Original Research Article

Study of uric acid in metabolic syndrome and it's correlation with individual components of metabolic syndrome

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Abstract

Aim: This study was designed to determine levels of serum uric acid (SUA) in patients of metabolic syndrome (MetS) and its correlation with individual components of MetS. **Material and Methods:** This was cross sectional study which included 75 cases of MetS and 50 controls. 75 cases were further divided in to 3 groups depending up on the number of components of MetS. Anthropometric parameters like height, weight, BMI (body mass index), Waist circumference (WC) were measured. Fasting blood sugar (FBS), serum total cholesterol (TC), serum triglycerides (TG), serum HDL (high density lipoprotein), LDL (low density lipoprotein), VLDL (very low density lipoprotein), systolic and diastolic blood pressure (SBP, DBP) and SUA were measured in each individual. And their correlations with each other were studied. **Results:** SUA was significantly increased in MetS patients than in controls. Level of serum SUA was increased with increase in components of MetS. SUA was positively correlated with WC, TG, SBP and DBP and negatively correlated with HDL. SUA was not correlated with FBS. **Conclusion:** SUA is significantly increased in MetS patients and it is significantly correlated with WC, TG, HDL, SBP and DBP.
Key Word: Metabolic syndrome, Serum Uric Acid, cardiovascular risk.

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INTRODUCTION

The metabolic syndrome (MetS) is characterised by abdominal obesity, dyslipidemia, elevated blood pressure and elevated plasma glucose. Dyslipidemia in MetS includes elevated triglycerides (TG), small dense low density lipoprotein particle (sdLDL) and low high density lipoprotein (HDL) cholesterol concentrations. Abdominal obesity and insulin resistance are the most important underlying risk factors of MetS[1]. Prevalence of MetS in Indian population is 29% in women and 23% in men[2]. It has been shown that significant correlations exist between SUA concentration, obesity and insulin resistance[3]. Relationship between SUA levels and MetS may be secondary to obesity, insulin resistance, and dyslipidemia[4]. Hyperinsulinemia and insulin resistance causes increased urate production as well as decreased renal urate excretion which leads to elevated SUA levels. It may probably due to the stimulating effect of insulin on urate reabsorption in the renal proximal tubule. Though uric acid makes significant contribution to serum antioxidant capacity, its raised levels paradoxically may lead to hypertension, endothelial dysfunction, platelet aggregation, thrombus formation, oxidative stress and lipid peroxidation. Asymptomatic Hyperuricemia is a strong predictor of future risk of Type 2 Diabetes Mellitus, hypertension and Cardiovascular Disease[5].Component of metabolic syndrome are closely associated with risk factors defined for cardiovascular diseases[6]. SUA seems inextricably linked to hypertension, dyslipidemia and disordered glucose metabolism, which

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play a causal role in the pathogenesis of cardiovascular disease. As such, SUA may be merely a marker of risk for cardiovascular disease[7, 8]. Several studies have shown that SUA level is associated with components of MetS[9]. The goal behind our study was to determine correlation of SUA with individual components of MetS.

MATERIALS AND METHODS

It was a Cross Sectional Study carried out in Government Medical College and Hospital, Aurangabad during period from January 2015 to July 2016. After written and informed consent, total 75 cases who met the criteria for MetS defined as per modified National Cholesterol Education Program (NCEP) adult treatment panel (ATPIII) between the age group 18 to 50 years were selected. Depending upon 5 components of MetS these 75 cases were further divided into 3 groups. Group 2 had 25 patients with any 3 components of MetS, group 3 had 25 patients with any 4 components of Mets and group 4 had 25 patients with all 5 components of MetS. Cases of MetS were compared with 50 apparently healthy controls which were included in group 1. Sample size is calculated using open EPI software. Participants were selected on the basis of detailed history, clinical examination and laboratory investigations. Detailed history of participants including age, sex and history of any medications, addictions and dietary habits was taken. Height, weight, BMI, waist circumference (cm) and blood pressure were measured in all participants. According to NCEP ATP III criteria a case of MetS is defined as having three or more of the following abnormalities 1) Waist circumference >90cm for men, >80cm for women (For Asians), 2) Serum Triglycerides >150mg/dl, 3) HDL Cholesterol <40mg/dl in men,<50mg/dl in women, 4) Fasting blood glucose >100mg/dl,5) Blood pressure >130/85 mmHg[1]. Permission of the institutional ethical committee was sought prior to the study.

Biochemical assessment

10 hour fasting venous blood samples were collected from all participants in Fluoride (2cc) and plain bulbs (4cc). Serum was separated after 1 hour by centrifugation at 3000 rpm for 10 minutes, and was tested for following parameters. Quantitative estimation of Uric Acid was done by Uricase end point method using kits from Accurex diagnostics, TC was done by Cholesterol Oxidase Peroxidase method (CHOD-POD), TG was done by Lipase/ Glycerokinase/ Glycerophosphate oxidase (GPO) method using commercial kits from Accurex diagnostics and HDL was estimated by Modified Polyvinyl Sulfonic Acid and Polyethylene Glycol Methyl Ether coupled classic precipitation method using commercial kits from ERBA diagnostics on fully automated biochemistry analyzer. Quantitative estimation of blood glucose was done by GOD-POD (Glucose Oxidase Peroxidase) method on semiautomatic chemistry analyzer. Serum VLDL and LDL were calculated by Friedewalds formula.

Statistical Analysis

The results were analyzed by Graph pad prism software, version 5. The results were interpreted as mean ± S.D. One-way analysis of variance (ANOVA test) was applied for comparing between groups and correlation coefficients were calculated (r value). P value was obtained from ANNOVA test and < 0.05 was considered statistically significant. Positive and negative r values were estimated to find out strength of correlation. These r values were interpreted as follows: r = 0 (no correlation), r = 0 - 0.3 (poor correlation), r = 0.3 - 0.7 (considerable correlation) and r = 0.8 or more (strong correlation).

OBSERVATIONS and RESULTS

Table 1: Demographic Characters in studied groups

Parameter	Group 1 (n = 50)	Group 2 (n = 25)	Group 3 (n = 25)	Group4 (n = 25)	p value
	Mean ± SD				
Age (years)	43.18±5.18	41.64± 5.61	42.80±5.78	42.96±5.21	0.703
Weight (kg)	63.99±6.98	77.08± 3.63	80.92±5.10	83.60 ± 4.45	<0.0001**
Height (m)	1.62 ± 0.06	1.60 ± 0.03	1.61 ± 0.04	1.61 ± 0.04	0.267
BMI (kg/m^2)	24.30±2.53	30.09± 2.05	31.28±1.95	32.17±1.24	<0.0001**
WC (cm)	77.46±4.62	91.88± 8.79	96.84±8.18	103.88±6.07	<0.0001**

**: highly significant p value

Table 1 represents demographic characteristic of Group 1, Group 2, Group 3 and Group 4. There is significant difference in weight, BMI, waist circumference in studied groups.

Table 2: Clinical and Biochemical parameters in studied groups

Parameter	Group 1 (n = 50)	Group 2 (n = 25)	Group 3 (n = 25)	Group4 (n = 25)	p value
			Mean ± SD		
SBP(mmHg)	117.0 ± 6.54	129.28 ± 13.53	134.08 ± 10.08	144.96 ± 6.56	<0.0001**
DBP(mmHg)	75.00 ± 4.85	81.20 ± 9.43	88.88 ± 7.00	93.12 ± 4.36	<0.0001**
FBS(mg/dl)	87.70 ± 6.90	119.84 ± 16.63	124.04 ± 22.67	146.72 ± 17.66	<0.0001**
Uric Acid(mg/dl)	4.82 ± 1.11 M=4.95±1.25 F=4.66±0.91	6.58 ± 0.45 M=6.65 ± 0.49 F=6.47 ± 0.37	6.93 ± 0.51 M=7.11 ± 0.43 F=6.71 ± 0.54	8.47 ± 0.53 M=8.51 ± 0.63 F=8.42 ± 0.41	<0.0001**
TC(mg/dl)	163.92 ± 13.56	178.68 ± 16.53	184.48 ± 22.11	203.24 ± 30.10	<0.0001**
TG(mg/dl)	122.34 ± 14.39	162.88± 16.55	181.24 ± 19.25	218.60 ± 47.67	<0.0001**
HDL(mg/dl)	50.86 ± 6.66	46.56 ± 9.18	37.84 ± 8.19	33.96 ± 9.60	<0.0001**
VLDL(mg/dl)	24.04 ± 2.86	32.32 ± 3.42	36.12 ± 3.88	43.48 ± 9.60	<0.0001**
LDL(mg/dl)	89.02 ± 13.39	99.80 ± 18.25	110.52 ± 20.58	125.80 ± 27.27	<0.0001**

**: highly significant p value

Table 2 presents SUA and other biochemical parameters in studied groups. There is significant difference in SBP, DBP, FBS, CysC, TC, TG, HDL, VLDL and LDL in studied groups. The mean value of SUA is significantly higher in cases of MetS than in controls (p value <0.0001) and it is significantly higher in group 3 as compare to group 2 and in group 4 as compared to group 3 (p value<0.0001). So as the components of metabolic syndrome increases the mean value of SUA increases.

Table 3: Correlation of Uric Acid with individual component of MetS in cases:

Parameters	Group 2 (r value)	Group 3 (r value)	Group 4 (r value)	P value
WC (cm)	0.582	0.619	0.701	< 0.05*
SBP(mmHg)	0.475	0.491	0.538	< 0.05*
DBP(mmHg)	0441	0.483	0.482	< 0.05*
FBS(mg/dl)	-0.031`	0.013	0.048	0.285
TG(mg/dl)	0.442	0.525	0.573	< 0.05*
HDL(mg/dl)	-0.411	-0.439	-0.524	< 0.05*

*: significant p value

As per **table 3**, SUA is positively correlated with WC, SBP, DBP and TG (p=<0.05) and negatively correlated with HDL (p=<0.05) which are statistically significant. SUA is not associated with FBS.

DISCUSSION

In present study we found that Uric Acid was significantly increased in MetS patients than in controls. There was increase in SUA concentration as components of MetS increases. Studies supporting our results are study by Madani MK et al in their study found that those with metabolic syndrome had higher serum UA levels than those without metabolic syndrome[10]. Cai Z et al in their study found that serum uric acid levels were significantly higher in subjects with the MetS than that in healthy subjects. They also found that an increased serum uric acid concentration is associated with a cluster of the MetS components[11]. Hyperinsulinemia in subjects with MetS decreases renal excretion of SUA that contribute to hyperuricemia[12]. Insulin may enhance renal urate reabsorption via stimulation of the urate-anion exchanger URAT1[13], and/or the Na dependent anion co-transporter in brush border membranes of the renal proximal tubule[14]. In the metabolic syndrome, impaired oxidative phosphorylation may increase systemic adenosine concentrations by increasing the intracellular concentrations of coenzyme A esters of long-chain fatty acids[14]. Increased adenosine can result in renal retention of sodium, urate, and water. Some have speculated that chronically increased extracellular adenosine concentrations may also contribute to hyperuricemia by increasing urate production[15]. Recent studies indicate that hyperuricemia may be partially responsible for the proinflammatory endocrine imbalance in the vascular smooth muscle cells and adipose tissue, which is an underlying mechanism of the low-grade inflammation and insulin resistance in subjects with MetS[16]. We found positive correlation of UA with WC and TG and negatively correlated with HDL. Numata T. et al in their study found that the presence of abdominal obesity and dyslipidemia in men and abdominal obesity in women revealed positive impacts on uric acid levels[17]. Lin S D et al in their study found that serum UA level associated with WC, TG and HDL[9]. Insulin resistance is associated with higher TG[18], WC[19, 20] and lower HDL-C[18]. The elevated UA level in our subjects who had abnormal TG, WC and HDL-C was due to concomitant higher insulin

resistance[9]. In addition TG synthesis accelerates the de novo synthesis of ribose-5-phosphate to phosphoribosyl pyrophosphate (PPRP) through the common metabolic pathway of NADP-NADPH, and as a result, uric acid production increases[21]. In present study UA was positively correlated with SBP and DBP. Study supporting our results is study by Kanellis J. et al showed association of higher UA with higher BP. UA may contribute to endothelial dysfunction and may play a causal role in the pathogenesis of hypertension[22]. Hyperuricemia can be the consequence of increased uric acid production or decreased excretion[23]. The mechanism by which uric acid causes metabolic diseases may involve a reduction in the concentrations of endothelial nitric oxide (eNO). Uric acid potently reduces the concentrations of endothelial nitric oxide in vitro and in vivo in experimental animals. In turn, a reduction in endothelial nitric oxide predisposes animals to develop features of the metabolic syndrome. Hyperuricemia in humans is also strongly associated with endothelial dysfunction[24]. Several potential mechanisms may explain how an impaired production of endothelial nitric oxide results in features of the metabolic syndrome. The endothelium is an elegant symphony responsible for the synthesis and secretion of several biologically active molecules. It is responsible for regulation of vascular tone, inflammation, lipid metabolism, vessel growth, arterial vessel wall and modulation of coagulation and fibrinolysis. The healthy endothelium is a net producer of endothelial nitric oxide (eNO). The activated, dysfunctional endothelium is a net producer of superoxide ($O2^{-}$) associated with the MetS, type 2 diabetes mellitus, and cardiovascular diseases[23]. In present study SUA is not related to FBS, which is supported by Lin S D et al who found that SUA is not significantly related to FBS[9]. Our results are supported by Woo J et al who found serum uric acid concentration was positively associated with central obesity, SBP, DBP and TG and negatively associated with HDL[24].Our study has certain limitations like the sample size of our study was relatively small. Selection of a clinic cohort may have increased the number of co morbidities in our study population. This 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.

CONCLUSION

Serum UA is significantly correlated with individual components of MetS except fasting blood glucose. UA showed strongest positive correlation with waist circumference.

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