

Association between serum uric acid level & metabolic syndrome in patients of a tertiary care Centre

Authors: Satyajit Koley*, Arindam Sur*

* Demonstrator, Department of Biochemistry, College of Medicine & JNM Hospital, Kalyani

Corresponding Author:. Arindam Sur Address- C/O Ranjit Kumar Sur,

Shyamashree Pally, P.O-Natagarh, Sodepur,

District-24 Parganas(North), Pin-700113

Email Address- arinmck@gmail.com

Mobile no- 9432252443

Abstract:

Introduction: Elevated uric acid is a common feature of metabolic syndrome (MetS) that includes risk factors like hypertension, obesity, dyslipidaemia and insulin resistance (IR).

Aims & Objectives: The study was conducted to detect any association between uric acid level and metabolic syndrome and its gender dependence.

Materials & Methods: 50 male and 50 female obese participants with suspected metabolic syndrome included in hospital based cross sectional study to estimate their triglycerides, total cholesterol, fasting plasma glucose, HDL-cholesterol, LDL-cholesterol, uric Acid, ALT, AST and also the anthropometric measurements like weight, height, waist circumference(WC),systolic blood pressure (SBP), diastolic blood pressure (DBP) were determined.

Results: Results showed that Total Cholesterol, Triglycerides & HDL-C are significantly correlated with increased uric acid level for both participants of either gender. However, FPG positively correlated only in cases of males.

Conclusion: The findings suggest that there is a significant correlation between metabolic syndrome and uric acid & preponderance in males compared to females.

Keywords: Metabolic syndrome, hyperuricaemia, dyslipidaemia, insulin resistance

Introduction:

Metabolic syndrome is increasing among adult population in world and it is predominant with increased age. Metabolic syndrome (MetS) includes risk factors like hypertension, obesity and dyslipidaemia & insulin resistance in a single patient. Hyperuricaemia often considered to be secondary to hyperinsulinaemia and primary role for uric acid in association with metabolic syndrome have been found

previously. Fructose has strong association with metabolic syndrome in rats and it raises uric acid. Decreased level of uric acid in fructose-fed rats prevents development of metabolic syndrome. Uric acid (UA) also can augment renal disease in experimental animals and is associated with gradually progressive renal disease in human being. It has been stated that fructose- and purine-rich foods both have the tendency to increase uric acid level may have a

role in development of metabolic syndrome and renal impairment that is happening all over the world (1).

It can be an indication to physicians that patients who present with such disorders are at much greater risk of morbidity and mortality from Type 2 Diabetes Mellitus (T2DM) and Coronary Heart Disease (CHD). Insulin resistance is the main underlying reason of metabolic syndrome.

The diagnosis of the MetS established when three or four of the following criteria's are satisfied: (2)

- a) Body mass index (BMI) ≥ 25
- b) Systolic blood pressure (SBP) ≥ 140 mmHg or Diastolic blood pressure (DBP) ≥ 90 mmHg;
- c) Triglycerides (TG) ≥ 150 mg/dl
- d) High density lipoprotein cholesterol (HDL-C) < 40 mg/dl in men and < 50 mg/dl in women;
- e) Fasting Plasma Glucose (FPG) ≥ 110 mg/dl
- f) Waist circumference (WC) ≥ 90 cm for men and ≥ 80 cm for women

However, whether uric acid is associated with cardiovascular mortality or not is still doubtful as several studies have suggested that hyperuricemia is merely associated with cardiovascular diseases because of confounding factors such as obesity, dyslipidaemia, hypertension, use of diuretics and insulin resistance.

The purpose of the present study is to investigate the prevalence of increased uric acid level in morbidly obese subjects as well as to find if there is any significant association between uric acid levels with the various parameters of metabolic syndrome and whether males or females are getting affected much with it.

Aims & objectives:

1. To identify whether there is any correlation between increased uric acid and metabolic syndrome parameters.
2. To check which gender is getting affected much with metabolic syndrome.

Inclusion Criteria:

- Both sex (M/F) are involved
- Age between 20 to 60 were granted
- Without any serious illnesses
- Apparently obese patients were selected
- Fasting for 12 hours

Exclusion Criteria:

- Patients with known elevated uric acid level, chronic kidney disease, haematological malignancies, hypothyroidism were excluded
- Alcoholic patients were excluded
- Patients taking Thiazides as antihypertensive were excluded
- Established long standing diabetic patients were excluded
- Subjects those are unwilling
- Patients taking any drug that can alter lipid profile were excluded
- Smokers were excluded

Methodology:

This is a Hospital based cross sectional descriptive epidemiological type of study that conducted at OPD of COMJNMH in collaboration with the department of BIOCHEMISTRY included total 100 cases among which 50 were males and 50 were females. It is a medium study with 100 sample size where power of the statistical test is 80%, effect size is 0.5 with level of significance 0.05. A Pilot study was conducted before starting the current study. Sample size calculation was done according to standard methods available.

Measurement of Parameters:

Uric Acid by Uricase method (ERBA system pack of TRANSASIA Bio-medical),

Triglycerides by GPO/PAP method (ERBA system pack of TRANSASIA Bio-medical),

Total Cholesterol by CHOD/PAP method (ERBA system pack of TRANSASIA Bio-medical),

Direct HDL-cholesterol estimation by PEG Precipitation method (ERBA system pack of TRANSASIA Bio-medical),

LDL-cholesterol (Calculated by FRIEDWALD'S formula),

Fasting Plasma Glucose by GOD-POD method (ERBA system pack of TRANSASIA Bio-medical),

Aspartate transaminase & Alanine transaminase were measured by Kinetic Enzymatic method (ERBA system pack of TRANSASIA Bio-medical).

All the biochemical parameters were assessed by full Auto-analyzer of ERBA at clinical laboratory.

Data Analysis:

Data were assessed by Kolmogorov-Smirnov Test which showed parametric distribution and Pearson's Correlation study was done between the study parameters by SPSS software.

Results & Discussion:

Metabolic syndrome is widely spread among adult population in world and its prevalence increases with age. With increase of uric acid insulin resistance property also increases which decreases the secretion of uric acid at renal tubular cells leading to hyperuricaemia. Hyperuricaemia first described in association with hyperglycemia and hypertension. There is also having an association between elevated uric acid level with other metabolic syndrome components like abdominal obesity and dyslipidemia (3). However, if increased uric acid level is significantly associated with cardiovascular mortality is still doubtful as several studies have suggested that

hyperuricaemia is not properly associated with cardiovascular impairment because several confounding factors are also present there like obesity, dyslipidaemia, hypertension, use of diuretics and insulin resistance (4). Association of hyperuricaemia with obesity and MetS was found in one population based study revealed that an increment of one standard deviation of serum uric acid level is associated with a 35% higher chance of developing MetS in males. (5). another study also showed that increased age and male gender are associated more with higher occurrence of MetS in adults (6).

Obesity, an important risk factor for type 2 diabetes mellitus have significantly raises in the past few years and probably representing as the most important parameter of the metabolic syndrome. The association of hyperuricaemia with obesity has been detected in last few years (1). Hyperuricaemia has been found to be associated with increased BMI in early studies. A positive correlation between serum uric acid level with bodyweight and body surface area have been found in previous study (7). In this study, waist circumference was found significantly associated with uric acid level with positive correlation in both sexes, with ($r = 0.417$, $p = 0.003$) for male and ($r = 0.564$, $p < 0.001$) for female. Obesity is an established risk factor for developing MetS (8). Association of increased uric acid level with overweight and MetS was found in several previous studies also (9, 10).

From our study we also found significant negative correlation between HDL-c and uric acid level in both sex where Males have shown ($r = -0.476$, $p < 0.001$) and female have shown ($r = -0.412$, $p = 0.003$). The possibility of occurrence metabolic syndrome inversely proportional with the HDL-c level as it is a good cholesterol in our body. HDL cholesterol is associated with UA level by the mechanism of insulin resistance (11). Association of insulin

resistance and abnormal glucose metabolism leads to increased uric acid level from the insulin-induced sodium retention in urine and decreased urinary UA clearance (12).

Investigators found association of triglycerides with increased uric acid level in general population (13). Synthesis of fatty acids in liver is associated with de novo purine synthesis that increases UA production (5). In this study, we found a significant positive correlation between increased uric acid level and high triglycerides in both sexes with ($r = 0.488$, $p < 0.001$) for male & ($r = 0.470$, $p < 0.001$) for female.

Diabetes Prevention Study Group showed that altered uric acid level were associated with fasting plasma glucose and persons with obesity and impaired glucose tolerance (14). Here we found significant positive correlation between fasting plasma glucose and uric acid level only in case of male ($r = 0.432$, $p = 0.002$) but female have shown an weak and insignificant positive correlation ($r = 0.253$, $p = 0.076$)

Thus we may comment that triglycerides, high density lipoprotein cholesterol and waist

circumferences are appropriate parameters of metabolic syndrome for obese male and female subjects and increased uric acid level positively correlated with waist circumference & triglyceride level and negatively with HDL-c level. The r values for males are showing more positive correlation of uric acid level with triglyceride & negative correlation with HDL-c in compare to females with exception of waist circumference where r value is greater in case of females than males. Moreover, male not female are showing significant correlation of increased uric acid level with fasting plasma glucose in this study.

Conclusion :

Raised uric acid level significantly associated with the Metabolic Syndrome in both sex. Males are showing more significant association with MetS than females as apart from showing significant correlation of uric acid with all common parameters of MetS for both sex, males having more strong and significant positive correlation of uric acid level with fasting plasma glucose than females in this study.

Table 1 : Showing the correlation coefficient & their significance between UA with metabolic syndrome parameters i.e SBP, DBP, WC, FPG, TG, HDL-C and TC, LDL-C, ALT,AST among males.

Uric Acid (Male)		SBP	DBP	WC	FPG	TC	TG	HDL-c	LDL-c	ALT	AST
	<i>r</i>	0.126	0.083	0.417	0.432	0.152	0.488	-0.476	0.209	0.026	-0.059
<i>p</i>	0.384	0.567	0.003*	0.002*	0.293	<0.001*	<0.001*	0.145	0.858	0.686	

(p = statistical significance, r = correlation coefficient * = significant p value)

Table 2 : Showing the correlation coefficient & their significance between UA with metabolic syndrome parameters i.e. SBP, DBP, WC, FPG, TG, HDL-C and TC, LDL-C, ALT, AST among females.

		SBP	DBP	WC	FPG	TC	TG	HDL-C	LDL-C	ALT	AST
Uric Acid (Female)	<i>r</i>	0.068	0.194	0.564	0.253	-0.042	0.470	-0.412	0.015	0.061	-0.096
	<i>p</i>	0.639	0.178	<0.001*	0.076	0.772	<0.001*	0.003*	0.917	0.675	0.508

(*p* = statistical significance, *r* = correlation coefficient * = significant *p* value)

References:

- Jin M, Yang F, Yang I, et al. Uric acid, hyperuricaemia and vascular diseases. *Front Biosci (Landmark Ed)* 2012; 17:656-669.
- Holme I, Aastveit AH, Hammar N, Jungner I, Walldius G. Uric acid and risk of myocardial infarction, stroke and congestive heart failure in 417,734 men and women in the Apo lipoprotein Mortality Risk study (AMORIS). *J Intern Med* 2009; 266:558-570.
- Expert Panel on Metabolic syndrome of Chinese Diabetes Society. Recommendations on Metabolic syndrome of Chinese Diabetes Society (in Chinese). *Chin J Diab.* 2004;12: 156-61. 86
- Fang J, Alderman MH. Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study, 1971-1992. *National Health and Nutrition Survey. JAMA.* 2000;283:2404-10.
- Mangge H, Zelzer S, Puerstner P, et al. Uric acid best predicts metabolically unhealthy obesity with increased cardiovascular risk in youth and adults. *Obesity* 2013; 21:e71-e77
- Hongo M, Hidaka H, Sakaguchi S, et al. Association between serum uric acid levels and cardio metabolic risk factors among Japanese junior high school students. *Circ J* 2010; 74:1570-1577.
- Schmidt MI, Watson RL, Duncan BB, et al. Clustering of dyslipidaemia, hyperuricaemia, diabetes, and hypertension and its association with fasting insulin and central and overall obesity in a general population. *Atherosclerosis Risk in Communities Study Investigators. Metabolism* 1996; 45:699-706.
- Rao GN, Corson MA, Berk BC. Uric acid stimulates vascular smooth muscle cell proliferation by increasing platelet-derived growth factor A-chain expression. *J BiolChem* 1991; 266:8604-8608
- Corry DB, Eslami P, Yamamoto K, Nyby MD, Makino H, Tuck ML. Uric acid stimulates vascular smooth muscle cell proliferation and oxidative stress via

- the vascular renin-angiotensin system. *J Hypertens* 2008; 26:269-275.
10. Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults: Executive summary of the 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). *JAMA* 2001; 285:2486-2497.
 11. Grujic V, Martinov-Cvejin M, Ac-Nikolic E, Niciforovic-Surkovic O. Epidemiology of obesity in adult population of Vojvodina. *Med Pregl* 2005; 58:292-295.
 12. Bedir A, Topbas M, Tanyeri F, Alvur M, Arik N. Leptin might be a regulator of serum uric acid concentrations in humans. *Jpn Heart J* 2003; 44:527-536.
 13. Ford ES, Li C, Zhao G. Prevalence and correlates of metabolic syndrome based on a harmonious definition among adults in the US. *J Diabetes* 2010; 2:180-193.
 14. Keenan T, Blaha MJ, Nasir K, et al. Relation of uric acid to serum levels of high-sensitivity C-reactive protein, triglycerides, and high-density lipoprotein cholesterol and to hepatic steatosis. *Am J Cardiol* 2012; 110: 1787-1792.