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RESEARCH

Trends in serum uric acid levels among Korean children and adolescents between 2016 and 2020: a nationwide study

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Abstract

The aim of this study was to examine trends in serum uric acid (SUA) levels over a recent 5-year period according to age, sex, obesity, and abdominal obesity among Korean children and adolescents. We conducted a serial cross-sectional analysis using nationally representative data from the Korea National Health and Nutritional Examination Survey from 2016 to 2020. The study outcome was trends in SUA levels. SUA trends were analyzed by survey-weighted linear regression analysis considering the survey year as a continuous variable. SUA trends were also analyzed for subgroups based on age, sex, abdominal obesity, or obesity. This study included 3,554 children and adolescents aged 10–18 years. SUA increased significantly over the study period in boys (p for trend = 0.043), but not in girls (p for trend = 0.300). In age-specific analyses, SUA increased significantly in the 10–12 years group (p for trend = 0.029). After adjusting for age, SUA increased significantly in the obese group of both boys (p for trend = 0.026) and girls (p for trend = 0.023), but not in the overweight, normal, or under-weight groups of either sex. After adjusting for age, SUA increased significantly in the abdominal obesity group of boys (p for trend = 0.017) and girls (p for trend = 0.014), but not in the non-abdominal obesity group of either sex.

Conclusion: In the current study, SUA levels significantly increased in both boys and girls with obesity or abdominal obesity. Further studies of the effect of SUA on health outcomes in boys and girls with obesity or abdominal obesity are needed.

What is Known:

- *High serum uric acid (SUA) is a risk factor for various metabolic diseases, including gout, hypertension, and type 2 diabetes.*

What is New:

- *SUA levels increased in boys and the 10-12 years group of Korean children and adolescents.*
- *SUA levels increased significantly in Korean children and adolescents with obesity or central obesity.*

Keywords Uric acid · Children · Adolescent · Obesity · Abdominal obesity

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Abbreviations

BMI	Body mass index
CVD	Cardiovascular disease
IR	Insulin resistance
KNANES	Korea National Health and Nutritional Examination Survey
MetS	Metabolic syndrome
SUA	Serum uric acid
WC	Waist circumference

Introduction

Uric acid (UA) is the final product of purine metabolism and a heterocyclic compound with the chemical formula C5H4N4O3 [1, 2]. It is produced primarily by the metabolism of endogenous purines in the liver and partially by the metabolism of ingested purines [3]. UA is produced intracellularly by xanthine oxidoreductase and circulates as plasma sodium urate [4]. Most UA in the body is excreted by the kidneys, while the remainder is excreted through the small intestine and bile ducts [5]. High serum uric acid (SUA) levels are the result of decreased UA clearance and/or increased UA production secondary to metabolic abnormalities or a purine-rich diet [2, 5, 6]. Previous studies have reported a consistent increase in SUA levels and the prevalence of hyperuricemia in recent decades [7–10].

Emerging studies have established that high SUA levels are closely associated with a number of cardio metabolic diseases, including obesity, metabolic syndrome (MetS), gout, dyslipidemia, hypertension, type 2 diabetes (T2DM), and chronic kidney disease [11–14]. A recent study indicated that SUA is associated with the prevalence of MetS and its components in general adults [15]. Several epidemiological studies have found that higher SUA levels are closely associated with increased liver enzyme and non-alcoholic fatty liver diseases, which comprise a spectrum of hepatic diseases associated with MetS [16, 17].

Whether UA contributes to MetS or is a consequence of MetS has not been established, but two studies conducted in Korea have reported strong associations between SUA levels and MetS in children and adolescents [18, 19]. Among the components of MetS, abdominal obesity in particular has been shown to be positively correlated with SUA concentrations [18, 19]. Previous studies have also reported that SUA levels are significantly associated with body mass index (BMI) and are significantly higher in overweight or obese populations than in normal-weight subjects [19–21]. In addition, increasing evidence suggests that elevated SUA levels in children and adolescents are predictive of the development of MetS and CVD later in life [19, 22, 23].

SUA levels vary according to age, sex, and environmental factors [8, 24–26]. SUA concentrations in children and adolescents increase gradually with age because renal excretion decreases to adult levels with puberty and body mass increases [27]. SUA levels are also higher in boys than in girls [28, 29]. SUA levels have been reported to rise considerably with age in boys but only increase slightly (and not by a statistically significant amount) with age in girls [28]. Since abnormalities in SUA concentration are closely associated with metabolic disorders, maintaining normal SUA levels may help to delay the onset of metabolic disorders in children and adolescents and reduce the risk of developing diseases associated with hyperuricemia. However, few previous studies have evaluated trends in SUA levels in Korean children and adolescents using a large-scale population-based design. Therefore, this study was conducted to investigate trends in mean SUA levels from 2016 to 2020 according to age, sex, obesity, and abdominal obesity among Korean children and adolescents based on data from the Korea National Health and Nutrition Examination Survey (KNHANES).

Methods

Study design and subjects

This cross-sectional study analyzed data from 2016 to 2020 obtained from KNHANES conducted by the Korean Centers for Disease Control and Prevention in accordance with the National Health Promotion Act. KNHANES is a cross-sectional, nationwide, representative survey conducted annually since 1998 to collect information on nutrient intake, non-communicable diseases (e.g., obesity, hypertension, diabetes, and dyslipidemia), and health behaviors in the Korean population. The KNHANES involves a multi-stage clustered probability design utilizing sampling units and households [30]. The survey is composed of a health questionnaire, examinations, and nutrition surveys for household members. The health interview and health examination are conducted by well-trained medical staff in the mobile examination centre during the all weeks of the year. Details on the KNHANES protocol has been described in a previous study [30].

As SUA levels have been investigated in individuals aged 10 years or older in Korea since 2016, we used data from the 2016 to 2020 KNHANES. The response rates were 76.6% for 2016–2018 (KNHANES VII) and 74.0% for 2019–2020 (KNHANES VIII). This study included data from a total of 3,554 Korean children and adolescents aged 10 to 18 years. Anthropometric data values were missing for 237 individuals, and SUA values were missing for 519 individuals.

This study was performed in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Severance Hospital (IRB No.4–2022-0796). Written informed consent was obtained from all participants or legal representatives of the children enrolled in this study.

Anthropometric measurements and laboratory tests

Anthropometric variables (body height, body weight, and waist circumference [WC]) were obtained by well-trained medical staff using a standardized protocol. BMI (kg/m^2) was calculated as weight in kilograms, divided by height in meters squared. Height was measured to the first decimal place (0.1 cm) using a stadiometer (SECA 225 in 2016–June 2019 and SECA 274 in July 2019–2020, Seca, Hamburg, Germany). Weight was measured to the first decimal place (0.1 kg) using an electronic balance (GL-6000–20, Gtech, Seoul, Korea). WC was measured at the midpoint between the inferior margin of the rib cage and the iliac crest. After resting for 5 min in a sitting position, blood pressure was measured in the right arm using a standard mercury sphygmomanometer (Baumanometer Wall Unit 33 (0850) in 2016–2019, Baum, Copiague, NY, USA, and Greenlight 300 in 2020, Accoson, Ayrshire, UK). Based on the 2017 Korean National Growth Charts, the study participants were classified into the following obesity groups based on BMI percentiles: underweight, less than the 5th percentile; normal, 5th percentile to less than the 85th percentile; overweight, 85th to less than the 95th percentile; or obese, equal to or greater than the 95th percentile. Abdominal obesity was defined as a WC > 90th percentile based on age- and sex-specific criteria.

Trained medical staff collected blood samples from each participant via the antecubital vein after an 8-h fasting period. The samples were processed and immediately refrigerated. Levels of SUA (mg/dL), total cholesterol (mg/dL), triglycerides (mg/dL), and high-density lipoprotein cholesterol (HDL-C) (mg/dL) were measured using a Hitachi automatic analyzer 7600/7600–210 (Hitachi, Tokyo, Japan). Hyperuricemia was defined when SUA levels were > 6.6 mg/dL at 10–11 years of age (both sexes) and > 7.7 mg/dL for males and > 5.7 mg/dL for females at 12–18 years of age [19].

Statistical analysis

We analyzed changes in mean SUA levels during the 5-year study period for the entire study population and for subgroups based on age, sex, obesity, and abdominal obesity. We employed one-way analysis of variance to compare continuous variables (mean SUA levels), and we used the Rao-Scott chi-square test to compare categorical variables (age groups, obesity, and abdominal obesity). To determine p-values for SUA trends, we performed survey-weighted linear regression analysis by considering the survey year as a continuous variable. The statistical significance of differences in SUA trends was also evaluated using survey-weighted linear regression analysis for each subgroup. In the BMI-specific and WC-specific analyses, we conducted the analyses after adjusting for age. To report representative estimates for the Korean population, we considered the sampling weights in all analyses.

Continuous variables are reported as weighted means with standard errors (SE), and categorical variables are reported as weighted percentages with SE. All statistical analyses for the complex survey design with clustering, stratification, and unequal weighting of the 5-year study period sample were performed using SAS, version 9.4 (SAS Inc., Cary, NC, USA). Significance was set as a p value < 0.05.

Results

Characteristics of the participants and trends in mean SUA levels

A total of 1,869 boys (mean age ± SE, 14.3 ± 0.1 years) and 1,685 girls (mean age ± SE, 14.2 ± 0.1 years) were included in this study (Table 1). Over the 5-year study time period (2016 to 2020), the mean BMI of boys increased significantly from 21.2 ± 0.3 kg/m^2 to 22.4 ± 0.3 kg/m^2 (p = 0.001), and the mean WC of boys increased significantly from 73.2 ± 0.7 cm to 76.3 ± 0.7 cm (p = 0.001). In contrast, there were no significant changes in BMI or WC of girls over the time period. The prevalence of hyperuricemia was 9.33% in boys and 9.68% girls, respectively.

Fig. 1 shows mean SUA trends from 2016 to 2020. Mean SUA increased significantly from 6.01 ± 0.04 mg/dL to 6.16 ± 0.09 mg/dL in boys (β coefficient = 0.057, p for trend = 0.043), while mean SUA did not change significantly in girls (β coefficient = 0.022, p for trend = 0.300). These trends persisted when age-adjusted mean SUA levels were analyzed, with a significant increase in SUA observed in boys but not in girls (Fig. 2).

Trends in mean SUA levels according to sex and age subgroups

We classified ages into three groups: 10–12, 13–15, and 16–18 years. When considering boys and girls together, mean SUA increased significantly (β coefficient = 0.064, p for trend = 0.029) from 2016 to 2020 in the 10–12 years group, while there were no statistically significant changes over time for the other two age groups (13–15 years: β coefficient = 0.040, p for trend = 0.254; 16–18 years; β coefficient = 0.047, p for trend = 0.160).

In age- and sex-specific analyses, there were statistically significant increases in mean SUA levels in boys aged 10–12 years (p for trend < 0.001), while there were no statistically significant increases in boys aged 13–15 years or 16–18 years. In girls, there were no statistically significant changes in SUA over time in all age groups (Fig. 2).

Trends in mean SUA levels according to the presence of obesity or abdominal obesity in boys and girls

Table 2 shows mean SUA trends in sex- and BMI-specific analyses between 2016 and 2020. Mean SUA levels increased significantly from 6.83 ± 0.10 mg/dL to 6.94 ± 0.16 mg/dL in boys with obesity (β

Table 1 Characteristics of study population

Characteristic	Males						Females					
	Overall	2016	2017	2018	2019	2020	Overall	2016	2017	2018	2019	2020
Unweighted number	1,869	394	388	371	380	336	1,685	382	358	330	343	272
Age, y	14.3 ± 0.1	14.4 ± 0.1	14.3 ± 0.2	14.2 ± 0.2	14.3 ± 0.2	14.2 ± 0.2	14.2 ± 0.1	14.3 ± 0.2	14.3 ± 0.2	14.3 ± 0.2	14.1 ± 0.2	13.9 ± 0.2
Height, cm	165.5 ± 0.4	165.4 ± 0.6	166.1 ± 0.7	166.2 ± 0.8	165.4 ± 0.9	165.2 ± 0.8	157.6 ± 0.2	157.9 ± 0.5	157.4 ± 0.5	158.1 ± 0.6	157.3 ± 0.6	157.5 ± 0.6
Weight, kg	60.0 ± 0.5	58.0 ± 0.7	58.8 ± 0.9	60.3 ± 1.1	60.7 ± 1.1	62.1 ± 1.0	51.3 ± 0.4	51.5 ± 0.8	51.4 ± 0.7	51.3 ± 0.6	51.5 ± 1.1	50.7 ± 1.0
SBP, mm Hg	111.2 ± 0.3	111.3 ± 0.3	110.4 ± 0.6	110.5 ± 0.6	111.9 ± 0.6	111.8 ± 0.9	105.9 ± 66.6	106.6 ± 0.7	105.8 ± 0.7	105.4 ± 0.6	105.2 ± 0.7	106.1 ± 0.7
DBP, mm Hg	67.3 ± 0.3	67.5 ± 0.5	66.5 ± 0.6	66.6 ± 0.6	67.6 ± 0.6	68.8 ± 0.7	66.6 ± 0.3	66.2 ± 0.5	66.5 ± 0.5	66.4 ± 0.6	65.9 ± 0.7	68.3 ± 0.7
BMI, kg/m^2	21.6 ± 0.1	21.2 ± 0.3	21.1 ± 0.2	21.7 ± 0.3	21.9 ± 0.3	22.4 ± 0.3	20.5 ± 0.1	20.5 ± 0.3	20.6 ± 0.2	20.4 ± 0.2	20.6 ± 0.3	20.2 ± 0.3
Obesity group [a]												
Underweight	8.5(0.8)	11.0(0.5)	8.3(0.4)	8.4(0.3)	8.2(0.4)	6.1(0.3)	8.8(0.8)	9.3(0.5)	8.2(0.4)	7.0(0.3)	10.6(0.4)	8.8(0.4)
Normal	66.4(1.4)	65.0(1.3)	73.3(1.5)	65.9(0.9)	65.4(1.3)	61.9(1.3)	71.1(1.3)	70.3(1.5)	70.1(1.5)	75.8(1.2)	65.8(1.3)	73.8(1.4)
Overweight	10.5 (0.8)	10.9 (0.4)	8.4 (0.3)	9.9 (0.3)	10.2 (0.5)	13.2 (0.4)	8. 5 (0.8)	8.3 (0.4)	10.2 (0.5)	7.8 (0.3)	10.0 (0.4)	6.2 (0.3)
Obese	14.7 (1.0)	13.2 (0.5)	10.1 (0.4)	15.8 (0.5)	16.2 (0.6)	18.8 (0.6)	11.6 (0.9)	12.1 (11.5)	11.5 (0.4)	9.4 (0.4)	13.6 (0.5)	11.1 (0.4)
WC, cm	74.0 ± 0.3	73.2 ± 0.7	72.2 ± 0.7	73.5 ± 0.7	75.0 ± 0.7	76.3 ± 0.7	67.7 ± 0.3	68.4 ± 0.6	67.2 ± 0.6	66.6 ± 0.5	68.5 ± 0.7	69.6 ± 0.9
Abdominal obesity [b]	9.7 (0.8)	8.6 (0.4)	7.3 (0.4)	10.6 (0.4)	8.1 (0.3)	15.0 (0.5)	9.9 (0.9)	13.9 (0.6)	7.2 (0.3)	7.8 (0.2)	11.8 (0.5)	11.9 (0.5)
SUA, mg/dL	6.01 ± 0.04	5.90 ± 0.09	5.96 ± 0.09	5.98 ± 0.09	6.16 ± 0.09	6.08 ± 0.09	4.65 ± 0.03	4.59 ± 0.06	4.67 ± 0.07	4.59 ± 0.06	4.73 ± 0.08	4.69 ± 0.08
TC, mg/dL	161.2 ± 0.8	159.7 ± 1.6	161.8 ± 1.6	162.5 ± 1.9	160.6 ± 1.8	161.8 ± 2.1	168.3 ± 0.8	169.3 ± 1.8	170.1 ± 1.8	167.5 ± 1.7	167.0 ± 1.8	167.3 ± 1.8
TG, mg/dL	87.2 ± 1.5	81.2 ± 2.6	85.8 ± 4.0	88.3 ± 2.9	88.7 ± 3.0	93.2 ± 4.1	89.8 ± 1.4	89.6 ± 3.2	85.5 ± 2.5	90.8 ± 3.4	84.1 ± 3.0	99.8 ± 3.8
HDL-C, mg/dL	50.3 ± 0.7	50.6 ± 0.6	50.2 ± 0.6	49.2 ± 0.6	50.9 ± 0.6	50.5 ± 0.6	53.5 ± 0.3	54.0 ± 0.7	53.1 ± 0.6	52.8 ± 0.6	54.6 ± 0.8	52.8 ± 0.7

Values are presented as weighted % (standard error) or weighted mean ± standard error

SUA serum uric acid, *WC* waist circumference, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *BMI* body mass index, *TC* total cholesterol, *TG* triglyceride, *HDL-C* high-density lipoprotein cholesterol

[a]Categorized according to BMI percentile: normal, less than the 85th percentile; overweight, 85th to less than the 95th percentile; or obese, equal to or greater than the 95th percentile

[b]Abdominal obesity was defined as WC > 90th percentile, using Korean WC reference data

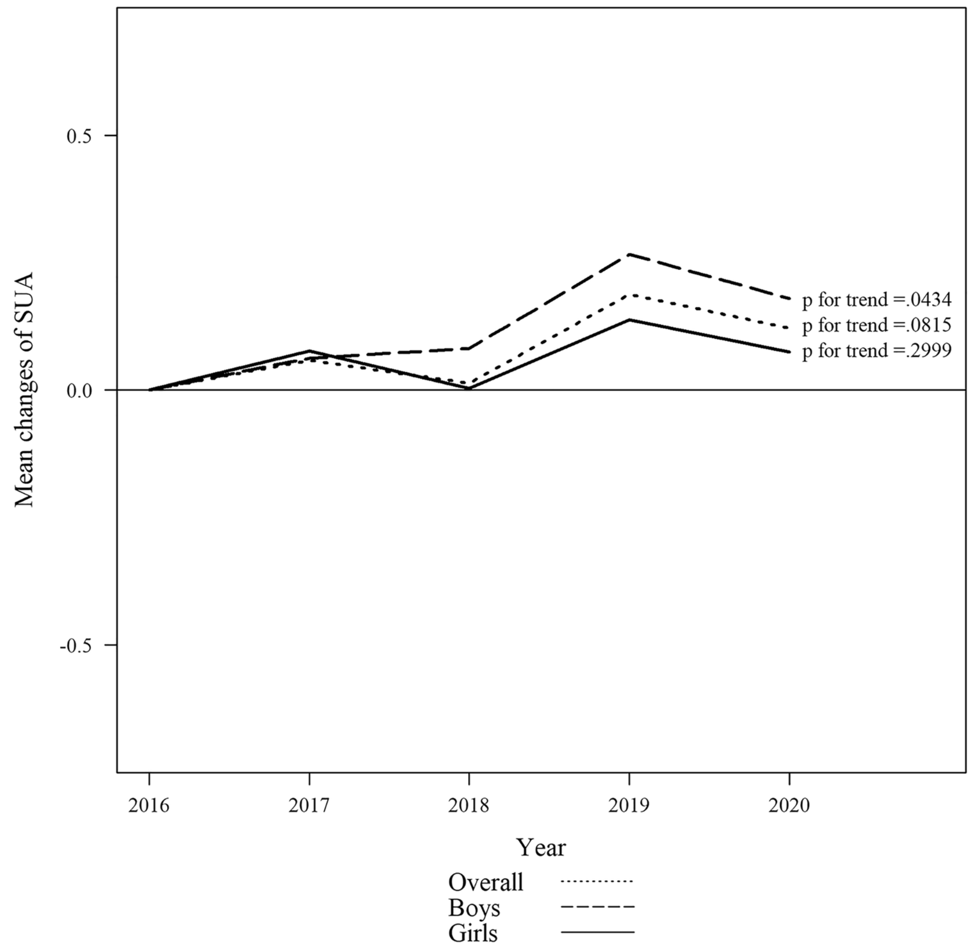

Fig. 1 Trends in mean serum uric acid levels among boys and girls from 2016 to 2020. SUA, serum uric acid

coefficient = 0.152, p for trend = 0.026), whereas there were no significant changes in boys who were underweight (β coefficient = 0.053, p for trend = 0.515), normal weight (β coefficient = 0.022, p for trend = 0.518) or overweight (β coefficient = –0.029, p for trend = 0.686). Mean SUA increased significantly from 5.12 ± 0.18 mg/dL to 5.74 ± 0.20 mg/dL in girls with obesity (β coefficient = 0.149, p for trend = 0.018), while there were no significant changes over time in girls who were underweight (β coefficient = -0.018, p for trend = 0.684), normal weight

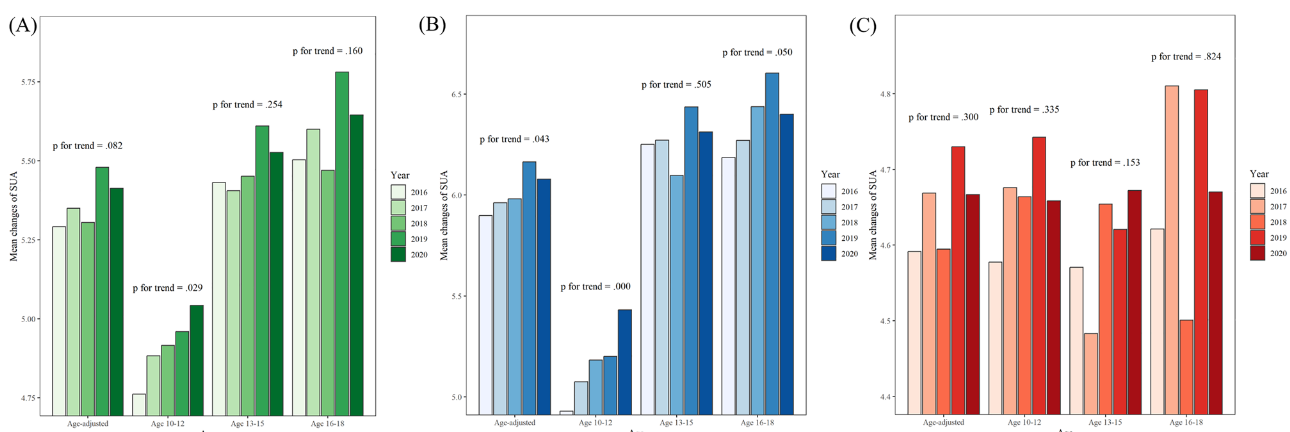

Fig. 2 Trends in mean serum uric acid levels according to age from 2016 to 2020 for (**A**) all study participants, (**B**) boys, and (**C**) girls. SUA, serum uric acid

Table 2 Trends in mean serum uric acid levels by sex and obesity subgroups

Group [a]	Serum uric acid, mg/dL (weighted mean ± standard error)					Age-unadjusted		Age-adjusted	
	2016	2017	2018	2019	2020	ß-coefficient	p for trend	ß-coefficient	p for trend
Boys									
Underweight	5.50 ± 0.27	5.49 ± 0.30	5.68 ± 0.27	5.87 ± 0.16	5.51 ± 0.21	0.053	0.515	0.091	0.205
Normal	5.77 ± 0.11	5.85 ± 0.10	5.80 ± 0.09	5.91 ± 0.11	5.85 ± 0.11	0.022	0.518	0.031	0.339
Overweight	6.48 ± 0.19	6.30 ± 0.17	6.60 ± 0.21	6.52 ± 0.24	6.28 ± 0.19	-0.029	0.686	0.001	0.989
Obese	6.40 ± 0.23	6.89 ± 0.20	6.61 ± 0.17	7.29 ± 0.19	6.94 ± 0.16	0.152	**0.026**	0.149	**0.026**
Girls									
Underweight	4.34 ± 0.10	4.01 ± 0.10	4.03 ± 0.10	4.38 ± 0.09	4.06 ± 0.09	-0.018	0.684	0.003	0.942
Normal	4.51 ± 0.06	4.58 ± 0.07	4.55 ± 0.07	4.56 ± 0.07	4.52 ± 0.06	0.001	0.979	0.000	> 0.999
Overweight	4.77 ± 0.24	5.00 ± 0.21	4.99 ± 0.10	4.93 ± 0.30	5.00 ± 0.17	0.029	0.706	0.031	0.681
Obese	5.12 ± 0.18	5.36 ± 0.21	5.06 ± 0.18	5.61 ± 0.17	5.74 ± 0.20	0.149	**0.018**	0.144	**0.023**

[a]Categorized according to body mass index percentile: normal, less than the 85th percentile; overweight, 85th to less than the 95th percentile; or obese, equal to or greater than the 95th percentile

(β coefficient = 0.001, p for trend = 0.979) or overweight (β coefficient = 0.029, p for trend = 0.706). After adjusting for age, similar trends remained, with significant increases in SUA over time in the obesity group for both boys and girls.

Table 3 shows trends in mean SUA levels in sex- and WC-specific analyses between 2016 and 2020. Mean SUA increased significantly from 6.26 ± 0.29 mg/dL to 6.94 ± 0.17 mg/dL in boys with abdominal obesity (β coefficient = 0.172, p for trend = 0.033), while mean SUA did not change significantly in boys without abdominal obesity (β coefficient = 0.028, p for trend = 0.329). Likewise, mean SUA increased significantly from 4.98 ± 0.20 mg/dL to 5.72 ± 0.19 mg/dL in girls with abdominal obesity (β coefficient = 0.152, p for trend = 0.028), but did not change significantly in girls without abdominal obesity (β coefficient = –0.005, p for trend = 0.785). After adjusting for age, similar trends remained, with significant increases in SUA over time for both boys and girls with abdominal obesity.

Discussion

In this study, we described trends in SUA levels according to age, sex, obesity, and abdominal obesity over a 5-year period in Korean children and adolescents. The average SUA levels during the entire 5 years were 6.01 ± 0.04 mg/dL in boys and 4.65 ± 0.03 mg/dL in girls. The SUA levels followed different trends according to age and sex. Increasing trends in SUA concentrations were significant only in boys. In age-specific analysis, there was a significant increase in SUA in the youngest age group (10–12 years). In age- and sex-specific analyses, SUA increased significantly only in boys aged 10–12 years. In sex- and BMI-specific analyses, SUA levels increased significantly in obese boys and girls, but not in the overweight, normal, or under-weight groups of either sex. In sex- and WC-specific analyses, SUA increased significantly in both boys and girls with abdominal obesity, but not in individuals without abdominal obesity in either sex.

Table 3 Trends in mean serum uric acid levels according to sex and abdominal obesity

Group [a]	Serum uric acid, mg/dL (weighted mean ± standard error)					Age-unadjusted		Age-adjusted	
	2016	2017	2018	2019	2020	ß-coefficient	p for trend	ß-coefficient	p for trend
Boys									
Non-abdominal obesity	5.87 ± 0.09	5.88 ± 0.08	5.92 ± 0.09	6.03 ± 0.08	5.93 ± 0.09	0.028	0.329	0.040	0.143
Abdominal obesity	6.26 ± 0.29	7.00 ± 0.20	6.56 ± 0.23	7.65 ± 0.23	6.94 ± 0.17	0.172	**0.033**	0.186	**0.017**
Girls									
Non-abdominal obesity	4.53 ± 0.05	4.60 ± 0.07	4.56 ± 0.06	4.59 ± 0.07	4.51 ± 0.06	-0.005	0.785	-0.005	0.810
Abdominal obesity	4.98 ± 0.20	5.54 ± 0.31	5.35 ± 0.21	5.71 ± 0.20	5.72 ± 0.19	0.152	**0.028**	0.181	**0.014**

[a]Abdominal obesity was defined as a waist circumference > 90th percentile, using Korean waist circumference reference data

A previous study based on nationally representative surveys found no significant changes in SUA or hyperuricemia trends in the United States adolescent population over the past 40 years [31]. However, the authors commented that SUA varied by age, race, sex, and obesity status [31]. They found that obese adolescents had higher uric acid levels than non-obese adolescents (5.79 mg/dL vs. 4.93 mg/dL; $p = 0.001$) [31]. These findings are in line with our results. In our study, we found increasing SUA trends in boys, but not in girls, as well as in children and adolescents with obesity or abdominal obesity, regardless of sex.

Cho et al. reported a close association between SUA levels and MetS or some components of MetS in Korean children and adolescents [18]. The odds ratio for the prevalence of MetS in the highest SUA group, compared to the lowest SUA group, was 2.897 (95% confidence interval [CI], 1.140–7.361) in boys and 5.173 (95% CI, 1.459–18.342) in girls [18]. For both boys and girls, subjects in the highest SUA quartile had an increased risk of abdominal obesity and low HDL-C [18].

Many cross-sectional studies have shown that increases in obesity and central obesity are associated with elevated SUA levels and a higher prevalence of hyperuricemia [15, 17, 32, 33]. Several studies have suggested that adipose tissue secretes UA and that activation of xanthine oxidoreductase is closely associated with obesity and insulin resistance (IR) [4, 33, 34]. A study conducted in Bangladeshi adults showed that SUA has a significant association with central obesity after adjusting for BMI [33]. They also found a strong association in overweight or obese women [33]. Obesity, itself, is associated with elevated SUA through overproduction and poor excretion of SUA [35]. Excess visceral fat also induces an elevated influx of plasma free fatty acids into liver and lead to UA production through activation of UA synthesis [35]. Additionally, recent evidence suggests that hyperuricemia is associated with IR and the subsequent development of T2DM [13, 36]: SUA plays a role in mediating obesity-induced IR. Although the mechanisms for the causal relationship between hyperuricemia and IR have not been fully elucidated, research with mice suggests that elevated SUA levels induce IR through inhibition of insulin signaling [4].

A study of MetS trends in Korean children and adolescents showed that both BMI and abdominal obesity prevalence increased significantly over 10 years from 2008 to 2017 [37]. In our study, BMI and WC increased significantly in boys from 2016 to 2020, although there was no significant increase in BMI or WC in girls over the same time period.

In light of the results of previous studies, we suggest that worsening trends in SUA levels among children and adolescents with obesity or abdominal obesity may be due to increased xanthine oxidoreductase activation and UA secretion by adipocytes and adipose tissue. Moreover, changes in dietary patterns secondary to coronavirus disease-19 (COVID-19) may have a substantial impact on children and adolescents with obesity or central obesity. A study investigating factors related to obesity in Korean adolescents before and during the COVID-19 pandemic reported that the prevalence of obesity increased slightly from 11.31% pre-pandemic to 12.48% during the pandemic, based on an analysis of the Korean Adolescent Risk Behavior Web-based Survey of middle and high school students in 2019–2020 [38]. According to a study on changes in the eating habits of Koreans during the COVID-19 pandemic, eating outside the home decreased sharply during the pandemic, while eating home-cooked meals increased; however, replacing home-cooked meals with delivered food also increased [38]. Adhering to regular mealtimes, which is commonly practiced while attending school or work, also decreased with the pandemic, while the proportion of irregular mealtimes increased [39]. Ammar et al. reported that unhealthy diet patterns, such as binge eating and snacking, increased in most countries in a survey focusing on West Asia, East Africa, and Europe that studied the effects of COVID-19 on individual lifestyles [40].

Fructose consumption may contribute to hyperuricemia by stimulating the catabolism of adenine nucleotides, and fructose intake has increased significantly over the past few decades [41]. This worsening trend of fructose intake is consistent with a substantial increase in metabolic diseases, including obesity, nonalcoholic fatty liver disease, cardiovascular disease and diabetes [42]. It has been reported that the typical intake of a Western diet of fructose is 49 g per day and only 8 g from natural sources [43], and a rise in fructose intake is associated with an increase in processed sugar and sugar-sweetened beverages. A recent study on the dietary intake of Korean adolescents showed that the intake of carbonated beverages has increased significantly [44]. In particular, the rate of participants with consumption of two or more carbonated beverages per day increased from 28.1% in 2015 to 36.9% in 2019 ($p < 0.01$). The rate of participants drinking two or more carbonated beverages was 39.8% in boys, which was higher than 24.9% in girls. In BMI-specific analysis, the rate of participants drinking two or more carbonated beverages in the obese group was 34.3%, which was higher than 31.7% in the normal group or 31.9% in the overweight group ($p < 0.001$) [44]. These findings are in line with the worsening trends of SUA in this study. In addition, a study surveyed on Korean children and adolescents from 2008 to 2018 reported that soft drink intake significantly increased (38.2–102.7 g/day; p for trend < 0.0001) and that soft drink intake was higher in boys than girls and in obese groups than in normal or overweight groups [45]. An increases in soft drinks intake leads to increased fructose intake, which could affect worsening trends in SUA levels. The aforementioned evidence could support our findings that SUA increased significantly in boys aged 10–12 years, obese boys, and obese girls. Further studies are needed to clarify theses age-, obesity- and sex-specific results.

Elevated SUA is associated with excessive cardiovascular mortality, hypertension, T2DM, and chronic kidney disease and is considered an indicator of MetS [46]. It is important to identify risk factors early in childhood to help prevent the development of T2DM and CVD. Since obesity is a major cause of hyperuricemia in children and adolescents, weight management through lifestyle modifications, such as diet, physical activity, and behavioral changes, is important in this age group [47]. In a study of 33 obese children, Togashi et al. demonstrated a significant decrease in SUA levels after a 3-month intervention involving diet and exercise [48]. Krzystek-Korpacka et al. reported that SUA levels decreased in 85.7% of females and 67.7% of males after a 1-year weight-loss program in children and adolescents 10–17 years of age [49]. Early, appropriate intervention is particularly important in relation to the chronic diseases causing hyperuricemia that begin in childhood. Therefore, large-scale clinical trials with long-term follow-up are required to determine whether lowering SUA levels can prevent and treat obesity, abdominal obesity, and MetS.

This study has some limitations. First, since we used data from KNHANES, the results of this study may not be generalizable to other races and countries. Second, our study was limited to identifying trends in SUA levels; the exact etiology of the worsening trends in SUA levels observed in individuals with obesity or central obesity could not be ascertained. Third, we could use only KNHANES data from 2016 to 2020 because of the lack of information about SUA levels before this time. Future studies are necessary to examine longer-term SUA trends in Korean children and adolescents. Nevertheless, this study is the first report evaluating trends in SUA levels according to age, sex, obesity, and abdominal obesity in Korean children and adolescents based on national representative health and nutrition survey data over a recent 5-year period.

Conclusion

In this study, we found that in Korean children and adolescents, SUA levels increased significantly in the youngest age group (10–12 years) and in the obesity and central obesity groups in both boys and girls. It is important to find and manage risk factors from an early age to prevent the development of cardiometabolic diseases, such as T2DM and CVD. Our findings suggest that SUA levels should be monitored regularly in Korean children and adolescents, especially those with obesity or abdominal obesity. Efforts should also focus on maintaining a healthy weight to reduce the number of individuals with obesity or abdominal obesity.

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Authors' contributions EYK, JWL, and YJK contributed to the conception or design of the work. HWL and NHS analyzed the data. EYK, HWL, JWL, YJK, and NHS contributed to the acquisition and interpretation of the data and drafting of the manuscript. All authors critically revised the manuscript, provided final approval, and agreed to be accountable for all aspects of the work, while ensuring integrity and accuracy.

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Data sharing statement The data analyzed in this study were obtained from the Korea National Health and Nutritional Examination Survey and are available at the following website: https://www.kdca.go.kr/contents.es?mid=a4050401000.

Declarations

Ethical approval This study was performed in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Severance Hospital (IRB No.4–2022-0796).

Conflict of interest The authors have no conflicts to declare.

References

1. Maiuolo J, Oppedisano F, Gratteri S, Muscoli C, Mollace V (2016) Regulation of uric acid metabolism and excretion. Int J Cardiol 213:8–14
2. de Oliveira EP, Burini RC (2012) High plasma uric acid concentration: causes and consequences. Diabetol Metab Syndr 4:1–7
3. Schlesinger N (2005) Dietary factors and hyperuricaemia. Curr Pharm Des 11:4133–4138
4. Tsushima Y, Nishizawa H, Tochino Y et al (2013) Uric acid secretion from adipose tissue and its increase in obesity. J Biol Chem 288:27138–27149
5. Bellomo G (2013) Uric acid and chronic kidney disease: A time to act? World J Nephrol 2:17–25
6. Rock KL, Kataoka H, Lai J-J (2013) Uric acid as a danger signal in gout and its comorbidities. Nat Rev Rheumatol 9:13–23
7. Wallace KL, Riedel AA, Joseph-Ridge N, Wortmann R (2004) Increasing prevalence of gout and hyperuricemia over 10 years among older adults in a managed care population. J Rheumatol 31:1582–1587
8. Zhu Y, Pandya BJ, Choi HK (2011) Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007–2008. Arthritis Rheum 63:3136–3141
9. Trifiro G, Morabito P, Cavagna L et al (2013) Epidemiology of gout and hyperuricaemia in Italy during the years 2005–2009: a nationwide population-based study. Ann Rheum Dis 72:694–700
10. Kumar AUA, Browne LD, Li X et al (2018) Temporal trends in hyperuricaemia in the Irish health system from 2006–2014: A cohort study. PLoS ONE 13:e0198197
11. Ali N, Mahmood S, Islam F et al (2019) Relationship between serum uric acid and hypertension: a cross-sectional study in Bangladeshi adults. Sci Rep 9:9061

12. Feig DI, Kang DH, Johnson RJ (2008) Uric acid and cardiovascular risk. N Engl J Med 359:1811–1821
13. Mortada I (2017) Hyperuricemia, Type 2 Diabetes Mellitus, and Hypertension: an Emerging Association. Curr Hypertens Rep 19:69
14. Ali N, Rahman S, Islam S et al (2019) The relationship between serum uric acid and lipid profile in Bangladeshi adults. BMC Cardiovasc Disord 19:42
15. Ali N, Miah R, Hasan M et al (2020) Association between serum uric acid and metabolic syndrome: a cross-sectional study in Bangladeshi adults. Sci Rep 10:7841
16. Molla NH, Kathak RR, Sumon AH et al (2021) Assessment of the relationship between serum uric acid levels and liver enzymes activity in Bangladeshi adults. Sci Rep 11:20114
17. Yang C, Yang S, Feng C et al (2018) Associations of hyperuricemia and obesity with remission of nonalcoholic fatty liver disease among Chinese men: A retrospective cohort study. PLoS ONE 13:e0192396
18. Cho MH, Kim YM, Yoon JH, Kim DH, Lim JS (2020) Serum uric acid in Korean children and adolescents: reference percentiles and association with metabolic syndrome. Ann Pediatr Endocrinol Metab 25:104–111
19. Lee JH (2019) Prevalence of hyperuricemia and its association with metabolic syndrome and cardiometabolic risk factors in Korean children and adolescents: analysis based on the 2016–2017 Korea National Health and Nutrition Examination Survey. Korean J Pediatr 62:317–323
20. Mazidi M, Katsiki N, Mikhailidis DP, Banach M (2018) The link between insulin resistance parameters and serum uric acid is mediated by adiposity. Atherosclerosis 270:180–186
21. Niu Y, Zhao X, Cai W, Feng Y (2021) Obesity-induced insulin resistance is mediated by high uric acid in obese children and adolescents. Front Endocrinol 1631
22. Jones DP, Richey PA, Alpert BS, Li R (2008) Serum uric acid and ambulatory blood pressure in children with primary hypertension. Pediatr Res 64:556–561
23. Ford ES, Li C, Cook S, Choi HK (2007) Serum concentrations of uric acid and the metabolic syndrome among US children and adolescents. Circulation 115:2526–2532
24. Maynard JW, McAdams-DeMarco MA, Law A et al (2014) Racial differences in gout incidence in a population-based cohort: Atherosclerosis Risk in Communities Study. Am J Epidemiol 179:576–583
25. Wakasugi M, Kazama JJ, Narita I et al (2015) Association between hypouricemia and reduced kidney function: a cross-sectional population-based study in Japan. Am J Nephrol 41:138–146
26. Kuwabara M, Niwa K, Ohtahara A et al (2017) Prevalence and complications of hypouricemia in a general population: A large-scale cross-sectional study in Japan. PLoS ONE 12:e0176055
27. Wilcox W (1996) Abnormal serum uric acid levels in children. J Pediatr 128:731–741
28. Oyama C, Takahashi T, Oyamada M et al (2006) Serum uric acid as an obesity-related indicator in early adolescence. Tohoku J Exp Med 209:257–262
29. Shatat IF, Abdallah RT, Sas DJ, Hailpern SM (2012) Serum uric acid in US adolescents: distribution and relationship to demographic characteristics and cardiovascular risk factors. Pediatr Res 72:95–100
30. Kweon S, Kim Y, Jang MJ et al (2014) Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). Int J Epidemiol 43:69–77
31. Kumar R, Khalsa DD, Carmody JB (2016) Serum uric acid and hyperuricemia in U.S. adolescents: 40-year trends. Clin Exp Rheumatol 34:S22–3
32. Palmer TM, Nordestgaard BG, Benn M et al (2013) Association of plasma uric acid with ischaemic heart disease and blood pressure: mendelian randomisation analysis of two large cohorts. BMJ 347:f4262
33. Ali N, Perveen R, Rahman S et al (2018) Prevalence of hyperuricemia and the relationship between serum uric acid and obesity: A study on Bangladeshi adults. PLoS ONE 13:e0206850
34. Cheung KJ, Tzameli I, Pissios P et al (2007) Xanthine oxidoreductase is a regulator of adipogenesis and PPARγ activity. Cell Metab 5:115–128
35. Matsuura F, Yamashita S, Nakamura T et al (1998) Effect of visceral fat accumulation on uric acid metabolism in male obese subjects: visceral fat obesity is linked more closely to overproduction of uric acid than subcutaneous fat obesity. Metabolism 47:929–933
36. Anothaisintawee T, Lertrattananon D, Thamakaison S, Reutrakul S, Ongphiphadhanakul B, Thakkinstian A (2017) Direct and indirect effects of serum uric acid on blood sugar levels in patients with prediabetes: a mediation analysis. J Diabetes Res 2017:6830671
37. Park SI, Suh J, Lee HS et al (2021) Ten-year trends of metabolic syndrome prevalence and nutrient intake among Korean children and adolescents: a population-based study. Yonsei Med J 62:344–351
38. Jang SH, Hwang H (2022) Multilevel Factors Associated with Obesity among South Korean Adolescents before and during the COVID-19 Pandemic. Child Obes. https://doi.org/10.1089/chi.2022.0053
39. 장석진, 박정민, 강주연 (2022) 코로나 19 이후 정부대응책 인식과 식생활 변화에 관한 연구-경제적, 심리적, 신체적 영향을 중심으로. 기업과혁신연구 45:3–31
40. Ammar A, Brach M, Trabelsi K et al (2020) Effects of COVID-19 home confinement on eating behaviour and physical activity: results of the ECLB-COVID19 international online survey. Nutrients 12:1583
41. Zhang C, Li L, Zhang Y, Zeng C (2020) Recent advances in fructose intake and risk of hyperuricemia. Biomed Pharmacother 131:110795
42. Jung S, Bae H, Song WS, Jang C (2022) Dietary fructose and fructose-induced pathologies. Annu Rev Nutr 42:45–66
43. Laughlin MR (2014) Normal roles for dietary fructose in carbohydrate metabolism. Nutrients 6:3117–3129
44. Yim HR, Yun HJ, Lee JH (2021) An investigation on Korean adolescents' dietary consumption: Focused on sociodemographic characteristics, physical health, and mental health. Int J Environ Res Public Health 18
45. Hwang SB, Park S, Jin GR et al (2020) Trends in Beverage consumption and related demographic factors and obesity among Korean children and adolescents. Nutrients 12
46. Johnson RJ, Bakris GL, Borghi C et al (2018) Hyperuricemia, acute and chronic kidney disease, hypertension, and cardiovascular disease: Report of a Scientific Workshop Organized by the National Kidney Foundation. Am J Kidney Dis 71:851–865
47. August GP, Caprio S, Fennoy I et al (2008) Prevention and treatment of pediatric obesity: an endocrine society clinical practice guideline based on expert opinion. J Clin Endocrinol Metab 93:4576–4599
48. Togashi K, Masuda H, Iguchi K (2010) Effect of diet and exercise treatment for obese Japanese children on abdominal fat distribution. Res Sports Med 18:62–70
49. Krzystek-Korpacka M, Patryn E, Kustrzeba-Wojcicka I, Chrzanowska J, Gamian A, Noczynska A (2011) The effect of a one-year weight reduction program on serum uric acid in overweight/obese children and adolescents. Clin Chem Lab Med 49:915–921