

The Prognostic Value of Serum Uric Acid in ST-Segment Elevation Myocardial Infarction

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Abstract

Background and Objective: Acute myocardial infarction is the leading cause of mortality and morbidity across the world. Acute myocardial infarction with ST-segment elevation has been considered a common cardiac emergency and has considerable morbidity and mortality. The role of uric acid (UA) in the mortality rate of ST-segment elevation myocardial infarction (STEMI) was examined in the present study. **Materials and Methods:** In this prospective study, 107 patients diagnosed with STEMI aged 18 years and older in the coronary care unit at Azadi Teaching Hospital, Duhok, Iraq from April 20, 2017 to December 20, 2017 were followed up for 1 month to determine the 30-day mortality in relation to serum UA level. **Results:** The mean age of patients was 55.27 ± 13.59 years. The inferior type of STEMI was the most prevalent one among the patients (45.1%). Serum UA was not significantly different in both the groups ($P > 0.05$). **Conclusion:** The study did not show UA as a risk factor for mortality in patients with STEMI.

Keywords: Mortality rate, risk factor, ST-elevated myocardial infarction, uric acid

INTRODUCTION

Acute myocardial infarction (MI) is defined as a myocardial necrosis event in which unstable ischemic syndrome is a causative factor.^[1] Acute MI is the leading cause of mortality and morbidity across the world. Acute MI with or without ST-segment elevation MI (STEMI or non-STEMI) is considered to be a common cardiac emergency and has considerable morbidity and mortality.^[2] STEMI happens when a major epicardial coronary vessel is obstructed due to thrombus formation or other factors. STEMI is a life-threatening condition and must be diagnosed and managed quickly through coronary revascularization such as percutaneous coronary intervention.^[3] Practically, acute MI is diagnosed through clinical evaluation, electrocardiogram (ECG), biochemical indicators, pathological evolution, and imaging techniques.^[2]

Since the past three to four decades, epidemiological features of acute MI have been changed substantially. Currently, low- and middle-income countries have been shifted to have considerable global burden of cardiovascular and acute MI.^[4]

Rupture or erosion in a vulnerable, fatty, and atherosclerotic coronary plaque has been shown to be an initial mechanism for acute MI. This mechanism leads to circulating blood exposure to highly thrombogenic core and matrix materials in the plaque.^[5] Currently, the number of cases due to erosion is increasing compared with the cases due to rupture factor.^[6] Total occlusion due to thrombus leads to STEMI.^[7] A partial occlusion, or occlusion in the presence of collateral circulation, leads to non-STEMI or unstable angina.^[8]

STEMI is one type of MI that the myocardium of heart muscle has died owing to blood supply obstruction. The ST-segment backs to the flat section in an ECG reading representing the interval between jagged heartbeats. This segment will appear abnormally elevated during MI.^[9] STEMI is a clinical syndrome depicted by characteristic

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symptoms of myocardial ischemia in relation to more than 20 min ST elevation (STE) and subsequent release in biomarkers of myocardial necrosis.^[7,10]

Significance of the study

Cardiac myocytes produce adenosine which is responsible for vasodilation of arteries. Under some circumstances, the adenosine level is raised substantially which results in hypoxia and tissue ischemia.^[11] Consequently, endothelium degrades adenosine to uric acid (UA) quickly. Due to the increase in UA concentrations and decrease in intracellular pH, UA effluxed to the vascular lumen.^[12] Therefore, it may be that the UA level is an indicator of ischemia severity and tissue hypoxia. The higher concentration of UA level has been shown to be a risk factor for coronary artery disease (CAD) or a prognostic factor for mortality and morbidity in patients with CAD. Some investigators showed the higher concentration of UA in STEMI mortality.^[13,14]

New therapeutic methods are established for those patients who develop heart failure following STEMI, and the aim is to reduce STEMI mortality. It is highly important to examine the role of serum UA to reduce mortality in STEMI patients. The role of serum UA in the 30-day mortality rate of STEMI was examined in the present study.

PATIENTS AND METHODS

Study design

In the prospective cohort study, 107 patients between 25 and 83 years were included. They have been diagnosed with STEMI in the Internal Medicine Department at Azadi Teaching Hospital in Duhok, Iraq.

Inclusion criteria

The patients met the eligibility criteria if they were 18 years and older, male or female, and met the diagnostic criteria of STEMI, including resting chest pain lasting for more than 30 min; having typical ischemic ST-elevation in ECG leads; and rise in cardiac troponins.

Exclusion criteria

In this study, the patients with following characteristics were excluded:

- Patients diagnosed with acute non-STEMI;
- Impaired renal function;
- Hypothyroidism;
- Malignancy;
- Gout;
- Inflammatory diseases;
- Those using corticosteroid or cytotoxic drugs.

Data collection methods

The questionnaire of collecting data consisted of three following sections: The first section had sociodemographic

factors and clinical history including age, gender, risk factors, and disease types. The second section consisted of biochemical indicators, including troponin, UA, creatinine, random blood sugar, total cholesterol (TC), and triglyceride (TG). In the last or third section, the mortality of patients was recorded following 1 month of hospital admission.

Measurement and diagnostic criteria

The general characteristics of the patients listed in the following were collected: age in year; gender as male or female; hypertension; diabetes mellitus; smoking; dyslipidemia; and family history of CAD.

The diagnosis of acute STEMI was established based on signs, symptoms, and biochemical indicators, according to the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines.^[7] Diagnostic STE is defined as new STE at the J-point in at least two contiguous leads >2 mm (0.2 mV) in men or >1.5 mm (0.15 mV) in women in leads V2-V3 and/or >1 mm (0.1 mV) in other contiguous chest or limb leads.^[1,15]

Laboratory measurements

Venous blood samples were taken from the patients in the morning in a fasting status. Serum UA, TC, and TG were measured with a 7600 Automatic Biochemistry Analyzer (Hitachi Limited Corporation, Germany). Baseline serum uric acid ≥ 7 mg/dL for men and ≥ 6 mg/dL for women was diagnosed with hyperuricemia.^[16]

Dyslipidemia was assessed through the biochemical measurement in the hospital according to the American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines (AACE)^[17] as follows:

- TC: desirable < 200 mg/dL, borderline high 200–239 mg/dL, high > 239 mg/dL.
- High-density lipoprotein-cholesterol: dyslipidemia low < 40 mg/dL in males and < 50 mg/dL in females.
- Low-density lipoprotein-cholesterol: optimal < 100 mg/dL, near optimal 100–129 mg/dL, borderline high 130–159 mg/dL, high 160–189 mg/dL, very high > 189 mg/dL.
- TG: normal < 150 mg/dL, high 150–199 mg/dL.

Statistical methods

The frequency percentage and mean standard deviation were used for descriptive purposes of the study such as mortality rate. The independent *t*-test, one-way analysis of variance (ANOVA), and Fisher's exact tests were performed for statistical difference of UA in sample size. The level of less than 0.05 was considered as statistically significant difference. Statistical Package for

Social Sciences (SPSS) version 23.00 (IBM) was used for statistical calculations.

Ethical considerations

The ethical approval of the present study was obtained from the Iraqi Board. The participation was completely optional. The current study did not apply any intervention on the patients.

RESULTS

The study found that of the 107 patients recruited in the study, more than two-thirds of them (75.7%) were males and remaining 24.3% were female patients. Hypertension and smoking were the most prevalent risk factors, 15.9% and 14.0%, respectively. Close to half of them had multiple risk factors for MI (45.8%). The mean of the patients was 55.27 (SD:13.59) years. The most common type of STEMI was inferior type (45.1%), followed by lowest was lateral (1.0%) and inferior and septal (1.0%). In the study sample size, mortality rate was 4.7%, as shown in Table 1.

The mean serum of UA and random blood sugar were 6.15 (SD: 1.96) mg/dL and 187.50 (SD: 111.72) mg/dL, respectively. The mean values of TC and TG were 205.52 (SD: 77.76) mg/dL and 211.21 (SD: 103.89) mg/dL, respectively. The median and interquartile values of

serum creatinine were 0.86 and 0.38 mg/dL, respectively [Table 2].

The impact of serum UA on mortality rate was examined in Table 3. The study did show that mortality has not been affected by serum UA ($P=0.435$). The mean value of UA in deceased patients following 1 month was 6.89 ± 1.98 mg/dL and the mean value of UA in live patients was 6.11 ± 1.96 mg/dL.

Similarly, the study showed that means of UA in different STEMI types were comparable ($P=0.679$) [Table 4].

DISCUSSION

This study showed that the mortality rate is 4.7% following 1 month of hospital admission. In addition, the investigator did not find UA as a risk factor for mortality in STEMI patients. Similar levels of UA were found in patients with different STEMI types.

Other investigators have examined the effect of UA on mortality and morbidity among patients with STEMI as well. For instance, Hajizadeh *et al.*^[18] enrolled 608 patients with STEMI in a prospective cohort study between December 21, 2012 and February 10, 2014 to find out the effect of UA on patients' mortality, morbidity, left ventricular ejection fraction, and atrial and ventricular arrhythmia. They showed that those patients with higher serum UA level have higher Killip class after STEMI. In agreement with the current study, they did not find that short- and mid-term mortality is associated with UA ($P=0.31$). Their finding is congruent with some other studies as well.^[13,19-22]

In our study, we examined the role of UA on short-term mortality (1 month) and found no significant association

Table 1: Baseline characteristics of patients

Patients' characteristics (n=107)	Frequency distribution	
	Frequency	Percentage
Gender		
Male	81	75.7
Female	26	24.3
Risk factors		
Hypertension	17	15.9
Diabetes mellitus	5	4.7
Smoking	15	14.0
Dyslipidemia	5	4.7
Family history	5	4.7
Multi-factor	49	45.8
Others	11	10.3
STEMI types		
Anterior	31	30.4
Inferior	46	45.1
Lateral	1	1.0
Septal	2	2.0
Inferior and lateral	7	6.9
Anterior and lateral	8	7.8
Anterior and septal	6	5.9
Mortality		
Yes	5	4.7
No	102	95.3
	Mean	Standard deviation
Age, years	55.27	13.59

Table 2: Biochemical indicators of patients

Biochemical indicators (n=107)	Frequency distribution	
	Mean	Standard deviation
Troponin (ng/mL)	12.71	9.79
Uric acid (mg/dL)	6.15	1.96
Random blood sugar (mg/dL)	187.50	111.72
Lipid profile		
Total cholesterol (mg/dL)	205.52	77.76
Triglyceride (mg/dL)	211.21	103.89
Serum creatinine (mg/dL)	0.86 (median)	0.38 (interquartile)

Table 3: Impact of serum UA on mortality in patients with STEMI

Mortality (n=107)	Uric acid (mg/dL)		
	Mean	SD	P-value (two-sided)
Patient outcome after 1 month			
Death (n=5)	6.89	1.98	0.435*
Live (n=102)	6.11	1.96	

*Independent t-test was performed for statistical analysis

Table 4: Level of UA in patients with different types of STEMI

STEMI types (n=107)	Uric acid (mg/dL)		P-value (two-sided)
	Mean	SD	
Anterior	6.18	1.45	0.679*
Inferior	6.00	1.86	
Lateral	8.2		
Septal	4.3	0.56	
Inferior and Lateral	6.64	2.09	
Anterior and Lateral	5.8	1.67	

*One-way ANOVA was performed for statistical analysis

between UA and mortality in patients with STEMI. The long-term mortality has also been investigated by Hajizadeh *et al.*^[18] and found no substantial relationship with UA. However, some other studies have shown a substantial serum UA and an increase in mortality in patients with STEMI. For example, Kojima *et al.*^[23] divided the study patients into four groups according to the serum UA level. They showed that the patients with serum UA level more than 4.5 mg/dL have 3.5 times higher mortality rate when compared with those with serum UA below 3.0 mg/dL. However, the mean of their patients was 67 years, significantly different from our study (55.27 years). In addition, Omidvar *et al.*^[24] showed that serum UA concentration of 7 mg/dL or greater plays a prognostic role for short-term and in-hospital mortality (30-day) in male hyperuricemic patients only with odds ratio of 3.76 for short-term mortality, but not for female patients, similar to some other studies.^[25]

In contrast to those studies showed higher serum UA as a risk factor for STEMI or not, the studies have shown that it is an independent risk factor for short- or long-term adverse events in patients with STEMI.^[26] It is significantly associated with cardiovascular disease and increase in mortality and occurrence of CAD in clinical and epidemiological investigations.^[27-29]

By taking into account the wide variety of studies conducted on UA role in STEMI patients mortality, it is evident that its role as a prognostic factor is controversial. However, the Framingham Heart study as one of the most important studies did not show this association.^[30] Therefore, most of the medical societies do not consider serum UA as a risk factor of short- or long-term mortality in patients with STEMI.^[30]

It is recommended that future attempts focus on average hospital stay in STEMI patients with hyperuricemia in comparison to patients with non-hyperuricemia. Different cut-off values for serum UA have been considered in these kinds of studies. Still, there is no internationally accepted normal range for male and female populations making hard to establish a between-study comparison.

Limitations of the study

The findings reported in the present study must be traced in the light of study design and sampling methods. The

study investigators were unable to follow the patients for longer than 1 month. Possibly, long-term follow-up with larger sample size is required to get the better picture of impact of UA on the cardiovascular system. In addition, the severity of disease has not been measured through Killip class to predict the mortality risk owing to time limitation of the present study.

CONCLUSIONS AND RECOMMENDATIONS

The present study shows 4.7% of mortality rate in patients with STEMI. In addition, the study did not show any association between serum UA levels and mortality rate in STEMI patients. It is recommended that clinicians attempt to reduce the level of UA in STEMI patients as it may lead to other medical conditions. Clinicians must trace the mortality expectation of STEMI patients in other risk factors such as smoking and dietary behaviors.

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