

Associations Between Body Mass Index, HbA1c Levels, Salivary MMP-9 Concentration, and Periodontal Parameters in Patients with and without Periodontitis

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Aim: Correlation among BMI, HBA1c, salivary MMP9, and periodontal parameters in patients with and without periodontitis.

Materials and Methods: 150 people participated in the case-control study and were divided into 75 patients with periodontitis (study group) and 75 with healthy periodontium (control group). Unstimulated saliva and serum samples were obtained from each participant before the clinical periodontal parameters' measurement involving PLI, BOP, PPD, and CAL, With age and BMI demographic factors. Saliva concentration of MMP9 and serum HBA1c were measured for each participant.

Results: The periodontitis group showed higher levels of salivary MMP9, serum HBA1c, and BMI measurement than the control group, with significant differences (P value <0.5). A positive significant correlation was found between MMP9 with PPD and CAL, also between BMI and PPD in the study group while for the control group, a positive significant correlation between MMP9 with BMI (P value <0.5)

Conclusion: The study shows a correlation between elevated levels of MMP9, HBA1c, and BMI with periodontitis. The complicated interaction between these factors in the onset and progression of periodontal disease is suggested by the positive correlations shown between BMI and PPD, as well as between MMP9 and PPD/CAL. More research is required to comprehend the underlying mechanisms completely and investigate potential therapeutic strategies that target these characteristics.

Keywords: Saliva, Periodontitis, HBA1C, BMI, MMP9

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Introduction

Persistent inflammatory reactions associated with pathological degradation of the alveolar bone and the periodontal ligaments are characteristic of periodontitis, characterized by a wide range of complex and continuously changing interactions between bacterial infections and harmful immune reactions.¹

Risk factors significantly affect an individual's reaction to periodontal infection. Identifying these risk variables enables patients to be targeted for treatment and prevention. Persons with high body mass index (BMI) scores reported being at risk for periodontitis. They had a 56% greater chance of developing periodontitis for every 1 kg/m² increase in their body mass index. This means that people with a higher BMI may be more likely to get periodontitis. Kim et al.'s systematic review and new meta-analysis from 2022 found that being overweight is linked to periodontitis. The study looked at 29 studies that reported the number of cases or risk ratios of BMI and periodontal disease. In 17 of them, the chance of periodontitis was higher in people who were overweight. Periodontal disease was 1.35 times more likely to happen in people who were overweight than in people who were not overweight. In diabetic patients, BMI could be associated with glycated hemoglobin (HbA1c).

Doctors frequently employ the hemoglobin A1c test in clinical settings to track patients' average blood sugar levels over a few months. Elevated levels of HbA1c can be used as a reliable marker to indicate inadequate glycemic control. In 2009, Hayashida discovered a strong link between periodontal health and HbA1c values in people who were not diabetic. A Cochrane analysis conducted in 2010 demonstrated a significant reduction of 0.4% in HbA1c levels following periodontal therapy. In 2013, a meta-analysis revealed that non-

surgical periodontal therapies were associated with decreased HbA1c levels, emphasizing the possible correlation between periodontal care and enhanced glycemic management. Vadakkekuttal 2017 also found that chronic periodontitis affected HbA1c levels in otherwise systemically healthy individuals. These findings indicate that periodontal inflammation may contribute to elevated HbA1c levels.

The proteolytic enzyme matrix metalloproteinase-9 (MMP-9) is accountable for type IV collagen degradation., a crucial structural constituent of the basement membrane. The enzyme above assumes a vital function in the etiology of periodontitis. Initial findings suggest a correlation between the expression of MMP-9 and the detrimental effects on periodontal tissue observed during the active phases of periodontitis. According to the findings of a study, MMP-9 has a substantial relationship to the higher rate of periodontal damage. Recent studies focus on the diagnostic accuracy of MMP-9 to differentiate periodontal health from disease. This study aims to investigate how BMI, HbA1c levels, salivary MMP-9 concentration, and periodontal parameters relate to one another in people with and without periodontitis.

Materials and Methods

Study design

An observational case-control study was conducted at the University of Baghdad College of Dentistry between January and June 2023. following the ethical principles of the Declaration of Helsinki, The College's Ethics Committee granted ethical approval. All participants provided informed consent and signed it after a comprehensive explanation of the study.

Sample Size Calculation

The sample size was calculated using the following formula:

$n = (Z^2 * p * q) / d^2$ where

n is the sample size

Z is the critical value from the Z-table for a desired level of confidence

p is the estimated prevalence of periodontitis

q is the estimated prevalence of healthy controls

d is the margin of error

Assuming a prevalence of periodontitis of 50% and a margin of error of 5%, the calculated sample size was 75 subjects per group. Participants were then divided equally into two groups: a control group with healthy periodontal conditions and a group diagnosed with unstable periodontitis.

Study Participants

150 people aged 30-60 years old shared in the study, which investigated the link between periodontal health with salivary and blood markers. Participants were divided into two equal groups: one with healthy gingiva (control group) and one with periodontitis. Healthy gingiva was defined as having minimal bleeding on probing (<10%), shallow gingival pockets (≤ 3 mm), and no bone loss. Periodontitis was characterized by periodontal pockets (≥ 5 mm or 4 mm, accompanied by BOP).

The study included participant enrolment, evaluation of eligibility, and examination of periodontal clinical parameters, and saliva samples. Conversely, serum sampling took place at the Baghdad blood bank. BMI measurement, the data was analyzed statistically.

Criteria of eligibility

Healthy individuals with at least 20 teeth, who hadn't used antibiotics or NSAIDs in the last 3 months, were eligible for the study. Periodontitis cases were defined if CAL was detected at ≥ 2 non-adjacent teeth or when buccal (facial) or lingual/palatal showed CAL ≥ 3 mm associated with PPD

>3 mm at ≥ 2 teeth. Smoking, alcohol consumption, chronic illnesses, compromised immunity, and oral lesions were excluded from participants.

Examination of the periodontium

Using a specialized tool (UCN-15 probe), a trained periodontist conducted a comprehensive examination of the gingiva. Every tooth in the mouth, except wisdom teeth, had six important sites of gingival health, and periodontal parameters tested by the examiner. One aspect of this was looking for plaque accumulation (PLI). Bleeding on probing (BOP%), pocket probing depth (PPD), and clinical attachment level (CAL).

Saliva sampling

Before saliva collection, participants fasted for 30 minutes and rinsed their mouths thoroughly with water to remove any potential contaminants. Whole, unstimulated saliva was collected into sterile test tubes²⁵. After centrifugation at 1000 rpm for 15 minutes, transparent saliva supernatants were carefully transferred to Eppendorf tubes using a micropipette for further analysis. The tubes were labeled and stored at -20°C until needed.

Serum sampling

Participants underwent venipuncture for blood collection, using gel and activator tubes. Following a 30-minute room temperature incubation to allow clotting, the tubes were centrifuged for 10 minutes at 3000 rpm to isolate the serum. The extracted serum was then portioned into 2 ml aliquots in sterile Eppendorf tubes and stored frozen at -20°C before analysis²⁶. Blood samples were collected and analyzed for glycated hemoglobin (HbA1c).

Measurement of BMI

The height (in meters) and weight (in kilograms) of each participant were recorded

for calculating the body mass index (BMI). Most people understand it as an indicator of a person's level of fatness²⁷ BMI was computed and expressed in kg/m² units by dividing the body weight in kilograms by the square of the height in meters. According to current recommendations from the WHO and the US Centers for Disease Control and Prevention

(CDC), an adult's normal BMI falls between 18.5 to 24.9, while a BMI between 25 and <30 is regarded as overweight, and a BMI ≥ 30 kg/m² is classified as obese.²⁸

Results

This study looked at clinical periodontal parameters, biomarkers, and demographics in both the healthy and periodontitis groups. Next, it evaluated the correlations between Body Mass Index, HbA1c Levels, Salivary MMP-9 Concentration, and Periodontal Parameters in Patients with and without Periodontitis.

Using the Shapiro-Wilk test, the data sets were analyzed to check normality and were normally distributed. The clinical periodontal data and demographics for the groups with periodontitis and healthy periodontium are displayed in Table 1. Different parameters showed statistically significant differences between the groups. Participants in the periodontitis group were slightly older than those in the healthy group. But at $p = 0.061$, this difference was not statistically significant. Notably, the clinical attachment level (CAL), probing pocket depth (PPD), bleeding on probing (BOP%), and plaque index (PLI) were found to be higher in periodontitis patients. All of these measurements showed statistical significance with p-values less than 0.01.

Furthermore, it was noted that the group with periodontitis had much higher salivary levels of MMP9 and serum levels of hba1c than the healthy group did, with a statistical significance ($p < 0.01$).

Sd: Standard Deviation, BMI: Body Mass Index, PLI: Plaque index, BOP: bleeding on probing, hba1c: Significant at $P < 0.05$

Table 1: Statistical analysis of demographic factors, periodontal parameters, and biomarkers concentration in both group

Groups	Healthy periodontium Mean $\pm$ Sd	Periodontitis Mean $\pm$ Sd	PValue Control vs Periodontitis
Age	32.69 $\pm$ 5.209	34.29 $\pm$ 5.193	0.0615 NS
BMI	28.11 $\pm$ 3.44	30.63 $\pm$ 4.16	<0.0001**
PLI%	29.65 $\pm$ 20.09	76.99 $\pm$ 18.22	<0.0001**
BOP%	5.58 $\pm$ 2.16	83.45 $\pm$ 16.8	<0.0001**
PPD	/	5.340 $\pm$ 0.98	/
CAL	/	3.64 $\pm$ 0.99	/
hba1c	5.66 $\pm$ 0.414	5.837 $\pm$ 0.36	0.0078*
mmp9	255.4 $\pm$ 69.28	374.9 $\pm$ 76.42	<0.0001**
Total number	75	75	/

** Significant at $P < 0.001$ S: Non-Significant

The Correlation between periodontal parameters with serum HbA1c and salivary MMP9 in periodontitis and control groups

The correlation between periodontal parameters (PLI, BOP), BMI, with salivary MMP9, and the level of HbA1c for the control group, as illustrated in Figure 1 using Pearson correlation coefficients, a significant positive correlation was found between salivary MMP9 and BMI (P value < 0.5)

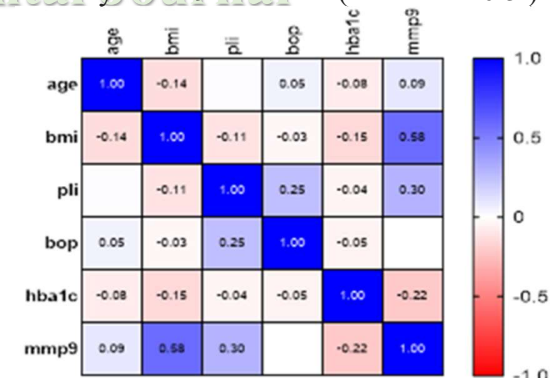


Figure 1: Correlation of the parameters in the control group

For the periodontitis group figure (2) exhibited there is a positive significant correlation between PPD with BMI (p-value < 0.05). Regarding salivary MMP9, there is a positive significant correlation with PPD, CAL.

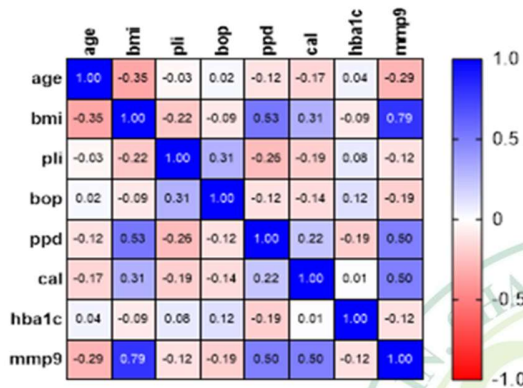


Figure 2: Correlation of the parameters in the periodontitis group

Discussion

The study showed that the BMI, HbA1c, and salivary MMP9 concentration significantly increased in periodontitis patients than healthy controls. Regarding salivary MMP9, there is a positive, significant correlation with PPD and CAL, and also a positive significant correlation between BMI and PPD in periodontitis patients, while for the control group, salivary MMP9 showed a positive, significant correlation with BMI.

The study's findings cannot be applied to individuals with different sociodemographic characteristics or environmental backgrounds because the sample size was restricted to a single university dental clinic. Furthermore, it was not possible to ascertain whether the onset and advancement of periodontal disease preceded an increase in HbA1c levels due to the use of case-control data collection. Longer-term, more thorough research is required to identify and clarify the causal relationship between HbA1c levels and the different stages of periodontitis.

The 2018 classification emphasizes staging according to disease severity and

management complexity, combining aggressive and chronic forms of periodontitis into a single category. Despite the new categorization providing a thorough framework, others contend that because periodontitis is a complicated condition with a wide range of clinical presentations, it may still not be precisely defined.^{29,30}

HbA1c screening for diabetes is convenient and effective in diagnosing diabetes. It may not be valid in certain subgroups, such as children, women with gestational diabetes, and those with prediabetes.³ Studies reveal a reciprocal association between glycemic control and periodontitis, implying that glycemic levels in diabetic patients might be considerably improved by periodontal treatment. They highlighted the significance of controlling periodontal health for better diabetes outcomes, with an average reduction in HbA1c of 0.43% observed after treatment.³²

The use of salivary biomarkers as a non-invasive substitute for conventional clinical evaluations in diagnosing and surveillance periodontal disease is becoming more widely acknowledged. These biomarkers can reveal a treatment's existence, intensity, and effectiveness. Studies reveal a correlation between increased levels of inflammatory mediators and periodontal disease clinical characteristics, indicating that these mediators may serve as markers of the severity of the illness.³³

Compared to people with healthy periodontal tissue, those with periodontitis had a noticeably higher salivary concentration of MMP9 as the result of this study, which may result from the loss of both soft and hard tissues and a breach in the basal membrane structure. During the active stage of periodontitis, an imbalance in the execution of host-derived proteinases, particularly MMP-9, results in bone loss, soft tissue injury, and deepening of periodontal

pockets.³⁴ This explains the positive significant correlation of MMP9 with periodontal parameters, PPD, and CAL. These results align with Kim in 2016, who found that high levels of salivary MMP-9 were associated with periodontitis.³⁵ Salivary MMP-9 levels are associated with obesity and periodontitis. In a study analyzing salivary proteomics in pregnant women, MMP-9 was found to be significantly up-regulated in the combination of obesity and periodontitis.³⁶ Another study developed a diagnostic algorithm for periodontitis using salivary MMP-9, which showed appropriate diagnostic ability.^{37,38} Additionally, a study evaluating the association of salivary MMP-9 with periodontitis found that high MMP-9 levels were associated with periodontitis.³⁹ These findings suggest that salivary MMP-9 may serve as a potential marker for periodontitis, particularly in the context of obesity.

Body Mass Index (BMI) is a widely utilized metric for assessing body weight relative to height, serving as a simple screening tool for obesity and related health risks. While it provides valuable insights into population health trends, its limitations necessitate a nuanced understanding of its implications. The BMI mean was equal to 30.63 in the periodontitis group. According to the WHO they are considered obese patients, and there is no correlation between BMI and periodontal parameters in the case group, these results were consistent with the study done by Castilhos et al. 2012. Although body mass index (BMI) and adiposity normally have a strong correlation, BMI can occasionally be misleading and misclassify total fat content and body fat distribution.⁴⁰ For instance, because muscle weighs more than fat, athletes with larger muscles typically have higher BMIs even when not obese. Furthermore, the tallest and shortest participants are frequently incorrectly labeled as obese.⁴¹ Although WC is a more accurate

predictor of disease than BMI, further research is required to decide which measure should be used to estimate the risk of disease: WC or BMI.⁴² (Kopelman, 2000). The BMI mean in the control group was 28.11 they are considered overweight according to WHO 2021 and a positively significant correlation was found between BMI and MMP9, in the majority of the investigations. The majority of the research indicated that adipocytes release proinflammatory cytokines including TNF- α and IL-6, MMP9 which increase the increasing the susceptibility to bacterial infection as periodontitis is a chronic condition that involves multiple factors. The buildup of microbial biofilm causes it and involves various interactions between specific bacterial species, harmful immune responses of the host, and different environmental factors.^{43,44} Dysbiotic plaque biofilm is the main etiologic factor for the chronic multifactorial inflammatory disease known as periodontitis.⁴⁵

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