Original Article

Prognostic Value of High-sensitivity C - reactive protein in Acute ST-segment Elevation Myocardial Infarction in Hospitalized Patients

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Abstract

Acute Myocardial Infarction (AMI) is an inflammatory condition. C-reactive protein (CRP) is a sensitive inflammatory marker. Elevated plasma CRP levels detected in the first few days of AMI is a predictor of unfavourable short and long term outcome. This cross sectional comparative study included 60 patients of 28-85 years with acute ST segment elevation myocardial infarction (STEMI) admitted within 24 hours of onset of chest pain in coronary care unit (CCU) of Sylhet MAG Osmani Medical College Hospital. Based on high-sensitivity C-reactive protein (hS-CRP) levels on the first day, the patients were divided into two groups: Group-I Low hs-CRP group (≤ 10 mg/L, n=22); Group-II High hs-CRP group (≥ 10 mg/L, n=38).

Clinical and echocardiographic prognostic variables were compared between two groups. The mean values of 1st and 3rd day hs-CRP levels of acute STEMI patients who developed the worse outcomes and who did not develop the outcomes are also compared. Among the in-hospital outcomes in group-I and group-II, (recurrent angina, cardiogenic shock, heart failure (HF), arrythmias, left ventricular ejection fraction (LVEF), wall motion abnormality (WMA), hospital stay and mortality) only arrhythmia was found significantly higher in high hs-CRP group (36.4% vs 76.3%, P<0.01). On the other hand, the patients who developed these worse outcomes had significantly higher mean values of both 1st day and 3rd day hs-CRP compared to those who did not develop these outcomes. Mean values of 1st and 3rd day hs-CRP (mg/L) of patients who develops recurrent angina or not was 68.42 (SD 12.56) and 110.14 (SD 10.66) vs 29.08 (SD 5.83) and 36.74 (SD 6.64) p<0.01. Among patients with arrhythmias, the values were 62.77 (SD 9.06) and 83.94 (SD 10.0) vs 14.23 (SD 2.92) and 35.20 (SD 7.65) p<0.001. Hs-CRP can be used as a simple and cost effective tool for prediction of in-hospital prognosis in patients with acute STEMI.

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Key Words: hS CRP (high sensitive C-reactive protein), acute ST segment elevation myocardial infarction (acute STEMI).

Introduction

AMI is a leading cause of death worldwide. In about 25% of all AMI, death occurs within few minutes, before reaching medical care. Half of deaths from AMI occur within 24 hours of onset and 40% within the first month[1]. Although patients treated by thrombolysis have a relatively good prognosis, long term mortality and incidence of nonfatal recurrent ischemic events remains high. Effective strategies and treatment of high risk patients need to be reassessed[2].Pivotal role of inflammation attracted the search to identify inflammatory markers for risk stratification in coronary artery disease. CRP is a sensitive marker of inflammation and has been shown to be associated with unfavorable short and long term outcome[3]. CRP values are stable over long period of time, not affected by food intake and shows almost no circadian variation. Traditional assays of CRP do not have adequate sensitivity to detect levels required for vascular disease prediction. To alleviate this problem, high sensitivity C-reactive protein (hS-CRP) assay have been developed[4]. The present study was conducted to assess the role of hs-CRP in predicting the in-hospital prognosis of acute STEMI.

Materials and Methods

Patients with acute STEMI admitted in Cardiology department of Sylhet MAG Osmani Medical College Hospital, presenting within 24 hours of onset, from 1st July 2004 to 30th June 2006 were evaluated for prognostic value of hs-CRP. Patients with previous MI, left bundle branch block, implanted permanent pacemaker, history of coronary artery bypass graft, congenital heart disease, valvular heart disease, active infection or chronic inflammatory disease, hepatic or renal dysfunction, malignancy, leukocytosis >18,000/mm3 and/or markedly raised ESR>80 mm in 1st hour were excluded from the study. The diagnosis of acute STEMI was done by history, clinical examination, ECG and cardiac bimarkers (CK-MB and Troponin-I), confirmed by WHO criteria. The prognostic variables were 1. Clinical (heart failure, cardiogenic shock, recurrent angina, arrhythmia, in-hospital mortality), 2. Biochemical (serum hs-CRP), 3. Echocardiographic (left ventricular ejection fraction, wall motion abnormality). After admission, 1st and 3rd day serum hs-CRP levels were measured in IMMULITE 2000 auto-analyzer, using immuno-luminometric assay method. Echocardiography was done between the 3rd and 5th day

to see left ventricular ejection fraction (LVEF) and wall motion abnormality (WMA). Based on the 1st day hs-CRP levels, patients were divided into two groups: Group-I Low hs-CRP group (hs-CRP level≤10mg/L) and Group-II High hs-CRP group (hsCRP>10 mg/L). The mean values of 1st and 3rd day hs-CRP levels of acute STEMI patients who developed the worse outcomes and who did not develop the outcomes are also compared.

Results

Of the total 60 patients of acute STEMI, 22 were low hs-CRP group (≤10 mg/L), and 38 were high hs-CRP group (>10 mg/L). The mean age of study subjects was 52.73±11.88 years (range 28-85 years, with 81.7% of 40-60 years age group), 52 (87%) male and 8(13%) female. About risk factor distribution, there were 48 (80%) smokers, 31(51.7%) hypertensive, 19(31.7%) diabetic, 4(6.7%) dyslipidemic, and 13(21.7%) had family history of CAD. Comparison of baseline characteristics and risk factors between low and high hs-CRP on the 1st day was shown in table I. No significant difference was observed with any parameters. There was also no significant difference of any fraction of lipid profile between two groups.

Distribution of baseline characteristics show that mean age and mean BMI were almost identical in both the hs-CRP groups (54.32 ± 12.79 vs 51.82 ± 11.39 years, p = 0.436 and 24.42 ± 2.65 vs 25.27 ± 2.63 kg/m2, p = 0.242 respectively). The mean time lapsed between onset of chest pain and arrival at hospital was found to be significantly greater in the high hs-CRP group (15.87 ±15.23 hours) than that in the low hs-CRP group (9.09 ±7.45 hours, p = 0.025) (table I).

Table I. Comparison of baseline characteristics between to hs-CRP groups.

Baseline characteristics#	1st day hs-CRP		p-value
	Low (≤10 mg/L) n = 22	High (>10 mg/L) n = 38	
Age (yrs)	54.32 ± 12.79	51.82 ± 11.39	0.436 NS
BMI (kg/m^2)	24.42 ± 2.65	25.27 ± 2.63	0.242 NS
Time lapsed (hrs)	9.09 ± 7.45	15.87 ±.15.23	0.025

Figures in the parentheses indicate corresponding percentages.

Data were analyzed using Chi-square (χ^2) test; df = 1. NS=not significant.

Data were analyzed using unpaired 't' test and were presented as mean ± SD.

NS= not significant.

Table II compares the risk factors between two hs-CRP groups. All the risk factors

like smoking, hypertension, diabetes and dyslipidemia were higher in the high hs-CRP group compared low hs-CRP group.

Table II. Comparison of risk factors between hs-CRP groups (n = 60)

Risk factors#	1st day hs - CRP		χ^2	p-value
	Low (≤10 mg/L) n = 22	High (>10mg/L) n = 38		
Smoking	17 (77.3)	31 (81.6)	0.161	0.947 NS
Hypertension	11 (52.4)	22 (57.9)	0.167	0.683 NS
Diabetes (FBS>7mmol/L)	8 (36.4)	20 (52.6)	1.482	0.224 NS
Dyslipidemia	20 (90.9)	36 (94.7)	0.328	0.468 NS

Table III compares the in-hospital outcome between groups. All the in-hospital outcome measures were found to be worse in the high hs-CRP group compared to the low hs-CRP group. However, only arrhythmia was found significantly higher in the high hs-CRP group (76.3%) than that in the low hs-CRP group (36.4%) p = 0.002. About 45% of the cases of high hs-CRP group experienced recurrent angina, where as 27.3% of the low hs-CRP group experienced the same complication (p = 0.180). Nearly 80% of the former group had heart failure compared to 63.6% of the latter group (p = 0.196). In the former group cardiogenic shock and mortality rate were 15.8% and 10.5% respectively, where as the same in the latter group were 9.1% each, though the differences between the groups were not statistically significant (p = 0.733 and 0.616). The mean hospital stay was higher in the high hs-CRP group compared to the low hs-CRP group (4.95 ± 0.653 vs. 6.97 ± 0.883 days, p = 0.830).

Table III. Comparison of in-hospital outcome between groups (n = 60)

In-hospital outcomes	Groups of 1st day hs - CRP		p-value
	Low (≤10 mg/L) n = 22	High (>10 mg/L) n = 38	
Recurrent angina#	6 (27.3)	17 (44.7)	NS
Heart-failure (Killip class)#	14 (63.6)	30 (78.9)	NS
Arrhythmias#	8 (36.4)	29 (76.3)	<0.01**
Cardiogenic shock#	2 (9.1)	6 (15.8)	NS
Hospital stay (days)+	4.95±0.653	6.97±0.883	NS
Mortality#	2 (9.1)	4 (10.5)	NS

Figures in the parentheses indicate corresponding percentage.

Data were analysed using Chi-square (χ^2) Test. + Data were analysed using t-Test and were presented as mean ± SEM.

** p<0.01, NS= not significant.

Table IV compares the mean 1st day hs-CRP levels between patients who developed and who did not develop the in-hospital worse outcome. The mean 1st day hs-CRP level was observed to be significantly higher among those who developed recurrent angina, cardiogenic shock, heart failure, arrhythmia, critical EF, akinesia, and/or died compared to those who did not, (p = 0.002, p = 0.004, p = 0.015, p < 0.001, p = 0.006, p = 0.019 and p = 0.036 respectively).

Table IV. Comparison of 1st day hs-CRP level between patients who developed and who did not develop the worse outcome

In-hospital outcomes	Mean 1st day hs-CRP level among (mg/l)	
	Developed	Not developed
Recurrent angina #	68.42 (SD 12.56)	29.08 (SD 5.83)**
Cardiogenic shock #	89.87(SD 23.82)	37.13 (SD 6.02)**
Heart failure #	53.49 (SD 8.19)	18.51 (SD 4.92)*
Arrhythmias #	62.77 (SD 9.06)	14.23 (SD 2.92)***
Critical EF (≤ 35 %)	73.72 (SD 7.24)	33.01 (SD 5.90)**
Akinetic WMA	69.61 (SD 13.83)	35.51 (SD 6.91)*
In-hospital mortality #	84.52 (SD 30.11)	39.68 (SD 6.17)*

*p<0.05, **p<0.01, ***p<0.001 in unpaired 't' test.
Data were presented as mean (SD).

Table V. compares the mean 3rd day hs-CRP levels between patients who developed and who did not develop the in-hospital worse outcome. The mean 3rd day hs-CRP level was found to be substantially higher among those who developed recurrent angina, cardiogenic shock, heart failure, arrhythmia, critical EF, akinesia, and/or died compared to those who did not, ($p = 0.002$, $p < 0.001$, $p = 0.042$, $p = 0.001$, $p < 0.001$, $p = 0.001$ and $p = 0.001$ respectively).

Table V. Comparison of 3rd day hs-CRP level between patients who developed and who did not develop the worse outcome

In-hospital Outcomes	Mean 3rd day hs-CRP level among (mg/l)	
	Developed	Not developed
Recurrent angina #	110.14 (SD 10.66)	36.74 (SD 6.64)**
Cardiogenic shock #	150.50 (SD 0.22)	54.66 (SD 7.06)***
Heart failure #	73.42 (SD 8.94)	41.36 (SD 11.56)*
Arrhythmias #	83.94 (SD 10.0)	35.20 (SD 7.65)***
Critical EF (≤ 35 %)	121.54 (SD 13.95)	44.02 (SD 6.45)***
Akinetic WMA	99.96 (SD 14.19)	48.66 (SD 7.63)***
In-hospital mortality #	150.50 (SD 0.29)	58.21 (SD 7.23)***

*p<0.05, **p<0.01, ***p<0.001 in unpaired 't' test.
Data were presented as mean (SD).

Discussion

This cross sectional comparative study was done to find the in-hospital prognostic value of hs-CRP in acute STEMI. Age range was 28-85 years (mean 52 years). Male to female ratio was 8:1. Similar age and sex distribution was also found in some studies in our country[5,6]. Age distribution and BMI of low and high hs-CRP groups were similar in our study.

Mean time lapsed between the onset of pain and arrival at hospital was found to be significantly greater in high hs-CRP group. The delayed arrival of high hs-CRP group might be a reason for their high serum CRP level.

Risk factors like-hypertension, diabetes mellitus, smoking, dyslipidemia and two cardiac biomarkers (Troponin-I & CK-MB)did not differ significantly between two groups, supported by a similar study[7]. Frequency of (Killip class-II,III & IV) heart failure though not statistically significant-was higher in hs-CRP group. In a study using hs-CRP value cut off point>3 mg/L- there was no significant difference[8], but in another study found significantly higher incidence in high hs-CRP group-using cut off point>10 mg/L on the 1st day[9]. In another study-predictive cut off point for heart failure after acute STEMI was 15 mg/L[10]. The differences in the findings of different investigators might be related to different cut off point used in different studies.

Incidence of critical and reduced LVEF was similar in two groups, consistent with a similar study[8] but not supported by another study[11] showing significant difference, might be due to higher sample size and higher cut point value.

Regional WMA was similar in two groups, but akinetic WMA- was significantly more frequent in the high hs-CRP group.

In-hospital adverse outcome-recurrent angina, cardiogenic shock were higher in high hs-CRP group, but not statistically significant. These finding are similar to some related studies[8,9]. Incidence of arrhythmia was significantly higher in high hs-CRP group, but in-hospital mortality didn't differ between groups. Tomoda & Akoi[8] showed an increased mortality in AMI with high hs-CRP(>3 mg/L) within 6 hour of onset. Suleiman[9] observed a significantly higher 30 day mortality using 1st day hs-CRP cut point >10 mg/mLin AMI. Lower cut point in our study and longer period of study in related studies made the differences of mortality statistics with acute MI.

In the present study, mean 1st and 3rd day hs-CRP values were significantly higher in patients who developed the adverse outcomes. Berton[10] also found significantly higher hs-CRP in acute STEMI on the 1st and 3rd day in patients who developed heart failure. Pietila[12] found that patients who died during 1st 6 months following acute STEMI had significantly higher hs-CRP, than those survived. Above findings agree with the present study indicating the predictive ability of serum hs-CRP for mortality.

Acute STEMI patients who develop high hs-CRP values should be considered to receive early invasive treatment in addition to closely monitored intensive medical management. Small sample size and non-randomization were limitations of our study.

The patients with serum hs-CRP levels >10 mg/L, measured within 24 hours of onset of symptoms- were associated with significant arrhythmia and akinetic WMA. Patients who developed in hospital worse outcomes (recurrent angina, cardiogenic shock, heart failure, arrythmias, critical EF, akinetic WMA, in-hospital mortality) had significantly higher mean values of both 1st and 3rd day hs-CRP compared to those who did not develop these outcomes. So, hs-CRP concentrations can be used as a simple and affordable tool for prediction of in-hospital prognosis in patients with acute STEMI.

We recommend further study with larger sample size with randomization to establish the prognostic value of hs-CRP in acute STEMI. We also recommend further studies to establish a cut point value of hs-CRP for prediction of worse outcomes in patients with acute STEMI.

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