VOLUME - 12, ISSUE - 05, MAY - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Medicine

ASSOCIATION OF URIC ACID WITH COMPONENTS OF METABOLIC SYNDROME AT A TERTIARY CARE CENTRE IN BENGALURU

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ABSTRACT

Background: Metabolic syndrome (MetS) is also known as syndrome X, insulin resistance syndrome is defined as a group of disease developed due to accumulation of multiple risk factors that includes resistance to insulin, dyslipidemia, abdominal obesity and hypertension. Metabolic syndrome, is associated not only with type 2 diabetes mellitus and cardiovascular disease, but also with many other systemic disorders such as cerebrovascular accident, chronic lung disease and fatty liver disease. Hyperuricemia (above 7.0 mg/dL in men and 6.0 mg/dL in women) has been reported to be closely related to diabetes, hypertension, obesity, renal function decline, and cardiovascular disease, most of which are principal contributors in the development and progression of MetS. The study aimed to assess the associations of serum uric acid with the components of MetS. **Methods:** This cross-sectional study was conducted in the hospitals attached to Bangalore medical college and research Institute. 110 patients with metabolic syndrome who satisfied the inclusion criteria were included. Data was collected in the form of history, clinical examination, and relevant investigations. Statistical analysis was performed using SPSS software, p value of <0.5 being significant **Results:** The mean age of the study participants was found to be 51.55+7.760 years of age. 62.7% of the study participants were males The mean serum uric acid level of the study participants was found to be 6.325+2.7910. 41.82% of the study participants who had metabolic syndrome had hyperuricemia. The association was found to be statistically significant between hyperuricemia and hypertension, central obesity, low HDL, high FBS among the study participants. **Conclusions:** Serum uric acid is closely associated with metabolic syndrome and its components. Serum uric acid can also be considered as a mandatory investigation in patients who has any of the five components of metabolic syndrome.

KEYWORDS : Serum uric acid; Metabolic syndrome; HDL; FBS; WC; BP; TG

INTRODUCTION:

The Metabolic Syndrome consists of a cluster of metabolic disorders, many of which promote the development of atherosclerosis and increase the risk of cardiovascular disease events [1]. Metabolic syndrome (MetS) is also known as syndrome X, insulin resistance syndrome and the deadly quartet. Metabolic syndrome, is associated not only with type 2 diabetes mellitus and cardiovascular disease, but also with many other systemic disorders such as chronic lung disease and fatty liver disease [2].

The prevalence of metabolic syndrome varies throughout the world. Metabolic syndrome is a rising disease entity and is growing into a significant public health problem [3]. Several studies have shown the Metabolic syndrome prevalence increases with age, making its diagnosis necessary due to 2.5-fold increase in cardiovascular mortality and a 5-fold higher risk of developing diabetes [4].

Serum uric acid (SUA) is the end product of purine metabolism or purine nucleotide catabolism [5]. Normal levels of uric acid provide a protective effect against free-radical oxidative damage [6]. Uric acid is formed by the liver, is excreted by kidneys with some production by the intestines [7]. When the regulation of SUA production and excretion is out of balance, the levels of SUA become abnormal. Causes include high intake of purine in the diet, renal failure, drugs, ethanol and malignancy. Hyperuricemia (above 7.0 mg/dL in men and 6.0 mg/dL in women) has been reported to be closely related to insulin resistance, hypertension, obesity,dyslipidemia, renal function decline, and cardiovascular disease, most of which are principal contributors in the development and progression of MetS [7–12]. The study aimed to assess the associations of serum uric acid with the components of MetS.

Objective Of The Study:

- To estimate the uric acid levels in patients with metabolic syndrome.
- To evaluate the association of uric acid with components of metabolic syndrome.

METHODOLOGY

Study Design: Cross-sectional study

Study Duration: 18 months (February 2021 to August 2022)

Study Area: Hospitals attached to Bangalore Medical College and Research Institute, Bangalore.

Study Participants: Patients with metabolic syndrome attending the Medicine OPD/IPD of Victoria Hospital and Bowring and Lady Curzon Hospital attached to BMCRI, Bangalore.

Inclusion Criteria

1. Age between 30-80 years
2. Patients fitting the Criteria for the metabolic syndrome according to National Cholesterol Education Program, Adult Treatment Panel III.

Exclusion Criteria

1. Renal disorders
2. Alcoholics
3. Smokers
4. Thyroid disorders
5. Hepatic disorders
6. Drugs which causes increased or decreased uric acid levels
7. Congestive cardiac failure.

Method Of Data Collection:

The study is a hospital-based cross-sectional study was carried out between February 2021 to August 2022 at hospitals affiliated to Bangalore Medical College and Research Institute, Bangalore. Approval and clearance were obtained from the institutional ethics committee, the patients fulfilling the inclusion criteria wer enrolled for the study after obtaining informed consent.

The study participants who were diagnosed with metabolic syndrome were included in the study, till the sample size was reached. Written informed consent was taken from the study participants before collecting the data. A pre-tested, semi-structured questionnaire was used to collect information on socio-demographic variables and detailed history regarding the illness by interview method. Examination were conducted in detail and routine laboratory parameters were tested.

Operational Definition:

Metabolic Syndrome: Study participants fulfilling the National cholesterol education programme: Adult treatment panel III i.e., any three of the five criteria below [13]:

1. **Central obesity:** waist circumference >80cm in females, >90cm males.
2. **Hypertriglyceridemia:** triglyceride levels >150mg/dl or specific medication.
3. **Low HDL cholesterol**: <50mg/dl for women and <40mg/dl for men or specific medication.
4. **Hypertension:** blood pressure >130mmhg systolic or >85mmhg diastolic or specific medication.
5. **Fasting plasma glucose level** >100mg/dl or specific medication or previously diagnosed type 2 diabetes.

Hyperuricemia was defined as a serum uric acid level of ≥7.0 mg/dL in men and ≥6.0 mg/dL in women [14].

Estimation of Sample Size:

On the basis of statistics obtained from Department of Medicine, Bangalore Medical College and Research Institute, an average of 8 cases per month fitting the criteria of the study with study duration of 18 months, we can expect to have N=144. Based on this population size, using YAMANE equation, for a known population size, sample size (n) equal to

- n =N/1+Ne2
- n=sample size
- N=population size
- e= margin of error (for 95% of confidence level, margin error =0.05)
- n=144/1+144*0.05*0.05 = 144/1.36 = 105.88

Therefore, after approximating, the sample size of the study participants was fixed at 110.

RESULTS:

Table 1: Socio-demographic Characteristics And Comorbidity Profile

Socio-Demographic Characteristics		Frequency	Percentage
Age	30-39 Years	7	6.36
	40-49 Years	41	37.27
	50-59 Years	46	41.82
	60-69 Years	11	10
	70-79 Years	5	4.55
	Mean+Sd	51.55+7.760	
Gender	Male	69	62.7
	Female	41	37.3
Comorbidity Profile	DM	52	47.3
	HTN	69	62.7
	IHD	18	16.4

41.82% of the study participants belonged to the age group 50-59 years of age. 37.27% of the study participants belonged to the age group 40-49 years of age. The mean age of the study participants was found to be 51.55+7.760 years of age. 62.7% of the study participants were males. 47.3% of the study participants had diabetes with 62.7% of the study participants had hypertension and 25.6% (n=28) of the study participants did not have any co-morbidities.

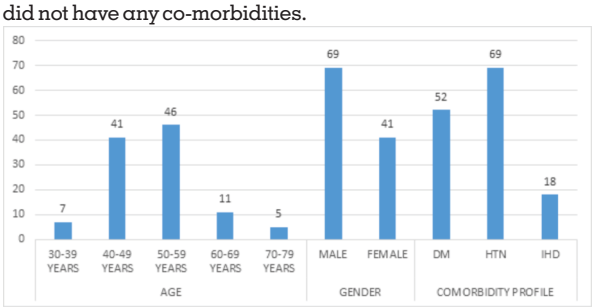


Figure 1: Socio-demographic Characteristics And Comorbidity Profile

Table 2: Mean Values Of Components Of Metabolic Syndrome

Components Of Metabolic Syndrome	Mean	Std. Deviation
SBP	142.75	20.721
DBP	92.23	14.374
WC	94.59	11.748
TG	169.10	45.075
HDL	39.31	6.537
FBS	171.86	55.472

The Mean SBP, DBP, WC, TG, HDL, FBS of the study participants were found to be 142.75+20.721, 92.23+14.374, 94.59+11.748, 169.10±45.075, 39.31±6.537 and 171.86±55.472 respectively.

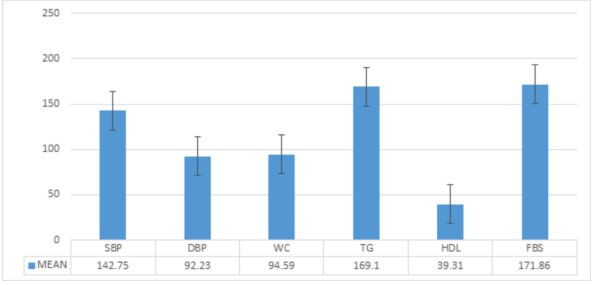


Figure 2: Mean Values Of Components Of Metabolic Syndrome

Table 3: Serum Uric Acid Levels

Serum Uric Acid	Frequency	Percentage
Normal	64	58.18
Hyperuricemia	46	41.82
Mean+Sd	6.325+2.7910	

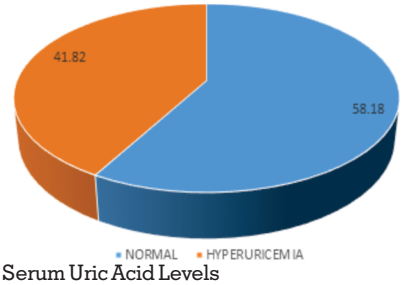


Figure 3: Serum Uric Acid Levels

The mean serum uric acid level of the study participants was found to be 6.325+2.7910. 41.82% of the study participants had hyperuricemia.

Table 4: Components Of Metabolic Syndrome

Components Of Metabolic Syndrome	Frequency N	Percentage %
Hypertension	70	63.3
Hypertriglyceridemia	85	77.3
Low Hdl Cholesterol	81	73.6

Central Obesity	57	51.8
Fasting Blood Glucose Level	107	97.3

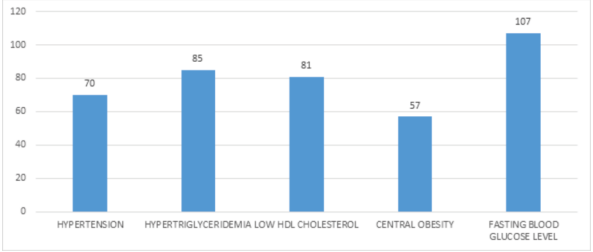


Figure 4: Components Of Metabolic Syndrome

Of the 110 study participants, 97.3% of the study participants were found to have FBS levels >100mg/dl. 77.3%% of the study participants were found to have triglyceride levels >150mg/dl. 73.6% of the study participants were found to have low HDL levels (<50mg/dl for women and <40mg/dl for men). 63.3% of the study participants were found to have Hypertension (blood pressure >130mmhg systolic or >85mmhg diastolic). 51.8% of the study participants were found to have central obesity (waist circumference >80cm in females, >90cm males).

Table 5: Mean Serum Uric Acid Levels With Components Of Metabolic Syndrome

Components Of Metabolic Syndrome		Serum Uric Acid Levels		P Value
		Mean	S. D	
Hypertension	Yes	6.226	1.8601	0.047
	No	5.157	1.7291	
Central Obesity	Yes	6.470	1.8210	0.062
	No	5.168	1.7620	
Hypertriglyceridemia	Yes	6.488	1.8132	0.065
	No	5.276	1.7924	
Low Hdl Cholesterol	Yes	6.398	1.8491	0.072
	No	5.121	1.6308	
High Fasting Blood Glucose Level	Yes	6.342	1.7997	0.037
	No	4.700	1.6000	

The mean uric acid levels of the study participants with and without hypertension was found to be 6.226+ 1.8601 and 5.157+ 1.7291 respectively. The mean uric acid levels of the study participants with and without central obesity was found to be 6.470+ 1.8210 and 5.168+1.7620 respectively. The mean uric acid levels of the study participants with and without hypertriglyceridemia was found to be 6.488+ 1.8132 and 5.276+1.7924 respectively. The mean uric acid levels of the study participants with and without low HDL cholesterol was found to be 6.398+ 1.8491 and 5.121+1.6308 respectively. The mean uric acid levels of the study participants with and without high FBS was found to be 6.342+ 1.7997 and 4.700+1.6000 respectively. As seen from the above table, the mean uric acid levels were found to be higher among the study participants (41.82%) . The association was found to be statistically significant between hyperuricemia and hypertension, high fasting blood glucose levels among study participants.

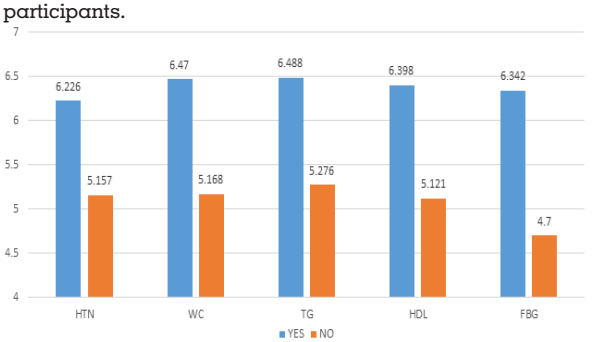
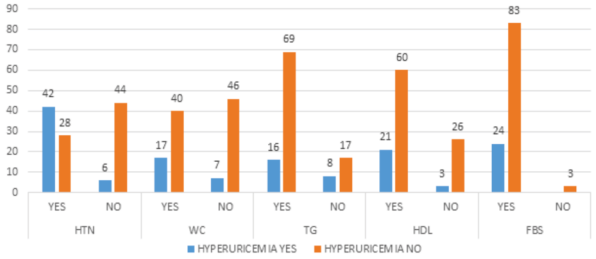


Figure 5: Mean Serum Uric Acid Levels With Components Of Metabolic Syndrome

Table 5: Association Of Serum Uric Acid Levels With Components Of Metabolic Syndrome

Components Of Metabolic Syndrome			Hyperuricemia		P Value
			Yes	No	
Hypertension (Systolic Blood Pressure >130mmhg Or Diastolic Blood Pressure >85mmhg)	Yes	Count	42	28	0.048
		%	60.0%	40.0%	
	No	Count	6	44	
		%	12.0%	88.0%	
Central Obesity (Waist Circumference >80cm In Females, >90cm Males)	Yes	Count	17	40	0.033
		%	29.8%	70.2%	
	No	Count	7	46	
		%	13.2%	86.8%	
Hypertriglyceridemia (Tg>150mg/Dl)	Yes	Count	16	69	0.131
		%	18.8%	81.2%	
	No	Count	8	17	
		%	32.0%	68.0%	
Low Hdl Cholesterol (<50mg/Dl For Women And <40mg/Dl For Men)	Yes	Count	21	60	0.044
		%	25.9%	74.1%	
	No	Count	3	26	
		%	10.3%	89.7%	
High Fasting Blood Glucose Level (Fbs>100mg/Dl)	Yes	Count	24	83	0.047
		%	22.4%	77.6%	
	No	Count	0	3	
		%	0.0%	100.0%	

60% of the study participants having Systolic blood pressure >130mmhg or diastolic blood pressure >85mmhg were found to have hyperuricemia. 29.8% of the study participants having waist circumference >80cm in females, >90cm males were found to have hyperuricemia. 18.8% the study participants having TG>150mg/dl were found to have hyperuricemia. 25.9% of the study participants having HDL <50mg/dl for women and 5<40mg/dl for men were found to have hyperuricemia. 22.4% of the study participants having FBS>100mg/dl were found to have hyperuricemia. The association was found to be statistically significant between hypertension, central obesity, low HDL, high FBS and hyperuricemia among the study participants.



DISCUSSION:

SUA is an antioxidant metabolite that maintains the stability of the vascular endothelium [15]. High SUA levels produce a pro-oxidant environment, endothelial dysfunction, and mitochondrial damage. Additionally, the increase of reactive oxygen species (ROS) and inflammatory proteins (interleukin-1, interleukin-6, and TNF-) are involved in the development of IR and MetS [16]. Previous studies have shown that elevated SUA levels predispose to IR and MetS [17, 18]. Some studies infer that high SUA levels may be both a risk factor and an outcome of some metabolic disorders [19, 20]. The purpose of the study was to determine if there was a relationship between hyperuricemia and MetS.

In the present study, 41.82% of the study participants belonged to the age group 50-59 years of age. 37.27% of the study participants belonged to the age group 40-49 years of age. The mean age of the study participants was found to be 51.55+7.760 years of age. 62.7% of the study participants were males.

In a study done by Mahajan A et al [7], 65% were males and 35% were females. The mean age of the study participants was found to be 53.53±12.14 years of age. In a study done by

Ni W et al [21], The mean age of the study participants was found to be 45.41+11.79. In a study done by Jeong J et al [22], The mean age of the study participants was found to be 53.69 ± 0.54. In a study done by Nejatinamini S et al [24], the mean age of the study participants was found to be 40.66 ± 6.01. In a study done by Reddy M et al [23], out of 40 study participants, 23 were males and 17 were females.

In the present study, The Mean SBP, DBP, WC, TG, HDL, FBS of the study participants were found to be 142.75+20.721, 92.23+14.374, 94.59+11.748, 169.10±45.075, 39.31±6.537 and 171.86±55.472 respectively. In a study done by Mahajan A et al [7], The mean systolic blood pressure was 140 ± 15 and the mean diastolic blood pressure was 86 ± 8. In a study done by Jeong J et al [22], The Mean SBP, DBP, WC, TG, HDL, FBS of the study participants were found to be 127.88 ± 0.46, 81.14 ± 0.32, 91.34 ± 0.27, 239.52 ± 6.95, 42.22 ± 0.29 and 115.56 ± 0.94 respectively. In a study done by Nejatinamini S et al [24], The Mean SBP, DBP, WC, TG, HDL, FBS of the study participants were found to be 122.8 ± 13.3, 85.7 ± 10.3, 95.10 ± 15.16, 200.1 ± 130.3, 42.7 ± 7.2 and 104.9 ± 12.1 respectively.

The mean serum uric acid level of the study participants was found to be 6.325+2.7910. 41.82% of the study participants had hyperuricemia. In a study done by Mahajan A et al [7], the mean serum uric acid level of the study participants was found to be 7.07±1.31. 64 (64%) had hyperuricemia. P value was statistically significant relating the positive association of higher uric acid levels with metabolic syndrome. In a study done by Ni W et al [21], the mean serum uric acid level of the study participants was found to be 5.67+1.37. In a study done by Jeong J et al [22], the mean serum uric acid level of the study participants was found to be 5.58 ± 0.04. In a study done by Reddy M et al [23], Mean serum uric acid levels was 7.9 mg/dL in men and 6.8 mg/dL in women and 28 subjects (65%) had hyperuricemia. In a study done by Nejatinamini S et al [24], the mean serum uric acid level of the study participants was found to be 5.87 ± 1.52. In a study done by Gunanithi K et al [25], Serum uric acid levels among patients with metabolic syndrome was found to be 8.02+1.82.

In the present study, 97.3% of the study participants were found to have FBS levels >100mg/dl. 77.3%% of the study participants were found to have triglyceride levels >150mg/dl. 73.6% of the study participants were found to have low HDL levels (<50mg/dl for women and <40mg/dl for men). 63.3% of the study participants were found to have Hypertension (blood pressure >130mmhg systolic or >85mmhg diastolic). 51.8% of the study participants were found to have central obesity (waist circumference >80cm in females, >90cm males).

In a study done by Reddy M et al [23], it was found that out of 28 patients with metabolic syndrome, 22 were having hypertension, 18 were diabetic, 16 were having dyslipemia (elevated triglyceride of more than 150 mg/dL, low high-density lipoproteins <45 in males and less than 55 mg/dL in females, 26 were having abdominal obesity. In a study done by Ni W et al [21], they found a high TG in 27.64%, a low HDL-C in 43.28%, a high blood pressure in 21.61%, an elevated concentrations of fasting glucose in 13.90%, and central obesity in 50.53% of the study participants.

In the present study, the mean uric acid levels of the study participants with and without hypertension was found to be 6.226+ 1.8601 and 5.157+ 1.7291 respectively. The mean uric acid levels of the study participants with and without central obesity was found to be 6.470+ 1.8210 and 5.168+1.7620 respectively. The mean uric acid levels of the study participants with and without hypertriglyceridemia was found to be 6.488+ 1.8132 and 5.276+1.7924 respectively. The mean uric acid levels of the study participants with and without low HDL cholesterol was found to be 6.398+ 1.8491 and 5.121+1.6308 respectively. The mean uric acid levels of the study participants with and without high FBS was found to be 6.342+ 1.7997 and 4.700+1.6000 respectively. The association was found to be statistically significant between the hypertension, high fasting blood glucose levels and the serum uric acid levels of the study participants.

In the present study, 60% of the study participants having Systolic blood pressure >130mmhg or diastolic blood pressure >85mmhg were found to have hyperuricemia. 29.8% of the study participants having waist circumference >80cm in females, >90cm males were found to have hyperuricemia. 18.8% the study participants having TG>150mg/dl were found to have hyperuricemia. 25.9% of the study participants having HDL <50mg/dl for women and <40mg/dl for men were found to have hyperuricemia. 22.4% of the study participants having FBS>100mg/dl were found to have hyperuricemia. The association was found to be statistically significant between hypertension, central obesity, low HDL, high FBS and hyperuricemia among the study participants.

In a study done by Jeong J et al [22], significant association between uric acid levels and risk of metabolic syndrome. Specifically, a high uric acid level was found to confer significant risk of metabolic syndrome regardless of the number of metabolic syndrome criteria met. In a study done by Nejatinamini S et al [24], serum uric acid had significant relationship with hypertriglyceridemia and low HDL-C.

In a study done by Gunanithi K et al [25], Serum uric acid levels showed positive correlation with fasting plasma glucose, serum triglycerides (pearsons correlation significant at $p<0.05$). In a study done by Sun HL et al [26], study participants with MetS had significantly higher BMI, WC, SBP, SDP, FPG, LDL-C, TG and UA than the study participants without MetS. In a study done by Sun HL et al [26], it was found that subjects with a high level of UA (> 5.5 mg/dL) had a 2-fold higher risk of having hypertension. In a study done by Lee MJ et al [27], significant synergistic effect of hyperuricemia and abdominal obesity on the odds for MetS components, such as hypertriglyceridemia and low HDL-C was found.

Though it was out of preview of this study, the possible mechanism for hyperuricemia in metabolic syndrome patients may be due to overproduction of uric acid caused by increased consumption of carbohydrate as it represents 60-70% % of average daily calories. This high intake of fructose and sucrose may explain the rise in obesity. The high prevalence of obesity may be explained by the accelerated urbanization that has been accompanied by nutrition transition, resulting in lower levels of physical activity, and the exchange of traditional foods high in complex carbohydrates for new foods high in refined carbohydrates. Hyperuricemia may be partially responsible for inflammatory imbalances in adipose tissues that lead to low-grade inflammation and insulin resistance. Also, metabolic syndrome may cause nucleic acid metabolism abnormalities, which stimulate adenosine monophosphate (AMP) deaminase that produce uric acid which promotes fat storage and insulin resistance. Uric acid is considered as one of the major factors that raises blood pressure by stimulating intracellular oxidative stress and activation of NADPH oxidase in the cytosol and mitochondria. Hyperuricemia may induce insulin resistance causing vasodilatation and increase blood flow that interfere with the action of nitric oxide, which facilitates glucose absorption. Other results suggest that hyperuricemia is caused by hyperinsulinemia acting on the renal tubules to facilitate the reabsorption of uric acid.

CONCLUSION:

High prevalence of hyperuricemia was found among the patients with metabolic syndrome . Serum uric acid is closely associated with metabolic syndrome and its components. serum uric acid can be considered as a mandatory

investigation in patients who has any of the five components of metabolic syndrome. If hyperuricemia identified and an attempt can be made to identify other components of metabolic syndrome. These kinds of patients maybe actively followed up for the development of new components and cardiovascular and cerebrovascular complications. Whether drugs that lower serum uric acid levels can actually prevent the development of new components and correcting hyperuricemia is beneficial in preventing complications, effect of appropriate anti-diabetic drugs, lipid lowering agents, anti-hypertensives and active weight reduction on serum uric acid level is beyond the scope of this study and it needs further research activity.

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