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Association between Serum Uric Acid and Blood Pressure in Overweight and Obese Children and Adolescents: A Multicenter Study

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A B S T R A C T

Childhood overweight and obesity are recognized as modifiable risk factors for the development of hypertension; however, the role of serum Uric Acid (UA) remains unclear. This study evaluated the association between UA and blood pressure in 173 overweight or obese patients aged 5-18 years (mean age 11.7 ± 2.9 years; 36.4% female). Among them, 28.9% were overweight and 71.1% obese. Mean UA level was 5.1 ± 1.2 mg/dL. Elevated UA, defined as above the population mean or greater than two Standard Deviations (SD) above the mean, was significantly associated with White-Coat Hypertension (WCH). Specifically, UA > mean was associated with WCH (OR =7.8, 95% CI 1.1-62.1; p=0.04) and UA > mean + 2 SD demonstrated a stronger association (OR =9.2, 95% CI 2.8-30.1; p<0.001). Our data supports the association between elevated UA and WCH.

Keywords: Obesity, Uric acid, Hypertension, Pediatrics, Ambulatory blood pressure monitoring

Abbreviations: UA: Uric Acid; SD: Standard Deviations; WCH: White-Coat Hypertension; HTN: Hypertension; BP: Blood Pressure; BMI: Body Mass Index; ABPM: Ambulatory Blood Pressure Monitoring; CI: Confidence Interval; NT: Normotension; MHTN: Masked Hypertension

1. Introduction

Childhood overweight and obesity are modifiable risk factors for Hypertension (HTN), with a prevalence ranging from 10.9% to 25% in overweight children[1].

Serum Uric Acid (UA) is a recognized cardiovascular risk factor in adults, likely due to its association with endothelial dysfunction[2]. Several studies have demonstrated a relationship between elevated UA and primary HTN in children, suggesting that elevated UA may indicate early cardiovascular risk[2,3]. UA concentrations naturally increase with age, differing by sex and pubertal stage. Renal retention is proposed as the main cause of increased UA levels during puberty, a process exacerbated by obesity[4].

The prevalence of hyperuricemia in paediatric patients with HTN ranges from 49% to 89%, depending on the diagnostic

threshold used[2]. This is supported by the Bogalusa Heart Study, which found that higher UA levels in childhood were associated with elevated Blood Pressure (BP) and future development of HTN[5]. Additionally, the prevalence of hyperuricemia among obese adolescents can reach up to 53%[6]. Despite these findings, there is limited local data on the association between UA levels and HTN in overweight and obese children.

2. Objective

To evaluate the association between UA levels and BP in overweight and obese children and adolescents.

3. Materials and Methods

3.1. Study design, setting and participants

This multicentre, prospective, cross-sectional study was conducted between December 2021 and October 2022 in three tertiary paediatric hospitals in Buenos Aires, Argentina: Hospital General de Ninos Dr. Pedro de Elizalde, Hospital de Ninos Ricardo Gutierrez and Hospital de Pediatria Juan P. Garrahan.

3.2. Inclusion criteria

Inclusion criteria were children and adolescents aged 6-18 years with overweight or obesity, defined by Body Mass Index (BMI) Z-scores between +1 and +2 and greater than +2, respectively; height >120 cm (the threshold required for Ambulatory Blood Pressure Monitoring (ABPM) reference values) and no antihypertensive treatment at enrolment.

3.3. Exclusion criteria

Exclusion criteria were chronic diseases associated with HTN, low birth weight or prematurity, neurological conditions requiring anticonvulsants and use medications like lipid-lowering agents, anti-inflammatories, hormonal therapies, corticosteroids, allopurinol or thiazides.

3.4. Sample size calculation and sample selection

A minimum sample size of 168 subjects was determined based on estimated prevalence of hyperuricemia and HTN in obese individuals, assuming a 45% prevalence of HTN among those with elevated UA versus 24.5% among those with normal UA levels. Calculations were performed using an 80% statistical power, 5% alpha error and a 95% confidence interval (CI) (StatCalc 4.1). Patients were enrolled by convenience sampling, based on eligibility during the recruitment period at all three centres.

3.5. Variables

3.5.1. Blood pressure assessment: BP was assessed using office BP measurements and 24-hour ABPM with a validated pediatric device. Based on these assessments, participants were categorized into four groups:

- **Normotension (NT):** Office systolic BP (SBP) and diastolic BP (DBP) <90th percentile for age, sex and height in three determination over three or more visits (for individuals <16 years) or average office SBP/DBP <130/85 mmHg (for those ≥16 years), with normal ABPM.
- **White-Coat Hypertension (WCH):** Office SBP and/or DBP ≥95th percentile (<16 years) or ≥140/90 mmHg (≥16 years), with normal ABPM
- **Masked Hypertension (MHTN):** Normal office BP, but elevated ambulatory SBP and/or DBP (>95th percentile for <16 years; ≥135/85 mmHg daytime or ≥120/70 mmHg nighttime for ≥16 years).
- **Sustained Hypertension (HTN):** Office SBP and/or DBP ≥95th percentile on three or more visits (<16 years) or ≥140/90 mmHg (≥16 years) and elevated ambulatory BP (>95th percentile or ≥130/80 mmHg over 24 hours, ≥135/85 mmHg daytime or ≥120/70 mmHg nighttime for ≥16 years).

The circadian BP pattern was also determined based on the nocturnal BP change: dipper, hyperdipper, non-dipper or riser.

3.6. Clinical and laboratory variables

Demographic and anthropometric data included age, sex, height, weight, BMI Z-score and waist circumference. UA was measured using the same enzymatic colorimetric method in all three participating centers. Two cutoffs were used for classification based on age: (1) above or below the population mean and (2) above or below two standard deviations (SD) from the population mean[7]. Laboratory parameters included fasting glucose, insulin, homeostasis model assessment of insulin resistance (HOMA-IR), lipid profile, liver enzymes, urea, creatinine, electrolytes, complete blood count and urinalysis.

3.7. Statistical analysis

Descriptive statistics were applied according to variable type and distribution. Associations between UA and BP categories were assessed using chi-square tests and odds ratios (ORs). Logistic regression was used to identify predictors of HTN. Statistical significance was set at $p < 0.05$, with 95% confidence interval (CI). Analyses were performed using SPSS v20.0.

4. Results

A total of 173 patients were included (mean age 11.7 ± 2.9 years; 36.4% female), of whom 28.9% were overweight and 71.1% obese. Significant inter-centre differences were found in sex distribution, obesity rates, BP values, cholesterol and LDL cholesterol. BP categories included 143 NT, 14 WCH, 11 MHTN and 5 HTN cases, with all HTN cases originating from a single centre. Mean UA level was 5.1 ± 1.2 mg/dl; 113 patients had levels above the mean and 24 above +2 SD. Additional population characteristics are shown in (Table 1).

Higher UA levels were significantly associated with higher BMI Z-score, waist circumference and metabolic syndrome (OR 2.2, 95% CI 1.1 - 4.6) (Table 2). Furthermore, UA > mean was linked to non-dipper pattern and WCH, whereas UA > 2 SD was associated with WCH, while normotension was protective (Table 3).

In multivariate analysis, only waist circumference was independently associated with UA > mean (Exp β = 1.1, 95% CI 1.01-1.06) and WCH with UA > 2 SD (Exp β = 14.1, 95% CI 1.6-123.9).

Table 1: Characteristics of the study population.

Subjects	HGNPE (n=60)	Garrahan (n=59)	HGNRG (n=54)	Total (n=173)
Sex F/M*	22 / 38	28 / 31	13 / 41	63 / 110
Age (years)	11.1 ± 2.8	11.8 ± 2.9	12.3 ± 2.5	11.7 ± 2.9

BMI (kg/m²)	28.2 ± 5.1	30.3 ± 6.1	28.9 ± 4.8	29.1 ± 5.4
BMI Z-score	2.1 ± 0.5	2.2 ± 0.4	2.1 ± 0.5	2.1 ± 0.5
Overweight / Obesity*	18 / 42	10 / 49	22 / 32	50 / 123
Waist circumference percentile > 90 / < 90	56 / 4	47 / 5	32 / 14	135 / 14
Personal History				
Gestational age (weeks)	39.1 ± 1.1	39.4 ± 0.8	39.4 ± 1.1	39.2 ± 1.1
Birth weight (kg)	3.4 ± 0.5	3.5 ± 0.5	3.4 ± 0.4	3.5 ± 0.5
Family history of HTN: yes/no	49 / 11	36 / 23	44 / 10	129 / 44
Clinical / Laboratory Assessment				
Office BP: HTN / pre-HTN / NT	4/12/1944	12 / 0 / 47	3 / 0 / 51	19 /12 / 142
Office BP + ABPM: NT / WCH / MHTN / HTN	47 / 3 / 4 / 0	40 / 7 / 7 / 5	56 / 4 / 0 / 0	143 / 14 / 11 / 5
24h SBP (mmHg)**	104.9 ± 8.6	112.5 ± 8.1	112.2 ± 11.1	109.8 ± 9.9
24h DBP (mmHg)**	60.2 ± 4.3	66.8 ± 5.9	64.3 ± 5.6	63.7 ± 5.9
24h MAP (mmHg)**	76.9 ± 4.8	83.1 ± 7.4	81.1 ± 5.9	80.3 ± 6.6
Urea (mg/dL)	24.6 ± 5.4	24.1 ± 6.6	26.4 ± 6.2	25.1 ± 6.1
Creatinine (mg/dL)	0.5 ± 0.1	0.6 ± 0.1	0.6 ± 0.4	0.6 ± 0.2
Glucose (mg/dL)	92.5 ± 8.5	93.1 ± 8.3	92.9 ± 6.6	92.8 ± 7.8
Insulin (μU/mL)	17.6 ± 9.9	19.1 ± 12.2	19.4 ± 12.8	18.6 ± 11.4
Total cholesterol (mg/d)**	163.9 ± 30.3	149.3 ± 33.1	160.3 ± 37.5	157.8 ± 34.1
HDL cholesterol (mg/d)	42.1 ± 8.7	42.9 ± 11.1	44.2 ± 9.6	43.1 ± 9.9
LDL cholesterol (mg/d)**	101.3 ± 24.1	96.1 ± 28.9	73.3 ± 47.2	90.7 ± 36.2
Triglycerides (mg/dL)	113.9 ± 46.3	105.9 ± 51.1	122.6 ± 67.2	113.8 ± 55.1
Uric acid (mg/d)	4.9 ± 1.2	5.1 ± 1.1	5.2 ± 1.4	5.1 ± 1.2
Uric acid > mean / < mean	37 / 23	39 / 20	37 / 17	113 / 60
Uric acid > 2SD / < 2SD	9 / 51	7 / 52	8 / 46	24 / 149

Data are presented as mean ± SD or n. Abbreviations: ABPM: Ambulatory Blood Pressure Monitoring; BMI: Body Mass Index; BP: Blood Pressure; DBP: Diastolic Blood Pressure; HDL: High-Density Lipoprotein; HGNRG: Hospital de Ninos Ricardo Gutierrez; HGNPE: Hospital General de Ninos Dr. Pedro de Elizalde; HTN, Hypertension; LDL: Low-Density Lipoprotein; MAP: Mean Arterial Pressure; MHTN: Masked Hypertension; NT: Normotension; SBP: Systolic Blood Pressure; SD: Standard Deviation; WCH: White-Coat Hypertension.*Chi-square $p < 0.05$, **ANOVA $p < 0.05$

Table 2: Association between uric acid levels and studied variables.

Variables	Uric acid > mean	Uric acid < mean	p	Uric acid > 2SD	Uric acid < 2SD	p
Sex F / M *	40 / 73	23 / 37	NS	8 / 16	55 / 94	NS
Age (years)**	11.9 ± 2.7	11.4 ± 3.1	NS	11.3 ± 2.3	11.8 ± 2.9	NS
Gestational age (weeks)**	39.2 ± 1.1	39.4 ± 0.9	NS	39.0 ± 1.1	39.3 ± 1.1	NS
Birth weight (kg)**	3.4 ± 0.5	3.6 ± 0.5	NS	3.3 ± 0.4	3.5 ± 0.5	NS
Obesity / Overweight*	84 / 29	39 / 21	NS	19 / 5	104 / 45	NS
BMI Z-score**	2.2 ± 0.5	2.01 ± 0.4	0.03	2.1 ± 0.6	2.1 ± 0.4	NS
Waist circumference (cm) **	95.0 ± 13.3	88.8 ± 11.8	0.004	94.3 ± 14.6	92.5 ± 12.8	NS
Dyslipidemia yes / no*	54 / 59	22 / 38	NS	11 / 13	65 / 84	NS
Metabolic syndrome yes / no*	40 / 73	12 / 48	0.03	7 / 17	45 / 104	NS

Data are presented as n or mean ± SD. Abbreviations: BMI: Body Mass Index, *Chi-square test; **Independent samples t-test.

Table 3: Association between uric acid levels and blood pressure categories.

Variables	Uric acid > mean	Uric acid < mean	OR (95% CI)	Uric acid > 2SD	Uric acid < 2SD	OR (95% CI)
Isolated HTN yes / no	26 / 87	11 / 49	1.3 (0.6 - 2.9)	6 / 18	31 / 118	1.2 (0.5 – 3.5)
Circadian rhythm: Non-dipper / Dipper	46 / 67	13 / 47	2.5 (1.2 - 5.1) *	11 / 13	48 / 101	1.8 (0.7 – 4.3)
NT yes / no	89 / 24	54 / 6	0.4 (0.1 – 1.1)	14 / 10	129 / 20	0.2 (0.1 – 0.5) *
WCH yes / no	13 / 100	1 / 59	7.7 (1.1 - 62.1)*	7 / 17	7 / 142	8.3 (2.6 – 26.7)*
MHTN yes / no	8 / 105	3 / 57	1.4 (0.4 – 5.6)	3 / 21	8 / 141	2.5 (0.6 – 10.2)
HTN yes / no	3 / 110	2 / 58	0.8 (0.1 – 4.8)	0 / 24	5 / 144	-

Data are presented as n. Abbreviations: HTN: Hypertension; MHTN: Masked Hypertension; NT: Normotension; WCH: White-Coat Hypertension; OR: Odds Ratio; CI: Confidence Interval, *Chi-square test, $p < 0.05$

5. Discussion

In this multicentre, prospective, cross-sectional study of overweight and obese children and adolescents, nearly 80% had normal BP and only 3% had HTN, likely reflecting the systematic implementation of early lifestyle interventions within the participating centres.

Elevated UA was common, with 65% of participants having UA levels above the mean and 13% above mean + 2 SD, consistent with previous reports, such as the 53% hyperuricemia prevalence found in obese adolescents[6]. Notably, we found a consistent association between elevated UA and WCH, where 50% of the WCH subgroup had UA levels > 2 SD. This aligns with the work of Mallamaci et al.[8], who described a similar link between white-coat effect and UA regulation. As hyperuricemia may contribute to early cardiovascular risk even without hypertension, this finding supports prior reports identifying children with WCH as having increased cardiovascular risk[9]. While hyperuricemia is associated with HTN risk, our small HTN sample limited had insufficient statistical power to confirm this relationship[5]. We did, however, observe the UA levels > mean was associated with non-dipper pattern and metabolic syndrome, consistent with previous findings[6,10].

6. Limitations

The primary limitation of this study is the variability in laboratory and BP measurements across centres, although standardized protocols were used. While the multicentre design may introduce heterogeneity, it also improves generalizability of our findings.

7. Conclusion

In conclusion, elevated UA was significantly associated with WCH in overweight and obese children and adolescents. However, the small number of HTN cases precluded a robust assessment of the relationship between UA and HTN.

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10. Ethical Approval

The study was approved by the ethics committees of all participating centres (Registry N. 5976, 5975 and 1373), conducted in accordance with the Declaration of Helsinki and obtained informed consent from participants or their guardians.

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