ORIGINAL ARTICLE

THE RELATIONSHIP OF HS-CRP IN TYPE 2 DIABETIC PATIENTS PRESENTING WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

OBJECTIVE: To determine the relationship of Hs-CRP with type 2 diabetes mellitus in patients with acute myocardial infarction.

Material And Methods: It was a cross-sectional study conducted at Hayatabad Medical Complex, Rehman Medical Institute, and Khyber Girls Medical College Peshawar. A total of 90 subjects were enrolled in the study. These subjects were split into two equal groups; Group 1 comprised patients having type 2 diabetes mellitus (T2DM) and acute myocardial infarction (acute MI). Group 2 comprised patients having T2DM only. Patients from both genders who presented within 6-12 hours of acute MI were included in group 1.

Results: Mean age of subjects of group 1 was greater than that of group 2 while the number of males within group 1 was greater than that of females. The median values of Hs-CRP were higher in group 1 subjects as compared to group 2. There was a significant difference between the values of both groups.

Conclusion: The Hs-CRP values were higher in diabetic patients with acute MI as compared to those with diabetes alone because the patients who suffered from acute MI had enhanced ongoing low-grade inflammatory process which was a possible reason for their MI.

Keywords: type 2 diabetes mellitus, coronary artery disease, hs-CRP, myocardial infarction, atherosclerosis.

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INTRODUCTION

Coronary artery disease (CAD) is a major cause of morbidity and mortality throughout the world[1]. CAD accounted for 382, 820 deaths in 2020 according to the Centers for Disease Control (CDC) [2].

T2DM is one of the strong risk factors for the causation of CAD. Patients having T2DM have 2 to 4 times the chances of developing CAD, or ischemic stroke, and a 1.5 to 3.6 times rise in death incidence [3]. More than 50% of patients having diabetes die due to CAD[4]. The prevalence of diabetes mellitus has increased dramatically throughout the world in the last two decades. Three hundred sixty-six million people had diabetes mellitus in 2011 and it is estimated that the number of cases is increasing and it will rise by 2030 to 552 million[5].

People with diabetes have an enhanced risk of developing atherosclerosis and therefore CAD. They experience high morbidity and mortality after acute MI than those without diabetes [6].

Atherosclerosis is a process associated with persistent low-grade inflammation. The process of inflammation is present during all stages of atherosclerosis and is closely related to atherosclerotic plaque formation and its rupture [7]. Therefore, the assessment of ongoing systemic inflammation is emerging as a tool in cardiovascular disease risk prediction. The main markers for the detection of this low-grade inflammation are Hs-CRP, Serum Amyloid A, IL-6, Homocysteine, Apolipoprotein B-100, and Soluble intercellular adhesion molecule type 1 [8]. Out of these markers, Hs-CRP has proven the most promising for risk prediction of cardiovascular events [8].

C-reactive protein is an acute-phase reactant produced by the hepatocytes during the process of inflammation. After an inflammatory stimulus, different cytokines in a cascade manner cause the production of interleukin-6

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(IL6), and IL6 finally causes the production of CRP from hepatocytes[7]. Hence inflammation and CRP production go side by side. Most of the clinical studies show that CRP is an independent marker for risk prediction of atherosclerosis[9], myocardial infarction, [10], hypertension[11], and cardiovascular events. The standard CRP estimation has been replaced by a more sensitive variant of CRP, high-sensitivity CRP (Hs-CRP). The Hs-CRP in today's world is proving itself to be the strongest and independent marker for risk prediction of atherosclerosis and CAD[8, 12].In studies conducted by Ridker et al and Danesh et al [13, 14] Hs-CRP levels were measured in apparently healthy individuals. These studies showed that Hs-CRP levels in the upper normal range, independently predicted major vascular events, like MI and cerebrovascular accidents.

According to CDC and AHA (American Heart Association), the Hs-CRP level stratification for the cardiac risk assessment in apparently healthy individuals is [15] High risk: >3.0 mg/ L Diabetic individuals due to hyperglycemia have higher levels of Hs-CRP than people without diabetes as hyperglycemia itself can lead to raised levels of the marker irrespective of other factors[16]. This study was an attempt to establish a correlation between Hs-CRP, diabetes, and its complications like CAD, and acute MI, and the prognostic importance of Hs-CRP in acute MI.

MATERIALS AND METHODS

The study was conducted after approval by the ethical committee of Khyber Girls Medical College (KGMC) and Hayatabad Medical Complex (HMC). Sampling was carried out at the cardiology and endocrinology units of HMC and Rehman Medical Institute (RMI), Peshawar. Samples were analyzed at the pathology departments of KGMC and RMI. It was a descriptive cross-sectional study. The study was conducted from February 2016 to November 2016. A total of 90 patients were selected for the study after informed consent. Subjects were selected according to the non-probability consecutive sampling technique. Known type 2 diabetic patients from both genders who presented with acute MI within 6-12 hours of acute MI to the cardiology units of HMC and RMI were included in the study. Known type 2 diabetic patients without acute MI from both genders were also included in the study. So, the study population comprised two groups of subjects. Group 1 subjects had T2DM and acute MI and group 2 subjects had diabetes mellitus alone.

Patients having acute infections, inflammatory disorders, any malignancy, type 1 diabetes mellitus, severe liver dysfunction, renal impairment, taking NSAIDs, low-dose Aspirin, and lipid-lowering drugs were not included in the study.

A venous blood sample (5ml) was collected from each subject. The serum was separated and stored in containers at a temperature of -70 0C for future measurement of Hs-CRP and other parameters. After the completion of the sample collection process, the serums of all patients were thawed and analyzed. The Hs-CRP concentrations were measured on Abbott's Architect ci 8200 analyzers by Immunoturbidemetric method using Abbott's FDA-approved kit (Multiagent CRP Vario).

SPSS 20 was used for statistical analysis. The Hs-CRP values were subjected to Kolmogorov Smirnoff and Shapiro-Wilk tests to assess the normality of the data. The data were not normally distributed. So for the Hs-CRP, median values and interquartile ranges (IQRs) were determined. The level of significance for the difference in the ages between the groups was determined by using an independent t-test while the medians of Hs-CRP of both groups were compared by using the Mann-Whitney U test. A value of $\leq .05$ at a confidence interval of 95% was considered significant.

RESULTS

The mean age of subjects in group 1 was 58.98 $\pm$ 9.10 years while that of group 2 subjects was 47.75 $\pm$ 4.51 years with a significant difference of 0.001. The number of male subjects in group 1 was more than females while the number of females was more than males in group 2. The median value of Hs-CRP in group 1 subjects was higher than that of group 2 subjects and there was a highly significant difference between both groups. On gender-wise analysis, the median Hs-CRP levels in group 1 were more in males as compared to females. There was a significant difference between both entities. In group 2, contrary to group 1, Hs-CRP levels were higher in females than males but without any significant difference.

Upon further analysis of subjects from both groups according to CDC and AHA risk stratification, it was found that most of the high-risk patients were in group 1 as compared to group 2 which had only 1 patient in the high-risk category. The majority of patients in group 2 were in the low-risk range while in the average-risk category the number of patients in both groups was almost the same.

DISCUSSION

The mean age of patients in group 1 (59.24 $\pm$ 8.35) in this study was comparable to that in the study done by Suleiman M et al [17] which was (61.33 $\pm$ 12.33). The present study showed that the number of male subjects in the group1 was greater than that of females and it was comparable to the study done by A U Saleh et al. [18] and Nayandak T et al. [19]. This might be because pre-menopausal females have got protection from CAD due to female sex hormones.

There was a significant difference between the median Hs-CRP levels of group 1 and group 2 subjects. This was in accordance with the study by G Chetan [20]. This difference indicates that the enhanced process of low-grade

Table 1: Frequencies of males and females in both groups

Groups	Males	Females
Group 1	29	16
Group 2	14	31
Total	43	47
Percentage	47.77%	52.22%

Table 2: Median Hs-CRP of both the groups

Groups	Median Hs-CRP	IQR	p-value
1	2.20	7.55) 7.80 – 0.25)	.003*
2	0.40	0.6) 0.20 – 0.80)	

*Mann Whitney U test

Table 3: Gender-wise analysis of Hs-CRP in group 1 and 2

Group	Gender	Number	Median	IQR	p-value
1	Male	29	3.80	0.40 – 9.00 8.6))	0.018*
	Female	16	0.50	0.10 – 2.13 2.03))	
2	Male	14	0.20	0.10 – 0.73 0.63))	0.208*
	Female	31	0.40	0.20 – 0.80 0.60))	

*Mann Whitney U test

Table 4: Hs-CRP risk stratification of both group subjects according to CDC and AHA guidelines

Hs-CRP cardiac risk levels according to AHA and CDC	Group 1	Group 2
Low risk- <1mg/L	16	34
Moderate risk 3-1- mg/L	12	10
High risk- >3mg/L	17	1

inflammation was going on in individuals who were diabetics and experienced acute MI as compared to individuals who did not experience any such event. On gender-wise analysis of both the groups, it was evident that the levels of the marker were higher in group 1 males as compared to females. It was consistent with the study done by Amrut D et al [21]. It means that males after acute MI are more prone to develop future complications. On the other hand, the values of the marker were higher in females than males in group 2 and it was in accordance with the study by G Chetan[20].

While comparing the median Hs-CRP levels of two groups according to CDC and AHA risk stratification, it was found that the number of individuals in group 1 was too high as compared to group 2 in high-risk category. So, the majority of group 1 individuals were prone to develop future complications of acute MI.

One can object that group 1 subjects had raised levels of Hs-CRP due to tissue damage and consequent inflammation as a result of acute MI. This question can be answered with the help of different studies. In a study done by Mahajan S.N. et al.[22], the mean Hs-CRP levels in acute MI subjects and unstable angina subjects were 9.8 ± 6.08 mg/L and 9.7 ± 4.36 mg/L respectively (no difference in values of both groups). Similarly, Berk et al (1990) found raised levels of CRP in 37 subjects with unstable angina as compared to 32 patients with stable angina. In the same way, Winter et al compared the CRP levels of patients with unstable angina and non-Q-wave acute MI and found a rise in the levels of both sets of patients. It means that higher levels of CRP in individuals with acute coronary syndromes are found due to the underlying process of inflammation inside the plaque and not as a result of myocardial damage as unstable angina is not associated with any tissue damage.

Although the number of group 1 individuals who were in the high-risk category was more as compared to group 2 yet the number of subjects in the moderate-risk category in group 2 i.e. 10 was not ignorable. It means those individuals were prone to develop CAD in the future.

This study signifies that Hs-CRP can be used as a marker for the risk prediction of future complications of acute myocardial infarction as well as for the risk prediction of developing CAD in diabetic patients in the future.

CONCLUSION

The study concludes that Hs-CRP is a very sensitive biomarker for the risk assessment of developing CAD and acute myocardial infarction. Moreover, it has got a very good prognostic value in the prediction of the development of future complications of acute MI.

It is recommended that such studies with a larger sample size should be conducted in Pakistan to establish the role of Hs-CRP as a marker for the prediction of CAD and its sequels.

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Following authors have made substantial contributions to the manuscript as under

Hussain M:	Conception of idea, Data collection, Analysis, Manuscript writing and Review
Ishaq A:	Discussion and Manuscript review
Shah S:	Data collection
Javed K:	Manuscript review , Statistical analysis
Parvez A:	Data collection and Manuscript review
Eman L:	Literature search

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.