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THE STUDY OF SERUM ACID IN DIABETES AND ITS CORRELATION WITH DIFFERENT COMPONENTS OF METABOLIC SYNDROME

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ABSTRACT

Background: Metabolic syndrome (MetS) is a significant public health issue worldwide and it has reached to pandemic proportions worldwide. In addition to MetS, elevated concentrations of uric acid are associated with a variety of cardiovascular conditions. Present study was aimed to study association between serum Uric acid levels and metabolic syndrome. **Material and Methods:** Present study was hospital based, cross sectional study, conducted in 150 cases of Metabolic syndrome of either sex with BMI >30kg/m2. Anthropometric measurements such as Height (in meters), Weight (Wt), Body mass index (BMI), Waist circumference, Hip Circumference (HC) & Blood Pressure were measured. A 12 hour fasting venous blood samples were collected for serum uric acid (SUA) estimation. **Results:** A total of 150 participants were enrolled in the study, 50 in each of the three groups, equal number of participants are taken in cross sectional study as convenient sample. Mean age was comparable among three groups, while mean body mass index, mean waist circumference & mean hip circumference had significant difference among group comparison The mean serum uric acid, fasting & PP Blood glucose had significant difference among group comparison (P<0.0001). The mean difference between SUA of MetS group and DM group is statistically nonsignificant. The mean difference of SUA levels between METs group and normal is statistically Significant. The mean difference of SUA between DM group and normal is statistically Significant. **Conclusion:** Serum uric acid levels were significantly increased in Metabolic syndrome patients. Serum uric acid showed a positive correlation with the waist circumference, body mass index, blood pressures both systolic & diastolic, Fasting blood glucose levels, Alanine transferase, Alkaline Phosphatase & Triglycerides in Metabolic syndrome patients.

Keywords: Serum uric acid, Metabolic syndrome, oxidative stress markers, waist circumference, body mass index,

INTRODUCTION

Metabolic syndrome (MetS) is a significant public health issue worldwide and it has reached to pandemic proportions worldwide.[1] About 20-30% of adult population worldwide is suffering from this disorder and it is a noncommunicable disease. Its prevalence increasing worldwide both in adults, children and adolescents.[2]

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The metabolic syndrome prevalence rate is estimated to be around 20-25 % in adult population worldwide.[3] Metabolic Syndrome is an aggregate of conditions that together increases the risk of developing cardiovascular disease (CVD) and Type 2 diabetes.[4] The commonly accepted underlying risk factors for Metabolic Syndrome include insulin resistance and abdominal obesity.

Serum uric acid is a byproduct of cell death, produced when there is cell destruction and nuclear degradation and final enzymatic product of purine metabolism. It is suggested that hyperuricemia is associated with MetS and they may have common pathophysiology.[5] In addition to MetS, elevated concentrations of uric acid are associated with a variety of cardiovascular conditions.[6] Present study was aimed to study association between serum Uric acid levels and metabolic syndrome

MATERIAL AND METHODS

Present study was hospital based, cross sectional study, conducted in department of XXX, at XXX medical college & hospital, XXX, India. Study was done during the period of January 2017 to August 2018. Study was approved by institutional ethical committee.

Inclusion criteria

- Group 1.50 cases of Metabolic syndrome of either sex with BMI >30kg/m2.
- Metabolic syndrome was defined as the presence of 3 or more of the following five criteria :
- 1) waist circumference (central obesity) ≥ 90 cm in males and ≥80 cm in females,
- 2) triglycerides ≥150 mg/dL or under treatment for elevated triglycerides,
- 3) high-density lipoprotein (HDL)-cholesterol < 40 mg/dL in males and < 50 mg/d in females or under treatment for reduced HDL,
- 4) SBP ≥130 mmHg or DBP ≥85 mmHg or under treatment for hypertension, and
- 5) Fasting glucose ≥100 mg/dL or under treatment for elevated glucose [13].

The study population was divided into 3 groups.

1. Metabolic syndrome patients with BMI =/ >30 of age group 30-70 yrs. Of either sex
2. Diabetic mellitus patients (T2DM defined by Expert Committee on the diagnosis and classification of DM) with BMI 25-29.9 of age group 30-70 yrs. known cases under antihyperglycemic therapy
3. Healthy individuals with normal BMI 20-24.9 of age group 30-70 yrs. Of either sex Willing to participate in present study

Exclusion criteria

- Presence of infectious disease at the time of evaluation or during the 15 days prior to enrollment
- Subjects with smoking, alcoholism, taking anti-inflammatory, antihistaminic, antifolate, anticonvulsant drugs.
- Patients with medical history of severe renal disease, severe hepatic disease, infectious disease or malignancy. Patients with HIV
- Pregnancy
- Not willing to participate in the study

Study was explained to participants in local language & written informed consent was taken. A pre-designed, pre-tested, semi-structured questionnaire was used to collect various socio-demographic data like name, age, sex, address along with data about physical examination and clinical history. Anthropometric measurements such as Height (in meters), Weight (Wt), Body mass index (BMI), Waist circumference, Hip Circumference (HC) & Blood Pressure were measured.

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A 12 hour fasting venous blood samples were collected from all participants in fluoride, plain and EDTA bulbs; again 2 hours postprandial blood sample was collected in fluoride bulb for blood sugar estimation. Serum was separated after 1 hour by centrifugation at 3000 rpm for 10 minutes, and was tested for plasma glucose (fasting & post prandial), serum gamma glutamyl transferase (GGT), serum uric acid (SUA), serum alanine transaminase (ALT), serum aspartate transaminase (AST), serum alkaline phosphatase (AST), serum total cholesterol, serum triglycerides & serum HDL-cholesterol.

Data was entered in Microsoft Excel and analyzed using SPSS version 24.0th. Normality of data was assessed for quantitative variable and data was found be normally distributed. So, Mean and SD were calculated for quantitative variables and proportions were calculated for categorical variables. Also, data was represented in form of visual impression like bar-diagram etc. One way Analysis of variance [ANOVA] was applied to check significance difference in three groups for different parameters. Tukey Post hoc test was used to check significant difference in two groups. P- value of <0.05 was considered statistically significant.

RESULTS

A total of 150 participants were enrolled in the study, 50 in each of the three groups , equal number of participants are taken in cross sectional study as convenient sample. Mean age was comparable among three groups, while mean body mass index, mean waist circumference & mean hip circumference had significant difference among group comparison (P<0.0001).

Table 1: General characteristics

Characteristics	MetS (group 1)	DM (group 2)	Normal(group3)	P-value
Age-Group (years)	45.44 ± 7.06	46.34 ± 10.35	45.34 ± 7.04	P=0.803, NS
Mean Body Mass Index	32.48 ± 2.18	27.69 ± 1.37	27.14 ± 1.41	P<0.0001 S
Mean waist circumference	99.61 ± 5.75	87.73 ± 3.84	86.16 ± 4.21	P<0.0001, S
Mean hip circumference	104.74 ± 4.63	98.32 ± 2.78	94.08 ± 5.44	P<0.0001, S

The mean difference between BMI of MetS group and DM group is statistically significant. The mean difference of BMI between MetS group and Normal group is statistically significant. (p value <0.0001). The mean difference of BMI between DM group and Normal group is statistically nonsignificant, (p value < 0.0001) as both the groups belong to overweight category 25-29.9 BMI.

The mean difference between WC of MetS group and DM group is statistically significant, The mean difference of WC between MetS & Normal group is statistically significant. The mean difference of WC between DM group and Normal group is statistically nonsignificant.

The mean difference between HC of MetS group and DM group was statistically significant. The mean difference of HC between MetS group and normal was statistically significant. The mean difference of HC between DM group and normal was statistically significant.

Table 2: Comparison among two Groups [Tukey Post Hoc test]

Groups	Body Mass Index		Mean Difference Waist Circumference		Mean Difference of Hip Circumference	
	Mean Difference	p-value	Mean Difference	p-value	Mean Difference	p-value

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METs Vs DM	4.79	P<0.0001, S	11.87	P<0.0001, S	6.42	P<0.0001, S
METs Vs Normal	5.34	P<0.0001, S	13.45	P<0.0001, S	10.66	P<0.0001, S
DM Vs Normal	0.550	P=0.241, NS	1.57	P=0.216, NS	4.24	P<0.0001, S

Systolic blood pressure & diastolic blood pressure had significant difference among group comparison (P<0.0001).

Table 3: Comparison of Mean SBP & DBP in Groups

Characteristics	MetS (group 1)	DM (group 2)	Normal(group3)	P-value
SBP	140.12 ± 11.39	135.32 ± 10.70	121.76 ± 7.13	P<0.0001, S
DBP	82.88 ± 9.378	79.50 ± 9.217	76.08 ± 4.313	P<0.0001, S

The mean difference between SBP & DBP of metabolic syndrome group and Diabetes mellitus (DM) group is statistically significant. The mean difference of SBP &DBP between MetS group & Normal group is statistically significant. The mean difference of SBP between DM group and Normal group is statistically significant.

Table 4: Comparison of Mean Difference of SBP & DBP two Groups

Groups	Mean Difference of GGT		Mean Difference of AST	
	Mean Difference	p-value	Mean Difference	p-value
METs Vs DM	5.07	P=0.001, S	3.14	P=0.122, NS
METs Vs Normal	27.14	P<0.0001, S	2.98	P=0.149, NS

The mean serum uric acid, fasting & PP Blood glucose had significant difference among group comparison (P<0.0001).

Table 5: serum uric acid, fasting & PP Blood glucose comparison

Characteristics	MetS (group 1)	DM (group 2)	Normal(group 3)	P-value
Mean serum uric acid (SUA)	5.99 ± 0.46	5.64 ± 1.01	4.47 ± 0.63	P<0.0001 S
Fasting blood glucose (mg/dL)	185.06 ± 12.31	177.10 ± 18.64	91.50 ± 14.38	P<0.0001 S
PP Blood glucose (mg/dl)	240.78 ± 34.517	108.32 ± 24.833	123.48 ± 11.174	P<0.0001 S

The comparison of Mean difference in SUA in groups is done by Tukey Post Hoc Test. The mean difference between SUA of MetS group and DM group is statistically nonsignificant. The mean difference of SUA levels between METs group and normal is statistically Significant. The mean difference of SUA between DM group and normal is statistically Significant .

The mean difference between FBG & PP BG of MetS group and DM group is statistically significant. The mean difference of fasting & post prandial blood glucose levels between MetS group & Normal group is statistically significant. The mean difference of Fasting & Post prandial Blood glucose levels between DM group and Normal group is statistically Significant.

Table 6: Comparison of serum uric acid, fasting & PP Blood glucose in two Groups

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Groups	Mean Difference of SUA		fasting blood glucose (mg/dL)		PP Blood glucose(mg/dl)	
	Mean Difference	p-value	Mean Difference	p-value	Mean Difference	p-value
METs Vs DM	0.35	P=0.047, S	7.96	P=0.028 S	132.46	P=0.047 S
METs Vs Normal	1.52	P<0.0001, S	93.56	P<0.0001 S	117.3	P<0.0001 S
DM Vs Normal	1.17	P<0.0001, S	85.60	P<0.0001 S	15.16	P=0.009 S

Mean VLDL was comparable among three groups, while mean total cholesterol, triglyceride, HDL & LDL had significant difference among group comparison (P<0.0001).

Table 7: Comparison of lipid profile in Groups

Characteristics	MetS (group 1)	DM (group 2)	Normal(group 3)	P-value
Mean TC	209.14 ± 12.84	177.10 ± 18.64	100.20 ± 12.47	P<0.0001, S
Mean TG	125.46 ± 26.76	108.32 ± 24.83	173.56 ± 20.03	P<0.0001, S
Mean HDL	43.38 ± 8.214	47.10 ± 12.122	49.48 ± 12.104	P=0.020, S
Mean LDL	138.87 ± 16.28	107.04 ± 20.51	98.04 ± 22.95	P=0.020, S
Mean VLDL	24.78 ± 5.57	21.74 ± 4.45	21.38 ± 11.40	P=0.059, NS

The mean difference between TC of MetS group and DM group is statistically significant. The mean difference of TC levels between METs group and normal is statistically significant. The mean difference of TC between DM group and normal is statistically Significant.

The mean difference between TG of MetS group and DM group is statistically significant. The mean difference of TG levels between METs group and normal is statistically significant. The mean difference of TG between DM group and normal is statistically significant.

Table 8: Comparison of total cholesterol & triglyceride in two Groups

Groups	Mean Difference of TC		Mean Difference of TG	
	Mean Difference	p-value	Mean Difference	p-value
METs Vs DM	32.04	P<0.0001 S	17.14	P=0.001, S
METs Vs Normal	108.94	P<0.0001 S	48.10	P<0.0001, S
DM Vs Normal	76.90	P<0.0001 S	65.24	P<0.0001, S

The mean difference between serum HDL of MetS group and DM group is statistically significant. The mean difference of HDL between MetS group & Normal group is statistically significant. The mean difference of HDL between DM group and Normal group is statistically nonsignificant.

The mean difference between serum VLDL of MetS group and DM group is statistically nonsignificant. The mean difference of VLDL between Metabolic syndrome group & Normal group is statistically nonsignificant. The mean difference of VLDL between DM group and Normal group is statistically nonsignificant.

The mean difference between serum LDL of MetS group and DM group is statistically significant. The mean difference of LDL between MetS group and normal group is statistically significant. The mean difference of serum LDL between DM group and Normal group is statistically nonsignificant.

Table 9: Comparison of HDL, LDL & VLDL in two Groups

Groups	Mean Difference of HDL	Mean Difference of LDL	Mean Difference of VLDL

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	Mean Difference	p-value	Mean Difference	p-value	Mean Difference	p-value
METs Vs DM	3.72	P=0.210, NS	31.82	P<0.0001, S	3.03	P=0.128, NS
METs Vs Normal	6.10	P=0.017, S	40.83	P<0.0001, S	3.40	P=0.076, NS
DM Vs Normal	2.38	P=525, NS	6.01	P=0.065, NS	0.37	P=0.970, NS

DISCUSSION

Metabolic Syndrome is an aggregate of metabolic conditions that together increases the risk of developing cardiovascular disease and Type 2 diabetes. Metabolic syndrome is a cluster of interrelated conditions characterized by dyslipidemia, hyperglycemia, high blood pressure and abdominal obesity. Some studies have reported that metabolic syndrome and its individual components are associated with serum GGT and Uric acid levels. Metabolic syndrome has insulin resistance which confers an increased risk of DM type 2. Apart from that, individuals with metabolic syndrome are susceptible to other conditions like fatty liver, asthma, cholesterol gallstones , polycystic ovary syndrome.

Several studies reported oxidative stress caused by the overproduction of reactive oxygen species (ROS) plays an important role in the development of MetS and in appearance of individual components, including obesity, systemic arterial hypertension (SAH), atherosclerosis, and type 2 diabetes (T2DM).[7] Any imbalance between the increase of oxidative stress and bodily antioxidant defenses can lead to metabolic changes and changes in cell signalling.[8]

In MS, the pro-oxidative state may impair insulin signal pathway and lead to damage to the endothelium. Thus, we can observe that this condition causes insulin resistance and promotes acceleration of the atherogenic process.[8,9] The increased oxidative stress associated with insulin resistance appears to be a major cause of accelerated atherosclerosis and also may lead to development of T2DM.[10]

In our cross sectional study, Serum Uric Acid (SUA) levels were significantly increased in metabolic syndrome group than diabetic overweight and normal overweight group. P value <0.0001. Serum SUA levels were significantly higher in diabetic overweight group as compared to normal overweight group. P value <0.0001.

Soltani Z et al.,[11] in their study found that serum uric acid plays a potential role in metabolic syndrome, kidney injury and cardiovascular events. There is a significant increase in uric acid levels in metabolic syndrome patients, p value <0.0001. Hyperuricemia has been attributed to hyperinsulinemia in metabolic syndrome.

Laura Billiet et al.,[12] in their cross-sectional population-based study found uric acid is involved in systemic inflammation and is commonly a part of cluster of metabolic disorders including abdominal obesity, dyslipidaemia, hypertension and impaired fasting glucose.

Arrigo Fransisco et al.,[13] in their studies reported a positive correlation between hyperuricemia and metabolic syndrome (MetS) in adults, which hyperuricemic subjects seem to more easily develop. We aimed to verify if serum uric acid (SUA) concentrations were positively associated with MetS prevalence and middle-term (4-year) incidence in older overall healthy subjects.

Hai-Lun Sun et al.,[14] conducted a study to assess association of serum uric acid in metabolic syndrome and diabetes patients. They found that serum uric acid levels are not high in all metabolic syndrome patients in group. Similarly, uric acid levels were not significantly higher in diabetes patients.

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Uric acid showed a statistically significant positive correlations with waist circumference, hip circumference, BMI, serum GGT, Triglycerides, LDL, and Fasting glucose levels in metabolic syndrome group. HDL values are lower in metabolic syndrome cases compared to Diabetic group & control groups which has statistically highly significant p value. Triglycerides and uric acid levels are slightly higher in metabolic syndrome cases compared to diabetic group; it has a statistical significance. Triglycerides and uric acid levels are slightly higher in MetS cases compared to normal group; it has a statistical significance.

As a whole we have noticed certain shortcoming of our study:

1. The sample size of our study was relatively small. Selection of outpatient department patients from institute may have increased the number of co morbidities in our study population.
2. Our study was cross sectional study so the direction of association cannot be ascertained and no casual interference can be made amongst the factors under consideration.
3. It is also possible that there is residual confounding from other variables that were included in the study analysis and unmeasured confounding from variables that were not evaluated in this study.

CONCLUSION

Serum uric acid levels were significantly increased in Metabolic syndrome patients. Serum uric acid showed as oxidative stress markers in patients of metabolic syndrome. Serum uric acid showed a positive correlation with the waist circumference, body mass index, blood pressures both systolic & diastolic, Fasting blood glucose levels, Alanine transferase, Alkaline Phosphatase & Triglycerides in Metabolic syndrome patients.

Conflict of Interest: None to declare
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