UDK: 616.311.2:[611.018.26:577.112

INFLUENCE OF SERUM ADIPONECTIN CONCENTRATION ON GINGIVAL HEALTH IN FEMALE PATIENTS WITH INCREASED BMI

ВЛИЈАНИЕ НА СЕРУМСКИТЕ КОНЦЕНТРАЦИИ НА АДИПОНЕКТИН ВРЗ ГИНГИВАЛНО ЗДРАВЈЕ КАЈ ПАЦИЕНТКИ СО ЗГОЛЕМЕН ВМІ

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Abstract

Relationship between circulating adiponectin levels and gingival health in women with high BMI

Chronic periodontal disease is an inflammatory condition characterized by a shift in the microbial ecology of subgingival plaque biofilms and the progressive host-mediated destruction of tooth-supporting structures. There has been considerable interest in drawing connections between periodontal inflammation and other chronic conditions. Although anti-inflammatory mediators, antagonize the pro-inflammatory activities, the balance between pro- and anti-inflammatory mediators is shifted towards inflammation. Recent data point out that inflammation is associated with lower levels of adiponectin. Adiponectin is adipocytokine secreted by the fat tissue that is involved in the energy homeostasis and the regulation of the metabolism of fat and carbohydrates and exhibits anti-inflammatory effect. The levels of circulating adiponectin are inversely related with body mass index and tend to be lower in obese subjects. The aim of our study was to determine connection between serum levels of adiponectin and gingival inflammation in obese women. **Materials and methods**: The study included 45 women, aged 21- 60 years with BMI range 25.8 – 50.2 kg/m^2. The study group was selected from the participants in the project MONODIET run at the Institute of Pathophysiology and Nuclear Medicine, at the Medical faculty in Skopje. The presence of endocrinologic disorders, pregnancy, lactation, hormonal or antilipidemic drugs were exclusion criteria. Adiponectin levels were determined by competitive radioimmunoassay and gingival inflammation was estimated clinically using the criteria proposed by Sillness Loe. The statistical analysis of the data was performed with Pearson's correlation and two sample unpaired t-test. The probability level <0.05 was considered statistically significant. **Results:** The adiponectin levels ranged from 3.3 ng/ml to 28.07 ng/ml. The mean value was 10.58+/- 4.7 ng/ml. The adiponectin levels showed negative correlation (r -0.7643, p<0.02, r-0,7776, p<0.002).) with gingival inflammation and bleeding as well.The results from our study showed inverse correlation between adiponectin and gingival inflammation and bleeding. In accordance with the obtained results we concluded that the lower levels of adiponectin lead to stronger clinical expression of gingival inflammation and bleeding. **Keywords:** Adiponectin, serum, BMI, gingiva, inflammation.

Апстракт

Хроничната пародонтална болест е воспалителна состојба која се карактеризира со промена во микробната екологија на биофилмовите на субгингивалниот плак и прогресивно уништување на структурите што го потпоруваат забот со посредство на домаќинот. Постои значителен интерес за поврзување помеѓу пародонталната инфламација и други хронични состојби. Иако антиинфламаторните медијатори ги антагонизираат проинфламаторните активности, рамнотежата помеѓу про- и антиинфламаторните медијатори е насочена кон воспаление. Неодамнешните податоци покажуваат дека воспалението е поврзано со пониски нивоа на адипонектин.Адипонектинот е адипоцитокин што се лачи од масното ткиво, кој е вклучен во енергетската хомеостаза и регулирањето на метаболизмот на мастите и јаглехидратите и покажува антиинфламаторно дејство. Нивоата на циркулирачки адипонектин се обратно пропорционални со индексот на телесна маса и имаат тенденција да бидат пониски кај обезни лица. Целта на нашата студија беше да се утврди врската помеѓу серумските нивоа на адипонектин и гингивалната инфламација кај дебели жени. **Материјали и метод:** Студијата опфати 45 испитаници од женскиот пол на возраст од 21- 60 години со вредност на ВМІ од 25.8 до 50.2 kg/m^2. Пациентките со ендокрини, метаболни пореметувања , бременост, лактација како и хиперлипидемија беа исклучени од студијата. Кај сите пациентки беше одреден БМИ, серумското ниво на адипонектин и клинички беше одреден индексот на гингивална инфламација по Sillness Loe. Адипонектинот беше одредуван на Институтот за патофизиологија и нуклеарна медицина со помош на компетитивна радиоимуноесеј метода . За статистичката анализа беше користен Pearson-овиот тест за корелации и Студентов t-тест за независни примероци. Степенот на веројатност <0.05 се сметаше за статистички сигнификантен. **Резултати:** Серумските вредности на адипонектин се движеа во распон од 3.3 ng/ml до 28.07ng/ml. Средната вредност изнесуваше 10.58+/- 4.7 ng/ml. Pearson-овиот тест за корелации покажа статистички значајна негативна корелација со индексот на гингивална инфламација и гингивално крвавење (r -0.7643, p<0.02, r-0,7776 p<0.002). Добиените резултати ни дозволуваат да заклучиме дека намалените нивоа на адипонектин кај пациентите учествуваат во клиничкото потенцирање на гингивалната инфламација и крвавење. **Клучни зборови:** адипонектин, серум, ВМІ, гингива, инфламација.

Introduction

Periodontal disease is a multifactorial condition characterized by the destruction of periodontal tissues due to an inflammatory response to bacterial plaque accumulation. Its pathogenesis involves the activation of the host immune responses, which leads to the release of pro-inflammatory cytokines such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). These mediators contribute to tissue degradation and alveolar bone loss[1]. Chronic inflammation in periodontal disease has also been associated with systemic conditions such as diabetes, cardiovascular disease, and obesity[2].

Recent research has highlighted the role of adipokines-bioactive molecules secreted by adipose tissue-in modulating inflammatory responses within periodontal tissues. Among these, adiponectin has garnered significant attention due to its anti-inflammatory properties and potential influence on periodontal health[3].

Adiponectin is a 30 kDa protein composed of 244 amino acids, structurally characterized by a collagen-like domain and a globular domain. It circulates in the blood in three forms: low-molecular-weight (LMW), medium-molecular-weight (MMW), and high-molecular-weight (HMW) oligomers. The HMW form is considered the most biologically active and is closely associated with insulin sensitivity and anti-inflammatory effects[4]. Adiponectin exerts its effects through two primary receptors, AdipoR1 and AdipoR2, which are widely expressed in various tissues, including the liver, skeletal muscle, and immune cells[5].

Adiponectin has been shown to inhibit the production of pro-inflammatory cytokines such as TNF-α and IL-6, which are elevated in periodontal disease while promoting the secretion of anti-inflammatory cytokines like IL-10, thus modulating the overall inflammatory response[6]. Additionally, Adiponectin influences the activity of osteoblast and osteoclast activity, contributing to bone remodeling. Studies suggest that adiponectin can inhibit osteoclasts genesis and reduce bone resorption, which is beneficial in preventing alveolar bone loss in periodontal disease[7].

Adiponectin plays an important role in improving insulin sensitivity, which is particularly relevant given the bidirectional relationship between diabetes and periodontal disease. Improved glycemic control may reduce the severity of periodontal inflammation and vice versa[8].

Emerging evidence also indicates a significant association between adiponectin levels and periodontal disease. Studies have shown that adiponectin exerts anti-inflammatory effects by inhibiting the expression of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukins (IL-1β, IL-6, IL-8) in periodontal ligament cells. In addition, adiponectin has been shown to counteract the stimulatory effects of periodontal pathogens like Porphyromonas gingivalis, thereby reducing the production of matrix metalloproteinases (MMP-1 and MMP-3) involved in tissue degradation[9].

Therefore, the aim of our study was to investigate the correlation between serum levels of adiponectin and gingival bleeding and gingival inflammation in women with high BMI

Material and methods

The study included 47 women, aged 21- 60 years with BMI values ranging from 25.8 to50.2 kg/m2. The study group was selected from the participants in the MONODI-ET project conducted at the Institute of Pathophysiology and Nuclear Medicine, at the Faculty of Medicine in Skopje. The presence of endocrinologic disorder, pregnancy, lactation, hormonal or antilipidemic drugs were exclusion criterium.

In all patients, BMI, serum adiponectin levels, and the gingival inflammation and gingival bleeding index were clinically assessed according to theSilness and Löe index.

All participants met criteria to have plaque index not higher than1 according to Green-Vermilion index.

Adiponectin levels were measured at the Institute of Pathophysiology and Nuclear Medicine using a competitive radioimmunoassay method. RIA is based on the competitive binding of a radiolabeled antigen (tracer) and an unlabeled antigen (from the sample) to a limited number of specific antibodies. The amount of radiolabeled antigen bound to the antibody is inversely proportional to the concentration of the unlabeled antigen in the sample.

For statistical analysis, Pearson's correlation test and Student's t-test for independentsampleswere used. A p-value<0.05 was considered statistically significant.

Results

The adiponectin levels among participants ranged from 3.3 ng/ml to 28.07 ng/ml. The mean value was 10.58+/- 4.7 ng/ml.

Table 1. Statistical comparation between levels of gingival inflammation and circulating levels of adiponectin

Inflammation		t	p
Index1	20,3 ng/ml.		
Index2	14,7 ng/ml.	2,39	0,0413
Index3	8,6 ng/ml.	3,48	0,0245

The results obtained from our study are presented in the following tables and graphics

Table 1 presents inflammation-related indices and their corresponding values of circulating adiponectin values. The columns include measured values (in ng/ml) and statistical data.

- **Index 1:** The measured value is 20.3 ng/ml.
- **Index 2:** The measured value is 14.7 ng/ml, with a t-value of 2.39 and a p-value of 0.0413. The p-value suggests a statistically significant difference at the 0,05 significance level.
- **Index 3:** The measured value is 8.6 ng/ml, with a t-value of 3.48 and a p-value of 0.0245. The lower p-value indicates a stronger statistical significance compared to Index 2.

Table 2. Statistical difference between levels of gingival bleeding on probing and circulating levels of adiponectin

G bleeding		t	p
Index 1	18,6 ng/ml.		
Index 2	12,3 ng/ml.	1,58	0,0493
Index 3	9,5 ng/ml.	2,89	0,059

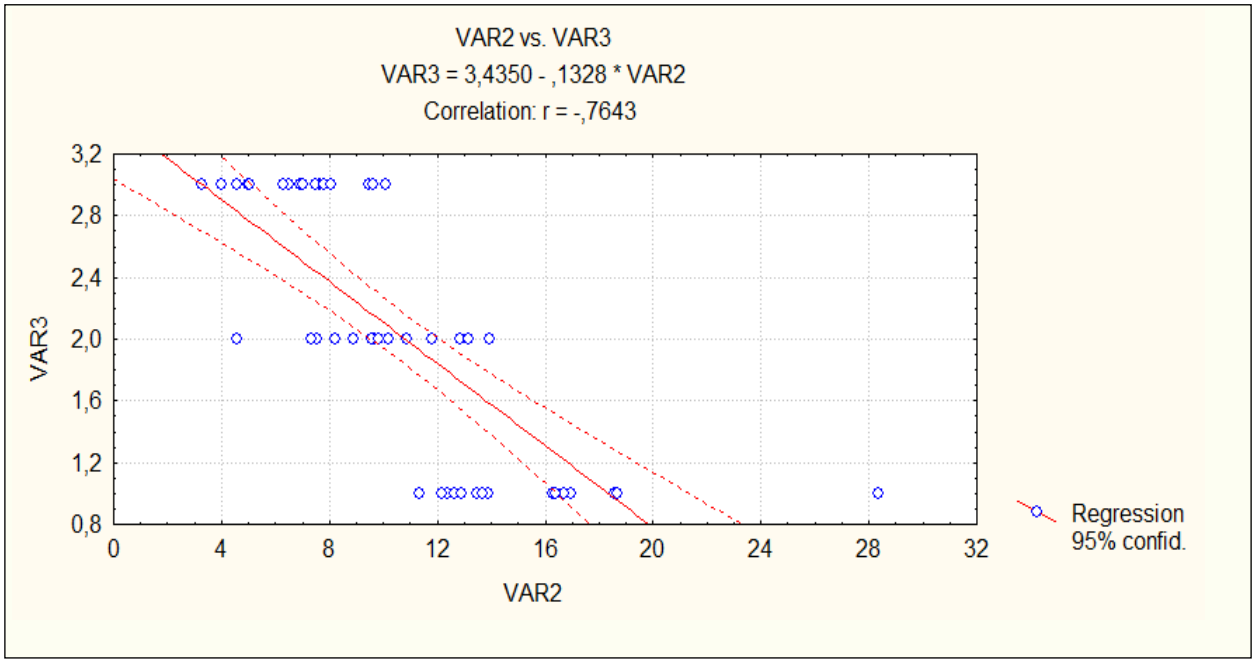
The statistical values (t and p) represent the results of a comparison, between different conditions or groups compared to the first group. A p-value below 0.05 generally indicates statistical significance, meaning the observed differences are unlikely due to random variation.

The table 2 presents data related to G bleeding and includes measured values of adiponectin serum levels, along with statistical parameters (t-value and p-value).

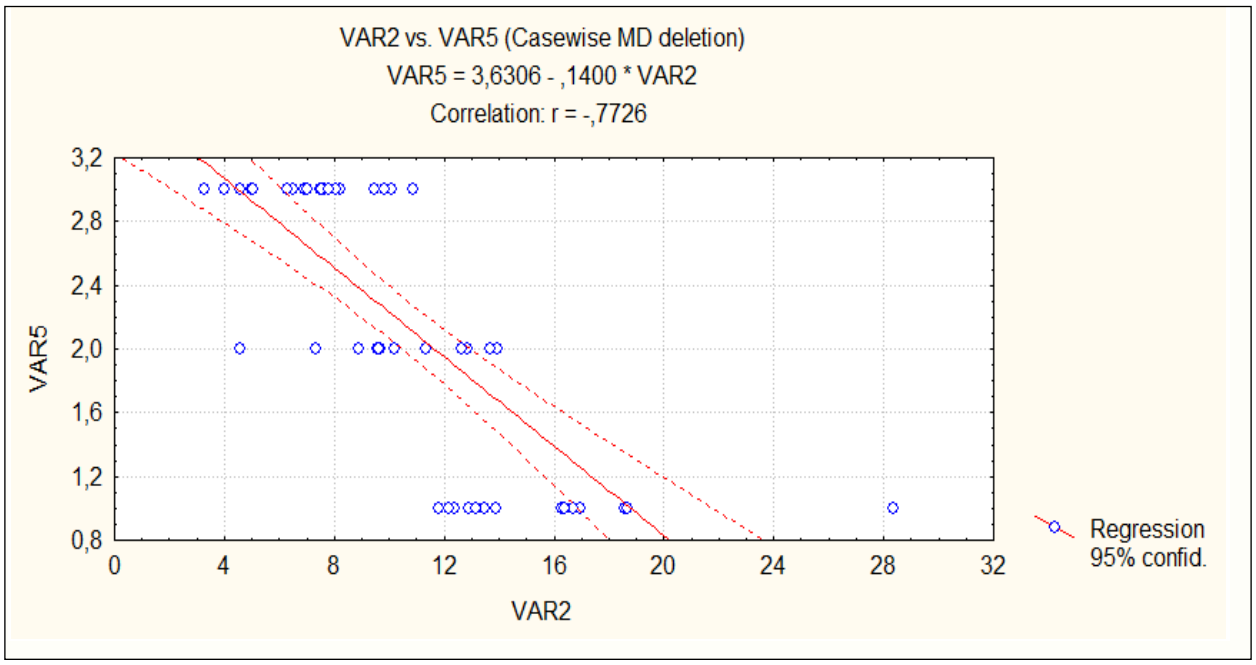
- **Index1:** The concentration is 18.6 ng/ml.
- **Index2:** The concentration is 12.3 ng/ml, with a t-value of 1.58 and a p-value of 0.0493. The p-value is close to the 0.05 threshold, indicating a statistically significant difference.
- **Index3:** The concentration is 9.5 ng/ml, with a t-value of 2.89 and a p-value of 0.059. The p-value is slightly above 0.05, suggesting that the difference is not statistically significant at the conventional level but may still indicate a trend toward significance.

Graph1 illustrates the relationship between adiponectin (VAR2) and gingival bleeding (VAR3) based on a regression analyses Correlation (r =-0.7643): The negative correlation coefficient (-0.7643) indicates a strong inverse relationship between adiponectin and gingival bleeding.

The graph 2 shows the relationship between adiponectin and gingival inflammation based on a regression analyses. This indicates that as adiponectin levels increase, gingival inflammation decreases. Correlation (r = -0.7726) The negative correlation coefficient (-0.7726)



Graph 1. Correlation between gingival bleeding and adiponectin



Graph 2. *Correlation between gingival inflammation and adiponectin*

suggests a strong inverse relationship between adiponectin and gingival inflammation.

Discussion

Periodontal disease arises from the interactions between periopathogenic bacteria and the host defense system. Bacterial products such as LPS, antigen, penetrate the gingival tissue triggering the inflammatory response. As a result of this interaction, inflammatory mediators such as cytokines, chemokines, adipokines, and arachidonic acid metabolites are released, which play an important role in disease progression and tissue destruction[10,2].

Adipokines are biologically active molecules produced by the adipose tissue. Adipokines such as adiponectin play an important role in periodontal inflammation.

Adiponectin possesses anti-inflammatory properties that may protect against periodontal inflammation by counteracting the effects of periodontal pathogens and their associated inflammatory responses[11,12].

The aim of our study was to assess the effect of adiponectin on gingival inflammation. Regarding gingival inflammation, our findings demonstrated that lower serum levels of adiponectin were associated with severe inflammation, while higher levels of adiponectin correlated with reduced inflammation (Table 1).

The negative correlation coefficient (-0.7726) indicates a strong inverse relationship between adiponectin and gingival inflammation. Higher adiponectin levels were associated with lower levels of gingival inflammation. Given adiponectin is an anti-inflammatory protein, this graph supports the hypothesis that higher adiponectin levels might help reduce gingival inflammation. The strong inverse correlation suggests that adiponectin could play a protective role in periodontal health (Graph 2.)

Adiponectin mediates its protective effects through several mechanisms, including:

Inhibition of Pro-inflammatory Cytokines: By suppressing the production of TNF-α and interleukins, adiponectin reduces the inflammatory response within periodontal tissues. Studies demonstrate that adiponectin is synthesized by oral epithelial cells and can modulate inflammatory responses induced by P.gingivalis lipopolysac charide. Adiponectin was found to downregulate pro-inflammatory cytokines such as IL-1β, IL-6, and IL-8, while upregulating anti-inflammatory mediators like IL-10[9].

Similar results were observed for gingival bleeding (Table 2, Graph 1). Higher adiponectin levels are associated with lower levels of gingival bleeding. Adiponectin, known for its anti-inflammatory properties, appears to have a protective role in reducing gingival bleeding. The strong inverse correlation suggests that higher adiponectin levels may contribute to better periodontal health by reducing bleeding in the gums.

Our findings align with previous research. For example, studies by Yamaguchi et al[6] also reported an inverse correlation between adiponectin levels and inflammatory markers in periodontal disease, reinforcing its protective

role in periodontal health. Similar results were observed by Fairlin P et al[13]., who demonstrated that higher adiponectin concentrations in gingival fluid were linked to reduced gingival inflammation and improved periodontal outcomes.

The same results were obtained for gingival bleeding (Table 2, Graph 1). Higher adiponectin levels are associated with lower levels of gingival bleeding. Adiponectin, known for its anti-inflammatory properties, appears to have a protective role in reducing gingival bleeding. The strong negative correlation suggests that higher adiponectin levels may contribute to better periodontal health by reducing bleeding in the gums. A study by Duzagac et al.[14] found that patients with chronic periodontitis had significantly lower serum adiponectin levels compared to healthy controls, suggesting a protective role of adiponectin in periodontal health.

Conversely, another study by Furugen et al.[15] reported elevated adiponectin levels in gingival crevicular fluid (GCF) of patients with periodontitis, indicating a localized anti-inflammatory response.

These findings highlight the complex role of adiponectin in periodontal disease, which may vary depending on the site of measurement (systemic vs. local) and the stage of the disease.

Thus, our study, together with previous research, supports the hypothesis that adiponectin is a significant modulator of gingival inflammation and bleeding, highlighting its potential as a biomarker for periodontal health.

Conclusion

Adiponectin plays a pivotal role in modulating inflammation and bone metabolism within periodontal tissues. Its anti-inflammatory and bone-protective properties make it a promising target for therapeutic interventions in periodontal disease. Future studies should focus on understanding the precise mechanisms of adiponectin action and exploring its potential in clinical applications for periodontal therapy.

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