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Gender Difference in Serum Levels of Uric Acid in Patients with Acute Myocardial Infarction

Abstract

Introduction: Serum uric acid (SUA) level has been shown to be increased in patients with cardiovascular disease. This increase is generally higher in women than men. However, there is conflicting evidence based on different population. This study was aimed to explore and assed gender-based differences in the level of SUA in an Iranian subjects with acute myocardial infarction (AMI). We also investigated the relationship between SUA and clinical characteristics including, BMI, Killip class, hypertension and diabetes.

Method: A total of 78 AMI patients, aged 20-90 years, comprised of 39 men and 39 women were enrolled in this cross sectional study. Venous blood samples were drawn from each of the participants after a nocturnal fasting on days 1, 3 and 4. Anthropometric indices, fasting plasma glucose, lipid profile and uric acid level as well as the ejection fraction (EF) were measured using standard protocols.

Results: The mean SUA level in women was significantly higher than that in male on days 1,3,4 (P=0.001, 0.002, 0.03 respectively). A strong association was found between SUA on day 3 and hypertension, even after adjustment for BMI (OR=2.29, 95% CI, 1.21-4.3). There was also a significant correlation between SUA and age in women (p=0.03). However, such relationship was no found for diabetes.

Conclusion: An increased level of SUA was observed in women. This increment was also associated with hypertension and age in women. Our results suggest a gender differences in the association of SUA level with AMI related adverse events.

Keywords

Myocardial infarction • Uric acid • Gender

Research Article

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Introduction

Myocardial Infarction (MI) is a leading cause of death and disability worldwide [1]. According to the World Health Organization (WHO), about 32.4 million MI and strokes take place globally every year [2]. It is estimated that around 23% of patient with MI are died before they ever reachhospitals and about 13% of which during or after a hospital admission [3]. Like other countries, the highest number of deaths (35.89%) in Iran are caused by cardiovascular disease [4]. Preventive measures, based on known MI related risk factors are required to decrease the incidence of the disease as well as the associated mortality rates. Several studies have reported the relationship between serum uric acid (SUA) level and MI

[5]. Elevated SUA level has been demonstrated to increase the risk of mortality in patients with MI andis considered to be an important prognostic marker for predicting mortality in these patients [6,7]. Suggesting that patients with the highest uric acid levels or with the greatest impairment in uric acid metabolism are at substantially increased risk for cardiovascular events [8].

Uric acid is the end product of the metabolism of purine. Hyperuricemia is generally defined as serum uric acid at least 6 mg/dL in women and at least 7 mg/dL in men [9,10]. Hyperuricemia, resulted from impaired xanthine oxidase activity, induces endothelial dysfunction, deterioration of left ventricular function, platelet adhesiveness and aggregation. This situation promote oxidative stress, leading to a vicious cycle that ultimately leads to severe heart failure [11].

Some epidemiologic have explored gender differences in the mean of SUA level and subsequent risk of cardiovascular disease among men and women [12,13]. It has been reported that increased levels of SUA are associated with ischemic heart disease more in women than in men [14]. However, the impact of hyperuricemia on MI between women and men has not been well understood. This study was aimed to explore the gender differences in the rate of uric acid production in patients with MI.

Method

A total of 78 patients with AMI (ST & Non-ST Elevation), aged 20-90 years, comprised of 39 men and 39 women admitted in cardiac care unit in Imam Khomeini hospital, Jiroft, Iran, were enrolled in this cross-sectional study. All patients with gout, chronic kidney diseases, hematological malignancy, hypothyroidism, rheumatologic diseases, chronic alcoholics and those receiving drugs possibly affecting the uric acid metabolism like diuretics, salicylates, ethambutol and pyrizinamide were excluded from the study.

All participants completed a standardized questionnaire including baseline characteristics including age, sex and past medical history of diabetes mellitus and hypertension. Informed consent was also obtained from them using protocols approved by the Ethics Committee of the JiroftUniversity of Medical Science.

For all subjects, height and weight were measured using a standardized method and scale (BC-418MA model, Japan). The body mass index (BMI) was calculated as kg/m2 and a BMI of 20-25 was considered normal, 25–30 over-weight, and >30 obese.Venous blood sample was drawn from the anterior cubital vein in the early morning after a nocturnal fasting, within 1, 3 and 4 days of admission. Serum level of lipid profile, glucose and uric acid were measured by routine laboratory methods using standard enzymatic techniques. Ejection fraction for all patients were also measured during the hospital stay. Killip classification as an indicator of a functional status of heart failure was used to assess the severity of heart failure in patients with ST-segment elevation myocardial infarction (STEMI).

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD). Categorical variables are shown as frequencies (percentages). Differences between quantitative variables were assessed by student's t-test. $\chi 2$ or Fisher's exact tests were used to compare categorical variables (if appropriate). Logistic regression analysis was used to calculate crude and adjusted odds ratios (ORs) and their 95% confidence intervals for association between SUA and the risk of disease. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS Inc.) version 18.0 software (Chicago, IL, USA). P-value <0.05 was considered as statistically significant.

Results

The baseline demographic and clinical characteristics of patients, analyzed on the basis of gender, are summarized in Table 1.The mean age of male and female were 58.6 ± 13.92 and 66.1± 12.79 years respectively. As expected, no significant difference was found for serum levels of TG, cholesterol, EF and FBS between males and females (P>0.05). There were 15.4% of male and 35.9% of female who had diabetes. In addition, the prevalence of hypertension was significantly higher in female than male (53.8% vs. 28.2%). Of the total number of patients, according to the Killip classification, 16.7% were in class I, 34.6%, in class II, 29.5% in class III, and 19.2% were in Killip class IV. In stratification analysis based on gender, the number of males and females in different classes of were as follow; 20.5% vs. 12.8% in class I, 38.5% vs. 30.8% in class II, 30.8% vs. 28.2% in class III and 10.2% vs. 28.2% in class IV(Table 2).

The data regard to the serum level of uric acid is presented in Table 3. As expected, the mean SUA levels on days 1, 3 and 4 were significantly higher in females than the males (P value were 0.00, 0.002 and 0.03 respectively). Both males and females had also shown the highest level for SUA on day 3 (5.3 mg/dl vs. 6.3mg/dl). In subgroup analysis based on Killipclass, there were no significant differences in SUA levels between men and women for different classes of Killipexcept than class 2, in which SUA was significantly higher in female than male subjects (p=0.04). Serum level of uric acid was also compared regard to the BMI groups in males and females. As shown in Table 4 about 47% of men and 43% of women were overweight/obese. The mean SUA level was significantly higher in woman than men with BMI ≥25 (p=0.01). According to Table 5,52.1% ofpatients had BMI between 20-25.

Although, no association was found between SUA levels with diabetes but, logistic regression analysis indicated a significant association between SUA on day 3 with hypertension after adjusting for BMI (Table 6). Each unit increase in SUA was associated with 2.29 fold increase in the odds of hypertension development (p=0.01). Linear regression analysis was also revealed a significant association of age with SUA (p=0.03). This relationship was stronger in women in which, each unit increase in age was associated with 0.05 mg/dl increase in SUA levels (Table 7).

Discussion

In this cross sectional study, a total of 78 patients with acute MI, comprised 39 male and 39 female were assessed for gender differences in serum levels of uric acid. There was a significant gender dependent correlation between levels of uric acid on days 1, 3 and 4 following admission. Women had a higher level of uric acid than men.A large body of evidence suggested that SUA levels may Significantly

Variable	Male		Female		Total		
	Mean	SD	Mean	SD	Mean	SD	p
Age	58.66	13.92	66.17	12.79	62.42	13.80	0.01
TG	132.64	70.48	122.20	56.23	127.42	63.56	0.27
TC	173.14	59.65	177.00	41.46	175.07	51.07	0.75
Ef	41.41	10.75	41.53	7.79	41.47	9.33	1
Fbs	132.87	54.58	117.20	56.25	125.03	55.6	0.22

Student T test were used for comparisons.

TG: Triglyceride, TC: Total Cholesterol, EF: Ejection Fraction, FBS: Fasting Blood Sugar

Table 1. Baseline characteristic of study population.

Variable		Male		Female		Total	
		n	%	n	%	n	%
Diabetes	Yes	6	15,4	14	35.9	20	25.6
	No	33	84.6	25	64.1	58	74.4
	Total	39	100	39	100	78	100
Hypertention	Yes	28	71.8	18	46.2	46	59
	No	11	28.2	21	53.8	32	41
	Total	39	100	39	1000	78	100
KillipClass	1	8	20.5	5	12.8	13	16.7
	2	15	38.5	12	30.8	27	34.6
	3	12	30.8	11	28.2	23	29.5
	4	4	10.2	11	28.2	15	19.2

Table 2. Distribution of clinical status of diabetes, hypertension and killip class male and female.

Variable	Female	Male	P -value
SUA on day 1 (mg/dl)	5.8± 1.8	5.1± 1.01	0.001
SUA on day 3(mg/dl)	6.3± 1.9	5.3± 1.2	0.002
SUA on day 7(mg/dl)	5.9± 1.9	5.2 ± 0.95	0.03

Independent student T test were used for comparisons.

Table 3. Comparison of serum uric acid in male and female.

Variable		Mean Difference	Pvalue
BMI	< 20	1.81	0.26
	≥20	0.99	0.01
KillipClass	1	0.42	0.64
	2	1.30	0.049
	3	0.86	0.28
	4	0.96	0.13

Student T test were used for comparisons

Table 4. Comparison of serum uric acid in male and female accord BMI and Killip class.

BMI	Male		Female		Total	
	n	%	n	%	n	%
<20	2	5.3	0	0	2	2.7
20-25	18	47.4	20	57.1	38	52.1
>25	18	47.4	15	42.9	33	45.2

Table 5. BMI of study population.

	B	SE	P	OR	CI
SUA on day 3	0.83	0.32	0.01	2.29	1.21-4.3

This model adjusted for BMI, B= Coefficients Regression, CI = Confidence Interval, OR: Odds Ratio

Table 6. Association between blood pressure and serum uric acid using logistic regression.

associated with cardiovascular related diseases, especially in women. Josef, et al. found a direct significant association between serum SUA level and CHD incidence, only in women. Severalstudies have also reportedSUAas a stronger predictor of CHD in women thanthe men [15]. On the other hand, in one study conducted by bySokhanvar,

Predictor		SUA		
		B	CI	P
Age	Male	0.01	-0.01-0.04	0.35
	Female	0.05	0.004-0.09	0.03

B= Coefficients Regression, CI = Confidence Interval

Table 7. Associations between Serum uric acid with age using linear regression.

et al. there was no significant difference in SUAin male and female [16].

Our results present a significant relationship between age and SUA, which was stronger in woman. It was proposed that estrogen has a role in excretion of uric acid [17]. Therefore, one reason for this difference may be attributed to the fact that increase in age is associated with reduction in estrogen level in women. There was also a significant difference in USA level between women and men with a BMI greater than 25. In line to our results, Kawamoto et al reported there apositive association betweenSUA and BMIespecially in women [18]. Daber, et al. was also reported a significant correlation between SUA and BMI [19].

With regard to the hypertension, a direct correlation was found with serum level of UA especially on day 3 after admission. Cicero et alwas also reported an association between SUA and hypertension [20]. This indicated a potential role of SUA in development of hypertension in AMI disease. It was proposed that UA lowering agents resulted on significant reduction in blood pressure [21]. Experiments conducted on animal models and cell cultures have revealed mechanisms by which UA could results in hypertension. Short-term hyperuricemia would result in hypertension due to activation of renin-angiotensin system which lead to a reduction in endothelial levels of nitric oxide. As such, the long term UA could cause microvascular renal disease and finally resulting the development of hypertension [22,23].

We couldn't find any association between hyperuricemia and diabetes even in gender groups. Likewise, Sokhanvar et al did not find a meaningful relationship between diabetes and hyperuricemia [16]. However,Kawamoto,et al. have reported a positive correlation of SUA with diabetes [18]. With regard to the subgroups of Killipclass,SUA was significantly higher in woman than man only in Killipclass

2. In some studies conducte by Kojima, et al.and Nadkar, et al.a significant correlation was reported for SUA concentration with Killip Class [11,24]. This correlation had also reported in Daber'study [25].

Conclusion

In conclusion, our results indicated a higher level of SUA in women than the men. Although, the median age of first acute MI was higher in women than men, but the results suggested an increase in SUA level as the age is increased. Also, high level of SUA was associated with hypertension and hypertention as two major risk factors for MI. However, further studies are needed to clarify more in subtle the effect of UA on MI. These finding may shed a light on promising use of SUA lowering drugs in preventing MI.

Conflict of Interest

The authors declare that they have no competing interests.

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