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RESEARCH ARTICLE

Correlation of on Admission Levels of Serum Uric Acid with Acute Myocardial Infarction: Case : Control Study

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Abstract

Background: There are insufficient researchers studied serum uric acid (SUA) concentrations in patients with acute myocardial infarction (AMI or MI) at time of admission. We undertook the contemporary work to evaluate the value of SUA levels in admitted AMI subjects. Materials and methods: The study subjects consist of 260 people divided in two groups, 100 age and sex matched healthy controls with 160 patients with AMI (28-80 years) diagnosed by clinical, laboratory findings, and echocardiography. Study populations were stratified according to their levels of SUA at their first 6-12 hours of admission, into three tertiles: first (<5 mg/dl), second (5-6 mg/dl) and the third (>6.3 mg/dl). The concentrations of the three serum UA tertiles were studied for their association with AMI patients. Research biochemical evaluations were directed using conventional techniques. An accepted level of significance was $P < 0.05$. Results: For all study subjects, the mean age was 50.5±13.5 years. The ratio of men to women was 3.5:1 and there were no statistically substantial variations amongst the groups as regards the age and gender. The higher tertiles where positively correlated with increasing ages of individuals. The most common risk factors for all subjects of the study were hypertension (56%), then smoking (55%), then diabetes mellitus (26%). The mean serum concentrations of UA were higher significantly in those with AMI (5.96 ±1.8) than in control group (4.39 ± 1.3 mg/dl; P=0.05). Those with AMI has higher odds ratio (6.3, *95% CI*: 2.26-17.6) than control group for the presence of highest Vis lowest SUA tertiles. Once several confounders (age, sex, diabetes mellitus, and hypertension) are being adjusted, the hazard ratios for developing AMI continue to be significant in the second and third tertiles of SUA. Conclusion: The outcomes of the study displayed that higher SUA concentrations are correlated with the incidence of AMI in admitted patients. High SUA levels independently can be considered as unconventional risk factor for the incidence of AMI.

Key words: *Acute myocardial infarction, Uric acid and hyperuricemia.*

Introduction

Uric acid is the metabolic end product of purine, the upper end of the normal range is 360µmol/l (6 mg/dl) for women and 400 µmol/l (6.8 mg/dl) for men in humans [1]. Uric acid had been shown to mediate inflammation, induce endothelial dysfunction and stimulate smooth muscle cell proliferation [2].

Since Gertler and colleagues in excess of fifty years ago, noticed a relationship between SUA and ischemic heart disease (IHD), at that time numerous researches have endeavored to found whether SUA is correlated to atherosclerotic events, independent of classical risk factors of IHD [3]. Hyperuricemia had serious prognostic influence of AMI especially among females [4], though it has valuable antioxidant effects at a cellular level in a "retrospective cohort of the Atherosclerosis Risk in Communities (ARIC) study" [5]. On the basis of the evidences currently available, it seems fair to suggest that raised oxidative stress is closely associated to cardiovascular events.

Consequently, high SUA concentrations may be an indication in which the bodies attempt to defend himself from the toxic influences of free radicals by cumulating much endogenous antioxidants, like UA.

Remarkably, UA inhibits enzymatic endothelial dysfunction and conserves its capability to stimulate vasodilatation during oxidative stress [6]. Uric acids can be an indicator of sodium retention accompanied with compromised hemodynamic reserves &/or distressed circulation [7]. However, there has been an inconclusive debate about whether UA can be licensed as an autonomous risk factor for death due to coronary vascular events [8]. There are insufficient researchers studied SUA concentrations in patients with AMI at admission. In light of the controversial association, this work designed to investigate the correlation between plasma UA concentrations and the presence of AMI in admitted patients.

Materials and Methods

Characteristics of Subjects

The study subjects consist of 260 individuals allocated into two groups; 100 healthy controls being matched for both sex as well as age (free of any cardiac illness) with 160 patients with AMI (28-80 years) diagnosed by history, clinical, laboratory, and echocardiographic findings. A systematic medical examination was performed to eliminate any other conflicting illness, which could probably affect the levels of SUA.

Study Protocol

This is a case-control cross-sectional study conducted in Merjan Teaching Medical City, Babylon. Research biochemical evaluations were directed using conventional techniques. Study population were stratified according to their levels of SUA at their first 6-12 hours of admission, into three tertiles: 1st tertile (< 5 mg/dl), 2nd tertile (5-6 mg/dl) and the 3rd tertile (>6.0 mg/dl). The concentrations of the three serum UA tertiles were studied for their association with admitted AMI patients. The measurements of SUA in AMI patients compared to that of control group. The authorization of the current work was approved by hospital local ethical committee and an oral consent of all subjects had been appropriately obtained.

Statistical Analysis

The data were analyzed by using a computerized SPSS/22 program and a significance level of (P<0.05) was accepted. Both chi-squares with fisher exact correlations had been used when needed to measure the strength of associations with Odds ratio. Both univariate and multivariate logistic regression model were implemented to evaluate the association among the tertiles of SUA and the presence of AMI and other conventional AMI risk factors.

Results

Patient Characteristics

Table (1) displayed that the demographic characteristics of the studied subjects. The mean age of all study subjects was 50.5±13.5 years with ratio of men to women was 3.5 to1 and there were no statistically significant variations between the groups regarding the age and gender. The commonest risk factors for all subjects of the study were hypertension (56%), then smoking (55%), then diabetes mellitus (26%).

Table 1: Characteristics of control and AMI patients

Characters	Total	AMI Patients (N=160)	Control (N=100)	*P-Value*
Mean age (year) Minimum - Maximum	50.5±13.5 28 - 80	60.99±12.9 34-95	39.6±11.6 20-71	> 0.05
Hypertension No (%)	90 (56)	82 (91)	8 (9)	< 0.05
Diabetes Mellitus No (%)	68 (26)	62 (91)	6 (9)	< 0.05
Smoking No (%)	144 (55)	76 (53)	68 (47)	< 0.05
Male No (%)	202 (78)	120 (59)	82 (41)	> 0.05
Female No (%)	58 (22)	40 (69)	18 (31)	> 0.05
	Serum Uric Acid Tertiles (mg/dl)			
	>6.0	5.0-6.0	<5.0	
Female	18	8	32	>0.05
Male	58	52	92	

Total	76	60	124		

IHD Patients	HT	44	CONTROL	HT	6
	HT+DM	38		HT+DM	2
	DM	24		DM	4
	IHD	54		Healthy	88

Table 2: Comparison of Serum Uric Acid Tertiles between Acute Myocardial Infraction and Control Subjects

Uric Acid Tertiles (mg/dl)	Total No. (%)	AMI Cases		Healthy Control		*P-Value*	*Odds Ratio*	*95% CI*	*P-Value*
		No (%)	Mean±SD mg/dl	No (%)	Mean±SD mg/dl				
< 5.0	124 (48)	58 (36)	5.96 ± 1.8	66 (66)	4.39 ± 1.3	< 0.001	0.29	0.13 - 0.61	<0.05
5.0-6.0	60 (23)	36 (23)		24 (24)			0.91	0.39 - 2.11	>0.05
> 6.0	76 (29)	66 (41)		10 (10)			6.3	2.26 - 17.6	<0.05
Total No	260	160	**Min-Max:** 2.9-10.7	100	**Min-Max:** 1.9-7.3				

Table 3: Presence prevalence of Acute Myocardial Infarction by Tertiles of Serum Uric Acid

Variables	Serum Uric Acid			*P-Value*
	Tertile-1	Tertile-2	Tretie-3	
Unadjusted OR	Ref.	0.91 (0.50 – 1.65)	6.31 (3.0 – 13.0)	0.001
Age adjusted OR	Ref.	1.08 (0.52 – 2.20)	4.60 (2.07 – 10.4)	0.04
Sex adjusted OR	Ref.	1.12 (0.59 – 2.15)	4.80 (2.25 – 10.21)	0.02
Multivariate model* OR	Ref.	1.06 (0.54 – 2.06)	6.84 (3.14 – 14.73)	0.01
Multivariate model** OR	Ref.	1.60 (0.80 – 3.19)	4.10 (1.8 – 9.19)	0.01
Multivariate model*** OR	Ref.	1.43 (0.66 – 3.08)	5.36 (2.2 – 12.58)	0.02

* Adjusted for diabetes, ** adjusted for hypertension, *** adjusted for diabetes & hypertension, OR: Odds Ratio, Values between brackets is 95% confidence intervals & Ref.: reference

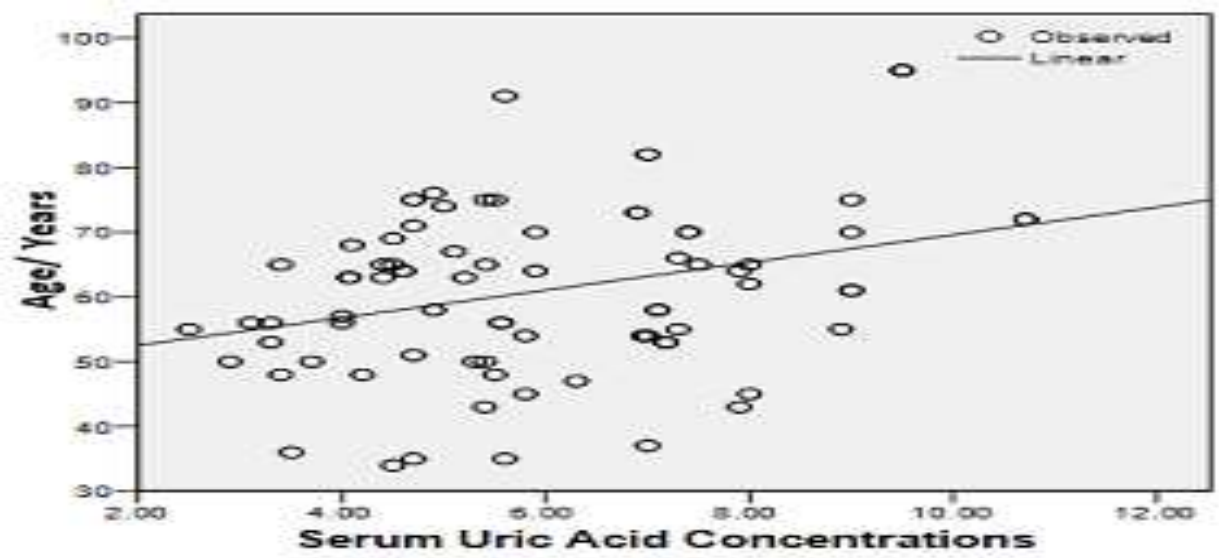

Figure 1: Correlation of Serum Uric Acid concentrations with the Age/Years of Studied Subjects

Serum Uric Acid Levels

There were no significant statistical differences in distribution of SUA levels between male and females Table 1. The higher UA tertiles where positively correlated with increasing ages of individuals

(Figure-1). Table 2 revealed that the mean serum concentrations of UA were higher significantly in those with AMI (5.96 ±1.8) than in control group (4.39 ± 1.3 mg/dl; *P*=0.05). Those with AMI has higher odds ratio (6.3) than control group for the presence of highest vis lowest SUA tertiles (95 % confidence interval, 2.26-17.6) as displayed in Table 3. With subsequent adjustment for age, sex, diabetes and hypertension the hazard ratios of AMI remained within the equivalent values relatively in the second and third tertiles of SUA (table-4). Once the involved variables was augment with the AMI, the hazard ratios were 0.91(*95% CI:* 0.50–1.65), 6.31(*95% CI:* 3.0–13.0), *P*-0.001 in the second and third tertiles of SUA, correspondingly. After the Odds ratio been adjusted for age, the risk of AMI presence attenuated slightly to 1.08 (*95% CI:* 0.52–2.20), 4.60 (*95% CI:* 2.07–10.4), *P*-0.04. For the time being, with adjustment for diabetes mellitus, the hazard ratios were same: 1.06 (*95% CI:* 0.54-2.06) and 6.84 (*95% CI:* 3.14-14.73), *P*-0.01 in the second and third tertiles of SUA, individually (multivariate model*).

On subsequent adjusting for hypertension (multivariate model**), no statistically significant alteration was observed with comparable risk ratios for AMI by SUA levels: 1.60 (*95% CI:* 0.80-3.19), 4.10 (*95% CI:* 1.8-9.19), *P*-0.01. As a final point, the study have reconsidered the investigation for AMI patients without the effects of variables included above (multivariate model***).

The correlation concerning SUA values and consequent evolution of AMI was of parallel extent: 1.43 (*95% CI:* 0.66–3.08), 5.36 (*95% CI:* 2.2–12.58), *P*-0.02 in the second and third tertiles, individually. As it were revealed, the risk for AMI in all the aforementioned analysis been associated with the uppermost tertile of SUA in all variant models.

Discussion

This study is an attempt to address the issue of the relation of SUA in the admitted patients with AMI. The data yielded by this study provides convincing evidence that higher SUA concentrations are coexisted with the occurrence of AMI in admitted patients; nonetheless, such association may persist after other risk factors being adjusted for AMI. Spahić et al puts forward the view that identified a positive correlation between SUA in healthy subjects and patients with IHD [9]. Further research in this area may include Baruah M. et al; who attempt to understand the behavior and reaction of SUA and C reactive protein in AMI subjects [10].

The data gathered in this study suggests that there was no significant statistical differences in distribution of SUA levels between male and females, although some of the current researches does not support such view. In a recent study, data revealed that UA levels are significantly elevated in men [5].For the time being, other recent systematic meta-analysis that evaluated the relationships between hyperuricemia and the risk for IHD; had exposed much controversy [4].

Explanations for these inconsistent results were unclear, but then again the high intra individual disparity in values of SUA that approaches the inconsistency amongst persons, may have decreased the power of the association seen in a number of studies. Additional explanation is that such revisions were limited by heterogeneity as regard to sample size [4]. Whether SUA values play a dissimilar role in both sexes is correspondingly uncertain [14]. In this study the, levels of SUA were significantly correlated with increasing ages of the studied subjects (figure-1).

Even though, much of the current debate revolves around this point in a current meta-analysis, owing to great disparities among studies that make it difficult to syndicate all five included studies (including 8,656,413 subjects, involving 1000 MI patients) and estimate a summary for such argument [11].With later modification for sex/age and past medical history of whichever hypertension or diabetes; the SUA levels continued as independent associated risk factor for the occurrence of AMI in a multivariate model (Table-3).

The study revealed that there was a significant increase in the strength of association for UA levels with the presences of AMI in the second tertiles and even higher in the third tertiles. The view is very much in line with findings that were observed by two previous studies in Hilla city [15, 16].The answer to the exact role of SUA with incidence of AMI is not as clear-cut as

popular views might suggest because numerous retrospective studies have recognized a considerable controversy exists

regarding such association [4]. Results from in-vitro and animal works propose a possible underlying role of SUA in coronary artery diseases. Uric acids upsurges proliferation and pro-inflammatory processes and subsidizes to endothelial dysfunction [3].

Hyper-uricemia (and/or uric acid accumulation) in addition to metabolic syndrome "defined as the coexistence of abnormal blood pressure, visceral obesity, dyslipidemia, and dysglycemia" are intensely associated [12].Cardiomyocytes known to produce adenosine as a vasodilator in response to conditions such as tissue hypoxia.

This adenosine will be degraded to UA by the endothelial cells; thereby accumulating the UA levels and reducing the PH inside the cells with subsequent rapid UA efflux to the vascular lumen [13]. On the basis of the evidences currently available, it seems fair to suggest that raised oxidative stress is closely associated to cardiovascular events. Consequently, high SUA concentrations may be an indication in which the bodies attempt to defend himself from the toxic influences of free radicals by cumulating much endogenous antioxidants, like UA. Remarkably, UA inhibits enzymatic endothelial dysfunction and conserves its capability to stimulate vasodilatation during oxidative stress [7].

Conclusions

The contemporary study clearly demonstrated that higher serum uric acids concentrations are associated with the incidence of AMI. High serum UA can be deliberated as risk factor for the occurrence of AMI independently.

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