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ROLE OF URIC ACID IN METABOLIC SYNDROME

General Medicine

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ABSTRACT

Introduction: Metabolic syndrome is a clustering of medical conditions. Evaluation of biochemical markers like Uric acid to predict an early onset of metabolic syndrome along with lifestyle changes to reduce cardiovascular morbidity and mortality.
Aims and Objectives: Assessment of role of Uric acid as a marker and its sensitivity & specificity in diagnosis of metabolic syndrome
Materials and Methods: A hospital based cross sectional study conducted on 200 subjects at MBGH, Udaipur.
Results: Out of 200 subjects,100 cases of metabolic syndrome and 100 age and sex matched control. Among cases, 61 out of 100 had UA values above normal. UA values were compared with respective parameters of metabolic syndrome. In 20 out of 25 CVD patients, higher levels of UA were noted.
Conclusion: Elevated levels of UA were found to be associated with metabolic syndrome and is strong predictor of cardiovascular risk and hence the role of primary prevention.

KEYWORDS

Metabolic Syndrome, Uric Acid (UA), Cardiovascular Disease (CVD).

INTRODUCTION

Metabolic syndrome, sometimes known by other names such as Syndrome X, insulin resistant syndrome, is a clustering of at least three of the five following medical conditions: central obesity, high blood pressure, high blood sugar, high serum triglycerides, and low serum high-density lipoprotein (HDL)[1]. Insulin resistance, metabolic syndrome, and prediabetes are closely related to one another and have overlapping aspects.

The criteria for metabolic syndrome have evolved since the original definition by the World Health Organization in 1998, reflecting growing clinical evidence and analysis by a variety of consensus conferences and professional organizations.

The rise in the prevalence of obesity in India is threatening to increase the burden of atherosclerotic cardiovascular disease (ASCVD)[2,3]. The prevalence of metabolic syndrome worldwide is 20-25% (IDF). Among the complications, cardiovascular events produce the greatest morbidity and mortality. Others include dyslipidaemia, hypertension, systemic inflammation, and a thrombotic tendency.

Recently there has been a trend in the cardiovascular field to group all these factors together under the heading of metabolic syndrome. This syndrome does not include, but is strongly associated with other complications of obesity, for example, fatty liver, cholesterol gallstones, obstructive sleep apnoea and polycystic ovarian syndrome.[4]

There has been a consistent effort to evaluate biochemical markers to predict an early onset of metabolic syndrome and subsequently intervene appropriately by means of lifestyle changes and drug therapy and thereby reduce cardiovascular morbidity and mortality. Studies are lacking among the adult Indian population.

Markers like adiponectin have been studied as a measure of increased adipose tissue but have not proven to be cost effective and easily available. Clearly a prompt, cost effective and easily available biochemical marker in required to predict an early onset of this syndrome. Uric acid is one such marker which is cost effective, easily available and performed as part of renal function tests.[5]

Elevated serum uric acid (SUA) levels often exist in patients with metabolic syndrome, and cross-sectional studies among various ethnic groups have shown that the prevalence of metabolic syndrome increases with increasing SUA levels. However, strong inter-correlations among the SUA and variables of metabolic syndrome included in diagnostic criteria make it difficult to determine whether an elevated SUA level is an additional active component of metabolic syndrome or just an associative link to metabolic syndrome or its components. Therefore, this study will determine the association between scrum uric acid levels and various components of metabolic syndrome.

The purpose of this study is to evaluate the utility URIC ACID as early diagnostic marker of metabolic syndrome.

AIMS AND OBJECTIVES

1. To assess the role of Uric acid as a marker in the diagnosis of metabolic syndrome.
2. To assess the sensitivity and specificity of Uric acid in the diagnosis of metabolic syndrome.

MATERIALS AND METHODS

This was hospital based cross sectional study was conducted on subjects who attended the Medicine Outpatient and Inpatient services (OPD and IPD) at MBGH, Udaipur. In our study, total 200 subjects were recruited comprising 100 cases of metabolic syndrome and 100 age and sex matched control (who were not fulfilling criteria of metabolic syndrome). The detailed clinical history, demographic profile, socioeconomic status, contact number and consent were taken and recorded. General physical examination as well as relevant systemic examination was done. Relevant investigations (LFT, RFT including URIC ACID, fasting lipid profile, fasting and post prandial plasma glucose, thyroid profile, USG abdomen) were done. All the collected informations were filled in predesigned proforma for final analysis.

INCLUSION CRITERIA

1. Patients aged above 18 years
2. Central obesity is defined as waist circumference ≥90cm for men and ≥80 cm for Women (Indian population)

Plus any two of the following four factors -

- Raised TG level ≥150 mg/dl or specific treatment for this lipid abnormality
- Reduced HDL cholesterol ≤40 mg/dl or specific treatment for this lipid abnormality
- Raised BP systolic ≥130 and diastolic ≥85 or treatment for previously diagnosed hypertension.
- Raised FPG ≥100 mg/dl or previously diagnosed type 2 DM

EXCLUSION CRITERIA

1. Hypothyroidism
2. Malignant diseases
3. Renal insufficiency.
4. Acute and chronic liver disease
5. Chronic alcohol consumption
6. Drugs (antiepileptics, oral contraceptive pills, erythromycin, cimetidine etc.)

Statistical Analysis

Data entered in M S excel and analysed using SSPS Version The result for each parameter (number and percentage) for discreate data and average (mean ± SD) for continuous data are presented in tables and figures.

1. Proportions were compared using Chi-square test of significance
2. Student 't' test was used to determine whether there was a statistical difference between study groups in parameter measured In all the above test, p value 0f less than 0.05 was accepted as indicating statistical significance. Data analysis was carried out using Statistical Package for Social Science (SPSS) package.

OBSERVATIONS

The mean duration of diabetes was 5.25±4.27 years in cases and 1.04±2.19 years in control group. The mean duration of hypertension was 4.58±4.73 years in cases and 1.03±2.1 years in control group. The mean duration of dyslipidaemia was 5.19±3.76 years in cases and 0.68±1.74 years in control group.

Among cases 55% had SBP above 130 mmHg and 83% had DBP above 80 mmHg. The value of both SBP and DBP among cases were highly significant.

The values of HbA1c, TG, LDL and fasting blood glucose were highly significant among cases.

Table 1: Serum uric acid levels in study population

Uric Acid (mg/dl)	Cases		Controls		Chi- Square value	P VALUE
	No.	%	No.	%		
<7.2/6	39	39	89	89	54.25	<0.001 (HS)
≥7.2/6	61	61	11	11		

Table 2: Serum uric acid levels in study population (Upper limit of Normal)

Uric Acid (mg/dl)	Cases		Controls		Chi- Square value	P VALUE
	No.	%	No.	%		
<6/5	21	21	63	63	36.20	<0.001 (HS)
≥6/5	79	79	37	37		

Reference range for normal values at MBGH, Udaipur:
Male: 3.5-7.2 mg/dl
Female: 2.6-6.0 mg/dl

Among cases, 61% had serum uric acid values above normal while only 11 % of control had high values. These values are highly significant.

Out of 55 patients with SBP > 130mmHg, 37 had UA level above the reference range comprising 37% of study population.

Table 3: Comparison and correlation of serum uric acid with HDL cholesterol, serum triglyceride and fasting blood glucose

		Uric Acid(mg/dl)				Chi-Square value	P VALUE
		<7.2/6 (n=39)		≥7.2/6 (n=61)			
		No.	%	No.	%		
HDL Cholesterol (mg/dl)	<40/50	19	48.72	41	62.21	3.391	0.006 (NS)
	≥40/50	20	51.28	20	32.79		
Triglyceride mg/dl	≤150	12	30.77	8	13.11	4.634	0.031 (NS)
	>150	27	69.23	53	86.89		
Blood Glucose Level	<100	11	28.21	14	22.95	0.350	0.554 (NS)
	≥100	28	71.79	47	77.05		

Table 4: Correlation of serum uric acid with cardio-vascular disease

		Uric Acid(mg/dl)				Chi- Square value	P VALUE
		<7.2/6 (n=39)		≥7.2/6 (n=61)			
		No.	%	No.	%		
Cardiovascular disease	No	34	87.18	41	67.21	5.05	0.025 (S)
	Yes	5	12.82	20	32.79		

Incidence of cardiovascular disease in cases with high serum URIC ACID levels was statistically significant.

Table 5: Sensitivity and specificity of serum uric acid in diagnosis of metabolic syndrome

Uric Acid Level	Patients with metabolic syndrome	Patients without metabolic syndrome	Total
Positive	61	11	72
Negative	39	8	128
Total	100	100	200

Sensitivity = 88.24%
Specificity = 95.83%

DISCUSSSION

The clustering of CVD risk factors that typifies metabolic syndrome is now considered to be the driving force behind a CVD epidemic. A need for early diagnosis of metabolic syndrome is essential to prevent and decrease mortality and morbidity due to cardiovascular disease. Studies are lacking in adult Indian population.

In our study, total 200 subjects were recruited comprising 100 cases of metabolic syndrome and 100 age and sex matched control. The mean age in study group was 58.2±10.35 and 58.17±10.34 in control group. Patient in this study group were found to be clustered in sixth decade of life with 37% belonging to this category. There were 49% males and 51% females in study group whereas 52% males and 48% females in control group.

Similar study done by B Kasapgolu et al[5], the mean age was 51.3±3.2 and gender distribution showed 62% females and 38% male in study group. This difference may suggest an equal incidence of metabolic syndrome in both sexes in Indian sub-continent.

The mean duration of diabetes was 5.25±4.27 in cases and 1.04±2.19 in control group. A total 75 out of 100 cases (75%) satisfied the IDF criteria of FPG>100mg/dl inferring impaired fasting glucose or type2 diabetes. These observations suggest a high prevalence of type 2 diabetes in patients with metabolic syndrome.

The mean duration of hypertension was 4.58±4.73 in cases and 1.03±2.1 in control group. The mean systolic blood pressure in cases was 134.8±14.2 and 121.7±8.5 in control group. A total 55 out of 100 patients (55%) satisfied the IDF criteria of SBP>130mmHg. The observations suggest that elevated systolic and diastolic blood pressure is an important contributing factor in metabolic syndrome.

In the reference study done by B Kasapgolu et al[5], similar results were found; mean SBP and DBP being 138.2±11.7 and 86.7±7.2 respectively.

The mean duration of dyslipidaemia was 5.19±3.76 in cases and 0.68±1.74 in control group. A total 80 out of 100 cases had TG>150 mg/dl including 39 males and 41 females. A total 76 out of 100 cases had HDL<40 for males and <50 for females. A total 53 out of 100 cases had LDL>100 mg/dl. The values of TG, HDL and LDL cholesterol were highly significant among cases. Hypertriglyceridemia was found in maximum number of cases in study group and predominant dyslipedemic abnormality.

The values in our study group with respect to lipid profile were lower than the reference study done by B Kasapgolu et al[5], where in mean TG was 273.8±25.2, LDL was 131.4±8.9 and HDL was 42.1±9.7. This difference may suggest variation in diet and familial metabolic parameters in particular geographic distributions.

In the evaluation of renal function tests, URIC ACID had the following results. The mean uric acid in study group was 6.89±1.37 and in control group was 5.13±0.98. Among cases, 61 out of 100 (61%) had uric acid

values above normal (males ≥7.2mg/dl and females≥6mg/dl) including 30 males and 31 females (P<0.001). In control group 11 of the subjects had uric acid levels above normal range.

Similar study "Hyperuricemia, Gout and Metabolic syndrome" done by Juan Gracia Puig; Maria Angeles Martinez, the mean uric acid in study group was 5.9mg/dl.

Uric acid values were compared with respective parameters of metabolic syndrome.

Out of 55 patients with SBP > 130mmHg, 37 had UA level above the reference range comprising 37% of study population. This correlation was statistically insignificant in our study. It is inconsistent with the previous studies which describes UA as an independent risk factor for development of hypertension. Reason for this may be small sample size. Further studies are required to find the correlation of UA with SBP.

Out of 80 patients with hypertriglyceridemia, 53 had uric acid level above the reference range comprising 53% of study population. The above observations suggest that uric acid had the highest correlation with hypertriglyceridemia.

Conen et al (2004) and Schachter (2005) showed the same result.[6]

Hyperuricemia and hypertriglyceridemia are suggested to be associated with insulin resistance syndrome. (Tai et al,1999; Bo et al,2001; Bosello and Zamboni,2000).[7]

In another retrospective study done for 2 years from 2005-2007 on 10,181 patients in Italia by Giuseppe Lippi, Martina Montagnana, Giovanni Targher, Gian Luca Salvagno and Gian Cesare Guidi, triglycerides were independently associated with high uric acid levels after adjustment for age and gender.[8]
Among the 61 patients with HDL<40 for males and <50 for females, 41 had UA above the reference range. This finding was not statistically significant.

Tao-Chun Peng et al in Taiwan studied in 2005 that serum HDL-C levels were significantly inversely associated.[9]

Giuseppe Lippi et al (2007) in Italia, UA was negatively correlated with HDL-C.[8]

Among 75 patients with FPG>100mg/dl, 47 had higher UA levels.

Yoo et al (2005) and Becker and jolly (2006) reported that hyperglycaemia was a remarkable risk factor of hyperuricemia.[10'11]

Nakanishi et al, 2003; studied on 3681 Japanese adults, it was found that increase in UA level in males increased the risk of type 2 diabetes.[12]

With respect to burden of cardiovascular disease, 25 out of 100 patients were suffering from CVD, including 10 males and 15 females. In 20 out of 25 patients, higher levels of UA were noted. These values were higher when compared with to study subjects without cardiovascular disease. This may suggest a direct correlation of UA levels with cardiovascular disease with higher values conferring increased CVD risks.

Niskanen et al suggested that UA may be an independent risk factor for cardiovascular disease.[13]

In an article written by Daniel I Feig (published in NEJM in 2008), UA was strongly correlated with cardiovascular risk.[14]

Validity measures were computed taking the reference values of UA≥7.2 in males and ≥6 in females. 61(61%) out of 100 patients had UA levels above normal while 11% in controls had high UA levels. Sensitivity and specificity of UA to diagnose the patients with metabolic syndrome was 88.24% and 95.83%.

An interesting observation noted in study group with respect to UA that most of the subject with level less than 7.2/6 mg/dl were clustered in the upper limit of normal (males>6mg/dl and females >5mg/dl). A total 79 out of 100 patients (79%) had UA values above normal with 18% falling in range of upper limit of normal. This therefore suggests that UA values even in upper limit of normal may have a predictive value in diagnosis patients with metabolic syndrome.

CONCLUSION

This study has critically evaluated the utility of UA as a diagnostic marker of metabolic syndrome. Elevated levels were found to be associated with metabolic syndrome and is strong predictor of cardiovascular risk. UA levels correlated well with all parameters of metabolic syndrome especially with hypertriglyceridemia with which it was the highest. It was also noted that there was a clustering of patients in the range of upper limit of normal values for UA indicating the possible need for considering even such values in context of metabolic syndrome and CVD risk. Considering the CVD risk, primary prevention may be emphasized in patients of metabolic syndrome with high UA values. Hence UA has position in algorithms for evaluation of metabolic syndrome and CVD risk assessment.

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