

Correlation between the Serum Levels of Uric Acid and HS-CRP with the Occurrence of Early Systolic Failure of Left Ventricle Following Acute Myocardial Infarction

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Abstract- Recent studies show that, Inflammation plays an important role in the initiation and progression of atherosclerosis and in the pathogenesis of acute cardiovascular events. There is a possible association between ventricular dysfunction following acute myocardial infarction and high Sensitivity C-reactive protein (HS-CRP) and uric acid. In this study we assessed the relationship between HS-CRP and uric acid with LVEF and Killip Class in patients with acute myocardial infarction (AMI). In a cross sectional study, 188 patients (63 females and 125 males) with AMI (STEMI) who were admitted in CCU ward in Emam Khomeini Hospital, Tehran/Iran, were entered. Uric acid and HS-CRP were measured within first day of admission. We measured ejection fraction (LVEF) and used Killip classification system. The mean age of patients was 60.4 ± 9.2 years. The mean of uric acid was 5.9 ± 1.6 , 6.6 ± 2.1 , 7.1 ± 2.1 and 9.4 ± 1.3 in patients with Killip Class I, II, III and IV, respectively ($P=0.005$). The mean of HS-CRP was 1.9 ± 1.4 , 14.2 ± 10.9 , 12.2 ± 10.9 and 15.7 ± 6.7 in patients with Killip Class I, II, III and IV, respectively ($P=0.005$). There was a relationship between HS-CRP and LVEF (Correlation coefficient= -0.788 , $P<0.001$), but there was not between uric acid and LVEF (Correlation coefficient= -0.111 , $P=0.129$). The plasma concentration of C-reactive protein correlated with LVEF and Killip Class in patients with AMI but serum uric acid was just correlated with Killip Class IV. It seems that plasma concentrations of HS-CRP and uric acid are useful for prediction of development of heart failure in AMI patients. More future studies are necessary for final judgment.

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Introduction

Cardiovascular disorders are the most common cause of mortality in industrial societies and one of the major reasons of death in developed countries. According to the burden studies conducted in Iran, cardiovascular disorders are the most common disorder among the Iranian population (1-3). Recent studies indicate that the role of inflammatory processes, whether as a factor to form atherosclerotic plaques or as a mediator for acute rupture of atherosclerotic plaque to form block and infarction are considerable (4,5). One of the most biomarkers which has been studied as a indicator for inflammatory process in cardiovascular disorders is High Sensitive C-Reactive Protein (HS-CRP) (6).some studies have shown the relation between serum level of HS-CRP with the prevalence of underlying

atherosclerosis and occurrence of cardiovascular accidents and its consequences such as heart failure following myocardial infarction (7-13).

Beside HS-CRP as a inflammatory factor, several studies indicated that serum level of acid uric has been brought up as a predictable factor for patients with Coronary Artery Disease (CAD) and Congestive Heart Failure (CHF) .It has been shown that there is a relation between the serum level of uric acid with LVEF, systolic pulmonary arterial pressure (PAP), and mortality among patients with heart failure (13-17) .

There are a few studies about the relation between serum level of acid uric with prognosis of patients with CHF and CAD and the occurrence of CAD. There is little number of studies about the role of serum level of uric acid as a predictor for patient with AMI (18-19). Therefore in this study, we would like to consider the

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relation between acid uric and HS-CRP with left ventricle failure (on the basis of ejection fraction ratio and Killip's class) following AMI. The results of this study can help us to assess the value of these markers in prediction of the occurrence of heart failure following AMI.

Materials and Methods

This study was conducted as a case control during 2009 to 2011 in CCU of Imam Khomeini Hospital, Tehran/Iran. The population in our study was patients with AMI (STEMI) who referred to the hospital for treatment. The criteria to select the patients in our study consisted of the patients with AMI diagnosed by cardiologist on the basis of the definition approved by American College of Cardiology Committee (ACC) and European Society of Cardiology(ESC) .This included typical rise and gradual fall of troponin level and or sever increase and decrease of CK-MB associated with at least one of the following parameters:

- 1-gradual appearance of pathologic Q wave on ECG (electrocardiogram) strip or
- 2- EKG changes indicating ischemia on the ECG strip (ST segment elevation).

Those who referred after 24 hours of cardiac attack onset, had a history of cardiac infarction or heart failure, apparent infection or diagnosis of infection on the basis of getting history and doing physical examination, existence of any malignancy or rheumatologic diseases, treatment with immunosuppressive drugs, history of apparent bleeding or surgery during last month and remarkable renal failure (creatinin> 1.2 mg/dl) at the time of admission were excluded from our study.

In this study all of the patients who met the requirement values to enter our study were considered in order, to complete the calculated size sample, thus we used available and census method to select our samples. According to the previous studies and variety of relative findings between HS-CRP and Uric Acid with heart failure among patients, in this study in a statistical significant level ($\alpha=5\%$) and power test of 80% ($B=20\%$), effect size=0.20 ($r=0.20$), the sample size was estimated around 200 persons.

At the time of admission for CCU, the entire history of patients was considered and reviewed by assistant of cardiology. Thereafter venous blood sample was taken by 5cc syringe in 2 laboratory tube and after delivery to the lab, the first tube was centrifuged with 300 g round for 10 minutes and then the achieved serum was considered by BT-3000 and BIOTECHNICA, Italy and

Spain kit, (detection of HS-CRP: limit=0.06 mg/L, sensitivity=60 mA. L/mg at 5 mg/L) and the second tube was used by this machine via PAP way for evaluation the level of Acid uric. The patients were considered by assistants of cardiology and his or her mentor in point of view of the occurrence of heart failure about 3-5 days post-infarction and ejection fraction was measured by using echocardiography over Simpson way with Mylab50 apparatus.

After gathering data of all of the patients, the data were entered into the computer sheets and SPSS-11.5 was used as software for statistical analysis .For this purpose we used ratio and frequency for qualitative variants, on the other hand mean and standard deviation were used for quantitative variants. At first we considered how variants were distributed and because of abnormal distribution, the comparison of means was considered by using Kruskall Wallis H test and the relation between quantitative variants with Spearman Rank Correlation was considered. The significant statistical limit of this study was $P<0.05$.

Results

The acquired results of the data of our study indicated that among 188 patients, 63 patients (33.5%) and 125 patients (66.5%) were female and male; respectively. The mean (\pm Standard deviation) of age for the patients was 60.4 ± 9.2 with a range between 37 to 75 years old.

In Table-1 the frequency and the ratio of classic cardiac risk factors have been shown.

The finding of the study has been shown that according to Kllip Class, 94 (50%) were in class I, 65 (34.6%) were in class II, 22 (11.7%) were in class III, 7 (3.7%) were in class IV. The findings have been showed that the mean of Acid uric serum level in patients in our study was 6.4 ± 1.9 mg/dl and in 36 patients (19.1%) was

Table 1. The frequency and the ratio of classic cardiac risk factors

Risk factor	Frequency	Ratio (%)
Hypertension	72	38.3 %
Diabetes	53	28.2 %
Hyper Lipidemia	45	23.9 %
Smoking	71	37.8 %
Positive family History for CAD	38	20.2 %

Table 2. The mean of uric acid and HS-CRP level on the basis of Killip Class

Patients Group	Variant Considerable	Killip Class				P Value
		I	II	III	IV	
female (n=63)	Uric acid	6.3±2.7	6.8±2.3	6.5±2.5	10.2±1.9	0.023
	HS-CRP	1.5±1.1	17.9±9.9	10.7±8.8	19.8±2.4	<0.001
Male (n=125)	Uric acid	5.7±1.3	6.4±1.8	7.9±1.7	8.2±1.1	0.011
	HS-CRP	1.9±1.6	11.1±5.8	14.7±5.4	10.4±7.1	<0.001
Total (n=188)	Uric acid	5.9±1.6	6.6±2.1	7.1±2.1	9.4±1.3	0.005
	HS-CRP	1.9±1.4	14.2±10.9	12.4±10.9	15.7±6.7	<0.001

more than normal range. The mean of serum level of HS-CRP was 7.9±5.4 mg/dl and in 98 patients (52.1%) the range of HS-CRP was abnormal and the mean of serum level of creatinin was 0.98±0.18 mg/dl. By using kolmogorov-smirnov, it was determined that quantitative variants of age, creatinin, EF, acid uric, and HS-CRP do not have normal distribution and frequency and in order to analytical analysis of their relations we need to use nonparametric tests.

In Table 2, the mean of values of acid uric and HS-CRP in all patients and among male and patients has been shown on the basis of Killip Class. These values indicates the existance of statistical significant differences among the acquired values in different classes of heart failure.

The content of the above-mentioned table shows that acid uric among class IV has a significant differences compare to the other classes ($P<0.001$). But there is no significant differences among other classes ($P<0.05$).

In Table-3 the correlation among quantitative variants has been shown.

In order to consider the independed relation among

considerable variations with class of heart failure, we used logistic multi variance regression test to consider the independed relation of variants with Killip Class. In this model of analysis , the relation between HS-CRP and acid uric with Killip class has been found.

Discussion

The acquired findings of the data of this study have been shown that most patients participating in our study were male. In spite of that, significant number of females were also participated in our study which this assisted us to clarify the relation between heart failure following AMI and serum level of Acid uric and HS-CRP on the basis of gender, separately.

The results of our study shows that the major proportion of patients were in class I and II of heart failure, and a minor proportion of them were in class III and IV. It was also of note that, in most of patients the serum level of acid uric was normal, but the proportion of patients with normal and abnormal HS-CRP was almost similar.

Table 3. Correlation among quantitative variants

Value	age	EF	crentinin	Uric acid	Hs CRP
age	-	r=0.253 P=0.001*	r=-0.005 P=0.949	r=0.094 P=0.198	r=-0.010 P=0.896
EF	r=0.253 P=0.001*	-	r=0.140 P=0.056	r=-0.111 P=0.129	r=-0.788 P<0.001*
crentinin	r=-0.005 P=0.949	r=0.140 P=0.056	-	r=-0.280 P=0.001*	r=-0.184 P=0.011*
Uric acid	r=0.094 P=0.198	r=-0.111 P=-0.129	r=0.253 P=0.001*	-	r=0.018 P=0.811
Hs_CRP	r=-0.010 P=0.896	r=-0.788 P<0.001*	r=-0.184 P=0.011*	r=0.018 P=0.811	-

* statistical significant value

In this study we found that there was a significant relation between heart failure and serum level of uric acid. The highest level of Acid uric was among class IV patients. But among patients in class I to III, there was not significant difference for the serum level of the uric acid. In other words, Killip class IV was associated with high level of uric acid. This finding has been found in both males and females; this could be resulted from the rise of the uric acid level due to tissue hypo perfusion in higher class of killip. On the contrary, the range of HS-CRP had a stronger relation with heart failure and class of failure, in a manner that whatever the class increases the serum level of uric acid will also increase and this difference was found among double groups. These findings indicated that there was a strong relation between inflammatory mediators such as HS-CRP with the occurrence of heart failure, and the level of uric acid was valuable once the heart failure was severe. According to the current study, the value of HS-CRP in prediction of the occurrence of heart failure following AMI was more than uric acid.

In our study, there was no relation between the age of patients and uric acid or HS-CRP. But there was a significant relation between EF and HS-CRP. No significant statistical relation between acid uric and EF was found. These relations was reversed, in other words, whatever EF decreased, acid uric and HS-CRP increased. But increasing of HS-CRP associated with decreasing of EF. Comparison of these results with the results of previous studies indicated similar findings. In a study conducted by Niskanen *et al.* (20), it was understood that the rate of mortality due to cardiac diseases in patients with high level of acid uric were 2.5 times more than patients with normal level of uric acid. Culleton *et al.* found that uric acid serum level had a significant statistical relation with the incidence of cardiovascular diseases and death due to cardiac diseases. In a study conducted by Ridker *et al.* (22) the serum level of CRP in healthy persons was 1.13 mg/L and in patients with MI 1.51 mg/L, in patients with ischemia were more than healthy persons. It was also of note that among patients with high level of HS-CRP, the risk of occurrence of MI was 2.9 times and the risk of stroke was 1.9 times in comparison to the patients with normal level of HS-CRP. Lazzari *et al.* (18) found that 21.5% of patients with AMI had a rise in acid uric level and the risk of mortality among these patients during hospitalization was 3.9 times more than patients with normal level of acid uric. It has been shown that there is a correlation between the occurrence of heart failure with uric acid level and HS-CRP.

In a study conducted by Nadkar and Jain (19), there was a significant statistical relation between acid uric and Killip class, immediately post-MI, *i.e* the rise of acid uric level will increase the occurrence of ventricular failure. These studies have been done on patients with heart failure and MI and several of them have been performed on healthy persons, but in both groups it seems that there is a relation between uric acid level and HS-CRP, cardiovascular accidents, and worse prognosis in case of such events.

Our findings shows that acid uric and specially HS-CRP are the markers which have a relation with heart failure among patients with AMI and the serum level of those could be as a predictor for the possibility of occurrence of sever heart failure in patients with AMI.

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