

SERUM URIC ACID IN METABOLIC SYNDROME-A CASE CONTROL STUDY

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ABSTRACT

The metabolic syndrome is a widely prevalent and multi-factorial disorder that presents in a distinct, heterogeneous phenotype. The clinical relevance of the metabolic syndrome is related to its role in the development of cardiovascular disease. The major features of the Metabolic Syndrome include central obesity, Hyper-triglyceridemia, low high-density lipoprotein (HDL) cholesterol, Hyperglycemia and Hypertension. Mean serum uric acid levels vary with variable components of metabolic syndrome. There is a direct linear relationship between serum uric acid level and number of metabolic syndrome patients. Increased levels of serum uric acid should be considered as an important marker in patients with metabolic syndrome and Hyperuricemia is an associated abnormality that should be considered in those with metabolic syndrome.

Aim & Objective of study is to evaluate the association between serum uric acid and metabolic syndrome and correlation of uric acid levels with various components of metabolic syndrome.

Type of study was conducted as a **case control study**. The patients included in the study group were adults of either sex having metabolic syndrome. Cases were taken as 100 and control as 50.

Study Period: August 2012 to July 2013

Material and Method: The study conducted in department of Medicine, Santosh Medical College, Ghaziabad, Uttar Pradesh. The study was approved by the departmental scientific review board and ethics committee of Santosh Medical College & Hospitals. A written informed consent was taken from the patients inducted into the study. A copy of patient information sheet was also given to the patient.

Result: It is seen when mean serum uric acid of triglycerides, HDL, Fasting plasma glucose, Blood Pressure and Obesity was compared to mean of uric acid of controls, results was significant.

Conclusion: Hyperuricemia should be considered as a component of metabolic syndrome and risk factor for cardiovascular diseases.

Keywords: Metabolic Syndrome, Hyperuricemia, Hyperlipidemia, Hyperglycemia.

INTRODUCTION

Metabolic syndrome is defined as abnormalities that confer increased risk of cardiovascular disease (CVD) and diabetes mellitus (DM).^[1] The major features of the Metabolic Syndrome include central obesity, **Hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, Hyperglycemia and Hypertension.**¹ It is a widely prevalent and multi-factorial disorder that presents in a distinct, heterogeneous phenotype. Although obesity and insulin resistance are not synonymous with the metabolic syndrome, they are the integral features in the derangement of adipocyte physiology and carbohydrate metabolism. This syndrome predicts the development of type 2 diabetes mellitus and cardiovascular disease.² The incidence of coronary disease along with carotid atherosclerosis is higher in patients with metabolic syndrome along with higher mortality from all such cases.^[2] There are currently two major definitions used for diagnosing metabolic syndrome provided by 1) **International Diabetes Federation (IDF)** and 2) **The Revised National Cholesterol Education Program (NCEP).** The revised NCEP and IDF definitions of Metabolic Syndrome are very similar and it can be accepted that they will identify many of

the same individuals as having metabolic syndrome.³

Table 1: Synonyms for metabolic syndrome.^{4,5,6}

• Android obesity syndrome	• Insulin resistance/hyperinsulinemia syndrome
• Syndrome of Affluence	• Atherothrombotic syndrome
• Plurimetabolic syndrome	• Metabolic cardiovascular syndrome
• GHO (Glucose intolerance)	• Syndrome X plus
• Hypertension/Obesity syndrome	• Deadly quartet Cardiovascular and metabolic syndrome
• Syndrome X	• Dysmetabolic syndrome X
• Metabolic syndrome X	
• Reaven syndrome	

There is a direct linear relationship between serum uric acid level and number of metabolic syndrome patients. Increased levels of serum uric acid should be considered as an important marker in patients with metabolic syndrome and Hyperuricemia.³ Hyperuricemia is defined as a serum Uric acid concentration in excess of urate solubility, which is about 420 Pmol/l in men and 360 Pmol/l in women.⁸ Hyperuricemia is also defined when the levels of uric acid is more than > 6mg/dl or it varies

from males (2.5mg/dl to 5.6mg/dl) and female (3.1 to 7mg/dl).⁹

Since hyperuricemia was first described as being associated with hyperglycemia and hypertension by **Kylin** in 1923^{7,10}, there has been a growing interest in the association between elevated UA and other metabolic abnormalities of hyperglycemia, abdominal obesity, dyslipidemia, and hypertension, as well as a continuing debating on hyperuricemia as an additional component of the metabolic syndrome^{11/12}. The prevalence of obesity, hypertension, diabetes, dyslipidemia, and hyperuricemia have been increasing over the last few decades due to rising living standards occurring with modernization and urbanization.¹³

The main objective of this study is to evaluate the association between serum uric acid and metabolic syndrome and correlation of uric acid levels with various components of metabolic syndrome.

MATERIALS AND METHOD

The study conducted in department of Medicine, Santosh Medical College, Ghaziabad, Uttar Pradesh. The study was approved by the departmental scientific review board and ethics committee of Santosh Medical college & Hospitals.

A written informed consent was taken from the patients inducted into the study.

A copy of patient information sheet was also given to the patient.

The study was conducted as a case control study.

The patients included in the study group were adults of either sex having metabolic syndrome.

Cases were taken as 100 and control as 50.

Study Period: August 2012 to July 2013

Inclusion Criteria:

A total of 100 subjects of old and newly diagnosed metabolic syndrome on the basis of IDF Criteria for central adiposity for the diagnosis of metabolic syndrome,

According to the guidelines any two or more having the following were considered:

- Circumference > 90 cms (M), > 80 cms (F) in the south asian individuals
- Hypertriglyceridemia: triglycerides >150mg/dl or specific medication.
- Low HDL cholesterol: <40 mg/dl and <50 mg/dl,

respectively for male and female or specific medication.

- Hypertension: blood pressure >130mmhg systolic or >85mmhg diastolic or specific medication.
- Fasting plasma glucose: >100mg/dl or specific medication or previously diagnosed Type 2 diabetes.

Exclusion Criteria:

Subjects of the study should not be having **ANY HISTORY** of

1. acute myocardial infarction or CVA.
2. gout, psoriasis, malignancy, renal stone.
3. Thyroid disorder
4. Renal failure
5. Hepatic disorder
6. Oncological disease
7. Subjects not taking drugs for hypoglycaemia, antioxidants, vitamin supplement or drugs that, are known to affect uric metabolism.

The patients attending the OPD were screened for the disease and a detailed and relevant present, past, personal, family and medical history was taken. Special emphasis was given on the obesity and co-morbid conditions associated with it, followed by baseline laboratory investigations to assess the metabolic status of the patient. After a 12 hour fasting period, venous samples were collected from all cases and control. Serum was used for analysis of uric acid and lipids. Patients fulfilling all inclusion and exclusion criterion were enrolled in the study.

STATISTICAL ANALYSIS

All the data was analyzed by SPSS statically software and basic parameter was compared using ANOVA test and chi square and p value was calculated.

RESULTS AND OBSERVATION

Study design: A Case Control Study with 100 subjects as cases and 50 subjects as control, which studied as role of serum uric acid with each component of metabolic syndrome, undertaken at Santosh Medical Collage and Hospital, Ghaziabad, Uttar Pradesh.

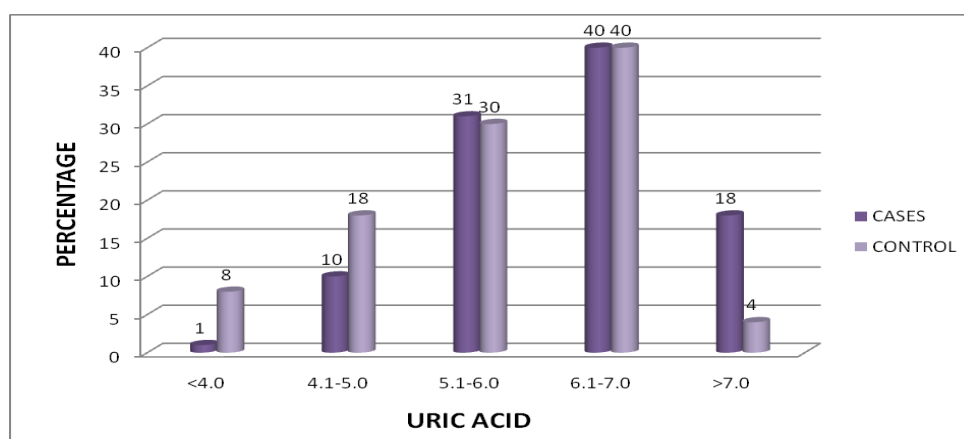
Table 2: Clinical Parameters Studied

S.NO	PARAMETER	CONTROLS (n=50)	CASES (n=100)	P VALUE
1.	AGE (yrs)	49.14+9.05	54.42+7.43	0.001*
2.	BMI (kg/m ²)	27.83+4.00	30.28+4.65	0.001*
3.	CENTRAL OBESITY(cms)	82.20+11.15	100.02+7.611	<0.001*
4.	DURATION OF DIABETES (yrs)	1.68+4.206	47.74+55.32	<0.001
5.	HBA1c (%)	5.91+0.73	6.38+0.78	0.001
6.	FASTING PLASMA GLUCOSE (mg/dl)	105.48+21.32	134.34+36.35	<0.001*
7.	PP(mg/dl)	139.80+40.74	190.63+64.09	<0.001*
8.	SYSTOLIC BLOOD PRESSURE(mmHg)	128.16+13.08	137.91+18.21	<0.001*
9.	DIASTOLIC BLOOD PRESSURE(mmhg)	80.44+8.51	88.19+11.40	<0.001*
10.	TC(mg/dl)	173.06+28.01	227.39+74.32	<0.001*
11.	TG(mg/dl)	106.00+34.85	188.09+44.76	<0.001*
12.	HDL(mg/dl)	47.04+12.92	55.20+18.69	0.002*
13.	LDL(mg/dl)	86.52+37.07	141.25+48.54	<0.001*
14.	VLDL(mg/dl)	23.92+6.52	43.72+23.48	<0.001*
15.	URIC ACID(mg/dl)	5.67+0.95	6.24+0.95	0.001*
16.	CREATININE(umol/l)	1.04+0.37	1.58+4.10	0.195
17.	UREA	24.53+- 6.12	24.22+-6.55	0.777

*Statically significant (p value <0.05)

Table 3: Serum Uric Acid (mg/dl)

URIC ACID	CONTROLS	PERCENT %	CASES	PERCENT %
<4.0	04	8.0	01	1.0
4.1-5.0	09	18.0	10	10.0
5.1-6.0	15	30.0	31	31.0
6.1-7.0	20	40.0	40	40.0
>7.0	02	4.0	18	18.0
TOTAL	50	100.0	100	100.0
MEAN+-SD	5.67+-0.95		6.24+-0.95	

**Graph 1: Comparison of Serum Uric Acid with Each Component of Metabolic Syndrome****Table 4: Uric Acid with Triglycerides**

Variables	Cases (100)	Controls (50)	P value*
TG >150	88	50	0.0001
Mean+-SD of Uric Acid	6.31+-0.93	5.67+-0.95	

*Independent sample t test

Table 5: Uric Acid with HDL

Variables	Cases (100)	Controls (50)	P value*
HDL Males<40, Females<50	37	50	0.007
Mean+-SD of Uric Acid	6.23+-0.94	5.67+-0.95	

*Independent sample t test

Table 6: Uric Acid with Blood Pressure

Variables	Cases (100)	Controls (50)	P value*
Blood Pressure >130/85	62	50	0.006
Mean+-SD of Uric Acid	6.17+-0.94	5.67+-0.95	

*Independent sample t test

Table 7: Uric Acid with Fasting Plasma Glucose

Variables	Cases (n100)	Controls (50)	P value*
Fasting plasma glucose >100 or IGT	88	50	0.0006
Mean+-SD of Uric Acid	6.27+-0.99	5.67+-0.95	

*Independent sample t test

Table 8. URIC ACID AND OBESITY

Variables	Cases(n 100)	Controls(50)	P value *
Central Obesity Males>90 Females >80	100	50	0.0006
Mean+-SD of Uric Acid	6.24+-0.95	5.67+-0.95	

*Independent sample t test

DISCUSSION

The constellation of metabolic abnormalities including centrally distributed obesity, decreased high-density lipoprotein cholesterol (HDL), elevated triglycerides, elevated blood pressure (BP), and hyperglycaemia is known as the metabolic syndrome.¹ This study has been conducted on the basis of newly approved and widely used definition of metabolic syndrome ie International Federation of Diabetes (IDF). In India **Deepa et al** compared the prevalence of MS in southern India and found that, by IDF 25.8% individuals >20 years were having MS as compared to 18.3% by ATP-III.¹⁴ In present study, we found that 50% of males in cases and 50% of females in cases and as controls 46% males and 54% females. **Sawant A et al**¹⁵.

Our study revealed a significant increase in serum uric levels in cases (6.24+-0.95) as compared to controls (5.67+-0.95), (p=0.001) corroborates with **Ishizaka N et al**¹⁶, who concluded that the prevalence of metabolic syndrome showed a graded increase along with increasing serum uric acid levels in both sexes (p<0.05).

Hyperuricemia is seen in individuals with insulin resistance because hyperinsulinemia reduces renal excretion of uric acid. In our study there was significant increase in serum uric acid levels when mean of cases (6.27+-0.99) in subjects who has insulin resistance or diabetes was compared to mean of controls(5.67+-0.95), (p=0.0006) which was statically significant. Similar to study by **Anthonia O**

Ogbera et al on Hyperuricaemia and insulin resistance¹⁷.

Positive relation between mean serum uric acid and triglycerides (6.31+-0.93) when compared to mean serum uric acid of controls (5.67+-0.95), (p=0.0001), in concordance with **ZhenZhen Cai, Xiaofeng Xu et al**¹⁸ which showed significant relation of uric acid with serum triglycerides (p<0.05). According to **Clausen JO et al**.¹⁹ there is a greater demand for NADPH during synthesis of triglyceride. The synthesis of fatty acids is associated with de novo synthesis of purines, therefore increasing the production of uric acid. When mean serum uric acid & HDL (6.23+-0.94) was compared to mean serum uric acid of controls (5.67+-0.95), There was a positive relation with HDL levels (p=0.007), similar to study of **Ahoud F.Al Meshaweh et al**.²⁰, showing similar results (p<0.05).

A positive relation was shown, when serum uric acid was compared with blood pressure, the mean of uric acid for cases (6.17+-0.94) who's BP was more than 130/85 according to the IDF criteria was compared to mean of uric acid for controls (5.67+-0.95), which resulted as significant (p=0.006). **Linc. KC, S.D, et al**^[22] which showed increase levels of uric acids with blood pressure (P<0.001).

There is also a co-relation of levels of serum uric acid with glycemia, in our study the mean of fasting plasma glucose(6.27+-0.99) was compared with mean of uric acid for controls (5.67+-0.95) which resulted in significant results (P=0.0006),

which matched the results of a study conducted by **Qin Li et al**^{21,23} showing a positive relation between hyperglycemia and uric acid ($P < 0.001$).

Central obesity, had a significant relation between uric acid and central obesity, the mean value of central obesity (6.24 ± 0.95) as compared to mean value of uric acids (5.67 ± 0.95) showed a significant result ($P = 0.0006$), similar **S.D Lin et al**²⁴ showing significant increase in uric acid when compared to obesity or waist circumference ($P < 0.001$). In the study conducted, on 100 patients of metabolic syndrome, 18 patients had clear evidence of hyperuricemia i.e. uric acid level was more than 7mg/dl. Hyperuricemia is a risk marker for coronary artery disease, these 18 patients are at risk for coronary artery disease and such patients should be repeatedly, periodically, evaluated for coronary artery disease. Similar to study conducted by **Kim SY, Albert DA et al**, that hyperuricemic patients (in which uric acid is above desirable range) are at risk of coronary artery disease.²⁵

Therefore the study has shown a significant relation between serum uric acid and components of metabolic syndrome.

SUMMARY & CONCLUSION

- The study was done in the department of medicine, Santosh Medical College and Hospitals, Ghaziabad (U.P) over a period August 2012 to July 2013.
- The aim was to study role of uric acid in metabolic syndrome.
- It is a prospective case control study.
- Total number of patients enrolled in the study was 100 as cases and 50 as controls.
- The majority of patients were in their 5th to 6th decade of life.
- The data was collected and findings and comparison was analysed and tabulated.
- It was seen that when the components of metabolic syndrome are compared with uric acid the results are significant.
- It was seen when triglycerides, HDL, Fasting plasma glucose, Blood Pressure and Obesity was compared to mean of uric acid of controls, results were significant. [TG 6.31 ± 0.93 , controls 5.67 ± 0.95 , $p = 0.0001$; HDL 6.23 ± 0.94 , controls 5.67 ± 0.95 , $p = 0.007$; Blood Pressure 6.17 ± 0.94 , controls 5.67 ± 0.95 , $p = 0.006$, Fasting plasma glucose 6.27 ± 0.99 , controls 5.67 ± 0.95 , $p = 0.0006$; Obesity 6.24 ± 0.95 , controls 5.67 ± 0.95 , $p = 0.0006$].

If uric acid levels are elevated it should therefore be regarded as a '**red flag**' and appropriate approach should be attempted to obtain the risk reduction. Serum uric acid may or may not be an independent

risk factor especially since its linkage to other risk factors is so strong.

From the present study it is concluded that:

1. There is a positive association between uric acid and metabolic syndrome.
2. There is a positive correlation between individual components of metabolic syndrome with Uric acid.
3. Hyperuricemia should be considered as a component of metabolic syndrome and risk factor for cardiovascular diseases.

A quote by Johnson RJ and Tuttle KR is appropriate for concluding:

'The bottom line is that measuring uric acid is a useful test for a clinician, as it carries important prognostic information. An elevation of uric acid is associated with an increased risk for cardiovascular disease and mortality.'

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Ethical Committee:	Permission taken

REFERENCES:

1. Robert H Eckel; chapter 242; the metabolic syndrome; page Harrison Principles of internal medicine 18th edition.
2. Atul Gogia, PK Agarwal; Deptts of medicine, Sri Ganga Ram Hospital; vol 60; year 2006; issue: 2; page 72-81.
3. Dr Dheaa K. AL-Omer; Dr Adnan T. Al-khafaji; Thi-Qar Medical Journal (TQMJ); Vol(1); No2007: (83-90)
4. American Heart Association (n.d.). What is metabolic syndrome? From <http://www.americanheart.org/presenter.jhtm?identifier=4756>, accessed
5. American Heart Association: What is metabolic syndrome? From <http://www.americanheart.org/presenter.jhtm?identifier=4756>, accessed.
6. Libby: Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 8th Ed.
7. Anthonia O gebara; Alfred O Azebabor; journal of diabetology and metabolic syndrome; 2010;
8. Reaven GM; Role of insulin resistance in human disease; Diabetes 1988; 37: 1595-607.
9. Zhenzhen Cai; Xiaofeng Xu; Hyperuricaemia and metabolic syndrome in Hangzhou; Asia pacific journal 2009; Vol 18; 81-87.
10. Fang J, Alderman MH (2000): serum uric acid and cardiovascular mortality the NHANES I epidemiological follow up study, 1971-1992. National Health and Nutrition Examination Survey 283:2404-
11. Kylin E 1923: Studien ueber das hypertonic-hyperglykamie-hyperurikamie syndrome. Zentral-blaet fuer Innere Medizin 44:105-27.
12. Liou TL, Lin MW, Hsiao LC, Tsai TT, Chan WL, Ho LT, Hwu CM (2006): Is hyperuricemia another facet of the metabolic syndrome? *J Chin Med Assoc* 69:104-9.

13. Zavaroni I, Mazza S, Fantuzzi M, Dall'Aglio E, Bonora E, Delsignore R, Passeri M, Reaven G (1993): Changes in insulin and lipid metabolism in males with asymptomatic hyperuricemia. *J Intern Med* 234:25-30.
14. DECODE Study Group (2003): Age- and sex-specific prevalence of diabetes and impaired glucose regulation in 11 Asian cohorts. *Diabetes care* 26:1770-80.
15. M Deepa, S Farooq, M datta, R Deepa, V Mohon: Prevalance of Metabolic syndrome using WHO, ATP-III and IDF definitions in Asian Indians:Chennai urban Rural Epidemiology Study (CU 34), 2010,23(2):127-134.
16. Savant A, Mankeshwar R, Shah S, Raghavan R et al, Prevalanc Of metabolic syndrome in urban India,Cholesterol; Article ID 920983;2012.
17. Ishizaka N, Ishizaka Y, Toda El et al, Association between serum.Uric acid, metabolic syndrome and carotid atherosclerosis,IP:122;17;2011.
18. Anthonia O gebra; Alfred O Azebabor; journal of diabetology and metabolic syndrome; 2010; 2:24.
19. Zhenzhen Cai; Xiaofeng Xu; Hyperuricaemia and metabolic syndrome in Hangzhou; Asia pacific journal 2009; Vol 18; 81-87.
20. Clausen JO et al, Analysis of the relationship between serum uric acid and insulin sensitivity index in a population based study
21. Ahoud F.Al-Meshaweh, Yaqoub Jafar, Mohammad Asem (2011): determinants of blood uric acid levels in a dyslipidemic Arab Population
22. PorteJr; Banting lecture 1990. Beta cells in type two diabetes.
23. Alterations in uric acid and pathophysiology of hypertension; Lancet; 2011
24. Qin Li, Zeng Yang: elevated levels of uric acid concentrations in those group of people who have increased risk for metabolic syndrome.
25. Bedir A, Topbas M, Tanyeri F, Alvur M, Arik N: Leptin might be a regulator of serum uric acid concentrations in humans *JpnHeart J* 2003, 44(4):527-536.
26. Kim SY; Guevera JP; Kim KM; Hyperuricemia and coronary heart disease: A systemic review and metanalysis; feb 2010;170-80.