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Prevalence of Hyperuricemia among Hospitalized Elderly Patients and Its Association with Metabolic Syndrome

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Abstract

There are few data available on the prevalence of hyperuricemia among elderly and its possible association with metabolic syndrome (MetS) so the aim of this study was to assess prevalence of hyperuricemia among hospitalized elderly patients as well as to assess its association with MetS. Cross sectional data from 200 hospitalized elderly patients were analyzed and the results were as follows: the prevalence of hyperuricemia was 21.0% in elderly men and 15.1% in elderly women. Multivariate logistic regression analysis revealed that BMI ≥ 30 (p = 0.031, OR = 1.1), hypertension (p = 0.019, OR = 1.8), high triglycerides level (p = 0.018, OR = 2.9) and hyperuricemia (p = 0.023, OR = 3.7) were independently associated with MetS. The study concluded that the prevalence of hyperuricemia among hospitalized elderly patients was 21.0% in elderly men and 15.1% in elderly women. There was an independent association between hyperuricemia and metabolic syndrome.

Keywords

Hyperuricemia, Metabolic Syndrome, Elderly

1. Introduction

The prevalence of hyperuricemia in the world population has steadily increased over the past 40 years [1]. There is a noted increase in serum uric acid levels in both sexes with increasing age [2]. With prolonged life expectancy, studying hyperuricemia in elderly has become even more important. Hyperuricemia is the major and primary risk factor of symptomatic gout [3], coronary artery disease and type 2 diabetes [4]-[6].

On the other hand, metabolic syndrome (MetS) is a major contributor to the development of medical condi-

tions which are similar to the associates of hyperuricemia, including [7] [8] cardiovascular diseases, type 2 diabetes, mild kidney disease, endothelial dysfunction and chronic inflammation [9].

The direct association between uric acid levels and metabolic syndrome remains controversial; Ju-Mi Lee and colleagues documented this association while Ferrara and colleagues didn't detect it [10] [11], so the aim of this study was to assess prevalence of hyperuricemia among hospitalized elderly patients as well as to assess its association with MetS.

2. Methods

2.1. Study Design

Cross sectional study.

2.2. Study Settings

Geriatrics medicine department, Ain Shams University hospital.

2.3. Study Participants

Two hundred hospitalized elderly patients, aged 60 years and over, agreed to participate in this survey study. All participants were subjected to complete history taking and physical examination. Arterial blood pressures were measured with a standard gauge mercurial sphygmomanometer. Hypertension was defined as a setting blood pressure ≥140/90 mmHg [12], or if hypertension had been verified earlier. W.C was measured by using a measuring tape, midway between the inferior margin of the ribs and the superior border of the iliac crest. The weight was measured in kilograms with the subject wearing light clothes, using Seca digital scale. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared [13].

2.4. Determination of MetS

MetS was determined according to the criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III). Thus, MetS was defined as the presence of three or more of the following five criteria: 1) waist circumference (W.C) ≥ 102 cm in males and ≥88 cm in females; 2) triglycerides ≥ 150 mg/dL or specific treatment for this lipid abnormality; 3) high-density lipoprotein (HDL)-cholesterol < 40 mg/dL in males and <50 mg/dL in females or specific treatment for this lipid abnormality; 4) systolic blood pressure (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 85 mmHg or treatment of previously diagnosed hypertension; and 5) fasting glucose ≥ 110 mg/dL or use of medication for hyperglycemia [14].

2.5. Laboratory Assessment

Three cm of at least 10 hours of overnight fasting blood samples were collected via venipuncture. Samples were allowed to clot for no more than 30 minutes, centrifuged and analysed enzymatically (Boehringer Mannheim, Germany) using standard laboratory methods in an automatic analyzer (Synchron CX 5). Fasting blood sugar, total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides (TG), serum uric acid and serum creatinine were measured.

Hypercholesterolemia was defined as a total cholesterol level ≥200 mg/dl. Hypertriglyceridemia was defined as a total TG ≥ 150 mg/dl. High LDL level was defined as a total LDL level ≥ 130 mg/dl. Low HDL level was defined as HDL level < 40 mg/dl in males and <50 mg/dl in females [15]. Hyperuricemia was defined as serum uric acid ≥ 7 mg/dl in men or ≥6 mg/dl in women [16] [17].

2.6. Exclusion Criteria

Patients taking medications that increase uric acid levels (e.g. thiazide diuretic) or using treatment for hyperuricemia (e.g. allopurinol) were excluded from this study.

2.7. Statistical Analysis

Data was analyzed using the 15th version of SPSS (Statistical Package for Social Science). The results were pre-

sented as mean ± SD for normally distributed data. Categorical data were compared between groups by χ^2 test. Continuous data were compared between groups using unpaired t test for normally distributed variables. Correlation coefficient was done to find linear relation between different variables using Spearman's correlation coefficient. Multiple logistic regression analysis was used to identify the independent variables of MetS. All factors introduced for multivariate analysis were previously analyzed by monovariate method. All proposed factors to be introduced for multivariate analysis, beside that they were all biologically plausible, were significant according to the findings obtained from data analysis. As for the technical manipulation, the "Enter" method was used after excluding insignificant variables. Insignificant variables or those giving inconsistent odds or risk ratios and confidence limits were excluded from the model step-by-step, together with comparing the maximum likelihood ratio. Significance was taken at 5% level.

3. Results

The study was carried out on 200 participants; 81 men (mean age 67.6 ± 6.3 years) and 119 women (mean age 68.5 ± 8.4 years). 43.5% of participants have hypertension, 36.0% have diabetes mellitus, 22.0% have ischemic heart disease (IHD), 19.5% have heart failure, 22.5% have cerebrovascular stroke, 23.0% have chronic liver disease (CLD), and 32.5% have chronic obstructive pulmonary disease (COPD).

The prevalence of hyperuricemia was 21.0% in elderly men and 15.1% in elderly women. There was a significant association between hyperuricemia and age as with increasing age there was an increase in the prevalence of hyperuricemia ($p = 0.005$). There were significant associations between hyperuricemia and W.C ($p = 0.001$ & 0.007 in elderly males & females respectively), BMI ($p = 0.002$), systolic blood pressure ($p = 0.001$), diastolic blood pressure ($p = 0.030$), TG ($p < 0.001$), HDL ($p = 0.003$), fasting blood sugar ($p = 0.001$), serum creatinine ($p < 0.001$), MetS ($p = 0.000$), ischemic heart disease (IHD) ($p = 0.010$) and stroke ($p = 0.009$) (**Table 1**).

In elderly males as well as elderly females, there were positive correlations between serum uric acid level and age, BMI, W.C, systolic blood pressure, diastolic blood pressure, triglycerides, fasting blood sugar and serum creatinine. There was a negative correlation between serum uric acid level and HDL (**Table 2**).

Studying the relation between MetS and the studied variables revealed significant associations between MetS and age ($p = 0.020$), female gender ($p = 0.032$), W.C ($p = 0.018$ & 0.049 in elderly males & females respectively), BMI (=0.001), systolic blood pressure ($p < 0.001$), diastolic blood pressure ($p = 0.002$), TG ($p = 0.001$), HDL ($p < 0.001$), fasting blood sugar ($p < 0.001$) and serum uric acid ($p < 0.001$) (**Table 3**).

Multivariate logistic regression analysis revealed that BMI ≥30 ($p = 0.031$, OR = 1.1), hypertension ($p = 0.019$, OR = 1.8), high triglycerides level ($p = 0.018$, OR = 2.9) and hyperuricemia ($p = 0.023$, OR = 3.7) were independently associated with MetS (**Table 4**).

4. Discussion

The current study revealed that the prevalence of hyperuricemia was 21.0% in elderly men and 15.1% in elderly women. Previous studies studying the prevalence of hyperuricemia suggested that the prevalence of hyperuricemia was ranging from 3.9% to 35.2% in men and 2.0% to 21.0% in women [18]-[26]. The differences in the prevalence rate between different studies are due to the differences in the populations being studied.

In this study there were significant association and positive correlation between age and uric acid. The age associated increase in uric acid was explained by age related changes in renal function; the kidneys are unable to remove uric acid from the body adequately [27].

In the studied participants, serum uric acid level was significantly associated and positively correlated with W.C and BMI in men and women. These relationships are consistent with other studies [28]-[30]. This may be explained by insulin resistance. Obesity may give rise to insulin resistance, even in individuals with normal glucose tolerance test. Insulin resistance is known to be inversely related to 24 hours urinary uric acid clearance [31]-[33].

Previous studies as well as this study reported that serum uric acid is more closely associated with impaired fasting glucose [34]-[40].

In this study hyperuricemia was significantly and positively associated with systolic blood pressure and diastolic blood pressure. Previous study has shown that the association between hyperuricemia and hypertension was partly mediated by obesity [41].

The present study reported that serum uric acid is significantly associated with HDL and TG. These results

Table 1. Participants' characteristics according to the presence of hyperuricemia.

	Normal uric acid (n = 165)	High uric acid (n = 35)	p value
	Age (years)		
60 - 70	73 (88.9%)	9 (11.1%)	
70 - 80	82 (82.9%)	17 (17.1%)	0.005
>80	10 (52.0%)	9 (48.0%)	
	Gender		
Females	101 (84.9%)	18 (15.1%)	0.321
Males	64 (79.0%)	17 (21.0%)	
Education ≤ 12 years	84 (78.5%)	23 (21.5%)	0.428
Education > 12 years	81 (87.1%)	12 (12.9%)	
	Marital status		
Single	37 (86.0%)	6 (14.0%)	0.818
Married	128 (81.5%)	29 (18.5%)	
W.C in males (cm) (mean ± SD)	104.6 ± 12.7	112.9 ± 16.6	0.001
W.C in females (cm) (mean ± SD)	100.6 ± 11.9	106.2 ± 13.4	0.007
BMI (Kg/m^2)	26.9 ± 7.1	30.9 ± 9.8	0.002
Systolic blood pressure (mm Hg)	136.36 ± 17.85	152.78 ± 19.85	0.001
Diastolic blood pressure (mm Hg)	77.95 ± 11.30	81.65 ± 10.57	0.030
Triglycerides (mg/dL)	140.2 ± 65.9	157.0 ± 45.5	<0.001
Total cholesterol (mg/dL)	189.0 ± 32.8	190.1 ± 31.9	0.251
HDL (mg/dL)	43.1 ± 10.8	42.9 ± 9.8	0.003
LDL (mg/dL)	115.5 ± 27.9	120.1 ± 26.2	0.073
Fasting blood sugar (mg/dL)	91.4 ± 12.0	109.2 ± 17.8	0.001
Serum creatinine (mg/dL)	0.8 ± 0.1	0.9 ± 0.3	<0.001
Metabolic syndrome positive	33 (62.3%)	20 (37.7%)	0.000
IHD	28 (63.6%)	16 (36.4%)	0.010
Stroke	26 (57.8%)	19 (42.2%)	0.009

W.C (Waist circumference), BMI (body mass index), HDL (high density lipoprotein), LDL (low density lipoprotein), IHD (ischemic heart disease).

Table 2. Correlation between serum uric acid and studied variables in males and females.

	Males		Females	
	r	p	r	p
Age (years)	0.360	0.048	0.56	0.002
BMI (Kg/m^2)	0.191	0.014	0.174	0.025
W.C (cm)	0.570	0.001	0.280	0.003
Systolic blood pressure (mm Hg)	0.282	0.002	0.194	0.012
Diastolic blood pressure (mm Hg)	0.174	0.023	0.253	0.011
Triglycerides (mg/dL)	0.215	0.032	0.289	0.003
Total cholesterol (mg/dL)	0.140	0.340	0.214	0.288
HDL (mg/dL)	−0.216	0.031	−0.228	0.022
LDL (mg/dL)	0.319	0.086	0.120	0.520
Fasting blood sugar (mg/dL)	0.380	0.030	0.365	0.001
Serum creatinine (mg/dL)	0.323	<0.001	0.349	<0.001

Table 3. Participants' characteristics according to the presence of metabolic syndrome.

	MetS – ve (n = 147)	MetS + ve (n = 53)	p value
Age (mean ± SD) in years	67.9 ± 6.5	69.9 ± 7.8	0.020
Females	81 (68.1%)	38 (31.9%)	0.032
Males	66 (81.5%)	15 (18.5%)	
W.C in males (cm) (mean ± SD)	111.7 ± 13.9	113.9 ± 13.7	0.018
W.C in females (cm) (mean ± SD)	104.4 ± 9.6	106.9 ± 10.0	0.049
BMI (Kg/m^2)	27.8 ± 5.8	29.6 ± 6.3	0.001
Systolic blood pressure (mm Hg)	126.7 ± 20.7	145.3 ± 29.1	<0.001
Diastolic blood pressure (mm Hg)	76.6 ± 14.9	82.5 ± 11.6	0.002
Triglycerides (mg/dL)	145.1 ± 38.0	156.8 ± 60.7	0.001
Total cholesterol (mg/dL)	198.0 ± 20.5	201 ± 21.3	0.174
HDL (mg/dL)	46.7 ± 6.0	41.2 ± 8.8	<0.001
LDL (mg/dL)	123.5 ± 13.3	127 ± 16.2	0.283
Fasting blood sugar (mg/dL)	90.3 ± 18.2	105.0 ± 23.6	<0.001
Uric acid (mg/dL)	5.1 ± 1.8	5.8 ± 2.1	<0.001

MetS (Metabolic Syndrome).

Table 4. Multivariate analysis of the independent factors affecting metabolic syndrome.

Variables	Odds Ratio	95% Confidence Interval	p Value
BMI ≥ 30	1.1	1.0 - 1.2	0.031
Hypertension	1.8	1.3 - 2.5	0.019
High TG	2.9	1.5 - 5.7	0.018
Hyperuricemia	3.7	1.1 - 11.8	0.023

are consistent with previous reports [42]-[44].

In the current study there was a significant association between hyperuricemia and serum creatinine. This comes in adherence to the results of a previous study which reported significant association between serum uric acid and renal function [45].

Many prospective studies as well as this study reported a significant association between hyperuricemia and IHD. The possible explanation for this link may include the atherosclerotic effect of uric acid; as elevated uric acid may cause endothelial dysfunction and facilitation of smooth muscle cell proliferation. These data have been well summarized in several reviews and meta analysis studies [46]-[49]. As well as this association, between hyperuricemia and IHD, may be secondary to the association between hyperuricemia and the other cardiovascular risk factors.

In this study the prevalence of hyperuricemia is significantly higher in patients with stroke than non stroke patients. This is mostly because of the association between serum uric acid and stroke risk factors such as hypertension and dyslipidemia. However the role of uric acid as a risk factor for stroke is still controversial [50].

The association between hyperuricemia and MetS has obtained much attention in recent years. The current study found an independent association between hyperuricemia and MetS. This is consistent with previous studies [51] [52]. The underlying mechanisms of the association between serum uric acid level and MetS remain poorly understood. Uric acid has been shown to reduce nitric oxide bioavailability and reducing endothelial nitric oxide supply which is a known mechanism for inducing insulin resistance and resultant hyperinsulinemia, which constitute the pathophysiological cause of MetS [53]. As well as animal studies have shown that hyperuricemia may lead to MetS. The possible mechanism is related to inflammation and oxidative stress. Uric acid in adipocytes of obese mice induces inflammatory oxidative changes leading to development of MetS [54]-[56]. It

has been suggested that hyperuricemia may be regarded as an intrinsic part [57] or surrogate marker [58] for MetS.

On the other hand many studies have shown that insulin resistance and resultant hyperinsulinemia, implicated in the pathogenesis of MetS, induces a significant reduction in the urinary excretion of uric acid leading to hyperuricemia [31]-[33].

The findings of the current study are consistent with previous reports [59]-[64], but can be distinguished from them as this study is the first study studying prevalence of hyperuricemia among hospitalized elderly in Egypt.

There are important implications of this study. First, the presence of hyperuricemia should trigger a high level of clinical suspicion and investigation for a potential coexistence of MetS as recognizing and treating MetS are important to prevent its serious complications [65]. Second, in MetS patients, physicians must search for hyperuricemia as decreasing uric acid levels may prevent or reverse the course of MetS [66].

5. Conclusion

The study concluded that the prevalence of hyperuricemia among hospitalized elderly patients was 21.0% in elderly men and 15.1% in elderly women. There was an independent association between hyperuricemia and metabolic syndrome.

Disclosure Statement

There is no financial support or relationship that may pose conflicts of interest.

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