e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2022; 12(12); 158-167

Original Research Article

Serum Uric Acid and CRP as Prognostic Predictor in Acute Myocardial Infarction

Singamaneni Manjusha, J. Rajesh, A. Shiva Prasad

Department of General Medicine, Mamata General and Super Speciality Hospital, Khammam

Received: 15-10-2022 / Revised: 22-11-2022 / Accepted: 11-12-2022
Corresponding author: Dr Singamaneni Manjusha
Conflict of interest: Nil

Abstract

Aim of the Study: To see for correlation of CRP and hyperuricemia with Killip's Class and mortality.

Material & Methods: 50 patients as cases (diagnosed as acute myocardial infarction) and 50 controls (healthy volunteers). All cases and controls were taken from Mamata General Hospital by applying inclusion and exclusion criteria. Patients were followed up for 7 days in the hospital and observed for complications such as complete heart block, cardiogenic shock, arrhythmias.

Results: Fifty patients presenting with acute myocardial infarction and fifty controls who satisfied the inclusion criteria were enrolled into the study. Data was collected and analysed with clinical and laboratory parameters.

Conclusion: Higher CRP and serum uric acid levels with Killip's class III & IV showed increased mortality. CRP >3.0 mg/dl and serum uric acid levels >7.5 mg/dl were associated with highest mortality.

Keywords: C-reactive protein (CRP), Acute Myocardial infarction (AMI), Cardio Vascular Diseases (CVD).

Introduction

Cardiovascular disease is responsible for 30% of all deaths in the world. About 80% of the global burden of CVD death occurs in low- and middle-income countries. India carries a significant portion of this CVD burden. Acute myocardial infarction continues to be the major public health problem in the industrialized and developing countries like India despite progressive research in diagnosis and management over last three decades. India suffers one of the highest CVD case fatality rates in the world according to an international registry (OASIS).

Although the use of prediction models like the Framingham's study greatly increases the detection of atherosclerotic risk, about 20% of myocardial infarction occurs in the absence of classical vascular risk factors. Many trials have been conducted to identify novel markers and risk factors of atherosclerosis. Similarly, there are only a few clinical predictors of prognosis in acute coronary syndromes (the Killip staging, TIMI and GRACE scores).

The need for biochemical cardiac markers in predicting major adverse cardiac events

(MACE) and mortality has been realized in the recent past. Recent studies have focused on the prognostic significance of novel markers like hs-CRP, lipoprotein a, homocysteine, BNP, IL-6 and uric acid. Uric acid is a marker of oxidative stress that reflects the inflammatory process occurring in atherosclerotic plaques and has also been linked to endothelial dysfunction and cell death. It is one of the most studied markers in ACS and other multifactorial diseases like obesity, hypertension, metabolic syndrome and stroke. Studies have ended up with conflicting results, with some studies showing a strong correlation, while others have not demonstrated a clear association. Similarly, a few studies carried out in populations with acute coronary syndrome have shown that uric acid is an independent marker of adverse cardiac outcomes in both short term and long term, while some studies refute it.

Acute inflammatory response is a major characteristic of cardiovascular occlusive event. Significant increase of serum C-reactive protein (CRP) occurs in inflammatory processes of different etiology, as a part of or independently of cardiac etiology [1,2].

In healthy individuals, CRP circulates in very low concentrations2, and individuals who are at the risk of development of cardiovascular diseases show systemic inflammatory response registered by increased serum CRP level. Apart from being a marker of inflammation, CRP contributes to development of atherosclerotic disease, and it is considered as the most powerful predictor of myocardial infarction and stroke [3].

Until now, various biomarkers have been studied in patients of acute coronary syndrome. However, no single marker gives definite prognostic information during the course of the disease. Little information is available about the role of different individual bio markers. Hence a study is attempted using 2 easily measured, broadly available biomarkers namely serum Uric Acid, and C-reactive protein targeting different risk indicators like purine metabolism, and inflammation as a tool for assessment in Acute myocardial infarction.

Aim of the Study

1. To assess serum c - reactive protein and serum uric acid levels determined on admission as a potential predictor in acute myocardial infarction.
2. To see for correlation of CRP and hyperuricemia with Killip's Class and mortality.

Material & Methods

50 patients as cases (diagnosed as acute myocardial infarction) and 50 controls (healthy volunteers) admitted in ICCU, Mamata General and Super Speciality Hospital, Khammam from September 2017 to August 2019.

All patients underwent clinical examination and detailed history, laboratory investigations such as routine blood investigations, serum CRP, serum uric acid. Samples were collected on day 0, 3, 5 from the onset of symptoms. ECG and echocardiography were taken.

Inclusion criteria: Patients with diagnosis of AMI based on WHO definition with any two of criteria namely-

1. Typical ischaemic chest pain,
2. Raised cardiac enzymes,
3. Typical electrocardiography (ECG) findings including development of pathological Q waves were included.

Exclusion criteria:

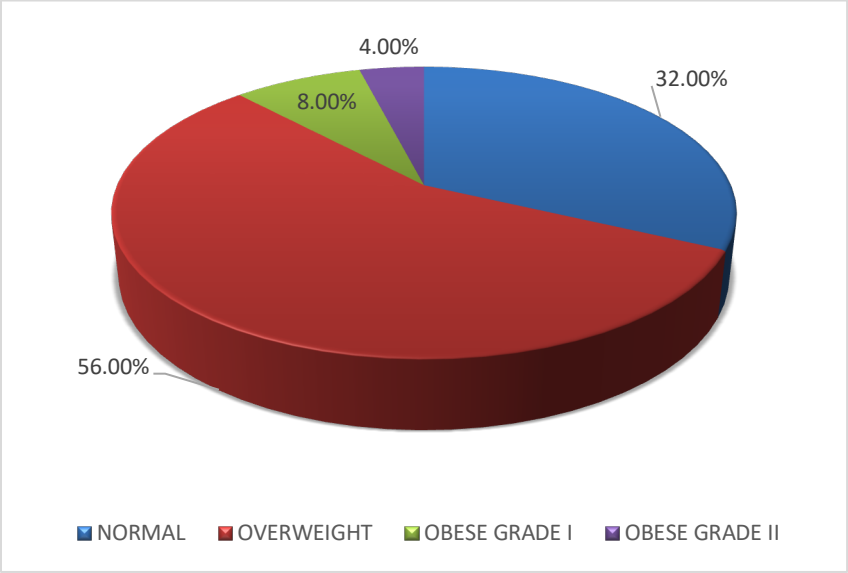
1. Patients with non-cardiac chest pain,
2. Acute infectious disease known (or) suspected neoplastic diseases,
3. Recent (less than 3 months) major trauma (or) surgery, burns Immune suppressive

drug therapy, immunological disorders, osteoarthritis, Rheumatoid arthritis, gout, ankylosing spondylitis, psoriatic arthritis were excluded from study.

Results

Table 1 : Mean age comparison between cases and controls

	GROUP	N	Mean	Std. Deviation	P VALUE
Age in years	CASE	50	58.320	12.4760	0.627 (NS)
	CONTROL	50	57.260	8.9484	



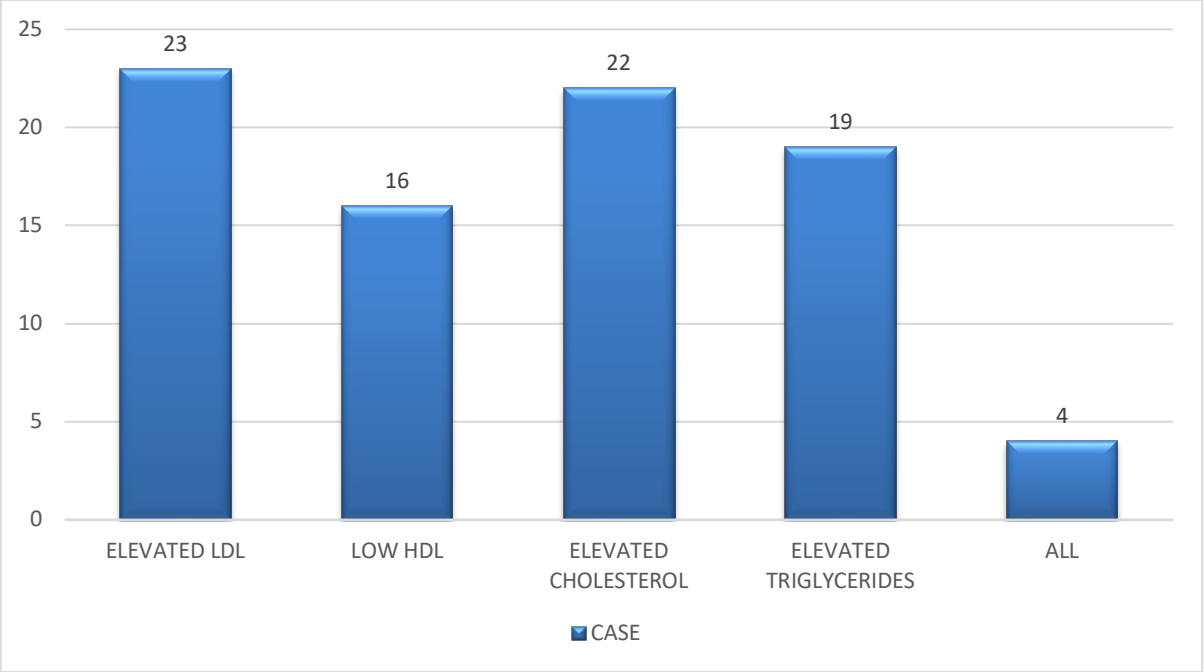
Graph 1: BMI distribution in cases

Table 2: Presenting complaints distribution in cases

	Frequency	Percent
CHEST PAIN	50	100.0
DYSPNEA	33	66.0
CHEST PAIN & DYSPNEA	33	66.0

Table 3: Risk factors distribution in cases

	Frequency	Percent
HYPERTENSION	31	62.0
DIABETES	21	42.0
SMOKING	27	54.0
ALCOHOL	16	32.0
ALL RISK FACTORS	4	8.0



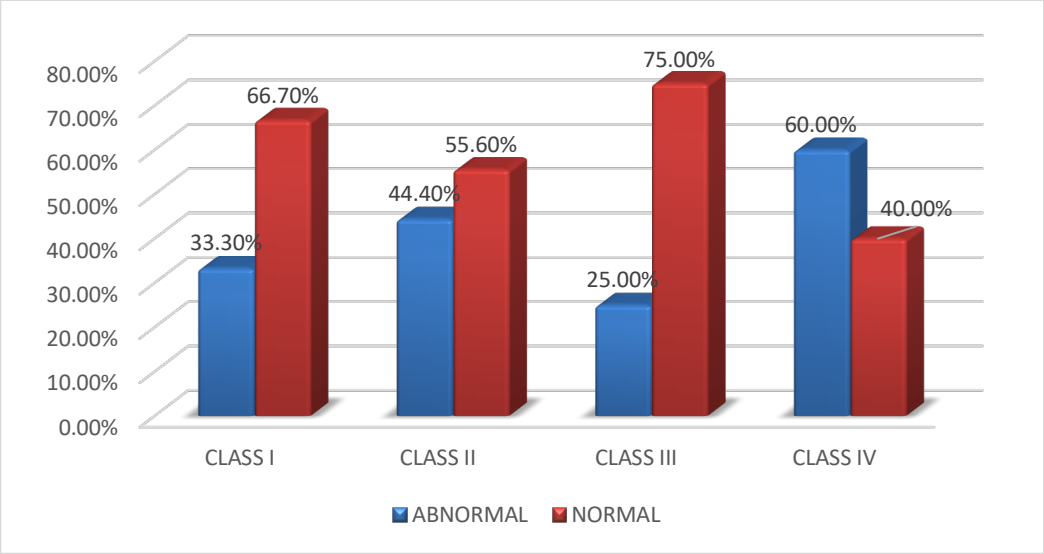
Graph 2: Dyslipidemia distribution in cases

Table 4: Type of acute myocardial infarction in cases

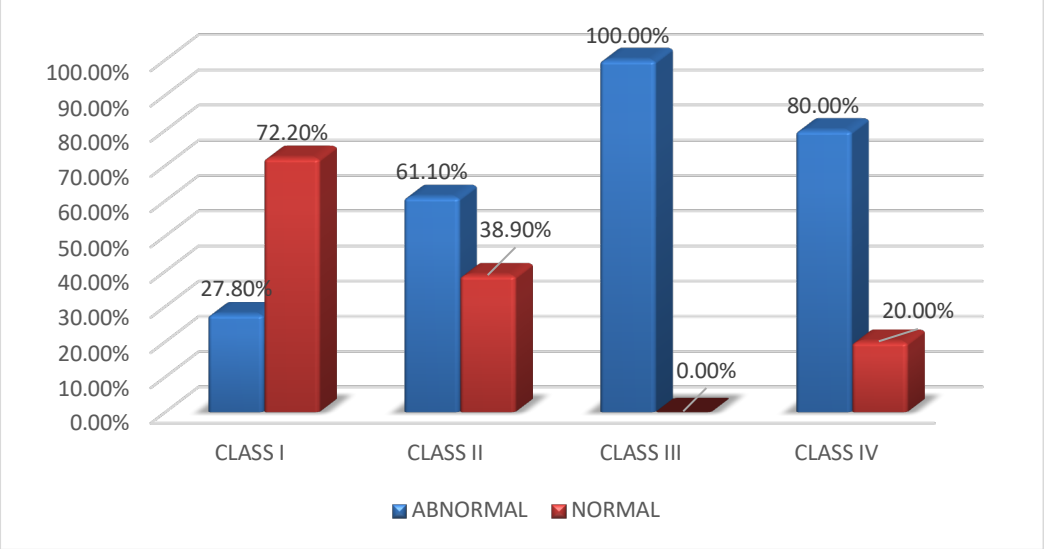
	Frequency	Percent
ASMI	4	8.0
AWMI	18	36.0
IWMI	7	14.0
LWMI	3	6.0
NSTEMI	18	36.0
Total	50	100.0

Table 5: Complications distributon in cases

	Frequency	Percent
CHB	3	6.0
CS	7	14.0
VF	1	2.0
VT	1	2.0
NO	38	76.0
Total	50	100.0



Graph 3: Killip Class comparison with Serum Uric Acid
Chi square = 2.404, P value = 0.493 (NS)



Graph 4 : Killip Class comparison with C Reactive Protein
Chi square = 11.490, P value = 0.009 (S)

Table 6: Ejection fraction comparison with serum uric acid

			SUA		Total
			ABNORMAL	NORMAL	
EF	<40	Count	14	16	30
		%	46.7%	53.3%	100.0%
	>40	Count	7	13	20
		%	35.0%	65.0%	100.0%
Total		Count	21	29	50
		%	42.0%	58.0%	100.0%

Chi square = 0.670, P value = 0.413 (NS)

Table 7 : Ejection fraction comparison with c reactive protein

			CRP		Total
			ABNORMAL	NORMAL	
EF	<40	Count	21	9	30
		%	70.0%	30.0%	100.0%
	>40	Count	7	13	20
		%	35.0%	65.0%	100.0%
Total		Count	28	22	50
		%	56.0%	44.0%	100.0%

Chi square = 5.966, P value = 0.015 (S)

Table 8: Relation between uric acid level and Killip's class and death

Killip's Class	Uric acid Day 0			Uric acid day 3			Uric acid day 5		
	<5.5	5.6-7.5	>7.6	<5.5	5.6-7.5	>7.6	<5.5	5.6-7.5	>7.6
	No of Deaths			No of Deaths			No of Deaths		
I	0	0	0	0	0	0	0	0	1
II	0	0	0	0	0	1	0	1	0
III	0	0	0	0	1	0	0	2	0
IV	0	0	0	0	2	1	0	2	2
Total	0	0	0	0	3	2	0	5	3

Table 9: Relation of elevated CRP correlation with Killip's class and death

Killip's Class	CRP Day 0			CRP Day 3			CRP Day 5		
	<1	1-3	>3	<1	1-3	>3	<1	1-3	>3
	No of Deaths			No of Deaths			No of Deaths		
I	0	0	0	0	0	0	0	1	0
II	0	0	0	0	1	0	0	1	0
III	0	0	0	0	1	1	0	1	0
IV	0	0	0	0	2	0	0	5	0
Total	0	0	0	0	4	1	0	8	0

Discussion

This prospective comparative study was conducted on 50 cases with acute myocardial infarction and 50 healthy volunteers to evaluate the prognostic value of C reactive protein and serum uric acid.

In our study the mean age of occurrence of ACS was 58.32 years. In controls it was 57.26 years. On performing unpaired t test, the difference was not found to be statistically significant (P value >0.05).

Out of 50 cases with ACS, chest pain was the most common presenting symptom in 100% of the patients followed by breathlessness in 66% of patients. This was higher compared to study done by Greenslade *et al* [4] in which chest pain was the predominant symptom occurred in 66% of patients with ACS followed by breathlessness which occurred in 41% of patients.

Out of 50 cases with ACS, Dyslipidemia was the major risk factor (84%) which occurred more frequently in our study when compared with Foussas *et al* study in which 64.6% patients had lipid abnormalities.

Hypertension emerged as the second major risk factor in our study seen in 62% of patients. 54% of patients had smoking as third major risk factor which was comparable with Kristin Newby *et al* [5] study in which smoking was observed in 50% of patients Both the studies reported lower levels when compared to our study.

In our study, out of 50 patients with ACS, 21 patients (42%) had diabetes as a risk factor. This was high when compared with Foussas *et al* in which 31% had diabetes mellitus and in Suleiman *et al* [6,[7]] it was seen in 30% of the study population.

In our study mean uric acid levels in the cases on day 0 was 5.466±1.435 and in the controls it was 3.642 ± 0.592. Average uric acid levels were higher in the case group as compared to the control group. This difference seen was also statistically highly significant ($p<0.001$).

In study done by Shirish Agarwal *et al* [[8]] uric acid levels in the cases on day 0 was 7.03±1.54 and in the controls it was 5.77±1.15.

According to study by MY Nadkar *et al* [9] the mean uric acid levels in case and control group were 5.23±1.95 and 3.78±0.74 respectively. Our findings correlate with these studies.

In our study correlation between levels of uric acid on day 0, day 3 and 5 along with Killip's class and the mortality of AMI was studied.

In a study by Trkulja V *et al* [10] a total of 621 patients (age 79 years, 64.7% men, 77.5% AMI with ST elevation, SUA 63-993 mmoL/L) were included. Higher SUA on admission is independently associated with higher in hospital mortality (RR, 1.016; 95% confidence interval [CI], 1.001-1.031, P =0.043) and higher thirty-day mortality (RR, 1.016; 95% CI, 1.003-1.029, P =0.018). Higher serum uric acid determined on admission is associated with higher in hospital mortality and poorer long- term survival after AMI. Our study findings correlate with their results.

Similar findings were also reported in a study by Prasanta Kumar Bhattacharya *et al* [[11]] where they observed that mean serum uric acid was higher in higher Killip classes compared to lower classes. They concluded that patients with a higher Killip class, signifying severe disease, were found to have a higher serum uric acid level. Further, patients with higher serum uric acid had longer hospital stay and significantly higher in-hospital mortality.

Thakur CP *et al* [12] in their study observed a statistically significant higher level of serum uric acid concentration in patients of acute coronary syndrome (5.80 ± 1.53) on the day of admission as compared to controls (3.8 ± 0.85). Higher serum uric acid (>7 mg/dl) level along with higher Killip's class (III, IV) was associated with higher mortality and major adverse cardiac events. These findings are similar to our study.

Ajmera D *et al* [13] also observed that on all three days of serum uric acid estimation, the serum uric acid levels were higher in AMI patients who were in higher KILLIP class as compared to lower KILLIP class group. They concluded that serum uric acid level is a strong and independent risk factor in predicting mortality and morbidity profile of patients of acute myocardial infarction. Also, serum uric acid level correlates well with KILLIP class.

Our study had 26% (n=13) mortality. Almost all the patients had elevated CRP values.

In our study mean CRP in the controls on day 0 was 0.43±0.31 and in the cases, it was 1.61±0.80. Average CRP levels were higher in the case group as compared to the control group in all the 3 days when checked. This difference seen was also statistically extremely significant ($p<0.001$). In our study,

the association of deaths in AMI with CRP levels and day of death of the patients was studied. This difference seen was statistically very significant.

In study done by M Baruah *et al* [14] CRP levels in controls and cases were 0.443±0.19 and 3.88±2.81. The CRP levels in AMI patients were slightly on the higher side when compared to our study, that may be because of the lab variations in the CRP values that can be taken as significant.

Adriano Caixeta *et al* [15] studied the predictive value of baseline C reactive protein on 30-day mortality in patients with acute coronary syndrome. Patients with CRP levels in 4th quartile had significantly higher mortality rates (2.3% vs 0.3%, p =0.0004).

In our study correlation between levels of CRP at day 0, day 3 and 5 along with Killip's class and the mortality of AMI was studied. CRP were grouped in 3 groups of <1, 1-3, >3.

All deaths occurred after admission day (day 0). Out of 13 deaths, 5 deaths occurred after day 1 and before day 3 and 8 deaths occurred after day 3. Killip's class I-1 death, class II-2 deaths, cIass III-3 deaths, class lV-7 deaths occurred.

So, we conclude that CRP levels were higher in patients with AMI with higher Killip's class. Higher mortality was also observed in patients with high CRP and higher Killip's class. Therefore, combination of Killip's class and CRP level after AMI is a predictor of mortality.

In the study done by M Baruah *et al* [16], serum CRP in AMI patient have a significantly higher value as compared to the control subjects (p< 0.01) on day 1, day 3, day 5, and at the time of discharge. This study showed that changes in CRP had a distinctive pattern, an acute phase response with persistent increasing trend with a peak CRP around 3rd day after onset of MI followed by a sustained and a gradual fall by 5th day, followed by decline not reaching baseline by 7th-9th day. The results obtained, matches with our study.

QQ Ma *et al* [17] observed that serum levels of CRP and Uric Acid were higher in patients with Acute Coronary Syndrome (ACS) as compared to control group (p<0.01). These findings were similar to our study.

Contrary to our study findings, Hundekari Prakash Pursnani *et al* [18] observed in their study that serum high sensitivity C - reactive protein was significantly (P<0.001) increased while serum uric acid was not significantly altered in acute myocardial infarction cases as compared to controls.

Out of 30 patients with ejection fraction <40%, 21 patients had increased CRP values and 9 patients had normal CRP values which is statistically significant. Our study shows no correlation with raised CRP and ejection fraction.

In study done by Pirambodo *et al* [19] correlation between CRP and ejection fraction in STEMI was assessed. No correlation was found between CRP and ejection fraction similar to our study.

Out of 30 patients with ejection fraction <40%, 14 patients had increased serum uric acid levels, and 16 patients had normal serum uric acid levels, but not statistically significant.

Li Chen *et al* [20] observed that Left ventricular end diastolic diameter (LVEDd) was larger in hyperuricemia patients than in non-hyperuricemia patients (53.52±6.19 vs. 52.18±4.89, P=0.041). The higher rate of left systolic dysfunction and diastolic dysfunction was discovered in hyperuricemia patients (36.4% vs. 15.1%, P<0.001; 68.2% vs. 55.8%, P=0.023).

Conclusion

- Potential predictor in acute myocardial infarction.

- Higher CRP and serum uric acid levels with Killip's class III & IV showed increased mortality.
- CRP >3.0 mg/dl and serum uric acid levels >7.5 mg/dl were associated with highest mortality.
- High serum uric acid on day of admission alone can be used in predicting the severity of AMI which makes it a simple tool for knowing the severity of AMI.
- The role of serum uric acid and CRP in influencing the course of ACS, a more elaborate multi centric study would have been desirable to precisely establish the role of serum uric acid and CRP in ACS. It is hoped that the present study will encourage new studies related to the above subject with a broader spectrum and for longer durations.

References

1. Shrivastava AK, Singh H V, Raizada A, Singh SK. C-reactive protein, inflammation and coronary heart disease. The Egyptian Heart Journal 2015; 67:89-97.
2. Matunović R, Stojanović A, Mijailović Z, Rađen G. Significance of determination of biomarkers of myocardial necrosis in acute coronary syndrome. Vojnosanit Pregl 2005; 62(5): 403-8.
3. Ridker PM. High-sensitivity C-reactive protein: Potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. Circulation 2001; 103 (13):1813-18.
4. Greenslade JH, Cullen L, Parsonage W, Reid CM, Body R, Richards M, *et al*. Examining the signs and symptoms experienced by individuals with suspected acute coronary syndrome in the Asia-Pacific region: a prospective observational study. Aim Emerg Med 2012; 60: 777-85
5. Foussas SG, Zairis MN, Lyras AG, Patsourakos NG, Tsirimpis VG, Katsaros K *et al*. Early Prognostic usefulness of C reactive protein added to thrombolysis in myocardial infarction risk score in acute coronary syndromes. Am J Cardiol 2005; 96: 533-7
6. Newby LK, Christenson RH, Ohman EM, Armstrong PW, Thompson TD, Lee KL, *et al*. Value of serial troponin T measures for early and late risk stratification in patients with acute coronary syndromes. The GUSTO-ha Investigators. Circulation. 1998; 98: 1853-9
7. Suleiman M, Aronson D, Reisner SA, Kapeliovich MR, Markiewièz W, Levy Y, *et al*. Admission C-reactive protein levels and 30-day mortality in patients with acute myocardial infarction. Am J Med 2003; 115: 695-701
8. Agrawal S, Aundhkar SC, Patange A et. al. Evaluate the role of serum uric acid in acute myocardial infarction as a prognostic marker. Int J Health Sci Res. 2014;4(5):120-128
9. Nadkar MY, Jam VI. Serum uric acid in acute myocardial infarction. J Assoc Physicians India 2008; 56: 759-62
10. Trkulja V, Car S. On-admission serum uric acid predicts outcomes after acute myocardial infarction: systematic review and meta-analysis of prognostic studies. Croat Med J 2012; 53: 162-72
11. Prasanta Kumar Bhattacharya, Mayank Agarwal, Debdutta Gautom, Hiranya Saikia. Role of Serum Uric Acid Level in Predicting Outcome in Acute Myocardial Infarction. National Journal of Laboratory Medicine. 2016; 5(4): 18-22
12. Thakur CP, Bhattacharjee K, Das D. Understanding the role of serum uric acid as a prognostic marker in acute coronary syndrome: a hospital-based study. J Evid Based Med Healthc 2018; 5(11): 986-990.

13. Ajmera D, Sharma NK, Chittorah S. A comparative study of serum uric acid level in various acute coronary syndromes and its short-term prognostic significance using KILLIP classification. Int J Adv Med 2019; 6: 1084-8
14. Mriganka Baruah, Chandan Kr Nath, Bikash Chaudhury, Runi Devi, Anand Shaker Ivvala. A study of serum uric acid and C reactive protein in acute myocardial infarction. IJBMSP 2012; 2(1): 21-24
15. Caixeta A, Stone GW, Mehran R, Lee EA, McLaurin BT, Cox DA, *et al*. Predictive value of C-reactive protein on 30-day and 1-year mortality in acute coronary syndromes: An analysis from the ACUITY trial. J Thromb Thrombolysis 2011; 31: 154-64
16. Mriganka Baruah, Chandan Kr Nath, Bikash Chaudhury, Runi Devi, Anand Shaker Ivvala.
    A study of serum uric acid and C reactive protein in acute myocardial infarction. IJBMSP 2012; 2(1): 21-24
17. Ma QQ, Yang XJ, Yang NQ, Liu L, Li XD, Zhu K, *et al*. Study on the levels of uric acid and high-sensitivity C-reactive protein in ACS patients and their relationships with the extent of the coronary artery lesion. Eur Rev Med Pharmacol Sci 2016; 20: 4294-4298
18. Hundekari, Prakash Pursnani, Nilima N. Dongre. Serum high sensitivity C-reactive protein, creatine kinase-MB, lipid profile and uric acid levels in acute myocardial infarction. J. Chem. Pharm. Res. 2015; 7(2):30-35
19. Rosa Priambodo, Bambang Irawan, Siti Nurdjanah. Correlation Between C-Reactive Protein and Left Ventricular Ejection Fraction in Anterior ST Elevation Myocardial Infarction. Acta Interna - The Journal of Internal Medicine 2012; 2(1): 16-22.
20. Li Chen, Xian-lun Li, Wei Qiao, Zhou Ying, Yan-li Qin, Yong Wang, *et al*. Serum uric acid in patients with acute ST-elevation myocardial infarction. World J Emerg Med. 2012; 3(1): 35–39