

Hs-CRP and Serum Uric Acid as Risk Factors and Prognostic Markers in Acute Myocardial Infarction.

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ABSTRACT

Background: To study the role of inflammatory markers like hs-CRP and S. Uric Acid as risk factors and prognostic markers in acute myocardial infarction. **Methods:** A total of 100 cases admitted in ICU/CCU under Department of Medicine/Cardiology, NIMS Medical College & Hospital Jaipur and 100 controls who were the normal age/sex matched during study period of 15 months i.e. August 2014 to October 2015 were taken into study based on inclusion and exclusion criteria. Blood samples were taken to measure hs-CRP and Uric Acid and patients were followed for 7 days in hospital. Tests of statistical significance were done using Chi-square Test, unpaired 't' test, Fisher test. **Results:** Out of 100 age and sex matched cases and controls, 63% were having positive hs-CRP compared to 2% in controls ($p < 0.001$). Hyperuricemia was found in 23% cases compared to 4% in controls ($p = 0.0002$). 44 patients developed different complications during follow up, out of which 40 were having positive hs-CRP ($P < 0.001$) and 22 were having hyperuricemia ($p < 0.001$). **Conclusion:** We found that hs-CRP and Uric Acid are risk factors for myocardial infarction and are good predictors of outcome following MI.

Keywords: Acute Myocardial Infarction, high sensitive c-reactive protein, Uric Acid.

INTRODUCTION

Acute coronary syndrome (ACS) is a unifying term representing a common end result of acute myocardial ischemia which includes ST segment elevation myocardial infarction (STEMI), Non ST segment elevation myocardial infarction (NSTEMI) and Unstable Angina.^[1] The term acute myocardial infarction (AMI) includes STEMI and NSTEMI.

Acute myocardial ischemia is usually but not always caused by atherosclerotic plaque rupture, fissuring, erosion or a combination with superimposed intracoronary thrombosis and is associated with an increased risk of cardiac death and myonecrosis.

Cardiovascular disorders are among the most common cause of death globally, hence WHO has called it as "modern epidemic".^[2] With increasing urbanisation prevalence of ACS is rising rapidly in developing countries.^[3] Acute coronary syndrome causes significant mortality and morbidity in Indians also.^[4]

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Atherosclerosis was previously known to result from a passive process of lipid accumulation. In recent studies it is considered to be an active process of cell activation, inflammation and thrombosis.^[5] Inflammation is the key mechanism in the pathogenesis of different stages of atherosclerosis which includes onset and progression of atheroma, plaque instability and rupture and restenosis

following angioplasty.^[6-8] The inflammatory process is enhanced by the cardiovascular risk factors, particularly elevated LDL cholesterol. It has been proved that modifying these risk factors reduces inflammation and helps in prevention of atherosclerotic events.^[9]

Obesity, Type 2 DM, Dyslipidemia are the traditional risk factors of IHD. Up to half of the events are reported to occur in apparently healthy individuals who have few or none of the traditional risk factors mentioned above. As a result attention has increasingly turned to the role of other risk factors such as inflammatory biomarkers.

Various inflammatory biomarkers including cytokines, adhesion molecules and acute phase reactant protein, are produced by vascular cells in the plaque. C Reactive Protein (CRP) is one of the acute phase reactant protein produced by liver which is a marker of systemic inflammation that increases in various types of injury, particularly bacterial infection.^[10] High sensitivity techniques were developed to detect lower serum CRP level than by previous laboratory methods, known as High sensitive CRP (hs-CRP), and these techniques should be used when assessing the cardiovascular risk associated with chronic vascular inflammation of atherosclerosis. Several studies proved that CRP is not only marker of inflammation but also plays an active role in atherogenesis.^[11]

Uric acid is the final product of the activity of xanthine oxidase (XO) in purine metabolism. Adenosine synthesized locally by vascular smooth muscle cells in cardiac tissue is rapidly degraded by endothelium to uric acid, which undergoes rapid efflux to vascular lumen due to low intracellular pH and negative membrane potential. Xanthine oxidase activity and uric acid synthesis are increased in vivo under ischemic condition and therefore elevated

serum uric acid may act as a marker of underlying tissue ischemia. It has been shown that elevated serum uric acid levels associated with increased cardiovascular morbidity and mortality.^[12] There is some evidence that, serum uric acid could promote oxidation of low density lipoprotein, cholesterol and lipid peroxidation.^[13] High SUA levels can also stimulate the release of free radicals, resulting endothelium damage thereby risk of developing MI.^[14]

Therefore, in this study we planned to study the relationship of serum level of uric acid and hs-CRP and their prognostic significance in AMI.

The findings of this study can help us to determine the relationship of hs-CRP and serum uric acid in patient with acute myocardial infarction and asses the value of these markers in prediction of the prognosis of the patient with acute myocardial infarction.

MATERIALS AND METHODS

- This study was carried out in the Department of Medicine/Cardiology, NIMS Medical College and Hospital, Shobha Nagar, Jaipur, Rajasthan from August 2014 to October 2015, over the period of 15 months.
- Study was done on both male and female acute myocardial infarction patients of age more than 18 years presented within 6 hrs with h/o chest pain, admitted in ICU/CCU under the Department of Medicine/Cardiology, NIMS Hospital, Jaipur and normal healthy controls

both male and female more than 18 years of age.

- Type of study : case control study with follow-up of cases
- Study design: longitudinal

Blood samples were collected at the time of admission for measurement of hs-CRP and Uric acid. Patients were admitted for in-hospital observation of prognosis following AMI. Complications developed during study period were noted.

RESULTS

Table 1: Incidence of hs-CRP among study population

In our study CRP were raised in 63 cases (63%) and in 2 controls (2%) out of 100 cases and controls respectively. it is statistically highly significant as p value < 0.001. thus inferring role of hs-CRP in acute myocardial infarction as a risk factor [Figure 1].

Table 2: hs-CRP and its association with complications of AMI

Out of 44 patients who were having complications following AMI 40 patients (90.9%) were having raised CRP levels where as among 56 patients without any complications only 23 (36.5%) were having raised CRP values [Figure 2]. It is statistically highly significant as P value is < 0.001. It shows that patients with elevated CRP values developed more frequent complications compared to patients who did not. Thus inferring hs-CRP is a marker of poor prognosis in Acute myocardial infarction.

Table 1: Incidence of hs-CRP among study population.

HS-CRP	Case		Control		Total	
	No.	%	No.	%	No.	%
Normal	37	37.00	98	98.00	135	67.50
Raised	63	63.00	2	2.00	65	32.50
Total	100	100.00	100	100.00	200	100.00

Chi-square = 82.051 with 1 degree of freedom; P < 0.001

Table 2: hs-CRP and its association with complications of AMI

hs-CRP	AMI with complications		AMI without complications		Total
	No.	%	No.	%	
<0.6 mg/dl(-ve)	4	10.81	33	89.19	37
≥0.6 mg/dl(+ve)	40	63.49	23	36.51	63
Total	44	44.00	56	56.00	100

Fisher Exact Test P < 0.001

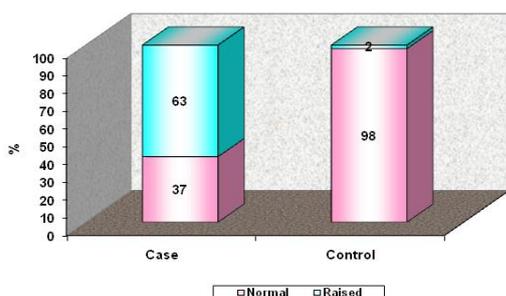


Figure 1: Incidence of hs-CRP on admission in study group

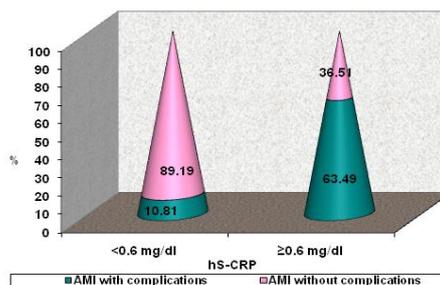


Figure 2: hs-CRP and its association with complications of AMI

Table 3: Incidence of uric acid among study population

In our study uric acid were raised in 23 cases (23%) and in 4 controls (4%) out of 100 cases and controls respectively. it is statistically highly significant as p value 0.0002 [Figure 3]. Thus, inferring role of uric acid in acute myocardial infarction as a risk factor.

Table 4: Uric acid and its association with complications of AMI

Out of 23 patients who were having raised uric acid levels 22 (95.65%) patients developed complications which is statistically significant (p< 0.001) [Figure 4]. This infers that elevated serum uric acid in acute MI is associated with frequent complications.

Table 3: Incidence of uric acid among study population

S. Uric Acid Day 0	Case		Control		Total	
	No.	%	No.	%	No.	%
Low	29	29.00	28	28.00	57	28.50
Normal	48	48.00	68	68.00	116	58.00
Raised	23	23.00	4	4.00	27	13.50
Total	100	100.00	100	100.00	200	100.00

Chi square: 16.8, with 2 degrees of freedom, p value: 0.0002

Table 4: Uric acid and its association with complications of AMI

S. Uric Acid Day 0	AMI with complications		AMI without complications		Total
	No.	%	No.	%	
Low	3	10.34	26	89.66	29
Normal	19	39.58	29	60.42	48
Raised	22	95.65	1	4.35	23
Total	44	44.00	56	56.00	100

Chi Square: 38.6, Dof: 2, p value: 0.0001

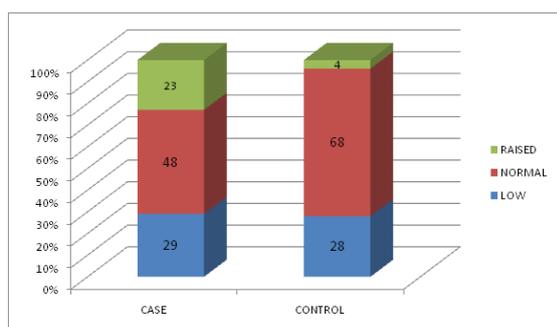


Figure 3: Incidence of uric acid among study population

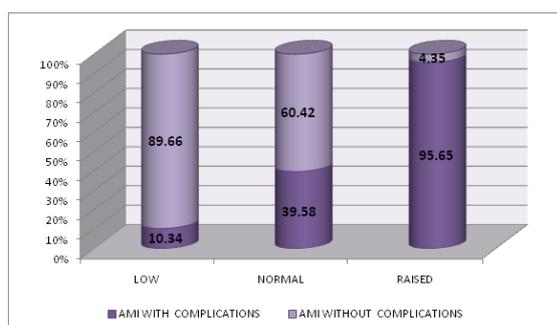


Figure 4: Uric acid and its association with complications of AMI

DISCUSSION

Correlation of level of hs-CRP and s. uric acid in acute myocardial infarction.

In our study of hs-CRP and S. uric acid levels in 100 patients with acute myocardial infarction, 63 % patients had positive hs-CRP (mean=0.61± 0.21) as compared to controls (mean = 0.28± 0.10) (P value

<0.001). This is in line with Liuzzo et al.^[15] (76%) and Mishra et al.^[16](62%).

23% patients with had higher serum uric acid level (mean =5.47±1.63) as compared to the healthy controls (mean = 4.60±0.95) which is statistically significant.(p <0.001). This is in line with Li Chen et al.^[17] (23%), Lazzari et al.^[18] (21.5%) and Gazi E et al.^[19] (18%).

Correlation of level of hs-CRP and S. uric acid (SUA) with complications following acute myocardial infarction.

In our study out of 44 patients who are having different complications like left ventricular failure, cardiogenic shock, conduction block and tachyarrhythmias; 40 patients (90.9%) had raised level of hs-CRP (≥ 0.6 mg/dl) (P< 0.001) and 22 patients with hyperuricemia (95.65%) were associated with above mentioned complications(P <0.001).

This is in line with Tomado et al.^[20], Winter et al^[21], Sinisa Car and Vladimir Trkulja^[22] and Kojima et al^[23].

CONCLUSION

In the present study we observed that hs-CRP (63%) and S. Uric Acid (23%) were elevated in patients of acute myocardial infarction and is consistent with previous studies in which higher levels of hs-CRP and S. uric acid had association with myocardial infarction.

We found that higher levels of hs-CRP and S. Uric Acid at the time of admission were associated with

higher incidence of complications following myocardial infarction.

Hence, this study may contribute to use serum CRP and Uric Acid levels as risk factors for prediction of impending cardiovascular events and also for prognosis following acute coronary event.

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