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Associations Between Serum Uric Acid Levels and Cardiometabolic Risk, Renal İnjury in Obese and Overweight Children

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What is already known on this topic?

Higher uric acid (UA) is associated with the risk factors characterizing Metabolic syndrome (MetS) and also with fasting insulin and insulin resistance (IR) in obese (OB) adults and adolescents. All these factors are predictive for both cardiovascular diseases and type 2 diabetes. Despite the appearing role of UA in contributing to obesity-related comorbidities such as MetS, cardiovascular risk factors, and kidney diseases, studies in overweight (OW)/OB children are rare and the results of the studies are still controversial.

What this study adds?

This study confirms associations of elevated serum UA with greater waist-to-hip ratio, lower HDL-cholesterol, hypertriglyceridemia, the presence of MetS and IR in OB and OW children. Moreover, the number of criteria related to MetS is significantly associated with the elevation of UA.

ABSTRACT

Objective: In this study we aimed to assess the association between serum uric acid (SUA) concentration
and metabolic syndrome (MetS) parameters and insulin resistance (IR). Our second aim was
evaluate whether hyperuricemia is related with renal injury and cardiovascular risk in obese (OB)
and overweight(OW) children.

Methods: This study was conducted on 128 OB/OW children and adolescents (ages: 8-18 years), of whom 52 (40%) with SUA elevation (SUA persantile>75), 76 with (60%) normal SUA level (SUAL).

Sex and age specific SUA persantiles were used and SUA persantile>75 was defined as hyperurisemia. Anthropometric data, blood pressure (BP) measurements and biochemical parameters including fasting blood glucose, insulin, total cholesterol, highdensity lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides (TG), aspartate aminotransferase (AST), alanine aminotransferase (ALT), homeostatic model assessments of insulin resistance (HOMA-IR) and SUAL were recorded. Oral glucose tolerance tests (OGTT) were performed on all patients. MetS was defined according to the International Diabetes Federation (IDF) criteria. Totalcholesterol / HDL-c ratio > 4 and TG to HDL-c ratio >2.2 were used as atherogenicindex (AI) and considered as cardiovascular risk.Urinary albumin excretion in a 24-h urinecollection and in a first-morning urine sample were measured. Renal injury was assessed by microalbuminuria according to the National Kidney Foundation criteria.

Results: The mean age of the participants was 13.1±2.6 years; 87(67,4%) were female and 41 (31,8%) were male. The mean weight and height of the subjects were 73 kg (SD±18.97 kg) and 155.4 cm (SD±12.11 cm) respectively. The group with hyperuricemia was not statistically different from the group without hyperuricemia in terms of age, sex, puberty stage and the degree of obesity. Increased SUAL were significantly associated with higher waist-to-hip ratio (WHR), insulin levels at fasting, 30th and 60th minutes of OGTT, HOMA-IR, lower HDL-c and presence of hypertriglyceridemia also with decreased HDL-c, increased AI, presence of IR and MetS. BP and microalbuminuria were notassociated with SUAL in our study analyzes. SUAL showed significantly positive correlation with waist circumference (WC), WHR, post-challenge glucose level at 60 minute, fasting insulin, post-challenge insulin levels at 30, 60, 90 and 120 minutes, HOMA-IR, Total cholesterol / HDL-c ratio,TG/ HDL-c ratio and the number of criteria related to MetS, also inverse correlation with HDL-c.

Conclusions: The presence of MetS, IR and dislipidemia rises with increasing SUAL independently of age, puberty, gender and body mass index (BMI) in OB/OW children. Patients with all of the MetS criteria had the highest SUAL. These results demonstrated that association between UA and metabolic and cardiovascular risk factors could be detectable as early as in childhood. Thus, we recommend monitoring SUAL in OB children and we believe that prevention of SUAL elevation in early life has a potential protective effect on metabolic impairment and subsequent comorbidities.

Keywords: Serum uric acid level, obesity, metabolic syndrome, insulin resistance, renal injury, cardiovascular risk, child.

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Introduction

Uric acid (UA) is the end-product of dietary and endogenous purine metabolism, produced by the liver and excreted by the kidneys (1). Serum uric acid level (SUAL) increase progressively with body growth fromearly childhood until the age of 15-17 (2). Obese (OB) individuals have higher concentrations of UA than in normal-weight peers. Hyperuricemia and obesity probably influence eachother based on multiple mechanisms, hyperuricemia may cause obesity by accelerating hepatic and peripheral lipogenesis (3). On the other hand, obesity may cause serum uric acid (SUA) elevation due to following factors: OB subjects have reduced renal clearance of UA and obesity is associated with elevated activity of xanthine oxidase and increased production of UA by adipose tissue (4).

The increased SUAL called hyperuricemia, is an independent risk factor for life style related diseases such as hypertension, renal diseases, cardiovascular diseases and also has apotential role in the development of Metabolic syndrome (MetS) (5). Morover, some recent prospective studies have revealed that hyperuricemia is a predictor of insulin resistance (IR) and type 2 diabetes mellitus development (5). However, the relationship between obesity-related metabolic risk factors and SUAL in childhood is still controversial; while some studies report a strong associations between these variables (6-7), others did not confirm an independent association(8-9). Therefore, in this study we aimed to investigate whether increased SUAL isrelated with the MetS risk factors (obesity (total body obesity measured by body mass index (BMI), or central obesity measured by waist-to hip ratio (WHR) or waist circumference (WC)), atherogenicdyslipidemia (increased triglycerides (TG),decreased high-density lipoprotein cholesterol (HDL-c), increased the ratio of total cholesterol/HDL-c and TG/HDL-c); hypertension (systolic and diastolic), hyperglycemia (abnormal glucose responses in Oral glucose tolerance tests (OGTT); fasting blood glucose, 2-h postprandial blood glucose)), hyperinsulinemia and IR measured by the homeostatic model assessments of insulin resistance (HOMA-IR) and to evaluate whether hyperuricemia isassociated with renal injury (microalbuminuria) and cardiovascular risk in OB and overweight (OW)children(10).

Methods

Study population

Children who visited the Pediatric Endocrinology outpatient clinic for a general obesity screening were enrolled to the study. Ethics committee approval was from Manisa Celal Bayar University (20.478.486). A total of 128 OB and OW children with a BMI greater than the 85th percentile for age and gender, according to data from the Center for Disease Control and Prevention (CDC-2000) (11), ages 8 to 18 were included in the study. We devided the patients into two groups acording to the presence of hyperuricemia. We excluded individuals diagnosed with type 1 or type 2 diabetes. Children whose obesity was the result ofa syndromal problem (Prader Willi, Laurence-Moon Biedle syndrome, etc.) or

whose obesity had an endocrinological cause such as Cushing's syndrome or hypothyroidism were excluded. Subjects referred to our clinic for known comorbidities of obesity (e.g. glucose alterations, arterial hypertension, dyslipidemia, liver steatosis, hyperuricemia etc.) or children who used current or past hormonal or interfering therapies (glucose or lipid-lowering drugs and/oranti-hypertensive medication), children with liver, kidney or other systemic diseases and family history of symptomatic hyperuricemia were also excluded from the study.

Procedures

Physical examination and laboratory results of all OB/OW patients were recorded. All of the evaluations were conducted by specially trained clinical research staff.

Anthropometric and clinical measurements

Child height and weight were measured by a wall-mounted stadiometer for height and a calibrated scale for weight. Children did not wear shoes for measurements. The weight of each subject was measured with all clothing removed except undergarments. WC was measured with a non-stretchable tape to the nearest 0.1 cm midway between the lowest rib and the highest point of the iliac crest paralel to the floor, without clothing and during expiration in a standing and relaxed position. Hip circumference (HC) was measured around the widest portion of the buttocks. WHR were calculated. Findings for pubertal development were recorded according to the classification of Tanner. Blood pressure (BP) was measured according to standard criteria at the right arm in the supine position after a five-minute rest, using a mercury sphygmomanometer with an appropriately sized cuff, and a stethoscope placed over the brachial artery pulse; three systolic and diastolic blood pressure (SBP, DBP) measurements were taken 2min apart and the average of the two last values was used in data analyses.

Laboratory tests

Biochemical variables inluding serum glucose, urea, creatinine, aspartat aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol, LDL-c, HDL-c, TG and SUA results were recorded. Each child underwent an OGTT following overnight fasting of 12–14 h. After subjects drunk glucose drink containing 1.75 g/kg glucose to a maximum of 75 g, blood samples were obtained every 30 min for 120 min, for measurement of plasma glucose and insulin. In all individuals, first-morning urinary albumin and creatinine were analyzed. Urine was collected for 24 h, and urinary albumin was measured. Samples showing pyuria and hematuria were excluded.

Classification

We calculated the BMI as weight (kg) divided by square of height (m^2). BMI-standard deviation score (SDS) and BMI percentiles were calculated using age and gender specific norms published by the CDC. Obesity was defined as BMI≥95th percentile and OW was defined as BMI≥85th percentile for age and sex. The extent of obesity was quantified using Cole's LMS method; obesity was stratified on the basis of a threshold BMI z score of 2.0 or more, namely, moderate obesity asa z score of 2.0–2.5, and severe obesity as a z score above 2.5 (12). WC percentiles were stratified according to sex and age, identifying abdominal obesity as the presence of WC≥90th percentile (13). WHR was used as an index of fat

distribution. A testicular volume of ≥4 mL in males, and breast development of stage 2 and over in females, were considered to be findings of puberty (14). Prepubertal stage was defined by Tanner stage I.

IR was evaluated with the aid of HOMA-IR index using a standard formula: fasting insulin (U/L)x fasting glucose(mmol/L) divided by 22.5. IR criteria were HOMA-IR >2.5 for prepubertal children and HOMA-IR >4.0 for adolescents (15). Impaired fasting glucose was defined as a fasting plasma glucose level between 100 and 125mg/dl without a history of diabetes mellitus(16). Impaired glucose tolerance was defined according to WHO criteria, a condition in which fasting blood glucose levels in venous plasma drop to <140 mg/dl and the 2 h post challenge blood glucose was between 140 and 200 mg/dL(16).

Hyperinsulinemia was defined as a fasting insulin ≥ 104.18 pmol/L (14,5mLU/L), or insulin during the OGTT test ≥104.18 pmol/L (145mLU / L), and/or ≥520.88 pmol/L (72,5mLU/L) at 2 h following the start of the OGTT (17).

MetS was defined according to the International Diabetes Federation (IDF) criteria. MetS can be diagnosed in children 10 to 16 years old when the following criteria are fulfilled: a WC≥90th percentile (sex and age specific), together with two more risk factors being these ones:

- fasting blood glucose levels ≥100 mg/dL (5.6 mmol/L),
- serum TG levels ≥150 mg/dl (1.7 mmol/L) or treatment for elevated TG,
- HDL-c<40 mg/dL (1.03 mmol/L) or treatment for low HDL-c,
- Either SBP ≥130 or DBP ≥85, or treatment for hypertension. SBP at least 95thpercentile for sex, age and height (18).

For children 16 years and older, the adult criteria can be used (ethnic-specific WC percentiles, for Turkish population; ≥94 cm for men, ≥80 cm for women and asex-specific cut off level for (HDL-c; <40 mg/dL (1.03 mmol/L) inmen or <50 mg/dL (1.29 mmol/L) in women). For children younger than 10 years of age, MetS can not be diagnosed, but vigilance is recommended if the WC is ≥90th percentile(19). Total cholesterol/HDL-c ratio is defined as atherogenic index (AI), >4 ratio (normal:2.5) was considered a cardiovascular risk (20). The TG to HDL-cratio>2.2 was considered atherogenic too (21). Hypertension was defined as BP above the 95th percentile for age and height according to the National Health and Nutrition Examination Survey (22). Microalbuminuria in children and adolescents was defined as an urinary albumin excretion rate of 30–300 mg/24 h in a 24-h urine collection, and 3–30 mg/mmol creatinine (30–300 mg/g creatinine) in a first-morning urine sample according to the National Kidney Foundation criteria (23). Hyperuricemia was defined as SUA value ≥75th percentile adjusted for age and sex (24).

Statistical analysis

Continuous variables were expressed as mean±standard deviation (SD) and categorical variables as number and percentage. Normal distribution was tested using the Kolmogorov-Smirnov test. Between-group comparison was performed by using the $\chi 2$ test for categoricalvariables, Fisher's exact tests for

categorical variables Student's t-tests (normally distributeddata) and Mann-Whitney U test were used for comparison of continuous variables.Correlations were sought by using the Pearson's correlation test. Statistical analyses were performed using Statistical Package for Social Sciences15.0(SPSS 15.0) program. P values < 0.05 were considered statistically significant.

Results

In this study, 128 (52 (%40) with SUA elevation and 76 (%60) with normal SUA) OB and OW children and adolescents were evaluated. The mean age of the participants was 13.1±2.6 years (min: 8, max: 18); 87 (67,4%) were female and 41 (31,8%) were male. The mean weight and height of the subjects were 73 kg (SD±18.97 kg) and 155.4 cm (SD±12.11 cm), respectively. Clinical and laboratory variables were compared in children with and without hyperuricemia, the results are presented in Table 1. The group with hyperuricemia was not statistically different from the group without hyperuricemia in terms of age, sex, puberty stage and the degree of obesity. Subjects with hyperuricemia had higher WHR and lower HDL-c compared with those with normal SUAL. Moreover, subjects with hyperuricemia showed higher insulin, either at fasting or as responses to OGTT at 30 and 60 minutes, were associated with higher IRthan those without hyperuricemia. Increased SUAL were significantly associated with the number of criteria related to MetS.

Table 2 shows that elevated uric acid levels were significantly associated with hypertriglyceridemia, decreased HDL-c, increased atherogenic index, presence of IRand MetS.

Table 3 shows the results of the correlation analysis between the variables with SUAL in all subjects. SUAL showed significantly positive correlation with WC, WHR, post-challenge glucose level at 60 minute, fasting insulin, post-challenge insulin levels at 30, 60, 90 and 120 minutes, HOMA-IR, total cholesterol to HDL-c ratio, TG to HDL-c ratio, the number of criteria related to MetS and inverse correlation with HDL-c.

Discussion

Physiological UA concentrations have antioxidant and endothelial protective effects in the extracellular environment. But the increased SUAL play a prooxidant role, might promote several harmful effects (25). The relationship between increased SUAL and obesity-related comorbidities such as MetS, IR, cardiovascular risk factors, and kidney diseases has been described in the OB adults and children (26-27). However, the results of the studies are still controversial.

The prevalence of MetS shows a gradual increase with increased SUAL from large populations of epidemiological studies (28). Despite the appearing role of SUA in contributing to MetS related metabolic impairment, studies in OW/OB children are rare. In the study of Ford et al. (7), including 1370 adolescents aged 12-17 years, patients with all MetS criteria were found to have the highest SUAL. In the STYJOBS/EDECTA cohort study of 299 OW/OB Japanese children aged 8-18 years, SUA was shown as the best predictor of unhealthy obesity. Patients in the highest quartile of the SUAL were found to be heavier, with worst lipid and insulin metabolism. Therefore, they emphasized that hyperuricemia should be considered as cardiometabolic risk factor in early childhood (29). Our study

confirms that the presence of MetS and the number of criteria related to MetS is significantly associated with the elevated SUAL in OB/OW children. A growing number of studies suggest that UA should be added to the list of determining factors of MetS (30-31). Thus SUA requires more attention in the evaluation of the metabolic risk profile of OB children and adolescents. The pattern of fat distribution rather than BMI is important for metabolic and cardiovascular diseases (32). Our results showed that increased SUAL was significantly associated with greater WHR and correlated with higher WC. The strong association found by us and others with WC confirms the strong link between UA and visceral adiposity (7, 24). The association of UA with regional distribution of abdominal adipose tissue in children is poorly understood. Increased dietary fructose consumption leads to hepatic lipogenesis, thus contributing to increased visceral fat accumulation and ultimately worsening of IR (33). Additionally dietary fructose activates the fructokinase metabolic system and upregulates de novo purine nucleotide synthesis in hepatocytes, thereby causing an increase SUA production and hyperuricemia (34). High SUAL-associated dyslipidemia has been shown to be as a result of low serum HDL-c levels, not increased LDL or VLDL levels. (15). This study confirmed associations of elevated SUA with lower HDL-c and hypertriglyceridemia. Recent evidence suggests that UA induces vascular inflammation and artery damage, leading to increased risk of atherosclerosis. Findings of the present study confirmed an association between SUA and increased atherogenic risk calculated with the ratio of TG to HDL-c and total cholesterol to HDL-c.

Recent prospective studies demonstrate that hyperuricemia is a predictor of IR (5). It was observed that, for every increase of 1 mg/dL in SUAL, there would be a 91% increase in risk of IR. The pathophysiological mechanisms of the connection between hyperuricemia and hyperinsulinemia/IR are not clearly established yet. Double correlation have been proposed, in general, IR and hyperinsulinemia are thought to increase SUA concentrations by reducing renal excretion and increasing production through the hexosemonophosphate shunt (1). Another possible link between hyperuricemia and IR could be the hyperuricemia-mediated endothelial dysfunction which may lead to lower insulin uptake by reduced blood flow in peripheral tissues and may worsen the IR (35). Consistent with these pathogenic evidences, hyperuricemic patients in our study had significantly higher insulin levels at 0., 30. and 60. minutes. SUAL showed significantly positive correlation withinsulin levels both at fasting and all minute responses after OGTT. We also found that SUA is significantly associated with the HOMA-IR. Cardoso and colleagues (9), showed the association between MetS and SUAL by IR; while glycemia was not different, HOMA-IR significantly varied among quartiles of SUAL. In our study, we found a significant correlation between UA and glucose levels only at post challenge 60 minute. Similarly Ricotti et al. (36), showed that hyperuricemic patients were at increased risk of having a 1 -hour post-OGTT glycemia which was also associated with increased metabolic risk.

The association of higher SUAL with higher BP has been reported in adults and children with numerous studies. (26, 37). The lack of an association between SUA and BP in our sample may be related to the fact that duration of exposure to increased SUAL and related inflammation and oxidative stress had not

been evaluated in our study. In adults, in addition to microalbuminuria, hyperuricemia is a well-established risk factor for chronic kidney disease (26). However, data concerning the relationship between hyperuricemia and renal injury in OB children are still lacking. We did not find a significant association in our study group. Long-term prospective studies are needed on this subject.

Our study has some limitations. We used percentages of the UA according to age and sex but SUAL may be affectedby pubertal stage, but we could not find UA reference values according to sex and pubertal stages in theliterature. Comprehensive studies are needed on this issue. The major limitation is the relatively small size of the population.

In conclusion we believe that the SUAL is a good alternative to assess cardiometabolic risk even at a young age. Chronic hyperuricemia appears to be involved in the pathogenesisof metabolic impairment leading to MetS and subsequent comorbidities. The prevention of the SUA elevation at an early age may have a potential protective effect on hyperglycemia, hyperinsulinemia, IR, dislipidemia and hypertension (38). Assessment of UA is easily feasible in routine test of primary care with widely available,very cheap and reliable methods. Therefore, the inclusion of measurement of SUAL in the assessment protocols forOB/OW children and adolescents is suggested. More prospective clinical researches are needed to evaluate the clinical significance and determine the costeffectiveness of measuring routinely SUAL in childhood obesity.

Ethics

Ethics Committee Approval: 20.478.486 (Celal Bayar University)

Informed Consent: No (retrospective study)

Authorship Contributions

Surgical and Medical Practices: Deniz Kızılay Özalp, Betül Ersoy

Concept: Deniz Kızılay Özalp, Semra Şen

Design: Deniz Kızılay Özalp, Semra Şen

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Analysis or Interpretation: Deniz Kızılay Özalp

Literature Search: Deniz Kızılay Özalp

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Conflict of Interest: No conflict of interest

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Table 1: Clinical and laboratory characteristics of the study groups.

Variables	Uric acid		p
	>75 Percentile (n=52)	<75 Percentile (n=76)	
Age (years)	13,2 ± 2,7	13 ± 2,6	0,66
Gender (%Female)	69,2	67,1	0,80
Puberty stage (% Pubertal)	92,3	93,4	0,82
Weight (kg)	74,1 ± 18,6	72,4 ± 19,2	0,61
Height (cm)	155,9± 12,8	155,1 ± 11,6	0,72
BMI (kg/m^2)	29,9± 4,4	29,5 ± 5	0,60
BMI SDS (kg/m^2)	2,03± 0,36	1,98± 0,35	0,44

Waist circumference (cm)	97,8 ± 11,6	94,5 ± 11,6	0,12
Hip circumference (cm)	105,6± 13,6	105,1± 11,9	0,83
Waist/Hip circumference ratio	0,93± 0,08	0,90 ± 0,06	**0,01**
SBP (mmHg)	116,6 ± 11,9	115,3± 13	0,58
DBP (mmHg)	73,1± 10,6	75,3 ± 11,6	0,29
GlcT0^{i}(mg/dl)	85,1 ± 7,5	86,0± 8,3	0,56
GlcT30^{i}(mg/dl)	136,3± 20,3	134,5± 21,9	0,64
GlcT60^{i}(mg/dl)	136± 29,8	132,6 ± 28,3	0,52
GlcT90^{i}(mg/dl)	126,2± 26,3	125,2± 33,1	0,85
GlcT120^{i}(mg/dl)	120,3 ± 22,1	122,1 ± 23,3	0,67
InsT0^{i}(mUI/L)	27,8± 12,8	23,4± 11,4	**0,045**
InsT30^{i}(mUI/L)	142,6 ± 77,5	117,8 ± 62,1	**0,049**
InsT60^{i}(mUI/L)	148,7 ± 91,6	113,3± 73,3	**0,017**
InsT90^{i}(mUI/L)	134,8 ± 91,3	117,8 ± 73,2	0,25
InsT120^{i}(mUI/L)	119,5± 89	105,7± 69,3	0,33
HOMA-IR	6,06± 3,1	5,04 ± 2,6	**0,083**
AST(IU/L)	27,5 ± 10,4	29,7± 21,2	0,49
ALT(IU/L)	31,7± 21,5	31± 28,1	0,87
Total cholesterol(mg/dl)	164,4± 28,3	158,3 ± 31,8	0,27
HDL-c(mg/dl)	45,2± 8,7	48,9± 10,1	**0,028**
LDL-c(mg/dl)	91,2± 21,3	83,8 ± 30,8	0,14
Triglycerides(mg/dl)	140,1± 66,5	124,7 ± 105,3	0,35
Urinary albumin excretion in a 24-h urine collection	10,1 ± 9	10,2 ± 11,7	0,98
Protein/Creatinine ratio in a first-morning urine sample	0,62 ± 0,64	0,52 ± 0,61	0,41
The number of criteria related to MetS (26);	2,01±0,9	1,60±0,7	**0,009**[a]

Abbreviations: ALT, alanine aminotransferase; AST, aspartat aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; GlcT0^{i}, fasting glucose; GlcT30^{i}, GlcT60^{i}, GlcT90^{i}, GlcT120^{i}, post-challenge glucose; HDL-c, high density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance; InsT0^{i}, fasting insülin; InsT30^{i}, InsT60^{i}, InsT90^{i}, InsT120^{i}, post-challenge insülin; LDL-c, low density lipoprotein cholesterol; SBP, systolic blood pressure; SDS, standard deviation score;

[a]Mann-Whitney U test

Table 2 shows that elevated SUAL were significantly associated with hypertriglyceridemia, decreased HDL-c, increased AI, presence of IR and MetS.

Table 2: Antropometric, clinical and metabolic variables of the study population according to the uric acid.

Variables	**Uric acid**		**P**
	>75 P (n=52) n(%)	**<75P (n=76) n(%)**	
Gender Male Female	 16 (30,8) 36 (69,2)	 25 (32,9) 51 (67,1)	0,8
The extent of obesity Overweight Moderate obesity Severe obesity	 11 (21,2) 25 (48,1) 16 (30,8)	 16 (21,1) 44 (57,9) 16 (21,1)	0,4
Puberty Prepubertal stage Pubertal stage	 4 (7,7) 48 (92,3)	 5 (6,6) 71 (93,4)	0,8
Waist circumference Increased (≥90 p) Normal (<90 p)	 52 (100) -	 76 (100) -	-
SBP Increased (≥95 p) Normal	 12 (23,1) 40 (76,9)	 14 (18,4) 62 (81,6)	0,52
DBP Increased (≥95 p) Normal	 7 (13,5) 45 (86,5)	 12 (15,7) 64 (84,3)	0,84

Glycemia Altered Normal	 13 (25) 39 (75)	 21 (27,6) 55 (724)	0,74
Triglycerides Altered (≥150 mg/dl) Normal	 18 (34,6) 34 (65,4)	 13 (17,1) 63 (82,9)	**0,023**
HDL-c Altered (<40 mg/dL) Normal	 19 (36,5) 33 (63,5)	 11 (17,8) 65 (85,5)	**0,004**
Atherogenic risk 1 Total cholesterol/HDL-c Present (>4) Absent	 20 (38,5) 32 (61,5)	 16(21,1) 60(78,9)	**0,03**
Atherogenic risk 2 TG/HDL-c Present (>2.2) Absent	 20 (38,5) 32 (61,5)	 33 (43,4) 43 (56,6)	0,044
IR Present Absent	 40 (76,9) 12 (23,1)	 41 (53,9) 35 (46,1)	**0,008**
Metabolic Syndrome Present Absent	 15 (28,8) 37 (42,3)	 9 (11,8) 67 (88,2)	**0,015**

Abbreviations: DBP, diastolic blood pressure; HDL-c, high density lipoprotein cholesterol; IR, insulin resistance; SBP, systolic blood pressure; TG,triglycerides.

Table 3: Corelation between risk factors of metabolic syndrome, cardiovascular and renal injury with serum uric asid levels.

Variables	Uric asid (n=128)	
	R	**P**
BMI (kg/m^2)	0,13	0,14
BMI SDS (kg/m^2)	0,05	0,57
BMI percentile	0,019	0,83
Waist circumference (cm)	0,32	**<0,0001**
Waist/Hip circumference ratio	0,20	**0,017**
SBP (mmHg)	0,07	0,42
DBP (mmHg)	-0,04	0,61
GlcT0'(mg/dl)	-0,07	0,37
GlcT30'(mg/dl)	0,09	0,27
GlcT60'(mg/dl)	0,21	**0,013**
GlcT90'(mg/dl)	0,11	0,21
GlcT120'(mg/dl)	0,10	0,25
InsT0'(mUI/L)	0,28	**0,001**
InsT30'(mUI/L)	0,30	**0,001**
InsT60'(mUI/L)	0,27	**0,002**
InsT90'(mUI/L)	0,19	**0,03**
InsT120'(mUI/L)	0,18	**0,03**
HOMA-IR	0,29	**0,001**
AST(IU/L)	-0,002	0,98
ALT(IU/L)	0,14	0,11
Total cholesterol(mg/dl)	0,06	0,45
HDL-c(mg/dl)	-0,26	**0,002**
LDL-c(mg/dl)	0,03	0,72
Triglycerides(mg/dl)	0,12	0,18
Total cholesterol/HDL-c ratio	0,27	**0,002**
TG/HDL-c ratio	0,24	**0,008**
The number of criteria related to metabolic syndrome	0,30	**<0,0001**
Urinary albumin excretion in a 24-h urine collection	-0,06	**0,46**

Protein/Creatinine ratio in a first-morning urine sample	0,03	**0,71**

Abbreviations: ALT, alanine aminotransferase; AST, aspartat aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; GlcT0', fasting glucose; GlcT30', GlcT60', GlcT90', GlcT120', post-challenge glucose; HDL-c, high density lipoprotein cholesterol; HOMA-IR, homeostatic model assessmensst of insulin resistance; InsT0', fasting insülin; InsT30', InsT60', InsT90', InsT120', post-challenge insülin; LDL-c, low density lipoprotein cholesterol; SBP, systolic blood pressure; SDS, standard deviation score; TG, triglycerides.