitis, and this is consistent with the fact that obesity influences the expression of adipokines into the saliva of obese individuals (19). Visfatin had a significant role in periodontitis by promoting the expression of pro-inflammatory cytokines, including TNF  $\alpha$  and MMP (20). Chemerin has been shown to be involved in the regulation of osteoclast activity, which is responsible for the resorption of alveolar bone in periodontal disease (21). Several studies demonstrated the positive correlation between salivary levels of both with periodontitis, which came in accordance with the study results (22–24). Another explanation is that obesity and periodontitis are closely associated by triggering the initiation of inflammatory processes in periodontal tissues leading to the production of chemokines and proinflammatory cytokines (25). Regarding the evaluated periodontal parameters, the study exhibited a significant correlation between salivary levels of Chemerin and Visfatin with all parameters and BMI for Group I subjects; this came in agreement with other studies (19, 25, 26). Members of this group show elevated levels of both studied biomarkers, indicating dysregulation of the inflammatory response and tissue destruction in periodontal disease (22, 27). Conversely, Group II subjects showed no significant correlation across all parameters, with the exception of a positive correlation with PI. It is known that

periodontal disease is associated with inflammation and metabolic disturbances, and adipokines play a role in both of these processes. Therefore, it is possible to speculate on the potential positive correlation between the plaque index and Chemerin/Visfatin based on their involvement in the inflammatory response, as increased plaque accumulation is known to trigger an immune response initiated by increased secretion of Chemerin and Visfatin (28, 29).

## 5. Conclusion

In conclusion, Chemerin and Visfatin produced by the host play a critical role in the pathogenesis of periodontal disease. They could be used as a potential biomarker for periodontitis.

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## Conflict of Interest

The authors declare that they have no conflicts of interest.

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## Ethical Clearance

Accepted by the research ethics of the college of dentistry, University of Baghdad has reviewed the submitted research project with ethical approval ref. no. 401 in 20-12-2021

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