KIDNEY DISEASES

Association of Serum Uric Acid With Cardiometabolic Risk Factors and Metabolic Syndrome in Iranian Adolescents
The CASPIAN-III Study

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Introduction. There is controversial evidence on association of serum acid uric (SUA) with cardiometabolic risk factors and metabolic syndrome in adults. This study aimed to investigate the associations of SUA levels, components of metabolic syndrome, and other cardiometabolic risk factors, in a nationally representative sample of Iranian adolescents.

Materials and Methods. This study included 132 participants who met the criteria of metabolic syndrome and 235 participants without metabolic syndrome. The participants were grouped according to the tertiles of SUA. Metabolic syndrome was defined according to the Adult Treatment Panel III criteria modified for children and adolescents. The relationship between SUA and cardiometabolic risk factors and metabolic syndrome was assessed by multivariable logistic regression analysis.

Results. The mean age of the participants was 15.21 ± 2.35 years, with no significant difference between the boys and the girls. The participants whose SUA was categorized in the 2nd tertile and those falling into the 3rd tertile had significantly higher systolic blood pressure ($P < .001$) as compared with the lower tertile(s). A similar trend was documented for the overall high blood pressure. Metabolic syndrome was associated with the 2nd and 3rd tertiles of SUA as compared to the lower tertile(s), in the adjusted model ($P < .001$), with the risk increasing by at least 2 times.

Conclusions. Our study showed that those adolescents with metabolic syndrome had higher SUA levels. Its association with some components of metabolic syndrome supports that SUA might be an additional component of metabolic syndrome even during adolescence.

INTRODUCTION

Metabolic syndrome is defined as a cluster of risk factors including anthropometric features and laboratory values, predisposing the individual to diabetes mellitus and increased risk for cardiovascular disease.[1,2] The association between cardiometabolic risk factors and metabolic syndrome is well documented.[3-5] These risk factors could persist into adulthood,[6-10] and

the American Heart Association advises for early preventive interventions against cardiovascular risk factors, starting in childhood.[11] Metabolic syndrome among children and adolescents has been studied extensively, and an epidemic of child and adolescent obesity has been established.[12-15] Although the developing countries were once mainly concerned with malnutrition of children, rapid rise of obesity in their pediatric populations has changed the landscape.[16] Iran has not been an exception, and nationwide studies on metabolic syndrome, cardiovascular risk factors and obesity among children and adolescents have been initiated in earnest since early 2000s.[17] Ever since, trends and prevalence of these factors have been regularly studied and reported.[18-21]

An increased level of serum uric acid (SUA) has been proposed as a cardiovascular disease risk factor in adults[22-24]; such association has been also described in the pediatric populations.[25-28] Associations between SUA levels, components of metabolic syndrome, and the utility of SUA levels for predicting metabolic syndrome in adolescents had controversial results; while some studies have reported strong associations among these variables,[29-31] others did not confirm an independent association based on multiple regression models. They suggested that this association might be gender-specific, limited to higher levels of SUA, and limited to a number of metabolic syndrome components[32-35]; yet some have argued, aptly, that with various confounders, physiologic roles of SUA, which in turn fits into an intricate web of feedbacks, and the inevitable limitations in our understanding of vascular physiology, the whole cycle remains to be determined.[36] This ongoing debate prompted us to design this study in order to examine the associations of SUA levels with cardiometabolic risk factors and metabolic syndrome in a representative sample of Iranian adolescents.

MATERIALS AND METHODS
Study Design and Population

The present study was designed as a cross-sectional study which was run on a national representative data of the 3rd round of the school-based surveillance system entitled "Childhood and Adolescence Surveillance and Prevention of Adult Noncommunicable Disease (CASPIAN III)" study (2009-2010). The aim and details of methods of

mentioned study has been described previously.[37]

From a total of 5625 students, aged 10 to 18 years, who were selected via multistage random cluster sampling method from urban and rural areas of 27 provinces in Iran, 132 participants meeting the criteria of metabolic syndrome and 235 randomly selected ones without these criteria were categorized as the study and control groups, respectively.

Ethics Considerations

Participation in the study was voluntary. The participants entered the survey after explaining the study objectives and protocols and obtaining oral consent from students and written consent from their parents. The Ethics Committee of Tehran and Isfahan University of Medical Sciences and other relevant national regulatory organizations (Ministry of Health and Ministry of Education) approved the study protocol. All of the questionnaires and information forms were completed anonymously.

Data Collection

In the data collection phase, all processes of examinations with calibrated instruments and recording of information in validated checklists were designed and conducted under the standard protocol by trained health care professional teams.[38] Via interview with parents or children, demographic information including family history of chronic diseases (hypertension, dyslipidemia, diabetes mellitus, and obesity), parental level of education (the highest total years of schooling), possessing a family private car and type of home, dietary behaviors, physical activity (PA), and sedentary lifestyle, was completed for all of the participants.

Clinical and Laboratory Measurements

Height and weight were measured, according to standardized protocols, without shoes and with light clothing to the nearest 0.1 unit of measure (cm for height and kg for weight). Body mass index (BMI) was calculated from weight and height (weight [kg]∕height squared [m^2]).[4,22] Waist circumference was measured over skin, midway between the lower border of the rib margin and the iliac crest at the end of normal expiration, to the nearest 0.1 cm. Both waist circumference and height were measured using a nonelastic tape. Abdominal obesity was defined as a waist-height

ratio greater than 0.5.[39]

Systolic and diastolic blood pressure were measured on the right arm, with the individual in a sitting position and at rest for at least 5 minutes, using standardized mercury sphygmomanometers and appropriate size cuff. Two measurements at 2-minute intervals were recorded, and the average was used for the statistical analysis.[40] Hypertension was defined as systolic and/or diastolic blood pressure equal to or greater than the 95th percentile for age, sex, and height.[41]

For each of the participants, a blood sample was drawn between 7:00 AM and 9:00 AM after 12 to 14 hours overnight fasting. Blood samples were delivered to the laboratory on the same day. Fasting blood glucose, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDLC), and low-density lipoprotein cholesterol (LDLC) were measured enzymatically by auto-analyzers. The HDLC was determined after dextran sulfate-magnesium chloride precipitation of non-HDLC.[42] The SUA was determined on a standard auto-analyzer with Uricase and reagent (Parsazmun Co, Tehran, Iran). Tertiles of SUA levels were considered for analysis of association of SUA with cardiometaboloc risk factors and metabolic syndrome criteria. The ranges of SUA levels in tertiles 1, 2, and 3 were 1.76 mg/dL to 4.40 mg/dL, 4.41 mg/dL to 6.03 mg/dL, and 6.04 mg/dL to 7.70 mg/dL, respectively.

Definitions

Cardiometabolic risk factors. According to the Adult Treatment Panel III criteria modified for children and adolescents, participants were classified as having metabolic syndrome if they had at least 3 of the 5 following criteria: abdominal obesity (waist-height ratio > 0.5), elevated blood pressure (either systolic or diastolic blood pressure $\geq$ 90th percentile for age, sex, and height), low HDLC level (< 50 mg/dL except in boys 15 to 19 years old for whom cutoff was < 45 mg/dL), high triglyceride level ($\geq$ 100 mg/dL), and high fasting blood glucose ($\geq$ 100 mg/dL). General obesity, high LDLC, and high total cholesterol were considered as other important cardiometabolic risk factors. General obesity and overweight were considered as a BMI greater than the 95th percentile and between the 85th and the 95th percentile for age and sex, respectively. According to the American

Heart Association, high LDLC and total cholesterol were defined as greater than 110 mg/dL and 200 mg/dL or gretaer, respectively.[43]

Socioeconomic status. Variables including parental education, parents' job, possessing private car, school type (public versus private), and having personal computer at home were summarized in 1 main component. This component explained 72.0% of variance. This main component was categorized into tertiles. The 1st tertile was defined as a low socioeconomic status (SES), 2nd tertile as an intermediate, and 3rd tertile as a high.

Screen Time. To assess the screen time (ST) behaviors, the average number of hours per day that participants spent watching TV/VCDs, personal computer, or electronic games was asked. The total cumulative spent time for ST was estimated. Information was recorded separately for weekdays and weekends. Analyzing correlates of ST, according to the international ST recommendations, ST was categorized into 2 groups of less than 2 hours per day (low) and 2 hours per day or more (high).[44,45]

Physical Activity. Through a validated questionnaire, information of the past week weekly frequency of leisure time PA outside the school was collected.[46] At least 30 minutes duration of exercises per day, that caused heavy sweating or large increases in breathing or heart rate, was defined as PA. The response options were as follow: none, 1 to 2 days, 3 to 6 days, and every day. For statistical analysis, each weekly frequency was categorized into 2 groups of up to 3 days per week (low) and 4 to 7 days (high).[47]

Statistical Analyses

Continuous and categorical variables are expressed as mean ± standard deviation and number (percentage), respectively. The Kolmogorov-Smirnov test was used to examine the normality of continuous variables. Continuous and categorical variables were compared between sexes by the *t* test and the chi-square test, respectively.

The mean of cardiometabolic risk factors across tertiles of SUA was compared by the 1-way analysis of variance test. Logistic regression analysis was used to examine the association of cardiometabolic risk factors and SUA. The aim of those analyses were to run 3 models: model 1, crude model (without adjustment); model 2, adjusted for age, living area, sex, PA, ST, and SES; and model 3,

additionally adjusted for BMI in all abnormality except obesity and overweight. *P* values less than .05 were considered significant. All statistical analyses were carried out using the SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc, Chicago, IL, USA).

RESULTS

The study participants consisted of 367 students with a mean age of 15.21 ± 2.35 years, with no significant difference between the boys and the girls (15.03 ± 2.34 years versus 15.30 ± 2.37 years, respectively). The majority of the participants (73.3%) were from urban areas. Characteristics of the participants are shown in Table 1; blood pressure was significantly lower in the boys. The girls had a significantly higher PA, but were more likely to have a high fasting blood glucose level.

Table 1. Characteristics of the Participants By Sex*

Characteristic	Total	Boy	Girl	*P*
Mean age, y	15.21 ± 2.35	15.03 ± 2.34	15.30 ± 2.37	.38
Living area				
Urban	264 (73.3)	109 (73.6)	155 (73.1)	.91
Rural	96 (26.7)	39 (26.4)	57 (26.9)	.91
Serum uric acid†	5.27 (2.45)	5.59 (2.51)	5.07 (2.42)	.20
Mean height, cm	157.41 ± 13.86	153.68 ± 10.30	160.01 ± 15.37	< .001
Mean weight, kg	53.77 ± 18.63	50.15 ± 13.74	56.36 ± 21.05	.001
Mean waist circumference, cm	74.27 ± 13.44	71.63 ± 11.03	76.12 ± 14.64	.001
Mean waist-height ratio	0.47 ± 0.07	0.46 ± 0.06	0.47 ± 0.07	.35
Mean body mass index, kg/m^2	21.29 ± 4.98	20.98 ± 4.65	21.52 ± 5.20	.29
Mean systolic blood pressure, mm Hg	107.83 ± 16.90	104.77 ± 17.45	109.91 ± 16.23	.004
Mean diastolic blood pressure, mm Hg	68.32 ± 11.52	66.75 ± 10.79	70.08 ± 11.681	< .001
Mean fasting blood glucose, mg/dL	87.95 ± 13.24	86.42 ± 12.62	89.01 ± 13.58	.07
Mean serum triglyceride, mg/dL	113.26 ± 65.73	113.25 ± 63.18	113.26 ± 67.59	.99
Mean high-density lipoprotein, mg/dL	42.58 ± 12.89	44.18 ± 12.67	42.06 ± 12.93	.12
Mean low-density lipoprotein, mg/dL	83.03 ± 26.15	83.291 ± 26.23	82.86 ± 26.17	.88
Mean total cholesterol, mg/dL	148.68 ± 32.97	150.30 ± 31.40	147.55 ± 34.06	.43
Physical activity				
Low	183 (58.3)	92 (66.7)	91 (51.7)	
Medium	88 (28.0)	27 (19.6)	61 (34.7)	
High	43 (13.7)	19 (13.8)	24 (13.6)	.01
Screen time				
Low	71 (22.0)	30 (21.9)	41 (22.2)	
High	251 (78.0)	107 (78.1)	144 (77.8)	.95
Abdominal obesity	138 (37.6)	55 (36.4)	83 (38.4)	.69
High systolic blood pressure	47 (13.0)	15 (10.3)	32 (14.8)	.20
High diastolic blood pressure	331 (90.9)	141 (95.3)	190 (88.0)	.17
High blood pressure	65 (18.0)	20 (13.7)	45 (20.8)	.08
High fasting blood glucose	76 (20.8)	20 (13.3)	56 (25.9)	.003
High serum triglyceride	91 (24.8)	35 (23.2)	56 (25.9)	.54
High total cholesterol	28 (7.7)	12 (8.0)	16 (7.4)	.84
High low-density lipoprotein	19 (6.0)	8 (6.3)	11 (5.9)	.87
Low high-density lipoprotein				
Metabolic syndrome	132 (36)	50 (33.1)	82 (32.8)	.34
Number of metabolic syndrome components				
1	97 (25.4)	33 (21.9)	64 (29.6)	
2	14 (3.8)	2 (1.3)	12 (5.6)	
3	111 (30.2)	46 (30.5)	65 (30.1)	
4	21 (5.7)	4 (2.6)	17 (7.9)	.003
Obesity	68 (18.7)	26 (17.2)	42 (19.7)	.55
Overweight	45 (12.4)	14 (9.3)	31 (14.6)	.13

*Values are mean standard deviation or count (percentage), except for serum uric acid.
†Values are median (interquartile range).

The prevalence of metabolic syndrome was not significantly different, while the girls tended to have more metabolic syndrome components than the boys.

Except for systolic blood pressure, which followed an ascending significant trend along with the ascending tertiles of SUA, there was not any significant difference between the mean values of cardiometabolic risk factors and SUA (Table 2). In a similar way, except for the higher frequency of high blood pressure associated with the SUA tertiles, there was not any significant differences between prevalence rates of cardiometabolic risk factors and SUA. There were no significant differences in the number of metabolic syndrome components between tertiles of SUA, either (Table 3).

Table 4 shows the association of cardiometabolic risk factors and SUA in the logistic regression analysis. The odds of a high systolic blood pressure were more than 2 times in the participants whose SUA was categorized in the 2nd tertile compared with their counterparts in 1st tertile ($P < .001$). Adolescents in the 3rd tertile of SUA, compared with the two other tertiles, were more likely to have high systolic blood pressure across all the three models ($P < .001$). For high diastolic blood

Table 2. Mean Values for Cardiometabolic Risk Factors By Tertiles of Serum Uric Acid

Parameter	Serum Uric Acid*			P
	Tertile 1	Tertile 2	Tertile 3	
Mean weight, kg	52.39 ± 15.91	56.03 ± 21.8	52.88 ± 17.49	.83
Mean height, cm	157.07 ± 12.79	159.08 ± 14.7	156.05 ± 13.92	.56
Mean waist circumference, cm	73.84 ± 12.15	75.40 ± 15.20	73.57 ± 12.79	.87
Mean body mass index, kg/m^2	20.87 ± 4.47	21.69 ± 5.77	21.32 ± 4.59	.49
Mean waist-height ratio	0.46 ± 0.07	0.47 ± 0.07	0.47 ± 0.06	.67
Mean systolic blood pressure, mm Hg	105.91 ± 13.33	107.43 ± 16.08	110.21 ± 20.45	.04
Mean diastolic blood pressure, mm Hg	66.79 ± 10.31	68.88 ± 12.07	69.28 ± 11.99	.09
Mean fasting blood glucose, mg/dL	86.99 ± 13.81	88.53 ± 14.07	88.31 ± 11.77	.43
Mean serum triglyceride, mg/dL	111.00 ± 66.13	109.97 ± 66.05	118.83 ± 65.17	.35
Mean high-density lipoprotein, mg/dL	45.07 ± 14.34	41.72 ± 11.72	42.02 ± 12.18	.06
Mean low-density lipoprotein, mg/dL	80.01 ± 26.90	85.26 ± 26.61	84.03 ± 24.86	.25
Mean total cholesterol, mg/dL	145.44 ± 31.81	149.04 ± 34.85	151.55 ± 32.14	.15

*The ranges of serum uric acid levels are 1.76 mg/dL to 4.40 mg/dL for tertile 1, 4.41 mg/dL to 6.03 mg/dL for tertile 2, and 6.04 mg/dL to 7.70 mg/dL for tertile 3.

Table 3. Prevalence of Cardiometabolic Risk Factors By Tertiles of Serum Uric Acid*

Parameter	Serum Uric Acid†			P
	Tertile 1	Tertile 2	Tertile 3	
Abdominal obesity	42 (34.4)	47 (38.2)	49 (40.2)	.64
High systolic blood pressure	7 (5.8)	19 (15.6)	21 (17.6)	.01
High diastolic blood pressure	5 (4.1)	15 (12.3)	13 (10.7)	.06
High blood pressure	9 (7.4)	26 (21.3)	30 (25.2)	<.001
High fasting blood glucose	21 (17.4)	26 (21.1)	29 (23.8)	.46
High serum triglyceride	28 (23.0)	28 (22.8)	35 (28.7)	.47
High total cholesterol	7 (5.8)	10 (8.1)	11 (9.1)	.61
High low-density lipoprotein	7 (6.4)	6 (5.9)	6 (5.7)	.97
Low high-density lipoprotein	47 (38.5)	62 (50.4)	64 (52.5)	.06
Metabolic syndrome	32 (26.2)	46 (37.4)	54 (44.3)	.12
Number of metabolic syndrome components				
1	36 (29.5)	32 (26.0)	29 (23.8)	.36
2	5 (4.1)	5 (4.1)	4 (3.3)	.36
3	27 (22.1)	38 (30.9)	46 (37.7)	.36
4	5 (4.1)	8 (6.5)	8 (6.6)	.36
Obesity	21 (17.4)	30 (24.6)	17 (14.0)	.09
Overweight	12 (9.9)	12 (9.8)	21 (17.4)	.12

*Values are count (percentage).
†The ranges of serum uric acid levels are 1.76 mg/dL to 4.40 mg/dL for tertile 1, 4.41 mg/dL to 6.03 mg/dL for tertile 2, and 6.04 mg/dL to 7.70 mg/dL for tertile 3.

pressure, this trend was only detected in the crude modeling of 2nd tertile. The overall high blood pressure was significantly associated with SUA in all models (P < 0.001).

A low HDLC was associated with falling into the 3rd tertile of the SUA with no adjustment for

Table 4. Association of Cardiometabolic Risk Factors and Serum Uric Acid in Logistic Regression Analysis*

Parameter	Serum Uric Acid†		
	Tertile 1	Tertile 2	Tertile 3
Abdominal obesity			
Model 1	1.00 (referent)	1.17 (0.69 to 1.98)	1.27 (0.76 to 2.15)
Model 2	1.00 (referent)	1.29 (0.69 to 2.41)	0.97 (0.52 to 1.83)
Model 3	1.00 (referent)	0.86 (0.35 to 2.08)	0.80 (0.36 to 1.77)
High systolic blood pressure			
Model 1	1.00 (referent)	3.00 (1.21 to7.43)	3.49 (1.42 -8.55)
Model 2	1.00 (referent)	3.20 (1.14 to8.93)	3.71 (1.33-10.35)
Model 3	1.00 (referent)	2.54 (0.87 to 7.45)	4.03 (1.41-11.54)
High diastolic blood pressure			
Model 1	1.00 (referent)	3.25 (1.14 to9.25)	2.79 (0.96 to 8.09)
Model 2	1.00 (referent)	2.60 (0.78 to 8.64)	3.12 (0.94to10.35)
Model 3	1.00 (referent)	1.98 (0.57 to 6.87)	3.18 (0.94to10.73)
High blood pressure			
Model 1	1.00 (referent)	3.37 (1.50 to 7.54)	4.19 (1.89 to 9.29)
Model 2	1.00 (referent)	3.45 (1.35 to8.78)	5.29 (2.10-15.32)
Model 3	1.00 (referent)	2.81 (1.06to 7.45)	5.61 (2.17-14.45)
High triglyceride			
Model 1	1.00 (referent)	0.98 (0.54 to 1.79)	1.35 (0.75 to 2.40)
Model 2	1.00 (referent)	1.22 (0.61 to 2.44)	1.12 (0.56 to 2.26)
Model 3	1.00 (referent)	0.91 (0.43 to 1.94)	1.12 (0.54 to 2.35)
Low high-density lipoprotein			
Model 1	1.00 (referent)	1.62 (0.97 to 2.69)	1.76 (1.05to 2.93)
Model 2	1.00 (referent)	2.15 (1.12 to4.12)	1.71 (0.90 to 3.26)
Model 3	1.00 (referent)	2.08 (1.08 to4.01)	1.71 (0.90 to 3.26)
High fasting blood glucose			
Model 1	1.00 (referent)	1.27 (0.67-2.42)	1.48 (0.79-2.74)
Model 2	1.00 (referent)	1.50 (0.72-3.26)	1.75 (0.82-3.76)
Model 3	1.00 (referent)	1.47 (0.68-3.16)	1.76 (0.82-3.78)
Having metabolic syndrome			
Model 1	1.00 (referent)	1.68 (0.97-2.89)	2.23 (1.30-3.82)
Model 2	1.00 (referent)	2.20 (1.11-4.36)	2.22 (1.11-4.42)
Model 3	1.00 (referent)	1.79 (0.77 to 4.16)	2.75 (1.23-6.17)
High low-density lipoprotein			
Model 1	1.00 (referent)	0.92 (0.29 to 2.83)	0.88 (0.28 to 2.72)
Model 2	1.00 (referent)	1.71 (0.46 to 6.33)	0.44 (0.07 to 2.57)
Model 3	1.00 (referent)	1.96 (0.51 to 7.43)	0.42 (0.07 to 2.46)
High total cholesterol			
Model 1	1.00 (referent)	1.44 (0.53 to 3.91)	1.62 (0.60 to 4.35)
Model 2	1.00 (referent)	2.13 (0.66 to 6.82)	1.38 (0.41 to 4.65)
Model 3	1.00 (referent)	1.80 (0.54 to 5.98)	1.42 (0.42 to 4.80)
Overweight			
Model 1	1.00 (referent)	0.99 (0.42 to 2.30)	1.90 (0.89 to 4.07)
Model 2	1.00 (referent)	0.86 (0.35 to 2.13)	1.73 (0.75 to 3.98)
Obesity			
Model 1	1.00 (referent)	1.55 (0.83 to 2.90)	0.77 (0.38 to 1.56)
Model 2	1.00 (referent)	1.93 (0.93 to 3.99)	0.62 (0.27 to 1.45)

*Model 1 was without adjustment; model 2, adjusted for age, living area, sex, physical activity, screen time, and socioeconomic status; and model 3, additionally adjusted for body mass index in all abnormalities except for obesity and overweight.
†The ranges of serum uric acid levels are 1.76 mg/dL to 4.40 mg/dL for tertile 1, 4.41 mg/dL to 6.03 mg/dL for tertile 2, and 6.04 mg/dL to 7.70 mg/dL for tertile 3.

other factors. This trend was seen for participants falling into the 2nd tertile only with the adjusted models (Table 4).

The prevalence of metabolic syndrome in the adjusted model for age, living area, sex, PA, ST, and SES was associated with the 2nd tertile of SUA ($P < .001$). This increasing pattern followed in all of models for the 3rd tertile members as compared with all the two other tertiles, with the risk increasing by at least 2 times (Table 4).

DISCUSSION

This study found that adolescents with metabolic syndrome had higher SUA levels, and SUA had significant associations with some components of metabolic syndrome. Participants whose SUA was categorized in 2nd tertile and adolescents in the 3rd tertile compared with lower tertiles, had significantly higher systolic blood pressure. Moreover, raised levels of SUA were associated with elevated blood pressure. Using tertiles of SUA levels, a difference was observed in the mean of participants' systolic blood pressure; this finding is consistent with some previous studies which used tertiles, quartiles, or quintiles to categorize adolescents based on their SUA levels.[26, 32, 35, 48] After dichotomizing various variables, the same association was still observable. Considering that increased estimated glomerular filtration rate is clustered with other metabolic syndrome risk factors,[49] and elevated blood pressure would lead to increased filtration of SUA in the kidney, these findings should be weighed cautiously against each other.

In our regression model, high systolic blood pressure meant 2- to 3-fold increases in odds of having a higher SUA level in the crude model, and the models adjusted for more covariates actually increased the odds, even further. Having elevated blood pressure also led to significant results, with increased odds of falling into higher tertiles of SUA levels for participants with elevated blood pressure; the odds increased further when the base model was adjusted for additional confounding factors.

Low serum HDLC levels, which had missed the marked narrowly when comparing the means of tertiles, increased the odds of having somewhat higher SUA levels; that is, being in the second tertile was more likely to be associated with low serum HDLC levels, as compared to being in the

1st tertile. This finding was not seen among those in the 3rd tertile. Having metabolic syndrome increased the odds of being in the upper tertile of SUA levels, as well. Both of these findings were corroborated by previous studies; Cardoso and colleagues[35] linked metabolic syndrome and SUA levels through insulin resistance; while glycemia was not different among quartiles of SUA levels, homeostasis model assessment of insulin resistance varied significantly among quartiles. Wang and coworkers[29] reported increased odds of having some of the metabolic syndrome components including low serum HDLC levels and elevated blood pressure, but that finding was almost limited to those in the highest quartile of SUA levels.

We used fasting blood glucose levels and other anthropometric measurements to determine insulin resistance, and did not find differences among tertiles of SUA levels, but since oxidative stress had not been evaluated in our study, we must be cautious in attributing the association between metabolic syndrome and SUA levels to serum HDLC levels. Others have suggested that dyslipidemia and subsequent increased free fatty acids could cause increased lipid peroxidation and an oxidative stress (prompting increased SUA levels),[35] or that influx of fatty acids into blood stream would directly increase purine synthesis (and hence SUA production) through pentose phosphate shunt[36,50]; although dyslipidemia in general was associated with increased odds of having higher SUA levels, that phenomenon was a result of low serum HDLC levels, not increased LDL or VLDL levels. A study which was focused on lipid profile and SUA levels did not find independent associations among the two in regression models,[32] although different lipid serum levels and SUA levels were correlated.

The nature of our study design did not permit inferring causality. One possible explanation for observed association of high SUA levels with low serum HDLC levels in the absence of any associations with serum triglyceride or LDL levels could be that higher SUA levels are a cause for metabolic syndrome. Adjusting the data for glomerular filtration rate could improve our regression models further. This population-based cross-sectional study was extracted from a large representative population-based survey which could improve generalizability of results.

CONCLUSIONS

This study suggests that adolescents with metabolic syndrome had higher levels of SUA; moreover, some components of metabolic syndrome were associated with higher levels of SUA. This association was independent of sex, BMI, or age. Further longitudinal studies are necessary to investigate the causal relation between SUA levels, metabolic syndrome components, and cardiometabolic risk factors, as well as their clinical implications.

CONFLICT OF INTEREST

None declared.

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