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Original Article

Association of Hyperuricemia with Metabolic Syndrome

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Abstract

Background: Uric acid levels are often increased in subjects with metabolic syndrome but it is unclear whether it plays a causal role or it is a marker for metabolic syndrome.
Objectives: To find the association of hyperuricemia with various components of metabolic syndrome.
Study type, settings: The cross sectional analytical study was carried out in Sir Ganga Ram Hospital, Lahore, Pakistan.
Subjects and Methods: Total 600 subjects of both genders aged 30-70 years were recruited in the study. Demographic, clinical and biochemical variables were recorded by using a questionnaire. Fasting blood sample was used to estimate plasma glucose, serum lipid profile and uric acid. The cut-off for hyperuricemia was serum uric acid level ≥7.0 mg/dl for males and ≥5.7 mg/dl for females. Metabolic syndrome was diagnosed if subjects had any 3 of the 5 criteria described as per ATP III guidelines. The data was analyzed using SPSS Version 20.
Results: The study included 216 (36%) males and 384 (64%) females with mean age 47±10 years. Out of total 447 subjects, 62 (13.9%) with metabolic syndrome had hyperuricemia. Whereas 62 (75.6%) subjects out of total 82 subjects with hyperuricemia had metabolic syndrome. Different parameters of metabolic syndrome were statistically correlated with hyperuricemia but none showed significant correlation. Chi square and Wald Statistic (Logistic regression algorithm) showed that by using G-to-S (general to specific) approach hyperuricemia was significantly associated with female gender but did not show any association with metabolic syndrome.
Conclusion: There was no association present between metabolic syndrome and hyperuricemia; therefore uric acid levels might not be important in the diagnosis of metabolic syndrome.
Key words: Hyperuricemia, metabolic syndrome, hypertriglyceridemia, LDL-cholesterol, cardiovascular disease, diabetes.

Introduction

Metabolic syndrome (Met S)comprises of general or central adiposity, elevated blood pressure, dyslipidemia, and hyperglycemia. Increased serum uric acid levels have been associated with hypertension[1], diabetes[2], obesity[3], insulin resistance[4], dyslipidemia[5] and cardiovascular diseases.

Previous studies have examined the putative association between serum uric acid levels and the metabolic syndrome[6,7]. Literature from Pakistan is lacking in studies related to association between serum uric acid levels and metabolic syndrome. Hyperuricaemia or elevated serum uric acid level is a biochemical entity that is not only a cardiovascular risk factor but also plays a role in renal and metabolic diseases[8]. Uric acid is the end product of purine metabolism in humans[9]. High plasma uric acid causes gout and is also associated with the metabolic syndrome and is a risk factor for cardiovascular diseases[10,11]. Hyperuricemia occurs in 16% cases dying due to any cause and in 39% due to cardiovascular disease[12]. Increased serum uric acid is associated with an increased prevalence of some of the parameters obesity, dyslipidemia and hypertension which are part of the metabolic syndrome or its components [13,14]. Very little progress on this association has been made in Pakistan. The prevalence of metabolic syndrome in Pakistan according to different definitions varies from 18% to 46% which is comparable to data from other South Asian countries[15]. Pakistan is gaining on the prevalence of metabolic syndrome and there is a need to pay attention to it. The present study was done to determine the frequency of hyperuricemia in metabolic syndrome patients and the association between hyperuricemia and the various metabolic syndrome components in our settings.

Subjects and Methods

This was a cross sectional analytical study. The sample size was estimated by using 5% level of significance and 5% margin of error with expected prevalence of 86.8%. The sample size came as 594, which was rounded off to 600 subjects. Adults aged 30-70 years were selected from the Ganga Ram hospital, Lahore. Recruited subjects were asked to come for lab investigations with 10-12 hours fasting in the hospital. After taking informed consent, demographic information and history of diabetes mellitus, hypertension was taken. All individuals also underwent anthropometric and blood pressure measurements and blood testing. Hyperuricemia was defined as serum uric acid level ≥7 mg/dl (males) or ≥5.7 mg/dl (females) Metabolic syndrome was defined as having ≥3 of the 5 criteria[16] : (i) Waist circumference ≥90 cm (males) , ≥80 cm (females); (ii) Serum triglyceride levels ≥150 mg/dl or on drug treatment for elevated triglycerides; (iii) Serum HDL-C levels <40 mg/dl (males) and <50 mg/dl (females), or on drug treatment for reduced HDL-C; (iv) Systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or on antihypertensive drugs and (v) Fasting blood glucose ≥110 mg/dl.

Waist circumference was measured using a measuring tape in a horizontal plane around abdomen at level of iliac crest. Measurement was made at the end of a normal expiration. Body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Blood pressure was measured in sitting position using a sphygmomanometer after resting for 5 minutes. For those showing a systolic blood pressure ≥140 mmHg and a diastolic blood pressure ≥90 mmHg, blood pressure was measured again on further 2 occasions after resting and average values were taken.

Blood samples (5ml) were collected after an overnight fast and sera were stored in tubes for batch analysis except blood sugar fasting which was analyzed on the same day. Blood glucose level was measured by glucose oxidase method[17]. Serum total cholesterol concentration was determined by enzymatic CHOD-PAP method[18] using reagent kit from Human, Germany. Serum uric acid level was measured by using kit of Human Germany[19]. Serum HDL-cholesterol was measured by precipitation method (HDL-cholesterol precipitant, and cholesterol concentration were determined by enzymatic CHOD-PAP method using reagent kit from Human, Germany)[20]. The LDL cholesterol concentration were calculated according to the Friedewald formula [LDL cholesterol (mg/l) = Total cholesterol - (Triglycerides/5 + HDL Cholesterol)][21]. LDL-C/HDL-C ratios were then calculated. Serum triglycerides concentration was determined by GPO- PAP method using reagent kit from Human Germany[22].

The data was entered and analyzed by using SPSS version 20.0 for Windows (SPSS Inc., Chicago, IL, USA). Age, height, weight, BMI, lipid profile, uric acid and blood sugar were described by using Mean ± S.D. The number of cases with metabolic and without metabolic syndrome were determined as per Adult treatment panel 111 guidelines. Frequency of hyperuricemia was noted in both groups with and without metabolic syndrome. Association of hyperuricemia with metabolic syndrome was described by cross tables using frequencies and percentages. Chi Square analysis was used to determine the association. To see the association of hyperuricemia with metabolic syndrome involving other confounder's, i-e age and gender, backward wald

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Statistic (logistic regression Algorithm) was used. *p*-Value of ≤0.05 was considered statistically significant.

Results

A total of 600 patients were enrolled, of whom 216 (36%) were males and 384 (64%) females. The overall prevalence of hyperuricemia was 82 (13.7%). Sixty two (13.9%) out of total 447 subjects with metabolic syndrome had hyperuricemia. Whereas 62 (75.6%) subjects out of total 82 subjects with hyperuricemia had metabolic syndrome. The prevalence of metabolic syndrome was 447 (74.5%) and out of these 62 (13.9%) had raised serum uric acid level. The mean age of the subjects was 47±10 years. Mean systolic blood pressure and diastolic blood pressure was (134.24±17.0) mmHg, diastolic blood pressure (84.64±10.93) mmHg.

Table 1: Association of the individual components of metabolic syndrome in relation to hyperuricemia with and without metabolic syndrome.

	Met_present (n=447)	*Met_absence (n=153)*	*p-Value*
	Hyperuricemia (n=62)	*Hyperuricemia (n=20)*	
High systolic blood pressure	51	10	0.004*
High diastolic blood pressure	37	6	0.020*
Diabeties	38	5	0.005*
Low HDL	54	6	<0.001*
Obesity	54	15	0.197
Hypertriglycerdemia	45	2	<0.001*

Table 2: Correlation coefficient (r) for individual component of metabolic syndrome in relation with serum uric acid.

Parameter	*Men (n=216)*		*Women (n=384)*	
	r	*p-Value*	*r*	*p-Value*
Waist(cm)	.102	.136	.062	.229
SBP	-.071	.302	.153	.003*
DBP	-.052	.447	.178	<0.001**
BSF	-.173	.011*	-.118	.021*
HDL-cholesterol	.035	.606	.005	.926
Serum triglyceride	.177	<0.001*	.053	.302

Hyperuricemia with and without metabolic syndrome was significantly associated with high blood pressure, diabetes, low HDL and hyper triglycerdemia (Table-1). Systolic and diastolic blood pressure and fasting blood sugar were significantly associated with hyperuricemia in females while only blood sugar fasting showed association in males (Table-2). Although different components of metabolic syndrome appeared to be statistically correlated with hyperuricemia in Table-2 but this significance was low because the correlation coefficient *r* showed a weak strength of association (≤0.178).

Table 3: Association of hyperuricemia in relation to age, gender and metabolic syndrome.

	B	*S.E.*	*Wald*	*Sig.*	*Exp(B)*
Model 1					
MetS present	-0.240	0.290	0.684	0.408	0.787
Gender men	-1.217	0.318	14.660	<0.001*	0.296
Age ≥45	0.225	0.250	0.814	0.367	1.253
Constant	3.933	0.793	24.584	<0.001*	51.063
Model 2					
Gender men	-1.158	0.309	14.083	<0.001*	0.314
age≥45	0.211	0.249	0.719	0.397	1.235
Constant	3.552	0.638	30.970	<0.001*	34.886
Model 3					
Gender men	-1.133	0.307	13.620	<0.001*	0.322
Constant	3.802	0.569	44.704	<0.001*	44.799

Table 4: Predictive status of the logistic model in table-3.

	Prediction		
	Hyperuri-cemic	*Non Hyperuri-cemic*	*% of Correct Hyperuricemia*
Model 1			
Hyperuri-cemic	0	82	0
Non Hyperuri-cemic	0	518	100
Overall percentage			86.33
Model 2			
Hyperuri-cemic	0	82	0
Non Hyperuri-cemic	0	518	100
Overall percentage			86.33
Model 3			
Hyperuri-cemic	0	82	0
Non Hyperuri-cemic	0	518	100
Overall percentage			86.33

Table 5: Association of hyperurecemia with metabolic syndrome.

	Hyperurecemia		*Normal*		*p-Value*
	n	*%*	*n*	*%*	
Age ≥45	51	62.2	310	59.8	0.686
Gender men	14	17.1	202	39.0	<0.001*
Mets present	62	75.6	385	74.3	0.804

Table-3 shows the results of logistic regression. Using general to specific (G-to-S) approach to see the association of hyperuricemia with metabolic syndrome involving other confounders i.e. age and gender in backward wald method. Female gender showed significant association with hyperuricemia (model 3). At step 2 (model 2) metabolic syndrome was removed from the equation while variable age was removed at step 3 (model 3). Results showed that gender was significantly associated with hyperuricemia. Non-hyperuricemia was predicted with 100% accuracy by all the three models while hyperuricemia was not predicted by all the three models and all hyperurecemic were reported as non hyperuricemic (Table-4).

The last optimal model in Table-3 showed that gender along constant was significantly associated with hyperuricemia and the cross table also showed the association of gender with hyperuricemia (Table-5).

Discussion

This study was done to find the association of hyperuricemia with various components of metabolic syndrome. The prevalence of metabolic syndrome was 74.5%. Present study showed correlation between serum uric acid concentration and hypertension, (Systolic BP, diastolic BP) were directly correlated and fasting blood sugar was inversely correlated with serum uric acid level in females while in males only fasting blood sugar showed significant inverse correlation. The association between uric acid levels and each component of metabolic syndrome were in consistent with findings of other study[23], due to the difference in ethnicity and cut-off values. These studies reported that hyperuricemic males were at more risk of hypertension[24,25]. The findings of present study are in agreement with another study suggesting that serum uric acid levels have non-linear relationships with diabetes[24].

The present study showed 13.6% prevalence of hyperuricemia and almost similar results were reported from china (13.10%-13.20%)[26,27]. The results of the logistic regression in the present study showed that by using G-to-S approach in backward wald method hyperuricemia was significantly associated with gender along with constant (model 3 in table 3), metabolic syndrome removed from the equation at step 2 (model 2) while age variable was removed at step 3 (model 3). It was observed that the Non-hyperuricemia was predicted with 100% accuracy by all three models while, hyperuricemia remained unpredictable. Similar lack of association between uric acid and metabolic syndrome were observed in other studies[28].

The results of the present study cannot be generalized for the community because of the limitation of the selection criteria for the targeted population. Further community based studies should be carried out to explore the relationship of hyperuricemia with metabolic syndrome.

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