Waist-to-height ratio as a novel marker of metabolic syndrome in patients with type 2 diabetes mellitus

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Abstract

Aim: Metabolic syndrome (MetS) is associated with chronic conditions, including type 2 diabetes mellitus (T2DM) and cardiovascular disorders. New markers are needed for the early detection and successful treatment of MetS, especially in patients with T2DM. The serum uric acid-to-creatinine ratio (UCR) and waist-to-height ratio (WHR) are novel markers in various chronic metabolic disorders. We aimed to compare WHR, UCR, and other metabolic and laboratory markers in T2DM patients with and without MetS.

Methods: Patients with T2DM who visited the outpatient clinics of our institution were enrolled in the study. Total diabetic subjects were 239 of which 180 were in MetS group while 59 were in without MetS group. Data from both study groups were compared.

Results: The serum UCR in the MetS and control groups was 6.3 ± 2.1 and 5.8 ± 1.6, respectively ($p = 0.04$). The WHR in the MetS and control groups was 0.65 (0.47–0.87) and 0.62 (0.35–0.84), respectively ($p < 0.001$). Significant positive correlations were observed between UCR and triglycerides ($r = 0.17$, $p = 0.009$), waist circumference ($r = 0.13$, $p = 0.046$), hip circumference ($r = 0.18$, $p = 0.006$), BMI ($r = 0.2$, $p = 0.002$), and GFR ($r = 0.4$, $p < 0.001$). Similarly, significant positive correlations were noted between WHR and systolic blood pressure ($r = 0.12$, $p = 0.049$), weight ($r = 0.5$, $p < 0.001$), BMI ($r = 0.7$, $p < 0.001$), and UCR ($r = 0.12$, $p = 0.047$). In the ROC analysis, the sensitivity and specificity of WHR (when higher than 0.64) in detecting MetS were 72% and 54%, respectively (AUC: 0.69, $p < 0.001$, 95% CI: 0.61–0.77).

Conclusions: We propose that WHR and UCR could be valuable tools for the early detection of MetS in patients with T2DM. The ease and low cost of evaluating WHR and UCR make them practical markers for monitoring and diagnosing MetS.

Keywords

Waist-to-height ratio, uric acid-to-creatinine ratio, type 2 diabetes mellitus, metabolic syndrome

Introduction

Metabolic syndrome (MetS) is a condition with increasing prevalence worldwide. It was first described by Reaven in 1988 with nomenclature of syndrome X. The core defect in MetS is insulin resistance which accompanied by obesity, cardiovascular disorders, hyperglycemia, and dyslipidemia [1].

The awareness of MetS has been increased recently, due to its association with cardiovascular and metabolic complications, such as type 2 diabetes mellitus (T2DM) and coronary heart disease [2]. Different definition criteria have been developed in diagnosis of MetS. Some of them include WHO-modified criteria of MetS and NCEP ATP III criteria for MetS. Most of them include hyperglycemia, hypertriglyceridemia, high blood pressure, low HDL-cholesterol, and abdominal obesity. Yet, novel markers to detect MetS earlier would be of benefit.

Serum uric acid is the end product of purine metabolism in mammals. It is associated with inflammatory and metabolic consequences. Elevated serum uric acid has been reported in T2DM [3, 4], hypertension [5], chronic kidney disease [6], metabolic dysfunction associated fatty liver disease [7], diabetic kidney injury [8], and even prediabetes [9]. Serum creatinine is mainly used as a surrogate marker of kidney functions. Elevated levels of serum creatinine predict poor renal outcomes. The proportion of serum uric acid-to-creatinine ratio (UCR) has been suggested as a disease marker in various conditions such as cardiovascular diseases [10], chronic kidney disease [11], and obesity [12].

Another novel anthropometric marker for metabolic conditions is waist-to-height ratio (WHR). Recent studies revealed the association between WHR and metabolic-inflammatory diseases including T2DM [13], MetS [14], and cardiovascular disorders [15]. Moreover, it was suggested to be a predictor of mortality [16].

In present study, we aimed to compare UCR levels of the diabetic patients with MetS to those without. We also aimed to compare WHR and other anthropometric and laboratory data of the subjects with and without MetS.

Materials and methods

Design, setting, and study population

Following institutional board approval (approval date: 18 July 2023 and approval number: 2023/240), T2DM patients diagnosed with MetS (according to NCEP ATP III criteria) and attending outpatient internal medicine clinics at our hospital from January 2022 to November 2023 were included in this study. The diabetic subjects without MetS served as the control group. Exclusion criteria included subjects with malignant conditions, hematological disorders, pregnancy, end-stage kidney disease, liver cirrhosis, and those receiving corticosteroids or other drugs that interfere with blood lymphocyte count (Lym). For approximately 95% power, the required sample size for detecting a 20% change was calculated as 200 in both groups using power analysis. To account for potential losses during follow-up, it was planned to include at least 220 patients in each group, with a 10% excess. Since subgroup analyses will also be conducted within the T2DM group, the required number tripled, resulting in a plan to recruit at least 660 patients.

Laboratory analyses

Patient files were utilized to record age, sex, height, weight, waist circumference, duration of T2DM, and systolic and diastolic blood pressures. Height and weight of the participants as well as waist and hip circumferences were recorded. Body mass index (BMI) was calculated by dividing weight (in kg) by the square of height (in meters). WHR was calculated by simply division of the waist circumference (in centimeters) by height (in centimeters). The waist to hip ratio (WHiR) was calculated with the following formula: waist circumference (cm)/hip circumference (cm). The arithmetic mean of blood pressure measurements taken during consecutive clinic visits in both arms was used as the blood pressure measure. Data on fasting plasma glucose (FPG), serum creatinine, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride, CRP, serum albumin, glomerular filtration rate (GFR), serum uric acid, glycated hemoglobin

(HbA1c), white blood cell count (WBC), hemoglobin (Hb), hematocrit (Htc), and platelet count (PLT) were obtained from the institutional database and documented. Serum UCR was calculated division of serum uric acid to serum creatinine. Data of the patients with MetS and without MetS were compared.

Statistical analyses

SPSS software (SPSS 15.0; IBM Inc., Chicago, IL, U.S.A.) was used for data analysis. The distribution of variables in the study groups was assessed using the Kolmogorov-Smirnov test. Homogenously distributed variables were compared with independent samples t test while the others were compared with the Mann-Whitney U test. The homogenous variables were expressed as means ± SD and the other were expressed as medians (min.–max.). Categorical variables were compared using the chi-square test and expressed as numbers and percentages. Pearson correlation analysis was used to determine the correlation between study parameters. The sensitivity and specificity of variables such as WHR and other indices of MetS were investigated using ROC analysis. A p-value of less than 0.05 was considered statistically significant.

Results

In present study, there were 239 T2DM patients, with 180 diagnosed with MetS and 59 were diabetics without MetS. Median ages of the patients with and without MetS groups were 59 (24–85) years and 57 (34–82) years, respectively (p = 0.31). It was found that 113 (63%) of the patients with MetS were female and 67 (37%) were male while 38 (64%) were female and 21 (36%) were male in diabetic subjects without MetS (p = 0.84).

There were no significant differences between MetS and control groups in terms of Hb (p = 0.58), Htc (p = 0.66), PLT (p = 0.26), diastolic blood pressure (p = 0.51), WHiR (p = 0.22), HbA1c (p = 0.79), creatinine (p = 0.09), total cholesterol (p = 0.57), LDL-cholesterol (p = 0.08), and albumin (p = 0.34).

Significant differences between MetS and control groups were observed in terms of systolic blood pressure (p = 0.009), fasting blood glucose (p = 0.005), triglyceride (p < 0.001), HDL-cholesterol (p < 0.001), waist circumference (p < 0.001), hip circumference (p = 0.001), weight (p = 0.002), BMI (p < 0.001), serum uric acid (p < 0.001), GFR (p = 0.005), and leukocyte count (p = 0.008). Table 1 summarizes the data of the MetS and control groups.

Table 1. Data of the MetS and control groups

Variables		Diabetics with MetS	Diabetics without MetS	p
		Mean ± SD or Median (min.–max.)	Mean ± SD or Median (min.–max.)	
Sex	Men (n,%)	67 (37%)	21 (36%)	0.84
	Women (n,%)	113 (63%)	38 (64%)	
UCR		6.3 ± 2.1	5.8 ± 1.6	0.04
Hb (g/dL)		13 ± 1.8	13 ± 1.8	0.58
PLT (k/mm^3)		278 ± 78	257 ± 70	0.26
Age (years)		59 (24–85)	57 (34–82)	0.31
SBP (mmHg)		130 (90–180)	129 (100–130)	0.009
DBP (mmHg)		80 (60–120)	79 (60–95)	0.51
Weight (kg)		81(50–150)	78 (38–131)	0.002
Height (cm)		162 (140–184)	162 (135–185)	0.12
Waist circumference (cm)		108 (70–144)	99 (54–134)	< 0.001
Hip circumference (cm)		112 (91–155)	112(53–133)	0.001
WHiR		0.94 (0.6–1.2)	0.94 (0.52–1.77)	0.22
BMI (kg/m^2)		30 (21–51)	28 (21–51)	< 0.001
WHR		0.65 (0.47–0.87)	0.62 (0.35–0.84)	< 0.001
Leukocyte count (k/mm^3)		7.7 (3.3–16.5)	6.8 (3.9–12.4)	0.008
Htc (%)		39 (30–50)	39 (30–52)	0.66

Table 1. Data of the MetS and control groups (*continued*)

Variables	Diabetics with MetS	Diabetics without MetS	*p*
	Mean ± SD or Median (min.–max.)	Mean ± SD or Median (min.–max.)	
Creatinine (mg/dL)	1 (0.5–6)	0.9 (0.6–2)	0.09
eGFR (%)	79 (7–124)	90 (33–118)	0.005
Total cholesterol (mg/dL)	191 (81–373)	191 (107–286)	0.57
LDL-cholesterol (mg/dL)	109 (31–345)	109 (44–182)	0.08
HDL-cholesterol (mg/dL)	46 (21–100)	53 (34–99)	< 0.001
Triglyceride (mg/dL)	167 (46–484)	102 (49–310)	< 0.001
Albumin (g/dL)	45 (32–58)	46 (38–52)	0.34
Uric acid (mg/dL)	5.6 (2.4–13.5)	5 (2.6–12)	< 0.001
Fasting blood glucose (mg/dL)	160 (70–573)	151 (64–418)	0.005
HbA1c (%)	8.1 (4.7–18)	7.3 (5–15)	0.79

UCR: uric acid-to-creatinine ratio; Hb: hemoglobin; PLT: platelet count; SBP: systolic blood pressure; DBP: diastolic blood pressure; WHiR: waist to hip ratio; BMI: body mass index; WHR: waist-to-height ratio; Htc: hematocrit; eGFR: estimated glomerular filtration rate; HbA1c: glycated hemoglobin; MetS: metabolic syndrome

Serum UCR of the MetS and control groups were 6.3 ± 2.1 and 5.8 ± 1.6, respectively (p = 0.04). WHR of the MetS and control groups were 0.65 (0.47–0.87) and 0.62 (0.35–0.84), respectively (p < 0.001).

Significant positive correlations were observed between the UCR and triglycerides (r = 0.17, p = 0.009), waist circumference (r = 0.13, p = 0.046), hip circumference (r = 0.18, p = 0.006), BMI (r = 0.2, p = 0.002), and GFR (r = 0.4, p < 0.001). A negative correlation between UCR and fasting blood glucose (r = –0.19, p = 0.004) was detected.

Significant positive correlations were noted between WHR and systolic blood pressure (r = 0.12, p = 0.049), weight (r = 0.5, p < 0.001), BMI (r = 0.7, p < 0.001), and UCR (r = 0.12, p = 0.047).

In ROC analysis, the sensitivity and specificity of WHR (when higher than 0.64) in detecting MetS were 72% and 54 %, respectively (AUC: 0.69, p < 0.001, 95% CI: 0.61–0.77). CRP, when higher than 0.58 mg/dL, has 71% sensitivity and 47% specificity in detecting MetS (AUC: 0.59, p = 0.04, 95% CI: 0.50–0.68). Serum HDL-cholesterol level (when lower than 49.2 mg/dL) has 75% sensitivity and 61% specificity in detecting MetS (AUC: 0.73, p < 0.001, 95% CI: 0.66–0.80). Among other markers of MetS, triglyceride has the highest sensitivity and specificity in detecting MetS. When triglyceride level was higher than 151 mg/dL the sensitivity and specificity of triglyceride were 64% and 85%, respectively (AUC: 0.80, p < 0.001, 95% CI: 0.74–0.87).

Discussion

The results of this analysis can be summarized as follows: 1) There was no statistically significant age difference between individuals with and without MetS diagnosed with T2DM, 2) In terms of gender, there were more females than males in the study cohort, 3) Significant differences between MetS and control groups were observed in terms of WHR, UCR, systolic blood pressure, fasting blood glucose, triglycerides, HDL-cholesterol, waist circumference, WHiR, weight, BMI, GFR, and WBC, 4) Significant positive correlations were observed between UCR and triglycerides, waist circumference, hip circumference, BMI, and GFR. A negative correlation between UCR and fasting blood glucose was detected. Significant positive correlations between WHR and systolic blood pressure, weight, BMI, and UCR, 5) WHR had significant sensitivity and specificity in detecting MetS.

We found elevated UCR in patients with MetS compared to the subjects without MetS. MetS is associated with inflammation [17]. Besides, the components of UCR, especially serum uric acid are closely associated with inflammatory and metabolic disorders such as atherosclerosis [18], stroke [19], MetS [20], and T2DM [21]. Furthermore, UCR has been introduced as a diagnostic and prognostic tool in various inflammatory conditions. These include chronic obstructive pulmonary disease (COPD) [22], cardiovascular disorders [10], and hypertension [23]. MetS is characterized by increased cardiovascular risk. Moreover,

elevated blood pressure is one of the 5 components of MetS. Similar to COPD, MetS is associated with a high burden of inflammation. Thus, the elevated UCR level in MetS is not surprising.

We found elevated WHR in patients with MetS compared to the subjects without MetS. In the literature, there are many studies highlighting the relationship between the components of MetS and WHR. In one study, the relationship between WHR and the risk of developing central obesity was mentioned [24]. Additionally, there are several reports highlighting the positive correlation between WHR and components of MetS, such as T2DM [25], and hypertension [26]. Given its close relationship with the components of MetS, WHR being a marker of MetS is inevitable, as demonstrated by this study and many others in the literature.

In a study conducted on young adults in Mexico, the triglyceride/HDL index, considered an indicator of cardiovascular diseases, was accepted as an indicator of MetS. Similarly, in our study, low HDL values were an indicator for patients with MetS [27]. Furthermore, in a study that published in 2022, authors highlighted that even moderate weight gain is associated with activation of inflammatory pathways [28]. In our study, those diagnosed with MetS had higher body weights in kilograms compared to those without MetS.

The most commonly and widely used inflammation marker is CRP. As a signature marker for systemic inflammation, CRP has been shown in epidemiological studies in humans to be a very strong factor related to obesity [15]. Similarly, in present study, CRP has emerged as a notable marker of inflammation in patients with MetS.

We reported a correlation between serum UCR and triglyceride levels. Few mechanisms could be possible for this finding. First, both elevated UCR and triglyceride levels are associated with insulin resistance, a key feature of MetS. Insulin resistance impairs lipid metabolism and promotes uric acid retention [29]. Second, hypertriglyceridemia can exacerbate renal dysfunction, reducing uric acid excretion and increasing serum uric acid levels [30]. Finally, high UCR and triglyceride levels contribute to oxidative stress and low-grade inflammation, creating a feedback loop that worsens both conditions [31].

There are several limitations of the present work. First, retrospective design which allows just reporting an association rather than causal relationship between study variables, and second, a relatively small study cohort. However, associations between UCR and MetS, and WHR and MetS are important findings and may contribute to the medical literature significantly.

Ultimately, our study found a relationship between MetS and UCR, as well as WHR. Additionally, a relationship was observed between CRP, an inflammation marker, and MetS. The ease and low cost of evaluating these indices make them useful for monitoring and diagnosing patients with MetS.

Abbreviations

BMI: body mass index

COPD: chronic obstructive pulmonary disease

GFR: glomerular filtration rate

Hb: hemoglobin

HbA1c: glycated hemoglobin

Htc: hematocrit

Lym: lymphocyte count

MetS: metabolic syndrome

PLT: platelet count

T2DM: type 2 diabetes mellitus

UCR: uric acid-to-creatinine ratio

WBC: white blood cell count

WHiR: waist to hip ratio

WHR: waist-to-height ratio

Declarations

Author contributions

EB: Conceptualization, Data curation, Methodology, Investigation, Writing—original draft, Formal analysis. GA: Conceptualization, Methodology, Writing—review & editing, Supervision. Both authors approved the final version of the manuscript.

Conflicts of interest

Gulali Aktas is the Editorial Board Member and a Guest Editor of Exploration of Endocrine and Metabolic Diseases, but he had no involvement in the journal review process of this manuscript. Elif Basaran declares that there are no conflicts of interest.

Ethical approval

The study was approved by the institutional ethics committee of the Abant Izzet Baysal University (approval date: 18 July 2023 and approval number: 2023/240).

Consent to participate

All participants have given informed consent to participate in the study.

Consent to publication

Not applicable.

Availability of data and materials

The data used and/or analyzed during the current study are available upon reasonable request to the corresponding author.

Funding

Not applicable.

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