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RESEARCH ARTICLE

PROGNOSTIC SIGNIFICANCE OF HIGH SENSITIVE–C-REACTIVE PROTEIN (HS-CRP) IN ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Background: Coronary Artery Disease is one of the leading cause of death, ranked "FIRST" worldwide among the eight killer diseases. It accounts for one-third of all deaths worldwide, two thirds of which occur in the developing countries. Elevated levels of hs–CRP found to be associated with deleterious effects on endothelial function and platelets, which increase risk of atherosclerotic plaque formation.

Keeping this in view, it is important to assess the global risk of CAD in patients and in asymptomatic individuals, using a combination of clinical assessment and measurement of biomarkers like hs-CRP as inflammatory markers and to correlate them with that of CAD, for early intervention of life saving prophylaxis and as a prognostic marker.

Aim and Objectives: To estimate the levels of hs-CRP in diagnosed patients with acute myocardial infarction and to correlate the level of hs-CRP with the outcome of the patient with acute myocardial infarction within (0-7) day.

Material and Method: A cross sectional study was conducted on randomly selected patients with clinically diagnosed acute myocardial infection admitted in NSCB Medical College, Jabalpur. After a thorough clinical examination and history taking, the procedure was explained to the subjects. 3ml of venous blood was collected to study the level of hs-CRP in each subject. Method of estimation: hs-CRP was estimated by Quantitative Nephelometric method.

Results: There was a male dominant presentation of acute myocardial infarction with sex ratio of 5.6: 1. Maximum presentation of acute MI was between 5th to 6th decade with mean age of 55.33 years. hs-CRP level were significantly high in acute MI patients with more complications like MR, CCF, Arrhythmia, low ejection fraction and increased ST segment elevation. hs-CRP level were significantly high in deranged lipid profile and in increase CPK-MB levels.

Conclusion: Acute MI is a devastating global health problem with rising incidence in developing countries like India. In our study, hs-CRP levels are significantly high in short and long term complication of acute MI. Thus, in patient of Acute MI, a low cost simple investigation, hs-CRP can be highly sensitive independent biomarker for acute MI, its complications and severity.

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INTRODUCTION

Acute myocardial infarction is a type of acute coronary syndrome, which is most frequently a manifestation of coronary artery disease. Coronary Artery Disease is one of the leading causes of death, ranked "FIRST" world wide (http:/www/worldlifeexpectancy.com/world-rankings-total-deaths) among the eight killer diseases. It accounts for one-third of all deaths worldwide, two thirds of which occur in the developing countries.

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The development of an atherosclerotic plaque involves a complex interaction between endothelium, inflammatory cytokines, and numerous blood elements. Myocardial infarction is the rapid development of myocardial necrosis. This usually results from plaque rupture with thrombus formation in a coronary vessel, resulting in an acute reduction of blood supply to a portion of the myocardium. (Enas, 2000) Elevated levels of hs-CRP found to be associated with deleterious effects on endothelial function and platelets, which increase risk of atherosclerotic plaque formation. Studies have shown a positive association between hs-CRP and coronary artery disease. In a survey of 388 British men aged 50-69, the prevalence of coronary artery disease increased 1.5 fold for each doubling of

CRP level. (Libby *et al*., 2000) In 2003, the American Heart Association and the Centers for Disease Control and Prevention published cardiovascular risk levels for the hs CRP test. An hs-CRP>3 mg/L indicates a high risk for cardiovascular disease. Fasting is not necessary for the hs-CRP test. (Ridker, 2003) Myocardial infarction is a common presentation of ischemic heart. WHO estimated that in 2002, 12.6% of deaths worldwide were from ischemic heart disease. Ischemic heart disease is the leading cause of death in developed countries, but third to AIDS and lower respiratory tract infections in developing countries. (World Health Organization, 2004) In the mid 1990s, immunoassays for C-reactive protein (CRP), with greater sensitivity than those previously in routine use, revealed that increased CRP values, even within the range previously considered normal, strongly predict future coronary events. These findings triggered widespread interest, especially, remarkably, in the US, where the clinical use of CRP measurement had been largely ignored for about 30 years. CRP production is part of the nonspecific acute – phase response to most forms of inflammation, infection, and tissue damage and was therefore considered not to provide clinically useful information. Indeed, CRP values can never be diagnostic on their own and can only be interpreted at the bedside, in full knowledge of all other clinical and pathological results. However, they can then contribute powerfully to management. (Pepys and Hirschfield, 2003)

Keeping this in view, it is important to assess the global risk of CAD in patients and in asymptomatic individuals, using a combination of clinical assessment and measurement of biomarkers (Eugene Braunwald, 2008) like hs–CRP as inflammatory markers and to correlate them with the of CAD for early intervention of life saving prophylaxis and as a prognostic marker.

Objective

1. To estimate the levels of hs-CRP in diagnosed patients with acute myocardial infarction.
2. To correlate the levels of hs-CRP with the outcome of the patient with acute myocardial infarction within (0-7) day.

MATERIALS AND METHODS

A cross sectional study was conducted on randomly selected patients with clinically diagnosed acute myocardial infection admitted in N.S.C.B. Medical College, Jabalpur. Patients diagnosed as Myocardial Infarction on the basis of clinical history, clinical examination, ECG changes, 2D ECHO, CPK-MB were included in the study while patients with hematological malignancy, chronic Kidney Diseases, patients of connective tissue disorders, cerebral stroke, pregnant females, DM, were excluded in the study group. After a thorough clinical examination and history taking, the procedure was explained to the subjects. 3ml of venous blood was collected to study the level of hs-CRP in each subject. hs-CRP was estimated by Quantitative Nephelometric method. (Pandian and Amuthan, 2005) These analyzer (Sysmex SF-3000 Nephelometer) were calibrated as per standards and stringent quality control is performed before they are ready for processing. All case report forms were checked for completeness and inappropriate or illogical responses. The forms were entered using Microsoft 2010 Excel worksheet. The databases were validated and all inconsistencies and differences were resolved. Statistical analyses were performed using STATA 12 for windows (STATA Corp LP, Texas, USA) Categorical data are presented as frequency counts (percent) and compared using the chi-square or Fisher's exact statistic as appropriate. Continuous data presented as means (± standard deviation) and compared using the t-test or analysis of variance as appropriate.

RESULTS

The mean age of cases observed at 52.20 (±8.99) for hs CRP<3, and 55.33(±8.85) for case with hs-CRP>3 No significant difference was found in Mean age of both cohort i.e. hs-CRP<3 and hs-CRP>3. Case with increase hs-CRP for either sex have almost equal for both sex (P > 0.05) (=0.133, P>0.05, NS) i.e. no association between raised hs-CRP and sex.

Table 1. Correlation between congestive cardiac failure with respect to hs-CRP

Congestive cardine failure	hs-CRP		Total
	hs-CRP<3	hs-CRP>3	
Present	15 33%	3066% 	45 45%
Absent	34 61.8%	21 38.2%	55 55%
Total	49	51 48.2%	100

CCF was present in 45(45%) of cases and out of which 30(66%) was found to have increase hs-CRP and when the CCF was absent only 21(38.2%) cases found with increase hs-CRP. Statistically, a significant association between presence of CCF and raised hs-CRP was seen. (16.48;P<0.01)

Table 2. Correlation between arrhythmia (vt & vf) with respect to hs-CRP

Arrhythmia	hs-CRP		Total
	hs-CRP<3	hs-CRP>3	
Present	7 26.9%	19 73.1%	26
Absent	42 56.8%	32.\ 43.2%	74
Total	49	51	100

Among 100 patient, 26 (26%) have arrhythmia. Out of 26, 19(73.1%) have increased hs-CRP and 7(26.9%) have decreased hs-CRP. Arrhythmia showed a strong association with increase hs-CRP (6.85; P<0.01)

Table 3. Distribution of Cases according to EF and hs-CRP

Group	EF	hs-CRP 1		Total
		hs-CRP < 3	hs-CRP > 3	
Case	<50 Abnormal	3 8.6%	32 91.4%	35 100.0%
	>50 Normal	46 70.8%	19 29.2%	65 100.0%
	Total	49 49.0%	51 51.0%	100 100%

Among 100 cases, 35 (35%) has decreased EF, out of these 32 (91.4%) have increased hs-CRP. While among the normal EF only 19 (29.2%) has increased hs-CRP. A highly significant correlation between abnormal echo and increase hs-CRP was seen. (35.218; P<0.0001)

Table 4. Correlation between MR as a complication with respect to hs-CRP

MR	hs-CRP		Total
	hs-CRP<3	hs-CRP>3	
Present	3	11	14
	21.4%	78.6%	
Absent	46	40	86
	53.5%	46.5%	
Total	49	51	100

Among 100 patient, 14 (21.4%) has MR. Out of 14, 11 (78.6%) have increased hs-CRP. Presence of MR is found to have a positive impact on increase hs-CRP. (4.95; P<0.05)

Table 5. Distribution of cases according to CPK and hs-CRP

Group	EF	hs-CRP		Total
		hs-CRP < 3	hs-CRP > 3	
Case	<30 Abnormal	17	4	21
		81%	19%	
	>30 Normal	32	47	79
		40.5%	59.5%	
	Total	49	51	100

Out 100 cases, 79 cases have increased CPK – MB. Out of 79, 47 (59.5%) have increased hs-CRP. The cases with abnormal CPK-MB level were found with increased hs-CRP. 21(21%) have normal CPK – MB, in which 4 (19%) have hs-CRP>3, (10.86; P<0.001)

Table 6. Distribution of cases according TC and hs-CRP

Group	EF	hs-CRP		Total
		hs-CRP < 3	hs-CRP > 3	
Case	<200	40	0.9	49
	Abnormal	81.6%	18.4%	
	>200 Normal	9	42	51
		17.6%	82.4%	
	Total	49	51	100
		49.0%	51.0%	

Among 100 patients, 51 have increased TC. Out of 51 cases, 42(82.4%) cases have increased hs-CRP. Strong and significant association of raised / abnormal TC and increase hs-CRP (23.11; P<0.001)

Table 7. Distribution of cases according to the ST Elevation MI / non ST Elevation MI with respect to hs-CRP

ST MI/NON MI	hs-CRP		Total
	hs-CRP<3	hs-CRP>3	
Present	17	45	62
	27.4%	72.6%	
Absent	32	6	38
	84.2%	15.8%	
Total	49	51	100
	49.0%	51.0%	

Out of total 100 cases, 62 (62%) has STEMI. Out of 62.45 (72.6%) cases have increased hs-CRP. 38 patients have NSTEMI, in which 32 (84.2%) have hs-CRP<3 and 6 (15.8%) have hs-CRP>3. (30.40; P<0.001)

DISCUSSION

A large body of evidence suggests that inflammation play a key role in pathogenesis of atherosclerosis. The chronic inflammatory process can develop into acute clinical event by rupture of plaque leading to acute coronary syndrome. In patient with acute coronary syndrome an increase CRP level at admission associated with proper short term and long term prognosis. In majority of atherosclerosis, the admission CRP value reflects the baseline inflammatory state of the patient. Those patients with acute coronary syndrome with High CRP level at admission usually are prone to more cardio-vascular complications. Present study was a hospital based cross-sectional observation study of 100 cases of acute myocardial infarction admitted in NSCB Medical College, Jabalpur during period of September 2012 to October 2015. Patients were studied by clinical evaluation, ECG, 2D ECHO, and biochemical analysis with screening of their serum hs-CRP levels. Main aims of the study were to study complication of acute myocardial infarction with serum hs-CRP levels as a prognostic marker. In the current study there is no significant difference between the two groups as regarding age, sex, which is comparable to the study of Pandian *et al*. given below.

Pandian *et al*. found that there was no significant difference between age, sex, ratio risk factors, where patients were classified into two groups (Group 1 CRP<3, Group 2 CRP >3). (Pandian and Amuthan, 2005) In our study, out of 100 cases, CCF was present in 45 (45%) of cases and out of which 30 (66%) was found to have increase hs-CRP and when the CCF was absent only 21 (38.2%) cases found with increase hs-CRP. Berton *et al*. (2003) showed that first-day high hs-CRP is a strong independent predictor of both heart failure progression and depressed LV ejection fraction in AMI. Sanchis *et al*. (Sanchis *et al*., 2004) found that high CRP levels were associated with reduced ejection fraction after AMI as the mean EF for patients with high CRP values (41$\pm$13 versus 58$\pm$13 for patients with low CRP values p=0.000). In our study, among 100 patient, 26 (26%) have arrhythmia. Out of 26, 19 (73.1%) have increased hs-CRP and 7 (26.9%) have decreased hs-CRP. Arrhythmia showed a strong association with increase hs-CRP. Mishra *et al*. (2011) found that the complications like arrhythmias were present in 71.0% patients of AMI with increased CRP response (> 3 mg/L) on admission as compared to 25.0% patients with normal CRP reponse. In our study, among 100 cases, 35 (35%) has decreased EF, out of these 32 (91.4%) have increased hs-CRP. While among the normal EF, only 19 (29.2%) has increased hs-CRP. A highly significant correlation between abnormal echo and increase hs-CRP was seen. Similar results were also observed by Pandian *et al*. (2005). Sanchis *et al*. found that high CRP levels were associated with reduced ejection fraction after AMI as the mean EF for patients with high CRP values. Among 100 patient, 14 (21.4%) has MR. Out of 14, 11 (78.6%) have increased hs-CRP. Presence of MR is found to have a positive impact on increase hs-CRP. Anzai and associates reported that increase peak CRP levels was an independent predictor of MR

cardiac rupture, ventricular aneurysmal formation. (Anzai *et al*.) In 2005, Fouss *et al*. concluded that hs-CRP levels had prognostic usefulness when added to the well – validated TIMI risk score for ST and non ST elevation MI and that both should be used to stratify risk in MI patients. In this study, it is found that increase in hs-CRP level correlates with degree of ST segment elevation. (Foussas *et al*., 2005) In our study, Out 100 cases, 79 cases has increased CPK–MB. Out of 79,47 (59.5%) have increased hs-CRP. The cases with abnormal CPK–MB level were found with increased hs-CRP. 21(21%) have normal CPK–MB, in which 4 (19%) have hs-CRP > 3. Our results are in consistent with the study of Pandian and Dibra *et al*. (2003).

Conclusion

This was a cross sectional observation study of 100 patients of Acute Myocardial Infarction. There was male dominant presentation of acute myocardial infarction with sex ratio of 5.6:1. Maximum presentation of acute MI was between 5th to 6th decade with mean age of 55.33 years. hs-CRP level were significantly high in acute MI patients with more complication like MR, CCF, Arrhythmia, low ejection fraction and increased ST segment elevation. hs-CRP levels were significantly high in increase CPK–MB levels. Acute MI is a devastating global health problem with rising incidence in developing countries like India. In our study, hs-CRP levels are significantly high in short and long term complication of acute MI. Thus in patient of Acute MI, a low cost simple investigation, hs-CRP can be highly sensitive independent biomarker for predicting acute MI, its complications and severity.

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