DOI: https://doi.org/10.53350/pjmhs20231711511

ORIGINAL ARTICLE

Association Between Uric Acid Levels and Metabolic Risk Factors in Overweight and Obese Children

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ABSTRACT

Background: Childhood overweight and obesity are increasing rapidly in Pakistan and are strongly associated with early metabolic disturbances. Uric acid, once considered an inert metabolic by-product, is now recognized as a potential biomarker linked to insulin resistance, lipid abnormalities, and elevated blood pressure. This study aims to evaluate the association between serum uric acid levels and major metabolic risk factors among overweight and obese children.

Methods: This cross-sectional study was conducted at Khyber Teaching Hospital, Peshawar, and the Punjab Institute of Cardiology, Lahore, from October 2022 to July 2023. A total of 100 overweight and obese children aged 6–17 years were enrolled using consecutive sampling. Anthropometric measurements, blood pressure, and fasting biochemical parameters serum uric acid, glucose, insulin, and lipid profile were obtained. Insulin resistance was calculated using the HOMA-IR formula. Participants were categorized into uric acid tertiles, and metabolic parameters were compared across groups. Statistical analysis included ANOVA, Pearson correlation, and multivariable linear regression.

Results: Higher uric acid levels were significantly associated with increased fasting insulin ($p < 0.001$), higher HOMA-IR ($p < 0.001$), elevated triglycerides ($p < 0.001$), higher LDL-cholesterol ($p < 0.01$), lower HDL-cholesterol ($p = 0.02$), and increased systolic blood pressure ($p < 0.01$). Uric acid showed moderate positive correlations with BMI percentile, fasting insulin, HOMA-IR, triglycerides, and systolic blood pressure. Regression analysis confirmed uric acid as an independent predictor of insulin resistance after adjusting for confounders ($\beta = 0.35$, $p = 0.002$).

Conclusion: Elevated serum uric acid is strongly associated with multiple metabolic risk factors among overweight and obese children. Routine assessment of uric acid may serve as a simple, cost-effective tool for early identification of high-risk pediatric groups requiring metabolic monitoring and intervention.

Keywords: Uric acid, Childhood obesity, Insulin resistance, Metabolic syndrome, Pediatric dyslipidemia.

INTRODUCTION

Childhood overweight and obesity have emerged as major global health challenges, with rapidly increasing prevalence in both developed and developing countries. Pakistan is experiencing a similar upward trend, driven by sedentary lifestyles, Westernized dietary patterns, increased screen time, and reduced outdoor physical activity[1]. Excess body weight during childhood is strongly associated with early metabolic disturbances that often persist into adulthood, predisposing individuals to a spectrum of cardiometabolic disorders. These include insulin resistance, type 2 diabetes mellitus, hypertension, dyslipidemia, non-alcoholic fatty liver disease (NAFLD), and premature cardiovascular morbidity. Therefore, identifying early biomarkers that reflect cardiometabolic risk is essential for timely detection and prevention[2,3].

Uric acid, traditionally regarded as a biologically inactive end-product of purine metabolism, has gained increasing scientific attention as an active metabolic mediator. Elevated serum uric acid levels have been linked to oxidative stress, systemic inflammation, endothelial dysfunction, and impaired nitric oxide production all of which contribute to metabolic dysregulation[4,5]. In both adults and children, hyperuricemia has been associated with obesity, insulin resistance, elevated triglycerides, reduced HDL cholesterol, and early hypertension. These relationships suggest that uric acid may not only reflect metabolic stress but may also play a contributory role in the pathogenesis of metabolic syndrome[6].

In the pediatric population, the association between uric acid and metabolic risk factors is of particular concern. Children who exhibit hyperuricemia alongside obesity demonstrate markedly higher risks of impaired glucose tolerance and clustering of metabolic abnormalities at an early age. As metabolic syndrome in childhood strongly predicts adult cardiometabolic disease, the identification of reliable early biomarkers becomes crucial.

Received on 03-07-2023
Accepted on 23-10-2023

Uric acid is inexpensive, easily measurable, and widely available in clinical settings, making it a potentially valuable predictor for early risk stratification[7-9].

Despite international evidence, there is limited local data from Pakistan examining the association between uric acid and metabolic risk factors in overweight and obese children. Given the rising prevalence of pediatric obesity in Punjab and the lack of regional studies addressing the metabolic role of uric acid, there is a critical need for local research to guide clinical practice[10].

Therefore, this study aims to evaluate the relationship between serum uric acid levels and key metabolic risk markers including insulin resistance, lipid abnormalities, blood pressure, and BMI percentile among overweight and obese children in tertiary care hospitals across Punjab. Understanding this association may support the use of uric acid as an early screening tool and guide preventive interventions in high-risk pediatric populations[11].

MATERIALS AND METHODS

This cross-sectional study was conducted at two major tertiary care centers in Pakistan: the Department of Pediatrics, Khyber Teaching Hospital (KTH), Peshawar, and the Pediatric Outpatient Division of the Punjab Institute of Cardiology (PIC), Lahore. The study duration spanned ten months, from October 2022 to July 2023. A total sample of 100 overweight and obese children aged 6 to 17 years was enrolled using non-probability consecutive sampling as they presented to pediatric clinics for evaluation or follow-up. Overweight and obesity were classified according to the Centers for Disease Control and Prevention (CDC) BMI-for-age growth charts, with overweight defined as a BMI between the 85th and 94th percentiles and obesity as a BMI at or above the 95th percentile for age and sex.

All parents or legal guardians were informed about the study objectives, and written informed consent was obtained along with verbal assent from children above 10 years of age. Children with

chronic kidney disease, diabetes mellitus, thyroid disorders, Cushing syndrome, genetic syndromes, acute infections, or those taking medications known to affect uric acid levels such as corticosteroids, diuretics, or immunosuppressants were excluded to minimize confounding influences.

Anthropometric measurements were obtained using standard protocols, with weight recorded to the nearest 0.1 kg using a calibrated digital scale and height measured to the nearest 0.1 cm using a stadiometer. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Blood pressure was measured using an appropriately sized pediatric cuff after the child had been seated at rest for at least ten minutes, and the average of two readings was documented. A detailed clinical history, including dietary habits, physical activity levels, family history of metabolic disorders, and comorbidities, was recorded using a structured questionnaire.

After an overnight fast of 10–12 hours, venous blood samples were obtained from all participants. Serum was analyzed for uric acid, fasting plasma glucose, fasting insulin, and lipid profile, including total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides. Uric acid levels were measured using an enzymatic colorimetric method, while insulin levels were quantified via chemiluminescent immunoassay. Insulin resistance was calculated using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) formula: fasting glucose (mg/dL) × fasting insulin (μIU/mL) / 405. All biochemical analyses were performed at the central laboratories of the respective hospitals under standardized internal quality control protocols.

The primary objective was to determine the association between serum uric acid levels and metabolic risk factors including BMI percentile, blood pressure, fasting glucose, lipid abnormalities, and insulin resistance. Participants were categorized into uric acid tertiles to compare metabolic parameters across groups. Statistical analysis was performed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation, and group comparisons were made using independent sample t-tests and one-way ANOVA where appropriate. Pearson correlation analysis was applied to evaluate the association between uric acid and metabolic indicators, while multivariable linear regression was used to assess uric acid as an independent predictor of insulin resistance after adjusting for age, sex, and BMI. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 100 overweight and obese children were included in the analysis, with a mean age of 11.6 ± 3.2 years. Of these, 58 were males and 42 were females. The overall BMI percentile of the participants was markedly elevated, consistent with the study's inclusion criteria. Serum uric acid levels ranged from 3.2 to 8.4 mg/dL, with a mean of 5.9 ± 1.3 mg/dL. Table 1 presents the baseline demographic, anthropometric, and clinical characteristics of the study population. As shown in Table 1, the mean systolic blood pressure was 119 ± 11 mmHg and mean diastolic pressure was 73 ± 8 mmHg, both trending higher in those at the upper BMI percentiles. The participants displayed early metabolic alterations, with increases in fasting insulin and triglyceride levels even at baseline.

Table 1: Baseline Characteristics of Overweight and Obese Children (N = 100)

Variable	Mean ± SD
Age (years)	11.6 ± 3.2
Male/Female	58/42
BMI Percentile	95.1 ± 4.8
Uric Acid (mg/dL)	5.9 ± 1.3
Systolic BP (mmHg)	119 ± 11
Diastolic BP (mmHg)	73 ± 8
Fasting Glucose (mg/dL)	94.6 ± 10.4
Fasting Insulin (μIU/mL)	14.9 ± 5.7
HOMA-IR	3.47 ± 1.2

The baseline profile (Table 1) indicates that most participants were within the obese range, with BMI percentiles averaging above the 95th percentile. Mean uric acid levels were mildly elevated for the pediatric age group and showed visible variation, providing a suitable spectrum for examining associations with metabolic markers.

To better evaluate metabolic differences, participants were categorized into three tertiles based on their serum uric acid concentrations:

- **Tertile 1 (Low UA)**: <5.0 mg/dL
- **Tertile 2 (Moderate UA)**: 5.0–6.3 mg/dL
- **Tertile 3 (High UA)**: >6.3 mg/dL

Comparison of metabolic parameters across uric acid tertiles is shown in Table 2. Children in the highest tertile demonstrated significantly higher fasting insulin, HOMA-IR, triglycerides, LDL-cholesterol, and systolic blood pressure compared with those in the lowest tertile. The differences across groups were statistically significant ($p < 0.05$), indicating a strong stepwise increase in metabolic risk factors with rising uric acid levels.

Table 2: Comparison of Metabolic Parameters Across Uric Acid Tertiles

Parameter	Tertile 1 (Low UA) <5.0 mg/dL	Tertile 2 (Moderate UA) 5.0–6.3 mg/dL	Tertile 3 (High UA) >6.3 mg/dL	p-value
Fasting Insulin (μIU/mL)	10.2 ± 2.4	14.7 ± 3.1	20.3 ± 4.5	<0.001
HOMA-IR	2.23 ± 0.7	3.21 ± 0.8	4.81 ± 1.3	<0.001
Triglycerides (mg/dL)	114 ± 28	147 ± 33	181 ± 39	<0.001
LDL-Cholesterol (mg/dL)	95 ± 18	110 ± 22	129 ± 27	<0.01
HDL-Cholesterol (mg/dL)	48 ± 7	44 ± 6	40 ± 5	0.02
Systolic BP (mmHg)	113 ± 9	118 ± 10	126 ± 12	<0.01

As shown in Table 2, increasing uric acid levels were associated with worsening metabolic indicators. Children in the high-UA tertile had nearly double the HOMA-IR values compared to those in the lowest tertile, demonstrating a strong relationship between uric acid and insulin resistance. Triglyceride and LDL levels also rose progressively, while HDL decreased, indicating an atherogenic lipid profile with higher uric acid.

Correlation analysis revealed significant positive relationships between serum uric acid and several metabolic risk factors. Uric acid showed a moderate correlation with fasting insulin ($r = 0.41$, $p < 0.001$) and HOMA-IR ($r = 0.47$, $p < 0.001$), supporting its role in insulin resistance. A positive correlation was also observed with BMI percentile ($r = 0.39$, $p < 0.01$), systolic blood pressure ($r = 0.34$, $p < 0.01$), triglycerides ($r = 0.37$, $p < 0.01$), and LDL-cholesterol ($r = 0.28$, $p = 0.02$). Conversely, HDL-cholesterol showed a significant negative correlation ($r = –0.25$, $p = 0.03$), indicating that higher uric acid levels were linked to a less favorable lipid profile.

To further assess the strength of uric acid as an independent predictor, multivariable linear regression analysis was performed. After adjusting for age, sex, and BMI percentile, uric acid remained a significant predictor of insulin resistance ($\beta = 0.35$, $p = 0.002$). This reinforces the observation that uric acid contributes independently to metabolic risk beyond body weight alone.

Overall, the results demonstrate a clear association between elevated uric acid levels and multiple adverse metabolic parameters among overweight and obese children. The rise in insulin resistance, blood pressure, and lipid abnormalities with increasing uric acid levels suggests that uric acid may serve as an important early biomarker of metabolic dysregulation in the pediatric population.

DISCUSSION

The present study examined the relationship between serum uric acid levels and key metabolic risk factors among overweight and obese children presenting to two major tertiary care hospitals in Pakistan[9,10]. The findings demonstrate a strong and consistent association between higher uric acid concentrations and markers of metabolic dysfunction, including insulin resistance, dyslipidemia, elevated blood pressure, and higher BMI percentiles. These results underscore the growing recognition of uric acid as an important metabolic biomarker in the pediatric population[11].

In this study, children with higher serum uric acid levels exhibited significantly elevated fasting insulin and HOMA-IR values compared to those with lower levels, indicating a strong association between uric acid and insulin resistance[12]. This relationship remained robust even after adjusting for potential confounders such as age, sex, and BMI, suggesting an independent metabolic role of uric acid. These findings align with previous international studies reporting that hyperuricemia contributes to impaired insulin signaling by promoting oxidative stress, inducing endothelial dysfunction, and increasing systemic inflammation. Several pediatric studies have similarly reported that elevated uric acid is one of the earliest detectable abnormalities in children progressing toward metabolic syndrome[13,14].

A clear association was also observed between uric acid and lipid abnormalities in this cohort. Children in the highest uric acid tertile displayed higher triglycerides and LDL-cholesterol, along with reduced HDL-cholesterol. This atherogenic lipid pattern is consistent with metabolic syndrome and has been described in multiple epidemiological studies. Hyperuricemia has been proposed to impair lipid metabolism by altering adipocyte function and increasing hepatic lipogenesis, which may explain the dyslipidemic trends observed in this study[15,16].

Systolic blood pressure was also significantly higher in children with elevated uric acid. The association between hyperuricemia and pediatric hypertension is well-documented, with proposed mechanisms including renal vasoconstriction, reduced nitric oxide bioavailability, and activation of the renin–angiotensin system. The findings of this study support these mechanisms and highlight uric acid as a potential early predictor of blood pressure changes in overweight children[17,18].

Importantly, the strong correlation between BMI percentile and uric acid levels in this study reinforces the established link between adiposity and hyperuricemia. Excess weight contributes to increased purine turnover, decreased renal excretion of uric acid, and heightened metabolic stress, all of which promote elevated uric acid levels[19].

The present study provides important local data on pediatric metabolic health in Pakistan, where research on childhood hyperuricemia remains scarce. Early detection of elevated uric acid in overweight and obese children may allow clinicians to identify high-risk individuals before the onset of irreversible metabolic complications. Screening for uric acid is simple, inexpensive, and widely accessible, making it a practical tool for early intervention in resource-limited settings[20,21].

However, this study has several limitations. Its cross-sectional design prevents the establishment of causality. The sample size, although adequate for association studies, may not fully represent the broader pediatric population. Dietary patterns, pubertal status, and genetic predispositions factors that may influence uric acid levels were not assessed. Despite these limitations, the study offers valuable insight and forms the basis for future longitudinal research to explore causal pathways and evaluate the effect of uric-acid-lowering interventions in children[22-25].

CONCLUSION

This study demonstrates that elevated serum uric acid levels are strongly associated with multiple metabolic risk factors in overweight and obese children, including higher BMI percentile, increased insulin resistance, adverse lipid profiles, and elevated systolic blood pressure. Uric acid remained an independent predictor of insulin resistance even after adjusting for confounding variables, underscoring its significance as an early metabolic biomarker. Given its affordability, availability, and strong predictive ability, routine measurement of uric acid may be beneficial in early identification of high-risk children who require targeted lifestyle modifications or medical follow-up. Early screening and intervention may help reduce the future burden of diabetes, hypertension, and cardiovascular disease in the pediatric population of Pakistan.

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This article may be cited as: Bahar S, Faiz MZ, Tariq A, Hammad AR, Mefleh RA, Khan MA: Association Between Uric Acid Levels and Metabolic Risk Factors in Overweight and Obese Children. Pak J Med Health Sci, 2023;17(11):511-513.