Value of serum uric acid estimation in patients with acute coronary syndromes

Dr. Ali Fawzi Abdalsahib Al-Zamily [(1)]

Abstract

One of the major causes of mortality and morbidity is the spectrum of ischemic heart diseases (IHD) which ranks on the top of the lists among medical indications for health care, hospital admission and mortality worldwide Debate regarding the prognostic role of serum uric acid can be easily concluded when reviewing literatures dealing with this subject. Some authors mention an association between occurrence of complications in patients with IHD and serum uric acid. The present prospective cohort study included 62 patients with acute coronary syndrome (myocardial infarction and unstable angina)who were admitted to the coronary care unit (CCU) at Al-Dewaniyah teaching hospital in Al-Dewaniyah province in Iraq. The study extended from January 2016 through December 2016. For each patient the following data were obtained: age, gender, history of aspirin intake, type of acute coronary syndrome (STEMI, NSTEMI and UA), Killip class (I, II, III and IV) and serum uric acid at time of admission. Patients were followed for development of complication and for the occurrence of death. Results showed significant positive correlation between serum uric acid level and severity, type of ACS and mortality rate.

Conclusion: high serum uric acid level is a poor prognostic factor in patients with acute coronary syndrome

Key words: ACS, IHD and serum uric acid

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(1) M. B. Ch. B., CABM, DM. Al-Dewaniyah teaching hospital/department of medicin/ Al-Dewaniyah province/ Iraq. Email: abdalsahib75@yahoo.com

Introduction

One of the major causes of mortality and morbidity is the spectrum of ischemic heart diseases (IHD) which ranks on the top of the lists among medical indications for health care, hospital admission and mortality worldwide [(1)]. Understanding the minute elements encountered in the whole picture of the pathophysiology of IHD may contribute enormously in improving the way in which health care professionals can diagnose, treat and anticipate future prognosis of this common disorder [(2)]. The story of IHD can be summarized in few words: intra-coronary artery thrombosis with resultant ischemia and if lasts for more than 20 minutes, it will lead to myocardial necrosis [(3)]. The main reason behind this article was the published argument that serum uric acid may somehow predict the outcome in patients with signs and symptoms suggestive of ischemic heart disease [(2)]. It is mentioned in substantial amount of literatures that adenosine secreted by cardiac myocytes can cause vascular dilatation, in response to hypoxia and ischemia, then endothelium degrades rapidly adenosine to produce uric acid which ultimately reaches intravascular compartment [(4)]; hence, measuring serum uric acid may serve as an indicator to the prognosis of patients with IHD [(5)].

Debate regarding the prognostic role of serum uric acid can be easily concluded when reviewing literatures dealing with this subject. Some authors mention an association between occurrence of complications in patients with IHD and serum uric acid [(6)]; others linked the rate of short term mortality after myocardial infarction to high level of serum uric acid [(7)]. Others found an association between long-term

hospital stay and the level of serum uric acid in patients with acute myocardial infarction [8].

The lack of uricase enzyme activity by human body is the reason behind uric acid being the final product following metabolism of purine [9]. The primary sites for uric acid metabolism in the body are the liver, kidneys, gastrointestinal tract and the heart after xanthine being oxidized by the enzyme xanthine oxidase (XO) [10]. The two determinants factor for the serum level of uric acid are represented by its rate of production and its rate of excretion by the kidneys. Hyperuricemia is defined as a level greater than 360 μmol/L in women and greater than 420 μmol/L in men, low normal levels are represented by concentrations of <250 μmol/L and <310 μmol/L in women and men, respectively, and levels in between are regarded high normal [11]. The development of high serum uric acid may be attributed to consumption of diets rich in purin such as alcohol, animal foods, sweetbreads and fructose, chronic disorders (diseases with high cell turnover and impaired renal function), intake of certain drugs such as diuretics and some inherited disorders (organic anion transporter mutations) [12]. Uric acid may be involved in a number of cardiovascular disorders. It has some anti-oxidant activity; however, it may cause some oxidative stress in high concentrations and in acidic environment [13]. Additionally, a lot of experimental researches showed that uric acid exerts effects on mononuclear inflammatory cells and vascular smooth muscle cells [14]. For that reason it has been postulated that high serum uric acid level may be a poor prognostic factor for cardiovascular diseases [13]. On the other hand, several authors linked high serum uric acids to conditions that are considered as risk factors for cardiovascular disorders such as dyslipidemia, hypertension and diabetes, and the picture is further complicated by some suggestion that uric acid is a byproduct rather than a cause for these conditions [13]. In conditions, such as heart failure and

hypoxia, there will be activation of the enzyme xanthine oxidase (XO) [14], with subsequent rise in serum acid level promoting oxidative stress and endothelial dysfunction [10]. It has been shown that inhibition of XO may reactivate endothelia function, however, the use of uricosuric agents, uric acid lowering agents, failed to produce similar effect [10]. So one can reach the following controversy regarding the exact role of sertum uric acid in cardiovascular diseases, is it a pathogen? Or it is just a mirror for another risk factor that takes the role of the true pathogen [14].

Taking into consideration coronary artery disease, a recent meta-analysis of 26 large prospective cohort studies showed a statistically independent association between occurrence of the disease and related mortality and high serum uric acid concentration [15]. There is little knowledge about the role of serum uric acid as an outcome predictor in patients with acute coronary syndrome. There are two studies that concluded an adverse prognostic role for high serum uric acid, at time of admission, in patients with acute coronary syndrome [16, 17]. The aim of the present study was to evaluate the prognostic role of serum uric, at time of admission, in patients with acute coronary syndrome.

Patients and methods

The present prospective cohort study included 62 patients with acute coronary syndrome (myocardial infarction and unstable angina) who were admitted to the coronary care unit (CCU) at Al-Dewaniyah teaching hospital in Al-Dewaniyah province in Iraq. The study extended from January 2016 through December 2016. For each patient the following data were obtained: age, gender, history of aspirin intake, type of acute coronary syndrome (STEMI, NSTEMI and UA), Killip class (I, II, III and IV) and serum uric acid at time of admission. Patients were

followed for development of complication and for the occurrence of short term death.

Data were introduced into an SPSS spread sheet and were analyzed using the 22nd version of this software in addition to medcalc software. Numeric variables were expressed as mean and standard deviation whereas categorical variables were expressed as number and percentage. Correlations were calculated using Pearson and Spearman correlations; Mann Whitney U test and Kruskal Wallis tests were used to study differences in mean serum uric acid. Chi-square test was used to study association between hyperuricemia and other variables. Receiver operator characteristic (ROC) analysis was used to determined serum uric acid cutoff value that predict negative outcome.

Results

The demographic characteristic and variables included in the present study are shown in table 1. Table 2 showed positive correlation between high serum uric acid level and type of ischemic heart disease (highest level with STEMI), severity of ACS and short term mortality with p-values (0.001, 0.004 and 0.028, respectively). Further association was presented in table 3 that solidify the results obtained in table 2. Cutoff values for serum uric acid that predict negative outcome are shown in table 4 and figures 1,2 and 3.

Table 1: Characteristic of the study group

Characteristic	Statistic
Age (mean ±SD) (range) years	(57.85 ±12.38) (35-85)
Gender	
Male (n, %)	25 (48.1)
Female (n, %)	27 (51.9)
History of aspirin (n, %)	10 (19.2)
Type of ACS	
NSTEMI	24 (46.2)
STEMI	22 (42.3)
UA	6 (11.5)
Killip class	
I (n, %)	7 (13.5)
II (n, %)	24 (46.2)
III (n, %)	18 (34.6)
IV (n, %)	3 (7.7)
Mortality (n, %)	12 (19.3)
Serum uric acid (mg/dl)	(7.16 ±1.49) (5.00 -10.65)
Hyperuricemia (n, %)	20 (38.5)

Table 2: Correlations of between serum uric acid and other variables included in the present study

Statistic	Gender	age	History of Aspirin intake	ACS*	Killip Class	Death
Correlation coefficient (r)	0.045	-0.187	0.187	0.438	0.393	0.304
P-value	0.752	0.185	0.184	0.001	0.004	0.028

*Acute coronary syndrome type (unstable angina, NSTEMI and STEMI)

Table 3: Mean serum uric acid and rate of hyperuricemia in relation to ACS type, Kllip class and mortality

Characteristic	Mean serum UA ±SD	P *	Hyperuricemia n (%)	P †
ACS				
UA	5.82 ±0.44		0	
NSTEMI	6.88 ±1.41	0.006	7	0.014
STEMI	7.83 ±1.45		13	
Killip Class				
I	5.98 ±0.88		1	
II	6.96 ±1.15	0.026	8	0.260
III	7.59 ±1.71		9	
IV	8.97 ±1.48		2	
Mortality				
Died	8.02 ±1.72	0.030	8	0.022
Alive	6.90 ±1.33		12	

* Mann Whitney U and Kruskal Wallis tests; † Chi-square test

Table 4: Cutoff values of serum uric acid that predict ACS type and class and death by receiver characteristic curve analysis

Characteristic	Cut off value	AUC	Interpretation	P-value	Sensitivity	Specificity
MI versus UA	> 6.2 mg/dl	0.797		<0.001	76.1 %	100 %
Class I and II versus III and IV	>7.2 mg/dl	0.645		0.088	65.0 %	62.5%
Death versus alive	>8.0 mg/dl	0.708		0.029	58.3 %	80 %

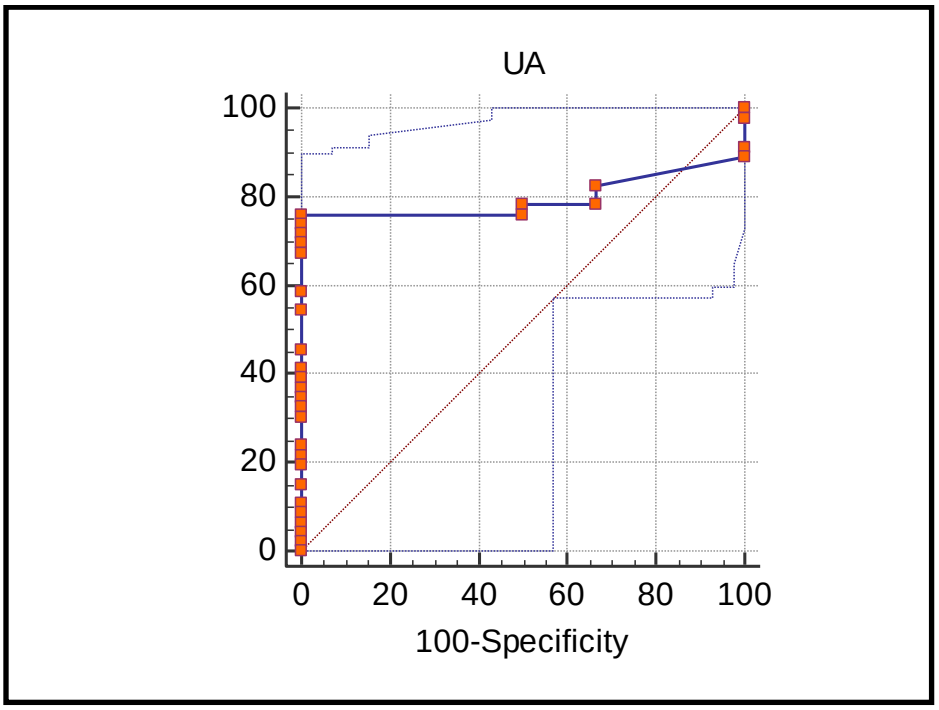

Figure 1: Receiver operator characteristic curve (ROC) for calculation of serum uric acid value for MI versus UA

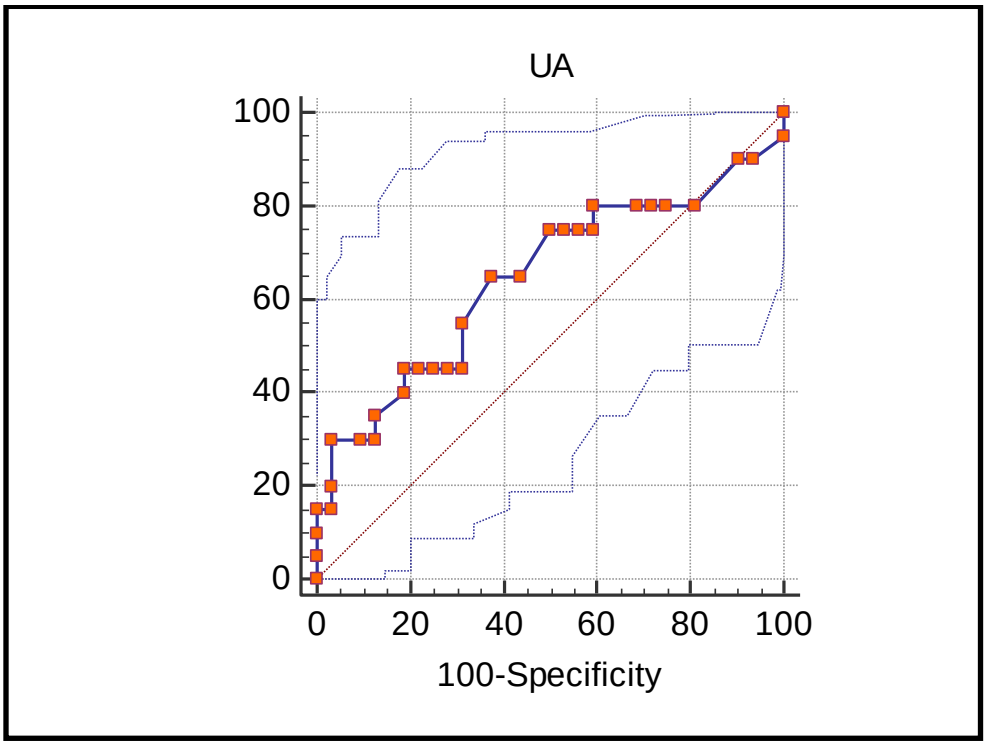

Figure 2: Receiver operator characteristic curve (ROC) for calculation of serum uric acid value for Killip class I and II versus III and IV

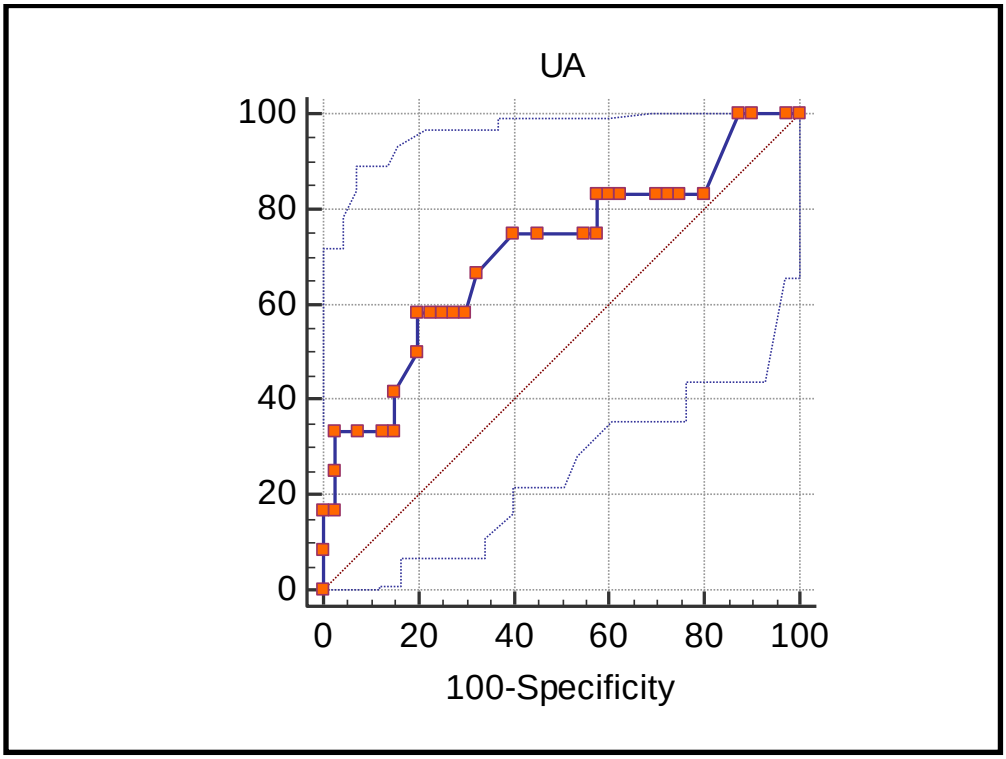

Figure 3: Receiver operator characteristic curve (ROC) for calculation of serum uric acid value for Death versus alive outcome

Discussion

The current study showed that hyperuricemia was associated with more severe form of IHD and greater rate of short mortality. In a study carried out in Turkey, Deveci et al studied 1012 patients to explore the association between severity of ischemic heart disease and the level of serum uric acid and the study came up with a conclusion of significant difference in mean serum uric acid in patients with coronary heart disease compared to those who are free of it regardless of the gender. Added, to that, this study showed a significant correlation between the severity of the disease and level of uric acid [(18)]. Another study, included 495 patients with ischemic heart disease, found a significant statistical association between the existence of ischemic heart disease, based on angiography, and high serum level of uric acid; nevertheless, severity of disease shoed no association with the level of serum uric acid [(19)]. A positive correlation between severity of ischemic heart disease and hyperuricemia was proved by Duran M et al in a study carried out on 246 patients with acute coronary syndrome [(20)]. In addition, Xiong Z et al observed a positive correlation between severity of ischemic heart disease, as assessed by angiograohy, and high level of serum acid [(21)]. The results of the above mentioned studies are comparable with our findings.

In contradiction to the findings of the present study, Lu P et al observed that there was no correlation between severity of ischemic heart disease and serum uric acid levels [(22)].

High serum uric acid concentrations have been shown to be associated with diabetics, obese, hypertensive and dyslipidemics. It has been postulated that a number of risk factors are responsible for the elevated serum uric acid and this by far makes the validity of serum uric

acid estimation as an independent risk factor questionable [23]; nevertheless several studies showed was no statistical difference in serum uric acid concentrations of diabetics versus non-diabetics and hypertensives versus non-hypertensives in patients with IHD [24].

Hyperuricemia has also been suggested as a marker of unfavorable prognosis and raised mortality rate globally [34]. Short term mortality has been shown, by Ndrepepa G et al, to be positively correlated with high serum uric acid levels in patients with all type of acute coronary syndromes [25]. Development of heart failure and long term complications, have been also shown, by Kojima S et al, to be predicted on the basis of high serum uric acid levels in patients with acute myocardial infarction (MI) [26].

High uric acid succeeded to predict poor outcome in patients with concomitant ischemic heart disease and pre-existing renal impairment. Outcome in dilated cardiomyopathy, calcific aortic stenosis, atrial fibrillation and metabolic syndromes has been linked, in several studies, to serum uric acid [27]. A number of studies re-discussed the possibility of xanthine oxidase inhibitors in delaying the progression of atheroma [28].

The xanthine oxidase inhibitor Allopurinol is being thoroughly studied for its possible benefit as additional treatment in patients with stable ischemic heart disease [29]. In conclusion; high serum uric acid level appears to be a poor prognostic indicator in patients suffering from acute coronary syndrome.

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