ORAL HEALTH

CORRELATION BETWEEN SALIVARY URIC ACID VALUES AND RISK FACTORS ASSOCIATED WITH METABOLIC SYNDROME

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Abstract

Introduction: The fast pace of modern life contributes to an increased prevalence of metabolism-related diseases. Since these diseases can be prevented through lifestyle modification, a new approach in medicine is needed, i.e. one that focuses on the early identification of individuals at higher risk. A promising noninvasive monitoring tool is the use of salivary biomarkers. Of particular interest is salivary uric acid, as a linear association between its serum and salivary concentrations has been demonstrated. Aim: To determine the correlation between various risk factors associated with metabolic syndrome and the salivary concentration of uric acid. Materials and Methods: A cross-sectional study was conducted among 156 students (aged 20–25 years) from the Faculty of Dentistry, Faculty of Medicine, and Faculty of Pharmacy at Ss. Cyril and Methodius University in Skopje. In the Biochemical Laboratory of the Faculty of Dentistry, body weight, height, waist circumference, blood pressure, and pulse of the studied participants were measured. Unstimulated saliva samples were collected using the spitting method. Uric acid concentration was determined spectrophotometrically using the enzymatic URICASE/PEROXIDASE method. The obtained data were statistically analyzed and correlated with anthropometric parameters, blood pressure, pulse, and body mass index. Results: The results showed a significant correlation between salivary uric acid levels and body weight ($p<0.001$), body mass index ($p<0.001$), waist circumference ($p< 0.001$), systolic blood pressure ($p<0.001$), and diastolic blood pressure ($p<0.001$). Conclusion: Our findings suggest that salivary uric acid may serve as a reliable noninvasive biomarker for detecting cardiometabolic risk factors.

ОРАЛНО ЗДРАВЈЕ

КОРЕЛАЦИЈА ПОМЕЃУ САЛИВАРНИТЕ ВРЕДНОСТИ НА УРИЧНА КИСЕЛИНА И РИЗИК-ФАКТОРИТЕ ПОВРЗАНИ СО МЕТАБОЛИЧКИОТ СИНДРОМ

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Цитирање: Анастасовска М, Попоски Б, Андоновска М, Идоска С, Идоски Е, Коколански В. Корелација помеѓу саливарните вредности на урична киселина и ризик-факторите поврзани со метаболичкиот синдром Арх Ј Здравје 2025; 17 (2) 87-89.

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Клучни зборови: плунка, урична киселина, метаболички синдром, оксидативен стрес, неинвазивна дијагностика

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Печатарски права: ©2025 Мартина Анастасовска, Бојан Попоски, Марија Андоновска, Санела Идоска, Енвер Идоски, Влатко Коколански. Оваа статија е со отворен пристап дистрибуирана под условите на нелокализирана лиценца, која овозможува неограничена употреба, дистрибуција и репродукција на било кој медиум, доколку се цитираа торигиналниот(ите) автор(и) и изворот.

Конкурентски интереси: Авторот изјавува дека нема конкурентски интереси.

Извадок

Вовед: Брзото темпо на живеење на современиот човек е една од причините за зголемување на стапката на заболувања поврзани со метаболизмот на човекот. Бидејќи овие заболувања можат да бидат превенирани преку менување на начинот на живот, се бара нов пристап во медицината кој би подразбирал идентификација на индивидуи со зголемен ризик за појава на овие заболувања. Еден од пристапите за неинвазивен мониторинг е користењето на саливарните биомаркери. Од особен интерес во истражувањата е саливарната урична киселина, бидејќи е откриена линеарна асоцијација на нејзините серумски и плунковни вредности. Цел: Да се утврди корелацијата помеѓу различните ризик-фактори кои се поврзуваат со метаболичкиот синдром и концентрацијата на саливарната вредност на уричната киселина. Материјал и методи: Беше спроведена студија на пресек (cross-sectional study), која вклучи 156 студенти (на возраст од 20–25 години) од Стоматолошкиот, Медицинскиот и Фармацевтскиот факултет во состав на Универзитетот „Св. Кирил и Методиј“ во Скопје. Во биохемиската лабораторија на Стоматолошкиот факултет беа измерени телесната тежина, висината, обемот на половината, крвниот притисок и пулсот на испитаниците. Нестимулирана плунка беше колекционирана користејќи го методот на исплукување. Концентрацијата на уричната киселина беше определена спектрофотометриски со ензимски метод (URICASE/PEROXIDASE). Добиените вредности беа статистички анализирани и корелирани со антропометриските параметри и вредностите на крвниот притисок, пулсот и индексот на телесна маса. Резултати: Резултатите покажаа значајна корелација помеѓу саливарните вредности на уричната киселина и телесната тежина ($p<0.001$), индексот на телесна маса ($p<0.001$), обемот на половината ($p<0.001$), систолниот крвен притисок ($p<0.001$) и дијастолниот крвен притисок ($p<0.001$). Заклучок: Нашите резултати укажуваат на можноста за користење на саливарната урична киселина како неинвазивен биомаркер за откривање на кардиометаболичките ризик-фактори.

Introduction

Excess body weight represents an increasingly serious public health problem in our population. This condition, together with metabolic syndrome, is considered a disease of modern society. Metabolic syndrome represents a cluster of interrelated metabolic abnormalities including abdominal obesity, elevated blood pressure, hyperglycemia, increased triglyceride levels, and decreased HDL-cholesterol values, which are factors that collectively increase the risk of developing cardiovascular diseases and type 2 diabetes mellitus[1]. Obesity most commonly arises as a result of dietary imbalance and is associated with increased morbidity and mortality from metabolic, endocrine, respiratory, cardiovascular, and other systemic diseases and health disorders[2]. The fast-paced lifestyle of modern society is one of the contributing factors to the growing incidence of metabolism-related diseases.

Various biological fluids are present in the human body, such as blood, urine, and saliva. These biological fluids play a crucial role in maintaining the homeostasis of organs and systems, as they contain proteins, metabolic degradation products, and minerals, making them valuable diagnostic media for a wide range of systemic and oral diseases. The growing prevalence of malignant, cardiovascular, and metabolic diseases has increased the demand for improved diagnostic procedures for early disease detection[3-5].

Among all biological fluids, saliva stands out as the most attractive diagnostic tool. This biofluid contains valuable information that enables early disease detection, leading to better treatment outcomes and improved prognosis[6-10]. Early detection of diseases often presents a challenge and typically requires multiple clinical and laboratory examinations, which may delay therapeutic intervention and worsen patient prognosis. Contemporary research therefore focuses on identifying noninvasive biomarkers for early disease diagnosis. An ideal biomarker should be specific to the disease, easily accessible, cause minimal discomfort during sample collection, and be cost-effective. Salivary diagnostics meet these criteria by providing an effective, noninvasive approach for early diagnosis, disease monitoring, and evaluation of therapeutic outcomes[10-13].

Whole saliva consists of secretions from the major and minor salivary glands, transudate from the oral mucosa, gingival crevicular fluid, serum-derived components, desquamated epithelial cells, microorganisms, and food residues. It is a complex biological fluid that contains hormones, enzymes, proteins, metabolites, antibodies, cytokines, and antimicrobial molecules. The analysis of these salivary constituents forms the basis for linking saliva to various systemic diseases[14].

Over the past decade, research on saliva has significantly expanded, attracting increasing interest as a diagnostic medium for detecting biomolecules associated with both health and disease. Considerable investments have been made to encourage scientists, governments, and industry to advance salivary research. An optimal diagnostic method should be functional, specific, sensitive, af-

fordable, and clinically applicable. Many of the methods developed for salivary diagnostics already meet these criteria, owing to the interdisciplinary collaboration of experts in chemistry, physics, biology, and technology[7,14].

Excess body weight profoundly affects human health and increases the incidence of diabetes and cardiovascular diseases. Since these conditions can be prevented or delayed through lifestyle modification, a new medical approach is needed, which focuses on the early identification of individuals at increased risk. One useful screening tool for identifying high-risk individuals is the detection of metabolic syndrome. The aim of this study was to determine the correlation between salivary uric acid concentrations and the various risk factors associated with metabolic syndrome.

This study was approved by the Ethics Committee of the Faculty of Dentistry - Skopje, Ss. Cyril and Methodius University in Skopje, and was conducted in accordance with the principles of the Helsinki Declaration.

Materials and methods

Study Design and Participants

A cross-sectional study was conducted among 156 students from the Faculty of Dentistry, Faculty of Medicine, and Faculty of Pharmacy, all part of Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia. The participants were between 20 and 25 years of age. Exclusion criteria included conditions known to affect salivation or uric acid metabolism, such as gout, renal insufficiency, Sjögren's syndrome, autoimmune diseases, acute infections, type 2 diabetes mellitus, and pregnancy. All participants completed a questionnaire to exclude any previous systemic diseases or conditions. Anthropometric measurements were performed, and unstimulated saliva samples were collected from each participant.

Anthropometric and Physiological Measurements

In the Biochemical Laboratory of the Department of Oral and Periodontal Diseases, Faculty of Dentistry – Skopje, the following parameters were measured for all subjects: body weight, height, waist circumference, blood pressure, and pulse rate. Measurements were performed in the morning, under standardized conditions.

Saliva Collection and Preparation

Unstimulated saliva was collected from all participants using the spitting method, following the recommendations of Navazesh[15]. The collection was carried out between 9:00 and 12:00 a.m., for 10 minutes. Participants were instructed to refrain from eating or drinking for at least two hours prior to sample collection. Saliva samples were centrifuged at 4000 rcf for 10 minutes at 4°C. From the supernatant, 1000 µL were transferred to Eppendorf tubes and stored at –20°C until analysis. Before biochemical determination, saliva samples were rapidly thawed by immersion in warm water.

Biochemical Analysis

The concentration of uric acid in saliva was determined spectrophotometrically using an enzymatic URICASE/PEROXIDASE method[16]. The assay was performed with a commercial reagent kit (Biosystems S.A., Barcelona, Spain). After a brief incubation at 37°C, a red-colored complex was formed. The absorbance, proportional to the uric acid concentration, was measured at 515 nm. All reagents used were of analytical grade purity.

Statistical Analysis

All data were analyzed using IBM SPSS Statistics software, version 24.0 (IBM Corp., Armonk, NY, USA). The results were expressed as mean ± standard deviation (SD). Comparisons between groups were performed using the Student's t-test, and correlations were evaluated using Spearman's rank correlation coefficient. The level of statistical significance was set at $p < 0.05$.

Results

Of all 156 students included in the study, 70 (44.9%) were male and 86 (55.1%) were female. The majority of students were from the Faculty of Dentistry (n=82, 52.6%), followed by those from the Faculty of Medicine (n=48, 30.8%) and the Faculty of Pharmacy (n=26, 16.6%), with a mean age of 22.85 ± 2.21 years in males and 22.11 ± 1.51 years in females; mean BMI 25.35 ± 4.18 kg/m² and 23.77 ± 3.52 kg/m², waist circumference 90.55 ± 15.38 cm and 74.61 ± 6.18 cm, systolic blood pressure 79.70 ± 13.16 mmHg and 78.83 ± 11.81 mmHg, diastolic blood pressure 121.60 ± 13.33 mmHg and 115.00 ± 16.09 mmHg, and pulse rate 87.30 ± 11.41 bpm and 97.94 ± 16.62 bpm, in males and females, respectively.

The mean salivary uric acid concentration in male participants was 134.65 ± 86.7 µmol/L, which was significantly higher than in females (96.06 ± 49.6 µmol/L) ($t = 3.345$, $p = 0.001$) (Table 1).

Table 1: Mean salivary uric acid concentration by gender

Parameter	Mean±SD (Male)	Mean±SD (Female)	t-value	p
Uric acid (µmol/L)	134.65±86.7	96.06±49.6	3.354	0.001

The mean salivary uric acid levels among participants with normal BMI (< 25 kg/m²) were 43.07 ± 14.2 µmol/L, whereas those with increased BMI (> 25 kg/m²) had 206 ± 71.8 µmol/L. Participants with higher BMI had significantly elevated uric acid concentrations ($t = –14.317$, $p < 0.001$) (Table 2).

Table 2: Mean salivary uric acid concentration by BMI group

Uric acid (µmol/L)	Mean±SD (BMI<25)	Mean±SD (BMI>25)	t-value	p
Male	29.71±10.05	45.24±5.44	-3.529	0.002
Female	69.96±35.2	251.25±44.1	-12.900	<0.001
Total	43.07±14.2	206±71.8	-14.317	<0.001

A positive correlation was observed between salivary uric acid levels and several risk factors associated with metabolic syndrome and cardiovascular diseases, including body weight, systolic and diastolic blood pressure, and waist circumference. No significant correlation was found between uric acid levels and pulse rate (Table 3).

Table 3: Correlation between salivary uric acid levels and risk factors associated with metabolic syndrome

Variables	r	p
Uric acid: BMI	0.906	<0.001
Uric acid: Waist circumference	0.846	<0.001
Uric acid: Systolic blood pressure	0.713	<0.001
Uric acid: Diastolic blood pressure	0.484	<0.001
Uric acid: Body weight	0.863	<0.001
Uric acid: Pulse	0.074	0.352

Discussion

Metabolic syndrome represents a combination of various metabolic disorders or risk factors, including obesity, increased waist circumference, elevated blood pressure, elevated triglycerides, decreased levels of HDL (high-density lipoproteins), and increased blood glucose levels[17,18]. Individuals who exhibit at least three of these risk factors are classified as patients with metabolic syndrome[18]. The need for screening of these factors that lead to the development of metabolic syndrome is evident. Their timely detection can help prevent serious cardiovascular complications[19.20]. However, identifying these risk factors is not always possible. There are several reasons for this: limited access to healthcare services, the high cost of certain diagnostic methods, and the reluctance toward invasive diagnostic procedures[21-23]. The use of noninvasive screening methods is a prerequisite for involving a larger number of individuals in preventive programs and for promoting healthier lifestyle changes[24].

One approach for noninvasive monitoring is the use of salivary biomarkers[25]. Several serum biomarkers such as C-reactive protein, adiponectin, and uric acid, which are associated with metabolic syndrome and cardiovascular diseases, can also be detected in saliva[26-28]. Of particular research interest is salivary uric acid, since a linear association has been identified between serum and salivary uric acid levels[29-31]. Although numerous studies have confirmed a positive correlation between salivary uric acid levels, metabolic syndrome, and cardiovascular diseases, the role of this metabolite is not yet fully understood.

Uric acid is the final degradation product of purine catabolism and has a significant antioxidative role in the extracellular environment[32]. It has been proven that uric acid is one of the main antioxidants in the human body, contributing approximately

55% of the total antioxidant capacity of plasma[33] and 70–85% of the total antioxidant capacity of saliva[29]. The enzymes responsible for uric acid formation also participate in the production of free radicals, which gives this metabolite both proinflammatory and prooxidant roles[34.35]. Whether uric acid is the cause of certain metabolic disturbances or a product formed as a result of them, it is currently being investigated as a potential biomarker for identifying individuals at risk for metabolic syndrome and cardiovascular diseases[36.37].

In our study, the amount of uric acid in saliva was significantly higher in male participants compared to females (Table 1), which is consistent with the findings of Uppin et al.[30], Riis et al.[27], and Viazzi et al.[38]. Participants with increased BMI values demonstrated significantly higher uric acid concentrations (Table 2). These results are in line with numerous studies reporting elevated serum and salivary uric acid concentrations among patients with metabolic syndrome[28,39-44].

In a study conducted on 2,380 patients, individuals with elevated uric acid levels had an odds ratio (OR) of 2.67, meaning they were 2.67 times more likely to develop metabolic syndrome[45]. Similar results were reported in a meta-analysis from 2025 (OR = 2.25)[46]. The association between uric acid and risk factors for metabolic syndrome has been confirmed in children, adolescents, and adults[40]. Soukup demonstrated a correlation between salivary uric acid levels and metabolic syndrome risk factors[28].

Our correlation analysis revealed a positive association between salivary uric acid levels and several risk factors related to metabolic syndrome and cardiovascular diseases, including body weight, systolic and diastolic blood pressure, and waist circumference (Table 3). No statistically significant correlation was found between uric acid levels and pulse rate. These results are consistent with recent studies showing that higher uric acid levels are significantly associated with components of metabolic syndrome[47,48]. Numerous studies[42,49-52] have indicated elevated uric acid concentrations in patients with metabolic syndrome. Ishizaka et al.[53] investigated the relationship between metabolic syndrome and uric acid concentration and found that the prevalence of metabolic syndrome increased proportionally with uric acid levels.

Large population-based analyses further show that individuals with hyperuricemia have greater waist circumference, higher blood pressure, and a higher prevalence of all five diagnostic criteria for metabolic syndrome[54]. These associations can be explained by several pathophysiological mechanisms. First, hyperinsulinemia associated with insulin resistance reduces renal excretion of uric acid, leading to its accumulation. Second, uric acid physiologically contributes to the worsening of metabolic disorders by inducing oxidative stress and reducing the bioavailability of nitric oxide in the endothelium, causing endothelial dysfunction and vasoconstriction - mechanisms that raise arterial pressure[54-56]. At higher concentrations, uric acid shifts from an antioxidant to a proinflammatory mediator, activating cytokines and promoting macrophage infiltration into adipose tissue, thereby exacerbating insulin resistance and encour-

aging the accumulation of abdominal fat[32,55]. This mechanism explains the strong link between uric acid and central obesity.

In other words, uric acid is not merely a marker but an active modulator of metabolic syndrome, participating in mechanisms of oxidative stress, inflammation, endothelial dysfunction, and fat accumulation[55].

Some studies have shown that hyperuricemia, through its proinflammatory effects, can enhance sympathetic tone and increase resting heart rate[57]. However, this effect is mainly observed in older individuals or in cases of pronounced autonomic dysfunction[58], which likely explains why no significant correlation was observed in our study.

Several studies have demonstrated that uric acid levels are significantly higher in individuals with metabolic syndrome and increase progressively with the number of metabolic abnormalities present. Therefore, uric acid concentration is considered an indicator of more severe cardiovascular disturbances[39,49,59]. Recent literature suggests that elevated uric acid levels may have both diagnostic and prognostic significance in the context of metabolic syndrome, proposing that hyperuricemia be included as a sixth diagnostic criterion, thereby expanding the current definition and allowing earlier identification of individuals at increased risk of developing metabolic syndrome[60].

The use of saliva as a diagnostic tool offers several advantages compared to serum or tissue samples. Its greatest advantage lies in the noninvasive method of collection. Additionally, its simple collection, storage, and handling make saliva a valuable biological fluid for disease diagnosis. New analytical technologies have enabled the detection of numerous salivary biomarkers, making salivary diagnostics an efficient tool for identifying various systemic and oral diseases.

Conclusion

Based on our results demonstrating a significant correlation between salivary uric acid concentrations and risk factors associated with metabolic syndrome, we believe that saliva can be used to determine uric acid concentration as a valid noninvasive biomarker for metabolic syndrome.

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