Original article

Correlation of plasma uric acid with blood pressure and dyslipidaemia in young Sudanese adults in Khartoum, Sudan

Huda Mahjoub Ali [1], Nouralsalhin A Alaagib [2*], Rabab Mohammed Elbashir [3]

[1]Department of Physiology, Faculty of Medicine, Shendi University, [2]Department of Physiology, Faculty of Medicine, University of Khartoum, [3] Department of Physiology, Faculty of Dentistry, University of Khartoum, Sudan

ABSTRACT

Background Uric acid (UA) is associated with a number of diseases like: obesity, metabolic syndrome, hypertension, renal diseases and heart diseases. Hyperuricaemia may occur prior to the development of metabolic syndrome and may be used as predictor of it.

Methods This is a cross-sectional study done on 150 subjects aged between 18-25 years. The weight, height and waist circumference (WC) were measured and Body Mass Index (BMI) was calculated. Skin fold thickness was measured from triceps region and body fat percent (BF %) was calculated. Blood pressure (BP) was measured and a fasting blood sample was taken to determine UA, total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and triglycerides (TGs).

Results Subjects were divided into three groups: obese (BMI ≥30kg/m^2, n=50), overweight (BMI 25-29.99 kg/m^2, n=49) and normal weight (BMI 18.5-24.99 Kg/m^2, n=51) group. UA showed insignificant difference between the three BMI groups. The correlations of UA with BP, BMI and WC were insignificant in this group of young adults. However, a significant positive association was found between UA and total cholesterol ($P<0.01$). A highly significant difference was found in the mean of HDL ($P < 0.005$) and LDL ($P < 0.005$) between the three BMI groups. The highest mean of LDL was found in the obese group.

Conclusion The positive correlation of UA with the total cholesterol in obese subjects indicates that Hyperuricaemia may predispose to cardiovascular problems even in young obese adults. Therefore it is important to assess uric acid in young obese adults.

***Correspondence to** nouralsalhin@gmail.com.*

BACKGROUND

Uric acid (UA) is the end product of an exogenous pool of purines and endogenous purine metabolism. [1] Recently, evidences have suggested that Hyperuricaemia may play a role in the development and pathogenesis of a number of metabolic, haemodynamic and systemic diseases other than gout e.g. obesity,[2,3] metabolic syndrome,[4] hypertension,[5] cardiovascular diseases (CVD),[6,7] endothelial dysfunction, and insulin resistance.[8]

The metabolic syndrome (Met S) is identified as a condition of increased risk for CVD and type 2 diabetes mellitus (T2DM) in both sexes.[9] Several definitions and clinical screening parameters for the Met S have been proposed by various organizations e.g. the World Health Organization (WHO), the International Diabetes Federation (IDF) and the National Cholesterol Education Program–Adult Treatment Panel III (NCEP–ATPIII).[10] The WHO put insulin resistance as the major criteria for diagnosis of Met S plus 2 additional risk factors including obesity, hypertension, high triglyceride (TG), reduced high-density lipoprotein cholesterol

(HDL), or micro-albuminuria. Patients with T2DM were not excluded from diagnosis.[11] The NCEP–ATPIII criteria did not require insulin resistance per se and no other single factor for diagnosis, but stated the presence of 3 of the following 5 factors as the basis for the diagnosis of Met S: abdominal obesity, elevated TG, reduced HDL, elevated BP, and elevated fasting glucose (impaired fasting glucose or T2DM).[12] The IDF also dropped the WHO requirement for insulin resistance but made abdominal obesity, with particular emphasis on waist measurement as a simple screening tool, necessary as 1 of the 5 factors required in the diagnosis of Met S.[13]

Hypertension, high waist circumference (WC) and Met S were reported as the major cardiovascular risk factors associated with Hyperuricaemia in black African population.[14] The association of UA with elements of Met S like hypertension has been studied extensively.[15-17] It was found that increase in UA is associated with higher BP in children[18] and adults.[17,19] Independent of traditional hypertension risk factors, the link between high UA and hypertension is more pronounced in younger individuals, in women and African Americans.[19] Lee et al reported that the association between Hyperuricaemia and essential hypertension was clearer in women and men under age of 60 years. They suggested that people under 60 years may obtain maximal benefit from the treatment of Hyperuricaemia to prevent and treat hypertension.[20]

One of the studies investigated the relation between UA and dyslipidaemia; they reported that normal levels of UA might be a good indicator of the level of TGs and very low density lipoprotein cholesterol (VLDL) in men in a wide range of age.[21] Serious cardiovascular complications have been linked with serum UA like stroke or ischemic heart disease.[22,23] and carotid atherosclerosis.[24,25] Therefore, early detection and treatment of hyperuricaemia may be preventive of hypertension and cardiovascular complications.

METHODS

This is an analytical cross-sectional study which included 150 young adult subjects: 67 male and 83 female, aged between 18-25 years from Medical Campus University of Khartoum. Participants were divided into three groups: normal weight group were 51 subjects (BMI 18.50-24.99 Kg/m^2), overweight group (BMI 25.00-29.99 kg/m^2) were 49 subjects and obese group (BMI $\geq$30.00kg/m^2) was composed of 50 subjects. Subjects with hypertension, diabetes, renal or cardiac diseases were excluded. Those who take medication that may affect plasma UA, smokers, alcoholics and females who have amenorrhea or pregnancy were also excluded from the study.

This study was approved by the Ethical Committee (EC) of Faculty of Medicine University of Khartoum. Students were recruited from the medical campus by advertisements in the lecture halls and social networking sites. After explaining the procedure, the participant signed an informed consent approved by the EC. A structured questionnaire was completed for each participant including personal information and medical history. Physical examination was done by the researcher to exclude any abnormality. Participants were asked to attend in the early morning to the laboratory at the physiology department in the Faculty of Medicine, University of Khartoum. Arterial BP was measured by the researcher for all participants using mercury sphygmomanometer (Mercurial Sphygmomanometer Desk Model, China). The mean BP was calculated using the following formula.[26]

Mean BP= Diastolic BP+1/3(systolic BP- Diastolic BP)

Fasting venous blood was taken and plasma UA, total cholesterol, LDL, HDL and TGs were measured. The following anthropometric measurements were also done:

Height (cm) and weight (Kg) were measured using a balance beam scale with a height rod (RGZ-120,

China). BMI (Kg/m2) was calculated as a ratio between the weight (Kg) and height squared meters.

Waist circumference (WC) in cm was measured by a flexible plastic measuring tape on the exposed abdomen at a level midway between the lowest rib and the iliac crest at the end of normal expiration and with the subject standing.

Triceps Skin fold thickness (mm) was measured using Harpenden caliper.[27] and was used to calculate the body fat percent (BF%) according to the following equation.[28]

$y_1 = 4.019 + 0.894\ x_1$

Where y_1 = BF% of the body weight; x_1 triceps skin fold (mm).

Data was saved and analyzed using Statistical Package for Social Sciences (SSPS) version 21. Descriptive statistics was done and displayed as means and standard deviation. Comparisons of the means of UA, lipid profile between the three groups (obese, overweight and normal weight subjects) was done using ANOVA test. The associations between BP, anthropometric measurements, lipid profile in the three groups were done using Spearman correlation test.

RESULTS

The age of the participants ranged between 17-25 years. The means of age, anthropometric measurements and mean BP in different BMI groups are shown in (Table 1). Obese group had the highest mean of WC (101.8 ± 10.6 cm), BF% (26.4 ± 4.9%) and mean BP (90.0 ± 6.3mmHg).

Table 1. Means of Age, BP and anthropometric measurements in different BMI groups

Variable	Normal weight n=51 Mean ± SD	Overweight n=49 Mean ± SD	Obese n= 50 Mean ± SD
Age (years)	18.9 ± 1.9	20.0 ± 2.0	19.5 ± 1.9
Weight (Kg)	59.7 ± 7.0	78.1 ± 9.6	95.1 ± 12.5
BMI (Kg/m^2)	21.5 ± 1.8	27.5 ± 1.5	33.0 ± 2.4
WC (Cm)	74.4 ± 6.2	87.4 ± ٧,٧	101.8 ± 10.6
BF %	17.7 ± 12.3	21.2 ± 5.3	26.4 ± 4.9
BF (Kg)	13.7 ± 3.9	19.8 ± 5.1	27.5 ± 5.5
Mean BP (mmHg)	82.0 ± 6.7	87.6 ± 7.8	90.0 ± 6.3

BP: Blood Pressure

BMI: Body Mass Index

WC: Waist Circumference

BF: Body Fat

Comparing lipid profile in the different BMI groups showed insignificant difference in the means of total cholesterol and TGs between the three BMI groups (Table 2). However, a highly significance difference was found in the mean of HDL ($P < 0.005$) and LDL ($P < 0.005$) between the normal weight, overweight and obese subjects. The highest mean of LDL was found in the obese group (Table 2).

Table 2. Comparison of lipid profile and uric acid between different BMI groups

Variables (mg/dl)	Normal Mean ± SD	Overweight Mean ± SD	Obese Mean ± SD	F	P Value
Cholesterol	156.6 ± 25.6	149.9 ±24.9	156.2 ± 27.4	1.0	0.3
TGs	77.3 ± 17.8	74.3 ± 21.3	81.1 ± 23.8	1.3	0.3
HDL	79.5 ± 16.2	33.0 ± 7.9	36.0 ± 8.3	258.0	0.005**
LDL	62.5 ± 18.9	77.2 ± 29	79.9 ± 34.6	5.6	0.000**
Uric Acid	3.8 ± .8	3.7 ± .8	3.6 ± .7	.276	.759

TGs: Triglycerides

HDL: High Density Lipoprotein

LDL: Low Density Lipoprotein

*P is significant at <0.05, **P is highly significant at ≤0.005

Comparison of the means of plasma UA showed no significance difference between the different BMI groups as shown in Table 2. However, plasma UA showed significant positive association with plasma cholesterol (P<0.01). The correlation between UA and BP was insignificant in the three BMI groups. In this group of young adults, the association of UA with BMI and WC was statistically insignificant.

DISCUSSION

The results of this study showed insignificant association between plasma UA and BP in this group of young adults. However, considerable number of studies found association between UA and BP.[17-19] Feig and Johnson showed a high correlation between serum UA and BP in children with primary hypertension.[29] UA has been claimed to have a role in the pathogenesis of hypertension in the young.[30] Animal models support a two-phase mechanism for the development of hyperuricaemic hypertension. Initially, UA induces vasoconstriction by activation of the renin-angiotensin system and by reducing the circulating nitric oxide,[31] which can be reversed by lowering UA. Over time, UA uptake into smooth muscle cells of the vessels causes cellular proliferation and secondary arteriolosclerosis that impairs pressure natriuresis, causing sodium-sensitive hypertension.[32]

The most widely recognized factors of Met S are atherogenic dyslipidaemia, elevated BP, and elevated plasma glucose. Subjects with these characteristics commonly manifest a prothrombotic state and a pro-inflammatory state.[10] Atherogenic dyslipidaemia consists of an aggregation of lipoprotein abnormalities that includes elevated serum TG and apolipoprotein BP, increased LDL and a reduced level of HDL.[10] Recently, the association between the plasma UA and dyslipidaemia has been suggested.[33,34] In our study we found a positive correlation between plasma UA and plasma cholesterol (TC) in young adult subjects. Comparable results were found by Sarmah et al who estimated the lipid profile (TC, TGs, HDL and LDL) in sixty hyperuricaemic Assamese people (Indian tribe) with no history of CVD. They reported a significant positive correlation between UA and TC.[35] Peng et al found that serum UA had a strong association with LDL, TGs, TC, Apo-B levels, ratio of TGs to HDL, and ratio of Apo-B to Apo-A1.[33] In vitro, UA induced an increase in the production of monocyte chemotactic protein-1, an adipokine that plays an essential role in inducing the pro-inflammatory state in human adipocytes.[36] Therefore, hyperuricaemia might be a mediator of pro-inflammatory endocrine imbalance in the

adipose tissue which can be considered as one of the mechanisms of insulin resistance in subjects with the Met S.[36] Zhu et al reported that Hyperuricaemia lead to inhibition of nitric oxide (NO) which lead to insulin resistance.[37] Furthermore, it has been reported that UA directly induces hepatocyte fat accumulation which may result in non-alcoholic fatty liver disease.[37,38]

CONCLUSION

The positive correlation of UA with cholesterol indicates that Hyperuricaemia may predispose to cardiovascular problems even in young age. Therefore it is important to assess UA in obese young adults. In addition, healthy life style and awareness about diets which increase UA and lipid profile are recommended to decrease the risk of cardiovascular diseases and metabolic syndrome.

REFERENCES

1. Chaudhary K, Malhotra K, Sowers J, Aroor A. Uric Acid-key ingredient in the recipe for cardiorenal metabolic syndrome. *Cardiorenal Medicine.* 2013;3:208-20.
2. Yamasaki T, Tomita K. Relationship between hyperuricemia and metabolic syndrome. *Nihon Rinsho Japanese Journal of Clinical Medicine.* 2008;66:766-70.
3. Ságodi L, Feher V, Kiss-Tóth E, Almasi A, Barkai L. Metabolic complications of obesity during adolescence, particularly regarding elevated uric acid levels. *Orvosi Hetilap.* 2015;156:888-95.
4. Wei C-Y, Sun C-C, Wei JC-C, et al. Association between hyperuricemia and metabolic syndrome: an epidemiological study of a labor force population in Taiwan. *BioMed Research International.* 2015;2015.
5. Nagahama K, Inoue T, Iseki K, et al. Hyperuricemia as a predictor of hypertension in a screened cohort in Okinawa, *Japan. Hypertension Research.* 2004;27:835-41.
6. Silva HAd, Carraro JCC, Bressan J, Hermsdorff HHM. Relation between uric acid and metabolic syndrome in subjects with cardiometabolic risk. *Einstein (Sao Paulo)*. 2015;13:202-8.
7. Su P, Hong L, Zhao Y, Sun H, Li L. Relationship between hyperuricemia and cardiovascular disease risk factors in a Chinese population: a cross-sectional study. Medical science monitor: *International Medical Journal of Experimental and Clinical Research.* 2015;21:2707.
8. Pingmuangkaew P, Tangvarasittichai O, Tangvarasittichai S. Association of elevated serum uric acid with the components of metabolic syndrome and oxidative stress in abdominal obesity subjects. *Indian Journal of Clinical Biochemistry.* 2015;30:286-92.
9. Emanuela F, Grazia M, Marco DR, Maria Paola L, Giorgio F, Marco B. Inflammation as a link between obesity and metabolic syndrome. *Journal of Nutrition and Metabolism.* 2012;2012:476380.
10. Alberti K, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. *Circulation.* 2009;120:1640-5.
11. Alberti KGMM, Zimmet Pf. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. *Diabetic Medicine.* 1998;15:539-53.
12. National Cholesterol Education Program (NCEP) Expert Panel on Detection E, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in

Adults (Adult Treatment Panel III) final report. *Circulation.* 2002;106:3143–421.

13. Alberti KGM, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. *The Lancet.* 2005;366:1059-62.
14. Moulin SR, Baldo MP, Souza JB, et al. Distribution of serum uric acid in black Africans and its association with cardiovascular risk factors. *The Journal of Clinical Hypertension.* 2017;19:45-50.
15. Emokpae AM, Abdu A. Serum uric acid levels among Nigerians with essential hypertension. *Nigerian Journal of Physiological Sciences.* 2013;28:41-4.
16. Lu Z, Dong B, Wu H, et al. Serum uric acid level in primary hypertension among Chinese nonagenarians/centenarians. *Journal of Human Hypertension.* 2009;23:113.
17. Sundstrom J, Sullivan L, D'agostino RB, Levy D, Kannel WB, Vasan RS. Relations of serum uric acid to longitudinal blood pressure tracking and hypertension incidence. *Hypertension*. 2005;45:28-33.
18. Alper Jr AB, Chen W, Yau L, Srinivasan SR, Berenson GS, Hamm LL. Childhood uric acid predicts adult blood pressure: *the Bogalusa Heart Study. Hypertension.* 2005;45:34-8.
19. Grayson PC, Kim SY, LaValley M, Choi HK. Hyperuricemia and incident hypertension: a systematic review and meta-analysis. *Arthritis Care & Research.* 2011;63:102-10.
20. Lee JJ, Ahn J, Hwang J, et al. Relationship between uric acid and blood pressure in different age groups. *Clinical Hypertension*. 2015;21:14.
21. Baliarsingh S, Sharma N. Serum uric acid level is an indicator of total cholesterol and low density lipoprotein cholesterol in men below 45 years in age but not older males. *Clinical Laboratory.* 2012;58:545-50.
22. Kang D-H. Potential role of uric Acid as a risk factor for cardiovascular disease. *The Korean Journal of Internal Medicine*. 2010;25:18.
23. Sinan Deveci O, Kabakci G, Okutucu S, et al. The association between serum uric acid level and coronary artery disease. *International Journal of Clinical Practice.* 2010;64:900-7.
24. Feng L, Hua C, Sun H, et al. Association between Serum Uric Acid Level and Carotid Atherosclerosis in Chinese Individuals Aged 75 Years or Older: A Hospital-Based Case-Control Study. *The Journal of Nutrition, Health & Aging.* 2018;22:508-12.
25. World Health Organization - Fact sheet: obesity and overweight. who. int/dietphysicalactivity/ publications/facts/obesity, 2016
26. Meaney E, Alva F, Moguel R, Meaney A, Alva J, Webel R. Formula and nomogram for the sphygmomanometric calculation of the mean arterial pressure. *Heart*. 2000;84:64-.
27. Durnin J. V. WJ. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. *British Journal of Nutrition*. 1974;32:77-97.
28. Parízková J. BP. Relationship between skinfold thickness measured by Harpenden caliper and densitometric analysis of total body fat in men. *Human Biology*. 1971;43:16-21.
29. Feig DI, Johnson RJ. Hyperuricemia in childhood primary hypertension. *Hypertension.* 2003;42:247-52.
30. Feig DI. The role of uric acid in the pathogenesis of hypertension in the young. *The journal of Clinical Hypertension.* 2012;14:346-52.
31. Sánchez-Lozada LG, Tapia E, López-Molina R, et al. Effects of acute and chronic L-arginine treatment in experimental hyperuricemia. *American Journal of Physiology-Renal Physiology.* 2007;292:F1238-F44.

32. Kang D-H, Park S-K, Lee I-K, Johnson RJ. Uric acid–induced C-reactive protein expression: implication on cell proliferation and nitric oxide production of human vascular cells. *Journal of the American Society of Nephrology.* 2005;16:3553-62.

33. Peng T-C, Wang C-C, Kao T-W, et al. Relationship between hyperuricemia and lipid profiles in US adults. *BioMed Research International*. 2015;2015.

34. Liu XZ, Li HH, Huang S, Zhao DB. Association between hyperuricemia and nontraditional adiposity indices. *Clinical Rheumatology*. 2018:1-8.

35. Sarmah D, Sharma B. A correlative study of uric acid with lipid profile. *Asian Journal of Medical Sciences.* 2013;4:8-14.

36. Baldwin W, McRae S, Marek G, et al. Hyperuricemia as a mediator of the proinflammatory endocrine imbalance in the adipose tissue in a murine model of the metabolic syndrome. *Diabetes*. 2011:DB_100916.

37. Zhu Y, Hu Y, Huang T, et al. High uric acid directly inhibits insulin signalling and induces insulin resistance. *Biochemical and Biophysical Research Communications.* 2014;447:707-14.

38. Wan X, Xu C, Lin Y, et al. Uric acid regulates hepatic steatosis and insulin resistance through the NLRP3 inflammasome-dependent mechanism. *Journal of Hepatology.* 2016;64:925-32.