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A study of serum uric acid levels in metabolic syndrome

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Abstract
Background: The relationships between uric acid and chronic disease risk factors such as metabolic syndrome, Diabetes, hypertension have been studied in adults. However whether these relationships exist in adolescents is unknown.
Metabolic syndrome is considered a collection of cardiovascular risk factors that generally includes central obesity, hypertension, high triglyceride and low HDL cholesterol levels. The prevalence of hyperuricemia has been increasing in recent years, not only in advanced countries but also in developing countries, along with the development of their economies. It has been suggested that hyperuricemia is associated with metabolic syndrome. Cardiovascular disease has been suggested to be associated with increased serum uric acid (UA) and with the components that contribute to metabolic syndrome.
Aims and Objectives:
1. To investigate the relationship between serum uric acid and metabolic syndrome.
2. To investigate the relationship between serum uric acid levels with the different components of metabolic syndrome.
Methods: 200 patients above the age of 18 years hospitalised in SIMS and RH satisfying the NCEP ATP III criteria for metabolic syndrome from October 2018 to August 2018 were taken for the study
Results: We studied a total of 200 patients of which 116 were females (58%) and 84 were males (42%) with a female: male ratio of 4:3. The mean age in our study was 116 for females and 108 for males. 63% of the patients were above the age of 50 years.
A mean uric acid level of 5.05±2.17 was seen in females and 5.92±2.44 in males. 68 (34%) of our subjects had elevated SUA levels with 36 females and 32 males. There was a prevalence of hyperuricemia in 38.1% of males and 31.1% of females. 73.5% of the patients with hyperuricemia were above the age of 50 years. The components of metabolic syndrome most commonly seen in females are high FBS levels, low HDL, high triglycerides and an increased waist circumference. The incidence of hypertension was the lowest among the components of metabolic syndrome. Increased serum uric acid levels had a direct positive statistical correlation with DBP and triglycerides with p values of 0.03 and 0.09 respectively.
The components of metabolic syndrome which were more commonly seen in males were elevated triglycerides, increased FBS and hypertension. Hyperuricemia was seen in 50% of patients with increased waist circumference. Elevated SUA levels had a definite statistical correlation with FBS and waist circumference with p values of 0.001 and 0.08 respectively.
Subjects with three, four and five components of metabolic syndrome had 32.1%, 32.5% and 37.5% incidence of hyperuricemia respectively.
Conclusion: We found hyperuricemia to be prevalent in patients with metabolic syndrome. There was a direct association between the components of metabolic syndrome and high serum uric acid levels. A statistical correlation was found between diastolic blood pressure and triglycerides with elevated uric acid levels in females. Increased serum uric acid levels had a significant statistical correlation with FBS and waist circumference. The incidence of hyperuricemia increased as the components of metabolic syndrome increased.

Keywords: Hyperuricemia, triglycerides, HDL cholesterol, metabolic syndrome

Introduction
Several epidemiological studies have shown that hyperuricemia is a risk factor for cardiovascular diseases (CVDs) in the general population [1-3]. The contribution of serum uric acid (UA) to atherosclerotic vascular disease, however, remains controversial [4]. Some studies argue that the observed association between UA and atherosclerotic vascular disease

is attributable to an indirect association of hyperuricemia with cardiovascular risk factors or clustering of these metabolic and hemodynamic risk factors, designated 'metabolic syndrome' (MS) [5, 6]. Recent evidence suggests that UA stimulates vascular smooth muscle proliferation and induces endothelial dysfunction. UA has been shown to decrease endothelial nitric oxide production and to lead to endothelial dysfunction and insulin resistance Target organ damage occurs through multiple mechanisms in metabolic syndrome. The individual diseases leading to metabolic syndrome produce adverse clinical consequences. For example, hypertension in metabolic syndrome causes left ventricular hypertrophy, progressive peripheral arterial disease and renal dysfunction [11]. However, the cumulative risk for metabolic syndrome appears to cause microvascular dysfunction, which further amplifies insulin resistance and promotes hypertension [12].

Metabolic syndrome promotes coronary heart disease through several mechanisms. It increases the thrombogenicity of circulating blood, in part by raising plasminogen activator type 1 and adipokine levels and it causes endothelial dysfunction [13]. Metabolic syndrome may also increase cardiovascular risks by increasing arterial stiffness. Additional mechanisms include oxidative stress [15], which has been associated with numerous components of metabolic syndrome [16].

Increasing evidence suggests that uric acid may play a role in MetS. Elevated levels of uric acid have been observed in MetS and were attributed to hyperinsulinemia, as insulin reduces renal excretion of uric acid. However, hyperuricemia often precedes the development of hyperinsulinemia. The strongest evidence of a role for uric acid in the development of MetS comes from studies in animal models showing that decreasing uric acid levels may prevent or even reverse features of MetS.

Previous studies in the United States, in both children and adults, have shown an association between elevated serum concentrations of uric acid and MetS

However, the association between an increasing number of metabolic components and serum UA has not been well studied. We sought to determine the association between serum UA and the number of risk factors that contribute to the metabolic syndrome and which factor is associated most with higher serum UA level in a rural health tertiary centre.

Objectives

1. To investigate the relationship between serum uric acid and metabolic syndrome.
2. To investigate the relationship between serum uric acid levels with the different components of metabolic syndrome.

Materials and methods

Source of data

200 patients with metabolic syndrome according to the NCEP ATP III criteria(modified for the South East Asian population) attending OPD and admitted in wards, Department of medicine, Shadan Institute of Medical Sciences, during the study period October 2018 to August 2018.

Method of collection of data

Patients presenting with metabolic syndrome were evaluated with a predetermined proforma and investigated for Serum Uric Acid, FBS/PPBS, RFT, LFT, Lipid profile, ECG, routine investigations.

Cases were selected as patients with metabolic syndrome based on NCEP ATP III criteria (modified for South East Asians) who came to the OPD or admitted to the department of medicine at SIMS during the study period.

Sample Size

The present study involved 200 who satisfied the inclusion criteria.

Inclusion criteria

Patients aged 18 and above with metabolic syndrome. (Revised NCEP/ATP III criteria).

The NCEP ATP III criteria is as follows

3 or more of the following

- Central obesity: Waist circumference >90cm (M), >80cm (F)
- Hypertriglyceridemia: Triglycerides >150mg/dl
- Low HDL cholesterol <40mg/dl (M), <50mg/dl (F)
- Hypertension: Blood Pressure >130mm systolic or >85mm diastolic
- Fasting plasma glucose >100mg/dl

Exclusion criteria

- Hepatic disorders
- Renal disorders
- Alcoholics, smokers
- Subjects on drugs which may increase serum uric acid such as diuretics, theophylline, ascorbic acid, aspirin, caffeine, cisplatin, diazoxide, epinephrine, ethambutol, levodopa, methyldopa, nicotinic acid, phenothiazines, were excluded.
- Drugs which may decrease serum uric acid such as allopurinol, azathioprine, clofibrate, corticosteroids, estrogen, guaifenesin, mannitol, probenecid, and warfarin were excluded.
- Myocardial Infarction
- Gout
- Thyroid disorder

Parameters Studied Fasting Blood Sugar

Fasting plasma glucose of more than 100mg/dl is a criteria of metabolic syndrome. Blood glucose was analyzed by glucose oxidase using semiautoanalyzer.

Blood pressure

Blood pressure (BP) was measured using a sphygmomanometer, with the patient in the supine position (average of three readings). Patients who were already known hypertensives and on medication were also taken as cases. The blood pressure readings had to be more than 130mmHg systolic blood pressure or more than 85mmHg diastolic blood pressure.

Dyslipidemia

After a 12-hour fasting period, venous blood samples were collected from all the cases. Blood samples were centrifuged and serum separated. Serum was used for analysis of uric acid and lipids (Total cholesterol, Triglycerides, LDL and HDL cholesterol). Total cholesterol, LDL and HDL were

analyzed by cholesterol oxidase method, triglycerides by glycerophosphate oxidase (GPO) method.

Waist circumference
Waist circumference (WC) was measured with the non elastic measuring tape positioned midway between the lowest rib and the superior border of the iliac crest while the patient exhaled normally. Males with waist circumference more than 90cm and females with waist circumference more than 80cm were taken as cases.

Uric acid
Uric acid was measured using the uricase method.

Other investigations
1. Blood Urea and Serum Creatinine
2. Liver Function Test
3. Complete Blood Picture
5. ECG
6. USG Abdomen

Statistical analysis
All the data was entered on excel and analysis was done using excel package.
Univariate analysis was carried out to study the differences in mean level among the factors.
Students t test and correlation analysis were done to find out significant differences between the two groups.
All tests were considered significant at $p < 0.05$ level.
SPSS version 15 for windows was the statistical package used for all statistical analysis of the data collected in the course of the study.

Results

1. Gender distribution

Table 1: Showing gender distribution of cases

Gender	No. of patients	%
Female	116	58.0
Male	84	42.0
Total	200	100.0

Of the 200 cases, there were a higher number of females in the study. There were 116 females and 84 males.

2. Age distribution

Table 2: Age distribution of patients studied

Age in years	Female		Male		Total	
	No	%	No	%	No	%
<20	0	0.0	2	2.4	2	1.0
21-30	6	5.2	6	7.1	12	6.0
31-40	10	8.6	12	14.3	22	11.0
41-50	24	20.7	14	16.7	38	19.0
51-60	32	27.6	22	26.2	54	27.0
61-70	34	29.3	24	28.6	58	29.0
71-80	10	8.6	4	4.8	14	7.0
Total	116	100.0	84	100.0	200	100.0

Most of the patients were between the age group of 50- 70 years. This was seen in both males and females. This age group accounts for 56% of the cases. There were also a significant number of patients between the 40 -50 age group.

Table 3: Distribution of patients studied with known history of diabetes and hypertension.

Previous history	Gender		Total (n=100)
	Female (n=58)	Male (n=42)	
HTN	52(44.8%)	44(52.4%)	96(48%)
DM	62(53.4%)	40(47.6%)	102(51%)

Of the 200 people studied 48% were previously diagnosed cases of hypertension. 51% of the 200 cases were known cases of Type 2 DM.

Table 4: SBP/DBP of patients studied

Vitals	Gender		Total (n=100)
	Female (n=58)	Male (n=42)	
SBP (mm Hg)			
• ≤130	40(34.5%)	24(28.6%)	64(32%)
• >130	76(65.5%)	60(71.4%)	136(68%)
DBP (mm Hg)			
• ≤85	44(34.5%)	24(28.6%)	68(34%)
• >85	72(64.7%)	60(71.4%)	132(66%)

We found 68% of the cases to have SBP> 130mm Hg and 66% to have a DBP >85mmHg. We found males to have a higher incidence of increased blood pressure among the cases studied.

Table 5: Blood sugar parameters of patients studied

	Gender		Total (n=100)
	Female (n=58)	Male (n=42)	
FBS (mg/dl)			
• <100	8(6.9%)	16(19%)	24(12%)
• 9100-125	38(32.8%)	20(23.8%)	58(29%)
• ≥126	70(60.3%)	48(57.1%)	118(59%)
PPBS (mg/dl)			
• <140	20(17.2%)	18(21.4%)	38(19%)
• 140-199	30(25.9%)	12(14.3%)	42(21%)
• 200 and more	64(55.2%)	54(64.3%)	118(59%)

Our study had 88% of patients who had a fasting blood sugar more than or equal to 200. Of these 29% had impaired fasting glucose and 21% had impaired glucose tolerance. 59% had overt diabetes.

Table 6: Waist Circumference (cm) of patients studied

Waist Circumference (cm)	Number of patients	%
Female ≤80 & male ≤90	52	26.0
Females>80& Males >90	148	74.0
Total	200	100.0

74% of the subjects had increased waist circumference i.e. for males > 90cm and for females >80cms. Of this 48 were females and 26 were males.

Table 7: Showing lipid parameters of patients studied.

	Gender		Total (n=100)
	Female (n=58)	Male (n=42)	
TGL (mg/dl)			
• ≤150	22(19%)	6(7.1%)	28(14%)
• >150	94(81%)	78(92.9%)	172(86%)
Total Cholesterol (mg/dl)			
• ≤200	88(75.9%)	60(71.4%)	148(74%)
• >200	48(24.1%)	24(28.6%)	52(26%)
HDL (mg/dl)			
• Male <40, Female <50	102(87.9%)	50(59.5%)	152(76%)
• Male>40, Female >50	14(12.1%)	34(40.5%)	48(24%)
LDL (mg/dl)			
• <70	32(27.6%)	14(16.7%)	46(23%)
• 70-150	80(69%)	64(76.2%)	144(72%)
• >150	2(1.7%)	6(7.1%)	8(4%)
VLDL (mg/dl)			
• <35	34(29.3%)	16(19%)	50(25%)
• 35-60	42(36.2%)	36(42.9%)	78(39%)
• >60	40(34.5%)	32(38.1%)	72(36%)

We found 86% of the subjects to have increased triglycerides. There were 48 females and 38 males. HDL was found in 51 females and 25 males with an incidence of 76%.

Table 8: Parameters of Metabolic syndrome in patients studied

Variables	No. of patients (n=100)	Males (n=42)	Females (n=58)	%
FBS >100 mg/dl	170	66	104	85.0
SBP>130 mm Hg	136	60	76	68.0
DBP>85 mmHg	136	60	136	68.0
Triglycerides >150 mg/dl	172	136	96	81.0
WC >90cm males and WC >80 cm females	148	52	96	74.0
HDL <40 mg/dl males & HDL <50 mg/dl in females	152	50	102	76.0

We found 85% of our subjects to have a raised FBS, of which there were 66 males and 104 females. Of the 68% of cases who had high SBP, there were 60 males and 76 females. A similar number of patients had high DBP. 76 males and 96 females had increased triglycerides. 52 male subjects and 96 females in our study had increased waist circumference. This brings the incidence of increased waist circumference to 74%. HDL was low in 76% of the patients. A higher percentage of females had low HDL levels than males.

Table 9: Number of criteria of metabolic syndrome of patients studied

Number of criteria	No. of patients (n=100)	%
1	0	0.0
2	0	0.0
3	62	31.0
4	80	40.0
5	58	29.0

31% of the cases had three components of metabolic syndrome. 40% had four components and 29% had all five components.

Table 10: Distribution of Serum Uric acid (mg/dl) in patients studied

Serum Uric acid (mg/dl)	No of patients	%
Female	N=58	
• <2.4	6	5.2
• 2.4-4	36	31.1
• 4-5	26	22.4
• 5-6	12	10.3
• >6	36	31.1
Male	N=42	
• <3.4	8	9.5
• 3.4-5	28	33.3
• 5-6	12	14.3
• 6-7	4	4.8
• >7	32	38.1

Of the 116 females in our study, 36(31.1%) had increased SUA levels i.e. more than 6mg/dl. 32 out of 84 males had increased SUA levels, which is more than 7mg/dl.

Table 11: Incidence of increased uric acid in patients studied

Uric acid	No. of patients (n=100)	%
Normal	132	66.0
Increased	68	34.0

Discussion

The present study was a prospective hospital based study to investigate the relationship between serum uric acid and metabolic syndrome and to investigate the relationship between serum uric acid levels with different components of metabolic syndrome. 200 patients with metabolic syndrome according to the NCEP ATP III criteria (modified for the South East Asian population) were studied.

Gender of study population

In the present study, where 200 cases of metabolic syndrome were involved, we found that 58% were females and 42% were males, indicating a predominance of female patients. This is in concordance with the results of other studies [5, 6].

Age in study population

Our study had more cases of metabolic syndrome between the age group of 50-70 years. This is consistent with findings in other studies that show the prevalence of the metabolic syndrome is highly age-dependent [7].

The uric acid levels in our study were similar to SUA levels in other studies [8].

The overall prevalence of hyperuricemia in our study was 34%. There was similar prevalence among both the genders with males having a slightly increased predominance. Similar results have been found in other studies. The pathogenic mechanism may be due to estrogen promoting uric acid excretion so it may be more important for men to prevent hyperuricemia [9, 10].

Increased uric acid levels with age

Most of the cases with increased uric acid levels were between the age group of 50- 70 years of age. This could be due a higher number of cases of metabolic syndrome within this age group as a whole. However, in terms of incidence of increased uric acid, the age group extends to 80 years of age. Similar findings were also found in a study [11].

We found a direct correlation between high SUA and FBS in both males and females in our study. However, there was a significant high statistical correlation only in males, with a p value of 0.001. Our study is similar to a study done [11]. A possible mechanism linking the association between hyperinsulinemia with hyperuricemia is a decrease of renal excretion of uric acid. Insulin can also enhance renal tubular sodium reabsorption [12] which in turn can reduce renal excretion of uric acid. (Article uamsdm)

There was a direct correlation between DBP and high SUA in both males and females in our study. It was statistically significant in females only with a p value of 0.03. This was comparable to a study [13]. There was a high incidence of hyperuricemia in subjects with high SBP in our study. However, it was not statistically significant in either males or females. Hyperuricemia is thought to arise from decreased renal excretion of urate. Altered lactic acid metabolism in hypertensive disease may also account for the altered renal transport of uric acid of the 100 patients, 31.3% of females and 50% of males with increased waist circumference had hyperuricemia. This shows a considerably higher prevalence in males over females. We also found a statistically significant correlation between waist circumference and SUA in males. However, a similar statistical significance was not seen in females.

In one study found statistically significant correlation between waist circumference and SUA in both males and females. In obese subjects, hyperuricemia is attributable to the overproduction of SUA and impairment in the renal clearance of UA owing to the influence of hyperinsulinemia secondary to IR. Leptin was also found to have a role in hyperuricemia in obesity [13, 14].

In our study, there was considerable association between SUA and triglycerides. We found a moderate statistical significance between triglycerides and SUA in females with a p value of 0.09. However, there was no statistical significance seen in males in our study significant p values. The potential mechanisms relating hyperuricemia to fasting hypertriglyceridemia are unknown. It has been speculated that it may be due to an increase in nicotinamide adenine dinucleotide phosphate oxidase (NADPH) requirement for de novo fatty acid synthesis in obese subject. With increasing NADPH, UA production is enhanced possibly increasing the SUA level.

There was a high incidence of hyperuricemia in subjects with low HDL in our study. However, we could not find a statistical significance between the above components in either males or females. statistical correlation between HDL and SUA in both males and females.

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Conflict of Interest: None

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Conclusion

- Hyperuricemia was prevalent in individuals with metabolic syndrome. 34% of our subjects had elevated SUA levels.
- Elevated SUA levels were found predominantly over the age of 50 years.
- Hyperuricemia was more prevalent in males with metabolic syndrome.
- Above the age of 50 years high SUA levels were seen equally in both males and females with metabolic syndrome.
- In males, there was a direct definite correlation between waist circumference and FBS with high SUA levels. This was statistically significant with a p value of 0.08 and 0.001 respectively.
- In females, there was a definite positive correlation between DBP and triglycerides with high SUA. This was found to be statistically significant with a p value of 0.03 and 0.09 respectively.
- There was no statistical correlation between SBP and HDL with increased SUA in either males or females in our study.
- The incidence of high SUA levels increased as the number of components of metabolic syndrome increased.

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