PREVALENCE OF HYPERURICAEMIA IN PATIENTS WITH METABOLIC SYNDROME AND ITS ASSOCIATION WITH SERUM URIC ACID

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ABSTRACT

BACKGROUND

Metabolic syndrome is an important risk factor for cardiovascular disease and type 2 diabetes mellitus. According to International Diabetes Federation, the risk factor associated with metabolic syndrome are central obesity, hypertension, increased fasting glucose, triglyceride level and decreased HDL. Recent studies also found that hyperuricaemia is also associated with insulin resistance and increased cardiovascular disease related morbidity. A cross-sectional study was conducted at Pondicherry Institute of Medical Sciences with an objective to find the prevalence of hyperuricaemia among patients with metabolic syndrome and also to find the association of risk factor of metabolic syndrome with serum uric acid level.

MATERIALS AND METHODS

103 patients (49 males and 54 females) who fulfilled the inclusion criteria were included in the study. Detailed medical history and physical examination including height, weight, BMI, waist circumference and blood pressure were recorded. Five millilitre of fasting blood sample was taken for lipid profile, serum uric acid and fasting blood glucose. Chi-square test was done to find out the association between metabolic syndrome and risk factors of hyperuricaemia with 'p' value of <0.05 were considered statistically significant. Pearson's correlation was used to assess correlation between variables. Univariate logistic regression was used to calculate regression coefficients and Odd's ratio for risk factors.

RESULTS

Out of 103 participants, 49 were males and 54 were females with mean age of 56.71 ± 11.015 and 54.98 ± 9.78, respectively. The prevalence of hyperuricaemia among males and females were found to be 18.36% and 14.81%, respectively, with overall prevalence of 16.5%. Hyperuricaemia was associated with increased age in males, but not in females. Age, BMI, diastolic blood pressure had very weak positive correlation with hyperuricaemia in both male and female, although they were not statistically significant (p >0.05). Exercise had negative influence on uric acid level in both gender, 41% less in males and 14% less in females. Diet also had positive influence on uric acid levels in both male and female.

CONCLUSION

The prevalence of hyperuricaemia among males is higher than females. The risk factors of metabolic syndrome like obesity, hypertension and increased cholesterol level are associated with hyperuricaemia.

KEYWORDS

Hyperuricaemia, Metabolic Syndrome, Cardiovascular Disease, Type 2 Diabetes Mellitus.

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BACKGROUND

Metabolic syndrome is a group of modifiable risk factors where central obesity and insulin resistance plays an important role along with genetics and physical inactivity.[1,2] Hyperuricaemia plays an important role in development and pathogenesis of gout, renal dysfunction and cardiovascular diseases.[3]

Hyperuricaemia is not only a cardiovascular risk factor, but it also associated with metabolic syndrome.[4] Hyperuricaemia has recently gained attention due to its increased prevalence in developing countries and rarely been investigated in country like India.[5]

Metabolic syndrome is closely associated with type 2 diabetes mellitus. It is stated that people with metabolic syndrome has five fold risk of developing type 2 diabetes mellitus.[6]

The underlying cause of metabolic syndrome is considered to be insulin resistance and central obesity.[7] Obesity contributes to hypertension, high serum cholesterol, low HDL levels and hyperglycaemia and is independently associated with development of coronary artery disease.[8,9]

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As metabolic syndrome is considered as a factor for development of type 2 diabetes mellitus and coronary artery disease, it is becoming increasingly important to identify people having metabolic syndrome so that interventions and treatment can be started early to prevent type 2 diabetes mellitus and coronary artery disease among them.

The rationale behind this study is to find out the prevalence and hyperuricaemia in patients with metabolic syndrome in Indian population and to assess the risk factors for metabolic syndrome and also to find out how much these risk factors influences the level of serum uric acid.

MATERIALS AND METHODS

A cross-sectional study was conducted at Pondicherry Institute of Medical Sciences with objective to find prevalence of hyperuricaemia among patients with metabolic syndrome and also to find the association of serum uric acid level with various risk factors of metabolic syndrome. 103 participants of age more than 18 years who fulfilled the International Diabetes Federation (IDF) criteria of metabolic syndrome that is waist circumference more than 90 cm in males and more than 80 cm in females plus two or more of the following- a. Blood pressure of more than 130/85 mmHg or a known hypertensive on treatment; b. Serum High-Density Lipid (HDL) less than 40 mg/dL and 50 mg/dL in males and females, respectively; c. Serum triglyceride of more than 150 mg/dL or on treatment for hypertriglyceridaemia; and d. Fasting blood glucose of more than 110 mg/dL or a known case of type 2 diabetes mellitus were included in the study.

Patients with chronic kidney disease, gouty arthritis, myeloproliferative disorders and lymphoproliferative disorders, patients on thiazide diuretics, hypothyroidism and pregnancy were excluded from the study.

Detailed medical history along complete physical examination including blood pressure, height, weight, body mass index and waist circumference was recorded with prior consent for all the participants. Five mL of blood was obtained from all the participants after 12 hours of fasting for lipid profile, serum uric acid and fasting blood glucose. All tests were done using the fully automated analyser COBAS INTEGRA 400 plus except for serum uric acid, which was done by Microlab 300, which is a semi-automated analyser. All biochemical tests were done using adequate internal and external quality checks.

Statistical Analysis

Data collected were analysed by using SPSS v. 16.0. Mean and standard deviation was used for continuous variables. Number and percentage were used for categorical variables. Chi-square test was done to find out the association between metabolic syndrome and risk factors of hyperuricaemia with 'p' value of <0.05 was considered statistically significant. Pearson's correlation was used to assess correlation between variables. Univariate logistic regression was used to calculate regression coefficients and Odds ratio for risk factors. Corrections for confounding factors were done using multivariate logistic regression.

Ethical Considerations

Approval from the institutes ethics committee was obtained, informed consent was obtained from all the participants before the data collection.

RESULTS

110 patients presented to medicine outpatient with features of metabolic syndrome, out of which, only 103 patients fulfilled the IDF criteria of metabolic syndrome were included in the study. Out of 103 participants, 49 were males and 54 were females with mean age of 56.71 ± 11.015 and 54.98 ± 9.78, respectively. The prevalence of hyperuricaemia among males and females were found to be 18.36% and 14.81%, respectively with overall prevalence of 16.5%. The risk factor analysis for association with hyperuricaemia revealed that none of them were statistically significant among both males and females (Table 1 and 2). Hyperuricaemia was associated with increased age in males, but not in females.

Age, BMI and diastolic blood pressure had very weak positive correlation with hyperuricaemia in both male and female, although, they were not statistically significant (p >0.05) (Table 3). Other risk factors had no correlation in both males and females (Graph 1).

Regression analysis in males showed that hypertension and antihypertensive medication, BMI and alcohol consumption had increased influence on hyperuricaemia. The influence of age is 27% for the increased uric acid levels in metabolic syndrome. BMI has 77%, consumption of alcohol has 56%, smoking has 18%, diet has 52%, statins has 40% and hypertension and antihypertensive medication has 92% positive influence on the increase of uric acid levels (Table 4).

In females too, BMI and hypertension had increased influence. In women, statins has an influence of 15% for the increased uric acid levels. Diet has 54%, BMI has 83%, hypertension and antihypertensive drugs has a positive influence of 60% on the increase of uric acid levels.

Exercise had negative influence on uric acid level in both the sexes, 41% less in males and 14% less in females. Diet also had positive influence on uric acid levels in both male and female.

Variables	N (49)	Mean Uric Acid Level ± SD	P value
Age			
30-39	14	3.425 ± 0.805	0.534
40-49	11	4.554 ± 1.505	
50-59	16	5.125 ± 1.704	
60 and above	18	4.472 ± 1.890	

BMI			
<18.5	1	3.400 ± 1.767	0.739
18.5-24.9	18	4.333 ± 1.496	
25-29	20	4.520 ± 2.028	
>29.9	10	5.270 ± 1.703	
Systolic BP			
≥130 mmHg	26	4.653 ± 1.628	0.879
<130 mmHg	23	4.578 ± 1.820	
DBP			
≥85 mmHg	27	4.500 ± 1.607	0.595
<85 mmHg	22	4.763 ± 1.839	
Fasting Plasma Glucose			
≥110 mg/dL	19	4.773 ± 1.488	0.671
<110 mg/dL	30	4.520 ± 1.843	
Total Cholesterol			
≥200 mg/dL	12	4.916 ± 1.667	0.491
<200 mg/dL	37	4.521 ± 1.725	
Triglycerides			
≥150 mg/dL	17	4.488 ± 1.480	0.701
<150 mg/dL	32	4.687 ± 1.829	
HDL			
≥40 mg/dL	18	4.705 ± 1.775	0.788
<40 mg/dL	31	4.556 ± 1.687	
On Statins			
Yes	8	5.037 ± 2.198	0.452
No	41	4.536 ± 1.610	
Exercise			
Yes	9	4.122 ± 1.558	0.339
No	40	4.730 ± 1.732	
Diet			
Mixed	44	4.590 ± 1.689	0.742
Veg	5	4.860 ± 2.011	
Alcohol			
Yes	23	4.747 ± 1.728	0.622
No	26	4.503 ± 1.706	
Smoking			
Yes	13	4.930 ± 2.029	0.446
No	36	4.505 ± 1.586	
On Anti-Hypertensive			
Yes	44	4.590 ± 1.689	0.742
No	5	4.860 ± 2.011	

Table 1. Independent t-Test Showing Various Risk Factors of Metabolic Syndrome and its Association with Mean Uric Acid Level in Males (SD- Standard Deviation)

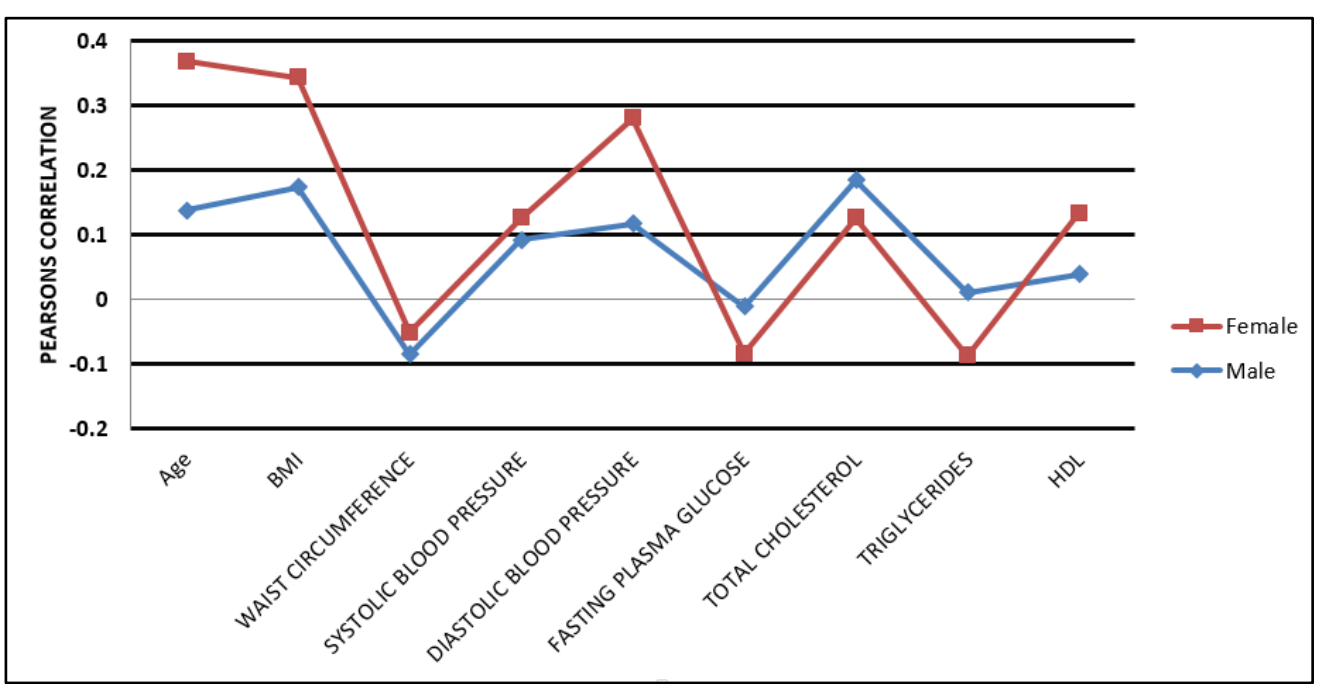
Variables	N	Mean Uric Acid Level ± SD	P Value
Age			
18-29	1	-	0.537
30-39	3	3.433 ± 1.270	
40-49	12	3.716 ± 1.063	
50 and above	38	4.192 ± 1.489	
BMI			
Less than 18.5	3	4.666	0.362
18.5-24.9	32	3.809	
25-29.9	18	4.361	
>30	1	2.800	
Blood Pressure			
SBP ≥130 mmHg	33	3.936 ± 1.426	0.570
<130 mmHg	21	4.157 ± 1.346	
DBP ≥85 mmHg	27	4.125 ± 1.195	0.588
<85 mmHg	27	3.918 ± 1.572	
Fasting Plasma Glucose			
≥110 mg/dL	32	4.112 ± 1.351	0.569
<110 mg/dL	22	3.890 ± 1.460	

Total Cholesterol			
≥200 mg/dL	17	4.123 ± 1.606	0.720
<200 mg/dL	37	3.975 ± 1.296	
Triglycerides			
≥150 mg/dL	12	3.791 ± 1.451	0.519
<150 mg/dL	42	4.088 ± 1.397	
HDL			
≥50 mg/dL	14	4.150 ± 1.590	0.693
<50 mg/dL	40	3.977 ± 1.328	
On Statins			
Yes	10	3.550 ± 0.986	0.237
No	44	4.129 ± 1.450	
On Hypertensives			
Yes	43	4.158 ± 1.439	0.157
No	11	3.490 ± 1.052	
Exercise			
Yes	8	4.187 ± 1.590	0.719
No	46	3.993 ± 1.366	
Diet			
Mixed	48	3.954 ± 1.401	0.312
Veg	6	4.566 ± 1.243	

Table 2. Independent t-Test Showing Various Risk Factors of Metabolic Syndrome and its Association with Mean Uric Acid Level in Females (SD - Standard Deviation)

Variables of Metabolic Syndrome	Male		Female	
	Pearson's Correlation	P Value	Pearson's Correlation	P Value
Age	0.137	0.348	0.230	0.094
BMI	0.173	0.235	0.170	0.903
Waist circumference	-0.086	0.557	0.034	0.809
Systolic blood pressure	0.091	0.593	0.034	0.839
Diastolic blood pressure	0.116	0.429	0.163	0.240
Fasting plasma glucose	-0.012	0.410	-0.072	0.603
Total cholesterol	0.184	0.184	-0.059	0.673
Triglycerides	0.010	0.473	-0.098	0.482
HDL	0.038	0.796	0.095	0.493

Table 3. Pearson's Correlation to Correlate between the Components of Metabolic Syndrome and Uric Acid Level in Males and Females



Graph 1. Pearson's Correlation to Correlate between the Components of Metabolic Syndrome and Uric Acid Level in Males and Females

	Unstandardised Coefficients		Sig.
	B	Std. Error	
Age	0.027	0.029	0.349
BMI	0.77	0.805	0.163
Waist	-0.071	0.044	0.119
SBP	-0.004	0.030	0.900
DBP	0.035	0.053	0.515
FBS	-0.013	0.011	0.247
Cholesterol	0.012	0.009	0.197
Triglyceride	-0.007	0.011	0.555
HDL	0.029	0.023	0.221
Exercise	-0.410	0.813	0.618
Alcohol	0.568	0.743	0.450
Smoking	0.187	0.794	0.815
Diet	0.527	0.990	0.598
Statins	0.407	0.748	0.591
HT and anti-HT	0.920	0.827	0.097

Table 4. Multivariate Logistic Regression for Influence of Components of Metabolic Syndrome on Uric Acid Level in Males (BMI- Body Mass Index, SBP- Systolic Blood Pressure, DBP- Diastolic Blood Pressure, FBS- Fasting Blood Sugar, HDL- High-Density Lipoprotein, HT- Hypertension, anti-HT- Antihypertensives)

	Unstandardised Coefficients		Sig.
	B	Std. Error	
Age	0.048	0.024	0.053
BMI	0.832	0.882	0.351
Waist	0.015	0.034	0.653
SBP	-0.030	0.020	0.139
DBP	0.058	0.041	0.165
FBS	0.004	0.013	0.766
Cholesterol	0.001	0.007	0.802
Triglyceride	-0.010	0.009	0.265
HDL	0.018	0.016	0.268
Exercise	-0.146	0.636	0.820
Diet	0.544	0.740	0.466
Statins	0.150	0.555	0.789
HT or anti-HT	0.609	0.641	0.348

Table 5. Multivariate Logistic Regression for Influence of Components of Metabolic Syndrome on Uric Acid Level in Females (BMI- Body Mass Index, SBP- Systolic Blood Pressure, DBP- Diastolic Blood Pressure, FBS- Fasting Blood Sugar, HDL- High-Density Lipoprotein, HT- Hypertension, anti-HT- Antihypertensives)

DISCUSSION

Metabolic syndrome is an important risk factor for cardiovascular disease and type 2 diabetes mellitus. It is also associated with high cardiovascular-related mortality and all-cause mortality.[10] In recent study by Fang et al showed that elevated serum uric acid level is not only associated with hypertension, obesity, metabolic syndrome, renal failure and cardiovascular disease, but also with high mortality rate.[11] Further a study by Li et al found that insulin resistance and increased serum uric acid has bidirectional casual effect.[12]

The overall prevalence of hyperuricaemia in South east Asian patients with metabolic syndrome was found to be 13.10% with male more than female (19.07% vs. 3.42%).[13] In a study conducted in India by Sachdev et al reported a prevalence of hyperuricaemia as 13.5% in patients with metabolic syndrome with men more than women 14.4% vs. 12.8%.[5] In our study, overall prevalence was found to be slightly higher (16.5%) with more men being affected than women (18.36% vs. 14.81%). In another study by Wang et al Guangdong Province in China reported a prevalence of hyperuricaemia as 32.6% much higher than other studies.[14] Wang et al also found that women were more affected than men in their study. They concluded that it maybe because of the older age of women participants. In our study, it was found that older men had high serum uric acid level as compared to women of same age.

The mean age of men and women in our study were 56.7 and 54.9, respectively, which was slightly higher than the study done by Sachdev et al. The hyperuricaemia in all the above study was found to be higher in the participants with age more than 50 years. Hyperuricaemia also increases with increase in postmenopausal women.

Hyperuricaemia has often been found in subjects with metabolic syndrome.[15] In a study by Sachdev et al,[5] hyperuricaemia has positive correlation with the components of metabolic syndrome. The study showed increased serum uric acid level is associated with hypertension, increased cholesterol level and type 2 diabetes mellitus. Similar result was found in the study by Chen et al[13] and Wang et al.[14] In our study, we found that increased BMI, increased cholesterol and hypertension, especially increased diastolic blood pressure were associated with hyperuricaemia in both males and females, although they were not statistically significant. Fasting plasma glucose was not positively

correlated to hyperuricaemia in both the gender. Alcohol consumption and diet rich in purine had increased the risk of hyperuricaemia in our study among men.

In males, alcohol consumption has 56% influence on increased uric acid levels and smoking has 18% influence on increased uric acid levels. None of the women consumed alcohol or smoked in our study. This may be due to the culture practiced in India. Ethanol increases urate synthesis, hence predominantly responsible for increasing the uric acid levels.[16]

Exercise was found to have negative correlation with hyperuricaemia similar to the study by Chen et al. We also studied the effect of statins on hyperuricaemia. Statins has influence of 40% on increase of uric acid levels in males, while in females, it was found to be 15%. The mechanism behind this is unclear. Further studies must be done to evaluate this.

CONCLUSION

The prevalence of hyperuricaemia among males is higher than females. The risk factors of metabolic syndrome like obesity, hypertension and increased cholesterol levels are associated with hyperuricaemia. Treatment and lifestyle modification should be considered to decrease the morbidity related to hyperuricaemia with metabolic syndrome.

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