ROLE OF HIGH SENSITIVITY C-REACTIVE PROTEIN (Hs-CRP) AS A PROGNOSTIC MARKER IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Background: Acute myocardial infarction (acute MI) is a major cause of morbidity and mortality worldwide and its incidence is increasing day by day.

C- reactive protein (CRP) is a biomarker for the risk prediction and prognosis of cardiovascular diseases. It is basically a marker for assessing ongoing inflammatory process. The research has proved that inflammation or more appropriately low grade inflammation plays a pivotal role in the etiopathogenesis of atherosclerosis. The measurement of hs-CRP, a variant of CRP for prognosis and risk prediction of coronary artery diseases has been part of many research projects since past two decades, throughout the world.

Objective: To determine the prognostic role of hs-CRP in individuals presenting with acute myocardial infarction.

Methodology: A total of 82 subjects having acute myocardial infarction were enrolled in this study. They were divided into two groups, A and B. Group A subjects consisted of individuals (38) with acute MI, who developed complications during their hospital stay while group B subjects consisted of individuals (44) with acute MI, who did not develop complications during their hospital stay.

Results: Statistically significant difference (<.001) was found in hs-CRP values of both the groups. The values were higher in group A subjects (4.342 mg/L ± 5.016 mg/L) than group B subjects (1.084 mg/L ± 1.428 mg/L).

Conclusion: The higher hs-CRP values in subjects with acute MI, who developed complications during their hospital stay proved the fact that higher hs-CRP values after acute MI were associated with development of complications and adverse outcomes.

Key words: Acute myocardial infarction (acute MI), hs-CRP, Prognostic role of hs-CRP

INTRODUCTION

Acute myocardial infarction (acute MI) is one of the major causes of morbidity & mortality throughout the world while atherosclerosis is the major cause of coronary artery disease (CAD) and associated acute coronary syndromes[1]. About 29.2% of all deaths in the world occur due to different types of heart diseases out of which 50% are due to CAD[2].

Atherosclerosis is a process associated with a persistent low grade inflammation. Low grade inflammation is involved in all stages of the atherosclerotic process, from the beginning of fatty streak to plaque progression and its complications[3]. Main markers for detection of this low grade inflammation are CRP (C-reactive protein), Serum amyloid A (SAA), IL-6 (Interleukin 6), Homocysteine, Apolipoprotein B-100, Apolipoprotein A-1, and soluble intercellular adhesion molecule type 1 (sICAM-1). Out of these markers, CRP has been the strongest risk predictor of cardiovascular events[4].

CRP is an acute phase protein[5] that is secreted from liver during the process of inflammation. Its secretion is stimulated by a number of inflammatory cytokines. In response to a pro-inflammatory stimulus, TNFα (tumor necrosis factor alpha) a cytokine is synthesized by macrophages which causes production of another cytokine interleukin1 (IL1), IL1 stimulates the production of IL6, produced by T cells and macrophages which finally causes production of CRP from hepatocytes[6].

The main role of CRP is to bind to phospholipids of pathogens or damaged cells to activate the complement system.CRP derives its name due to its property of reacting with C substance of *Streptococcus pneumoniae* (the protein which reacts with the C substance of *Streptococcus pneumoniae* or pneumococcus)[7].

A lot of studies show that CRP is an independent marker for risk prediction of atherosclerosis[8], myocardial

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infarction,[9] hypertension[10] and cardiovascular events. It has been found that CRP predicts the risk of both recurrent ischemia and death among patients with acute coronary syndromes admitted in coronary care units[11,12]. The CRP measurement as a marker of vascular inflammation and predictor of coronary artery disease has been replaced in recent past by a more sensitive variant of CRP, high sensitivity CRP (hs-CRP). The hs-CRP is emerging as the strongest and independent risk predictor for the development of atherosclerosis and coronary artery disease[6,13].

The recommendations of CDC (Centre for Disease Control**)** and AHA (American Heart Association) for hs-CRP level stratification for the cardiac risk assessment in apparently healthy individuals are[14]:

Low: < 1 mg/L

Average: 1.0 to 3.0 mg/L

High: >3.0 mg/ L

A study conducted by Badiger RH et al, in 2014 shows that high hs-CRP levels in patients with acute myocardial infarction make the patients prone to develop complications during their hospital stay[15]. A similar study done by Praveen P et al, in 2018 concluded that raised hs-CRP levels were associated with development of complications in patients presenting with acute myocardial infarction including death, cardiac failure, arrhythmias and post infarction angina[16].

METHODOLOGY

Study was performed after approval by the ethical committee of Khyber Girls Medical College Peshawar. Sampling was carried out at the cardiology unit of Hayatabad Medical Complex, Peshawar, while analysis of samples was done at Pathology departments of Khyber Girls Medical College and Rehman Medical Institute, Peshawar. It was a descriptive cross sectional study. Sampling was done on non probability convenient basis. Patients were selected as per criteria laid down by the American Heart Association. Study was conducted from February 2015 to February 2016.

Total 82 individuals were selected for the study. They were divided into two groups;

Group A: Those having acute myocardial infarction and developed complications during their hospital stay.

Group B: Those having acute myocardial infarction and developed no complication during their hospital stay.

Patients from both genders with history of hypertension, obesity, dyslipidemia and smoking were included in this study.

Patients having acute infections, inflammatory disorders, any malignancy, severe liver dysfunction, taking NSAIDs, low dose Aspirin and lipid lowering drugs like statins were excluded from the study.

A fasting venous blood sample was collected from each subject. Parameters like hs-CRP, Troponin I and CKMB were measured by using Abbott's Architect *ci* 8200 analyzer. The hs-CRP was measured by Immunoturbidemetric method using Abbott's FDA approved kit (Multigent CRP vario). ECG and Echocardiogram of every patient was done. The other parameters like fasting blood glucose and lipid profile were measured by using Microlab 300, semiautomatic analyzer. The full blood count was measured on Sysmex automatic analyzer.

SPSS 23 was used to derive different statistical parameters. Mean ± standard deviations were derived for the target variables. Student's t test was applied to test the statistical significance between the means of two groups. A p value of 0.05 was taken as significant at a confidence interval of 95%.

RESULTS

Out of total 82 subjects, 38 (46%) developed complications after acute MI during their hospital stay.

In group A, 24 (63%) males were affected while14 (36%) females were affected. In group B a total of 36 (81%) males had acute MI as compared to 8 (19%) females. Regardless of presence or absence of complications the number of males was more as compared to females.

Mean age of the subjects with complications was slightly greater (59.13 ± 8.240 years) than those without complications (54.81 ± 15.23 years). No statistically significant difference (.109) was found between the ages of two groups.

On analysis it was found that there was a highly significant difference (<.001) between the mean hs-CRP levels of the subjects with complications of acute MI (4.342 mg/L ± 5.016 mg/L)and the subjects having no complications (1.084 mg/L ± 1.428 mg/L). There was a mean difference of 3.258 mg/L ± 3.588 mg/L between the subjects of two groups.

The individuals belonging to group A, i.e. the subjects who developed complications during their hospital stay were further divided into two groups;

a. Those having type 2 diabetes mellitus

b. Those not having type 2 diabetes mellitus

On analysis it was found that number of patients who developed complications and had type 2 diabetes mellitus as well, was more (22) than patients who had complications of acute MI without any evidence of type 2 diabetes mellitus (16). There was a statistically significant difference (.003) between the mean levels of hs-CRP in diabetic patients (5.227 mg/L ± 5.702 mg/L)

Table 1: No. of subjects with and without post MI complications

Total no of subjects	No of subjects with complications (Group A)	No of subjects without complications (Group B)	% of complicated cases
82	38	44	46%

Table 2: Gender wise distribution of complicated and uncomplicated cases

Gender	Group A	Group B
Males	24 (63%)	36 (81%)
Females	14 (36%)	8 (19%)
Total= 82	38(46%)	44(54%)

Table 3: Mean age of subjects of complicated and uncomplicated cases

Group	Mean age	Std. Deviation	p value
A (With complications)	59.1316	8.24021	.109
B (Without complications)	54.8182	15.23654	
Total	56.8171	12.60720	

Table 4: Mean hs-CRP levels in Group A and B patients

	Group	Mean	Std. Deviation	t value	p value
hs-CRP	A (With complications)	4.342	5.016	3.871	<.001
	B (Without complications)	1.084	1.428		
	Mean difference	3.258	3.588		

Table 5: Mean hs-CRP levels in diabetic and non diabetic subjects with complications

	Group	Number	Mean	Std. Deviation	p value
hs-CRP	A (With complications)	22	5.227	5.702	.003
	B (Without complications)	16	1.037	1.516	
	Mean difference		4.19	4.186	

as compared to non diabetic patients (1.037 mg/L ± 1.516 mg/L). There was a mean difference of 4.19mg/L±4.186mg/L between both the groups.

DISCUSSION

In present study it was observed that out of total 82 subjects, 38 (46%) developed complications after acute MI during their hospital stay.

There were 24 (63%) males in group A and 14 (36%) females while the number of males in group B was 36(81%) and those of females was 8 (19%). So the number of males was higher in both the groups as compared to females. This was in accordance with the study conducted by Khan Z A et al[17]. In both the groups the lesser number of females supports the fact that females have got more protection from coronary artery disease and its sequels due to their sex hormones.

The mean hs-CRP levels of the patients who developed complications were significantly higher than those who did not develop complications. These results were consistent with the study conducted by Raju H. Badiger et al[15]. This shows that the patients with complications had accelerated low grade inflammation leading to advanced atherosclerosis as compared to the patients who did not develop complications.

On further analysis it was found that greater number of group A individuals (subjects with complications) were diabetics (22) while lesser number of individuals (16) of group A were non diabetics and there was a statistically significant difference (.003) between the two groups. This finding points towards the fact that diabetic individuals have enhanced low grade inflammation as compared to non diabetics; therefore diabetics are more prone to have acute coronary syndrome and complications associated with it[18].

Moreover, it was also evident from the results that the group A individuals who developed complications during their hospital stay had means hs-CRP levels > 3mg/L (4.342 mg/L ± 5.016 mg/L) which were above the upper cut off limit for the individuals at high risk for developing ischemic heart disease (IHD) and its sequels as defined by AHA and CDC. On other hand mean hs-CRP levels of group B individuals (1.084 mg/L ± 1.428 mg/L) who did not develop complications were < 3mg/L which was consistent with the AHA/CDC recommendations (hs-CRP levels < 3mg/L are associated with low to moderate risk of developing IHD and its sequels). These findings were consistent with the studies done by Kiran Babu TG et al.[19] and Punekar J et al[20].

CONCLUSION

The study showed that hs-CRP is a strong risk predictor and prognostic marker for assessing the future outcomes of patients presenting with acute MI. The increased levels of the marker in patients with acute MI are associated with more chances of development of complications and mortality. The reason behind this correlation is the presence of accelerated low grade inflammation in these individuals.

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