Academic Journal of Medical Sciences
ISSN: 2708-2725
ORIGINAL ARTICLE

Hyperuricemia and Components of Metabolic Syndrome in Obese Children and Adolescents

Asaad Abid Atiya Al-Talabi[1*], Wurood Jalil Hasan [2],Kamal Ismail Mashallah[3]

Author's Information
1.M. B. Ch. B. /F.I.C.M.S.pediatric
2.M.B.Ch.B./C.A.B.P.
3.M.B.Ch.B./C.A.B.P.

Corresponding author:
Dr. Asaad Abid Atiya Al-Talabi

Funding information
Self-funded

Conflict of interest
None declared by author

ABSTRACT

Background: *Metabolic syndrome (MS) encompasses a set of factors that lead to the development of cardiovascular disease (CVD) and diabetes mellitus (DM), represented by central obesity, dyslipidemia, glucose metabolism abnormalities, and high blood pressure (HBP), which is closely associated with insulin resistance*
Objective: *to analyze the association between serum uric acid concentrations with indicators of general obesity, of visceral adiposity, and with other biochemical measurements related to the metabolic syndrome in obese schoolchildren and adolescents.*
Method: *A cross-sectional, prospective study in which 823 students were evaluated within the age of 6-15 years (range in which the prognostic value of the components has been studied of the metabolic syndrome), attending a school that serves children from low socioeconomic strata (selected due to geographical proximity). We exclude Those presenting with: Diabetes mellitus, neurological diseases under treatment with anticonvulsants, depression, that they would receive medication lipid-lowering or anti-inflammatory drugs or hormone of the growth or LH-RH analogues, or corticosteroids of chronic use.*
Results: *Significantly higher concentrations were found of uric acid (UA) in children with hyperinsulinism, according to the suggested cut-off points for schoolchildren or teenagers (normal insulin: 0.179 ± 0.049 vs hyperinsulinemic: 0.224 ± 0.068 mmol/l; $p < 0.01$), no significant differences according to the various cutting points of HOMA. There was no association between uric acid (UA)and values of systolic blood pressure, or diastolic (hyperuricemic: greater than x + 1 z: 68.1 ± 14.2 vs normal uric acid: 62,9 ± 11,1 mm Hg).*
Conclusion: *Obese children and teenagers in the current study show an association with elevated uric acid as well as a link to higher ALT and insulin*

Keywords: ***Uric acid, Metabolic syndrome, Children, Insulin.***

1. INTRODUCTION

Metabolic syndrome (MS) encompasses a set of factors that lead to the development of cardiovascular disease (CVD) and diabetes mellitus (DM), represented by central obesity, dyslipidemia, glucose metabolism abnormalities, and high blood pressure (HBP), which is closely associated with insulin resistance. Currently, there is no single criterion for defining it; it is not a single disease, but rather a combination of health problems that can occur simultaneously or sequentially in the same individual (1,2). MS is a clear health problem, not only because of its high prevalence but also because of its role as a risk factor for other diseases that carry significant morbidity and mortality. Therefore, it is important to obtain data that allow for the design of proposals to improve timely treatment and prevent further complications (3,4). Uric acid (UA) is the end product of purine metabolism, a nucleotide that is abundant in nature, especially in the form of nucleic acids. Hyper uric acid (UA)is common in patients with obesity, essential hypertension, dyslipidemia, and hyperglycemia, a group of factors that characterize MS. Some authors consider hyper uric acid (UA)a characteristic of MS, although serum UA levels are not yet considered a diagnostic criterion for MS, among other reasons because the pathophysiological alteration that triggers the increase in serum UA is not fully understood (5,6). Although it has been suggested that UA may simply be a consequence of increased UA uptake in the proximal tubule secondary to hyper insulin , there is considerable data indicating that serum UA levels could play an active role in contributing to the development/progression of MS (7). Numerous studies have demonstrated the association between UA concentrations and individual MS components, but the prevalence of MS using UA concentrations has not yet been established (8). The clinical and biochemical criteria for determining the presence of MS are clearly defined; however, there are emerging factors related to metabolic disorders that should be included, as is the case with UA (9). More importantly, it is important to know whether UA contributes independently to the development of MS or is simply a byproduct of other processes that cause this disorder, and whether UA can act as a biomarker to predict the future development of MS (10). Obese children and adolescents have frequent metabolic alterations associated with their clinical signs. The so-called metabolic syndrome was initially described for young adults as a set of

clinical alterations and metabolic, with a predictive value for the risk of type ii diabetes and cardiovascular disease in older ages: increased abdominal perimeter, increased systolic and diastolic blood pressure, hypertriglyceridemia, decreased HDL cholesterol and hyperglycemia. This set of proposed alterations has also been studied in pediatric populations and also seems to have a good predictive value for these conditions of adult life in schoolchildren and adolescents (11,12). The aim of this study was to analyze the association between serum uric acid concentrations with indicators of general obesity, of visceral adiposity, and with other biochemical measurements related to the metabolic syndrome in obese schoolchildren and adolescents.

2. METHODOLOGY

A cross-sectional, prospective study in which 823 students were evaluated within the age of 6-15 years (range in which the prognostic value of the components has been studied of the metabolic syndrome), attending a school that serves children from low socioeconomic strata (selected due to geographical proximity).

Exclusion criteria: Those presenting with: Diabetes mellitus, neurological diseases under treatment with anticonvulsants, depression, that they would receive medication lipid-lowering or anti-inflammatory drugs or hormone of the growth or LH-RH analogues, or corticosteroids of chronic use.

284 children (34.5%) were found with a BMI > 2 SD of the WHO growth standards. Of these children were selected in a random 100 children whose parents were asked for a consent written and informed (more assent to those children > 8 years old); finally 88 children and adolescents were incorporated into the study. The sample size was calculated according to the coefficient of correlation between visceral adiposity and basal insulin observed by Goran et al. (13); an alpha error was used from 5% and a power of 80%. The sample required for the study was 75 individuals and was considered a 15% of possible losses.

They were measured under standardized conditions: weight, height, abdominal circumference (1 cm above the iliac ridges), blood pressure; pubertal development according to the Tanner's criteria. Visceral adiposity was assessed by abdominal ultrasonography, measuring the spine-edge internal segment of the anterior rectus muscle and the presence of fatty liver.

It was performed by the same pediatric radiologist trained in the same ultrasonographic equipment, the measurements were repeated 3 times, being recorded the average. Fasting metabolic measurements were: basal IR, glucose (HOMA), serum lipids, aspartate aminotransferase enzymes (AST) and alanine aminotransferase (ALT) and UA. The insulin estimate is made by radioimmunoassay (RIA DCP kit, LA, USA), being classified as hyperinsulinism in prepubertal subjects with fasting insulin ≥ 10 mIU/mL and in the pubertal ≥ 15 mIU/mL.

Triglycerides were measured with the ATP technique peroxidase (reagent kit 7D74). Hypertriglyceridemia was considered to plasma triglycerides ≥ 100 mg/dl. The HDL cholesterol was measured directly (kit 3 K 33HDL/1E68 HDL calibrator). According to Cook's criteria et al.(14) we consider cardiovascular risk cholesterol HDL ≤ 40 mg/dl.

The study was previously approved by the Research ethics of the our hospitals and. Parents and children (> 8 years old) were asked to sign a written and informed consent.

The statistical analysis included descriptive statistics, Pearson linear correlation, "t" of Student to evaluate differences between parametric continuous variables; they performed several logistic multiple regression models to study associations between clinical variables and uric acid (UA)categorized.

In addition, ROC curves were carried out of sensitivity-specificity to analyze the points of cutting more suitable for associations between transferees with ultrasound fatty liver, ultrasound distance column muscular anterior rectum or insulin , or between uric acid (UA)and the other metabolic variables.

3. RESULTS

The characteristics of the children and adolescents studied were shown in (**Table 1**). The serum uric acid (SUA) concentrations were 0.199 ± 0.056 mmol/l, no statistically significant differences between males and females (0.201 ± 0.052 vs 0.196 ± 0.062 mmol/L). The upper limit of normality of our sample (x + 2 SD) was similar to that described for adults (0.321 mmol/l = 4.95 mg/dl); 7% of children they had concentrations above that limit and another 18% the they had between +1 and +2 SD. Significantly higher concentrations were found of uric acid (UA) in children with hyperinsulinism, according to the suggested cut-off points for schoolchildren or teenagers (normal insulin: 0.179 ± 0.049 vs hyperinsulinemic: 0.224 ± 0.068

mmol/l; p < 0.01), no significant differences according to the various cutting points of HOMA. By means of ROC analysis the best cut-off point was sought of sensitivity-specificity of associated AST and ALT Alanine Aminotransferase to alterations of insulin , or to the presence of fatty liver, or spine-muscle ultrasound distance anterior rectum. > 26 U/l of ALT was found to be associated better in the presence of fatty liver (sensitivity of 56.8%, specificity of 74.4%, area under the curve of 63%). They were not found statistically significant differences of uric acid (UA)according to AST categories, or BMI magnitude, perimeter abdominal, abdominal perimeter/size, ultrasound measurements of intra-abdominal adiposity or ultrasound suspicion of fatty liver. There was no association between uric acid (UA)and values of systolic blood pressure, or diastolic (hyperuricemic: greater than x + 1 z: 68.1 ± 14.2 vs normal uric acid: 62,9 ± 11,1 mm Hg). Several multiple regression models were tested logistics with normal vs altered uric acid (UA)(> +1 z) as a variable dependent, leaving the ALT Aminotransferase as the only statistically significant associated (p < 0.033) (**Table 2**).

Table 1. Characteristics of obese children and adolescents (n = 77)

Variable	Mean ± SD	Range
Age (years)	10.1 ± 2.2	6.0-15.5
Gender (M/F)	34/43	-
Height (cm)	139 ± 10.1	117.4-159.1
BMI (z-score)	4.0 ± 1.4	1.3-7.5
Abdominal perimeter (cm)	86.9 ± 9.8	66.0-111.0
ultrasonographic column-anterior rectus muscle segment (cm)	5.39 ± 1.2	3.2-7.95
Total cholesterol (mg/dl)	159.9 ± 39.2	105-312
HDL (mg/dl)	42.8 ± 6.9	29-59
LDL (mg/dl)	98.7 ± 19.8	53-180
Triglycerides (mg/dl)	91.6 ± 33.7	39-176
F. Blood glucose (mg/dl)	82.2 ± 9.4	61-102
Fasting Insulin (uU/ml)	11.1 ± 6.5	2.2-23.9
HOMA-IR	2.1 ± 1.3	0.2-7.1
ALT Transferase (U/l)	25.8 ± 11.3	7-79
AST Transferase (U/l)	23.7 ± 19.6	8-143
SUA(mmol/l)	0.199 ± 0.056	0.092-0.367

Table 2. Logistic regression model evaluating risk factors associated with hyperuricemia (x + 1 SD > 0.243 mmol/l) in children and teenagers

Variable	Odds Ratio	Standard error	z	p > z	95% conf.	Interval
z BMI	0.962	0.213	-0.12	0.901	0.6393	1.4830
HOMA-IR	0.74	0.52	-0.43	0.670	0.1857	2.950
Visceral Fat	1.32	0.403	0.93	0.352	0.7315	2.408
Age	1.043	0.148	0.30	0.765	0.789	1.379
ALT	1.066	0.0331	2.06	0.039	1.0033	1.133
F. Insulin	0.9731	0.1365	-0.19	0.846	0.739	1.281

4. DISCUSSION

The association of UA with the frequency of MS in our population is particularly relevant. Considering the scarcity of epidemiological studies that provide information on the status of our population. Obese children and adolescents have frequent alterations metabolic factors associated with its clinical signs. The so-called metabolic syndrome was initially described for young adults as a set of clinical alterations and metabolic, with a predictive value for the risk of type diabetes ii and cardiovascular disease in ages more advanced: increased abdominal perimeter, increased of systolic and diastolic blood pressure, hypertriglyceridemia, decrease in HDL cholesterol and hyperglycemia. This all of the proposed alterations have also been studied in pediatric populations and also seems to have a good predictive value for those conditions of adult life in schoolchildren and adolescents (15-17). Several studies have shown that the measurements of general obesity (BMI) have a lower association with risk of metabolic alterations typical of the syndrome metabolic; the abdominal perimeter, and even better the measurements ultrasonographic of intra-abdominal adiposity, are better indicators of these alterations than the IMC (18,19). Other metabolic alterations have been proposed as well associated with metabolic syndrome in adulthood, including hyperuricemia , but these have been little studied in the pediatric ages and we do not have information in the national level (20). Our results show that the increase in uric acid (UA) is associated with other metabolic parameters of the metabolic syndrome, in obese schoolchildren and adolescents. If

the metabolic component is mostly associated with the set of clinical and metabolic alterations of the metabolic syndrome are the alterations of insulin , the observed association between increased uric acid (UA)and hyperinsulinism is in line with this pathophysiology (21). There is no association between increased HOMA and increased uric acid (UA)may be associated with the fact that it has not been possible to demonstrate in schoolchildren, and especially in teenagers, HOMA cut-off points concordant with insulin resistance. Which is in agreement with that mentioned by Dikker O, et al. (22). There is currently no consensus to establish points of cut that define uric acid (UA)in children (23), have proposed to define uric acid (UA)as the average +1 of the uric acid (UA) concentrations of a normal population, according to the age. The ultrasonographic suspicion of fatty liver and the increase in transferases is also associated with alterations of insulin, the same as the increase in of ultrasound indicators of intra-abdominal adiposity (24,25). However, we did not observe an association between serum uric acid levels (SUAL) with severity of general obesity (BMI) or with perimeter abdominal, nor with ultrasonographic suspicion of liver fatty. Some previous studies have observed an association between an increase in SUAL and an increase in blood pressure, as part of the metabolic syndrome (26).

5. CONCLUSIONS

Obese children and teenagers in the current study show an association with elevated uric acid as well as a link to higher ALT and insulin.

Ethical Approval:

All ethical issues were approved by the author. Data collection and patient's enrollment were in accordance with Declaration of Helsinki of World Medical Association, 2013 for the ethical principles of researches involving human. Consent was obtained from each participant and data were kept confidentially.

6. BIBLIOGRAPHY

1. Swarup S, Ahmed I, Grigorova Y, Zeltser R. Metabolic syndrome. InStatPearls [internet] 2024 Mar 7. StatPearls Publishing.

2. Fahed G, Aoun L, Bou Zerdan M, Allam S, Bou Zerdan M, Bouferraa Y, Assi HI. Metabolic syndrome: updates on pathophysiology and management in 2021. International journal of molecular sciences. 2022 Jan 12;23(2):786.

3. Jemal A, Girum T, Kedir S, Bedru A, Mosa H, Assfa K, Oumer A. Metabolic syndrome and its predictors among adults seeking medical care: A trending public health concern. Clinical Nutrition ESPEN. 2023 Apr 1;54:264-70.

4. Reynolds K, He J. Epidemiology of the metabolic syndrome. The American journal of the medical sciences. 2005 Dec 1;330(6):273-9.

5. Barrera-Cruz A, Rodríguez-González A, Molina-Ayala MA. Current scenario of obesity in Mexico. Rev Med Inst Mex Seguro Soc 2013;51(3):292-99.

6. López-Suárez A, Elvira-González J, Bascuñana-Quirell A, RosalObrador J, Michán-Doña A, Escribano-Serrano J, et al. Serum urate levels and urinary acid excretion in subjects with metabolic syndrome. Med Clin (Barc) 2006;126(9):321-324.

7. Soltani Z, Rasheed K, Kapusta DR, Reisin E. Potential role of uric acid in metabolic syndrome, hypertension, kidney injury, and cardiovascular diseases: is it time for reappraisal? Current Hypertension Reports 2013;15(3):175-181.

8. Reyes JAE, Navarro J, Cruz IM, Castro DLJ, Landgrave GJ, Narváez PC, Landgrave GI, Oregón LA, Espinosa LFR. Prevalence of metabolic syndrome in relation to uric acid levels. Medicina Interna de México 2009;25(4):278-284.

9. Kaur J. [Retracted] A Comprehensive Review on Metabolic Syndrome. Cardiology research and practice. 2014;2014(1):943162.

10. Copur S, Demiray A, Kanbay M. Uric acid in metabolic syndrome: does uric acid have a definitive role?. European journal of internal medicine. 2022 Sep 1;103:4-12.

11. Al-Hamad D, Raman V. Metabolic syndrome in children and adolescents. Translational pediatrics. 2017 Oct;6(4):397.

12. Park H, Choi JE, Jun S, Lee H, Kim HS, Lee HA, Park H. Metabolic complications of obesity in children and adolescents. Clinical and Experimental Pediatrics. 2023 Nov 16;67(7):347.

13. Goran I, Bergman N, Gower A. Influence of total vs. visceral fat on insulin action and secretion in African American and white children. Obes Res. 2001:423---31.

14. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: Findings from the third National Health and Nutrition Examination Survey,1988-1994. Arch Pediatr Adolesc Med. 2003;157:821---7.

15. Wittcopp C, Conroy R. Metabolic syndrome in children and adolescents. Pediatrics in review. 2016 May 1;37(5):193-202.

16. Mainieri F, La Bella S, Chiarelli F. Hyperlipidemia and cardiovascular risk in children and adolescents. Biomedicines. 2023 Mar 7;11(3):809.

17. Kavey RE. Combined dyslipidemia in children and adolescents. Endotext [Internet]. 2023 May 10. Available at: https://www.ncbi.nlm.nih.gov /sites/books/NBK395577/.

18. Grundy SM. Obesity, metabolic syndrome, and cardiovascular disease. The Journal of Clinical Endocrinology & Metabolism. 2004 Jun 1;89(6):2595-600.

19. Engin A. The definition and prevalence of obesity and metabolic syndrome. Obesity and lipotoxicity. 2017:1-7.

20. Billiet L, Doaty S, Katz JD, Velasquez MT. Review of hyperuricemia as new marker for metabolic syndrome. International Scholarly Research Notices. 2014;2014(1):852954.

21. Foster C, Smith L, Alemzadeh R. Excess serum uric acid is associated with metabolic syndrome in obese adolescent patients. Journal of Diabetes & Metabolic Disorders. 2020 Jun;19:535-43.

22. Dikker O, Aktaş A, Şahin M, Doğan M, Dağ H. The association of serum uric acid levels and various uric acid-related ratios with insulin resistance and obesity: A preliminary study in adolescents. Children. 2023 Aug 31;10(9):1493.

23. Kubota M. Hyperuricemia in children and adolescents: present knowledge and future directions. Journal of nutrition and metabolism. 2019;2019(1):3480718.

24. Esteghamati A, Jamali A, Khalilzadeh O, Noshad S, Khalili M, Zandieh A, et al. Metabolic syndrome is linked to a mild elevation in liver aminotransferases in diabetic patients with undetectable non-alcoholic fatty liver disease by ultrasound. Diabetology & Metabolic Syndrome. 2010 Dec;2:1-7.

25. Stolk RP, Wink O, Zelissen PM, Meijer R, Van Gils AP, Grobbee DE. Validity and reproducibility of ultrasonography for the measurement of intra-abdominal adipose tissue. International journal of obesity. 2001 Sep;25(9):1346-51.

26. Loeffler LF, Navas-Acien A, Brady TM, Miller ER III, Fadrowski JJ. Uric acid level and elevated blood pressure in U.S. adolescents. National Health and Nutrition Examination Survey 1999-2006. Hypertension. 2012;59:811---7.

Citation:

Al-Talabi A.A.A, Hasan W.J, Mashallah K.I Hyperuricemia and Components of Metabolic Syndrome in Obese Children and Adolescents. AJMS 2024; 11 (2): 43-51