An assessment of Angiographic and Clinical correlation among High-sensitivity C-reactive Protein with acute ST-elevation Myocardial Infraction

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ABSTRACT

Objective: To assess the relationship between hs-CRP (high sensitivity C-reactive protein) and acute ST-elevation myocardial infarction (STEMI), and the association of hs-CRP with common coronary disease risk factors and angiographically important coronary artery disease.

Study Design: A cross-sectional analytical study.

Place and Duration: From 3rd Mar 2020 to 3rd Aug 2020 at the Department of Cardiology in Ch. Pervaiz Elahi Institute of Cardiology Multan.

Methodology: A total of 150 patients diagnosed with STEMI were included in the study after passing through selection criteria. All the participants were evaluated for hypertension, diabetes, and smoking status. Blood samples were collected to analyze hs-CRP values following a protocol. Based on angiographic findings patients were divided into three groups: mild, moderated, and severe coronary artery disease.

Results: The result found out significant relation between mean hs-CRP values and hypertension, diabetes, dyslipidemia, and Killip class ($p<0.05$). Although, the values of mean hs-CRP for double and triple coronary vascular diseases were higher than the single vascular disease (SVD, 0.62 mg/dl; DVD, 0.71 mg/dl and TVD, 0.87 mg/ml), no significant difference can be found in terms of a number of vessels involved. It was found out that mean hs-CRP values for three groups based on Syntax score are directly related to syntax scores. (Syntax score ≤22, 0.62 mg/ml; Syntax scores >22–32, 0.79 mg/ml and syntax score >32, 1.91 mg/dl), however, the difference remained insignificant.

Conclusion: The study has found hs-CRP as a potential candidate for navigating the development of ST-elevation myocardial infarction and predicting its prognosis.

Keywords: Coronary artery disease, Myocardial infarction, Clinical findings, Angiographic findings, Inflammatory markers, hs-CRP, Clinical correlation.

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INTRODUCTION

Cardiovascular diseases have a major share in the global mortality rate[1], which mandates the investigation of all the possible causes and pathogenic mechanisms of the diseases and the efforts to improve their diagnostic and treatment schemes. Inflammation is perceived to play a significant role in the pathogenesis of atherosclerosis, from the formation to the definite establishment of plaque till it is finally ruptured[2]. Similarly, the inflammatory processes also play a major role in arterial fibrillation, valvular diseases, heart failure, and arterial hypertension. In the last few decades, several researchers have developed an association between the inflammatory process and atherosclerotic diseases[3]. In about 50% of total incident cases of coronary artery disease (CAD) established risk factors are found to be causative agents of the disease while the other half remain idiosyncratic[4]. C-reactive protein (CRP) has been recognized as one of the prominent and reliable markers for systemic inflammation owing to its strong diagnostic ability, easy

availability, economical testing cost, and easy handling[5]. It is a pentameric protein made up of five similar, 23-kD, non-covalently associated subunits that bind to calcium and are produced in reaction to interleukin-1 (IL), IL-6, tumor necrosis factor[4,5].

The level of CRP starts to rise within four to six hours following the injury and multiplies by a hundredfold within the next one to two days. Moreover, its half-life is less than 24 hours[6]. The analytic capacity of CRP for the identification of blood vessel damage lies in the 0.1-0.5 mg/dl range, a level that is also found in several healthy persons who don't have any inflammation[7]. The High-sensitivity CRP (hs-CRP) is a well-established, standardized assay with a detection limit of less than 0.02 mg/dl. Various researches have claimed that the hs-CRP has significantly higher predictive capacity than those of conventional cardiovascular risk markers[8]. However, the relation between the two variables has, so far, not been well-established.

The study was designed with an objective to assess the relationship between hs-CRP and acute ST-elevation myocardial infarction (STEMI), and the association of hs-CRP with common coronary disease risk factors and angiographically important coronary artery disease.

METHODOLOGY

This cross-sectional analytical study was conducted at the Cardiology ward of Ch. Pervaiz Elahi Institute of Cardiology, Multan, for the period of six months from 3rd Mar 2020 to 3rd Aug 2020. The study included a total of 150 patients who were diagnosed with acute STEMI and were selected through a random sampling technique. Whereas, the patients diagnosed with non-ST elevation myocardial infarction (NSTEMI) or unstable angina, with any other unknown inflammatory or infective disease, and necrosis were excluded from the study. The study was conducted after getting the informed consent of the patients and the approval board of the hospital.

Acute MI was diagnosed following the "Joint Task Force's" Third Universal Definition[9]. The diabetic status of the patients was confirmed to those having fasting plasma glucose levels greater than 126 mg/dl, having glycated hemoglobin greater than the level of 6.5%, or those who were on hypoglycemic agents. The hypertensive condition was defined as having systolic/diastolic blood pressure greater than 140/90 mmHg or being under any antihypertensive medication. Those who were actively smoking for the last six months were characterized as smokers. A self-designed questionnaire was administered to gather data relating to age, gender, body mass index (BMI), family history, risk factors assessment, and blood pressure. Baseline evaluation included assessment of Killip class and calculation of thrombosis in MI (TIMI) score of every patient[10]. The blood samples were collected when patient first reported to the Coronary Care Unit (CCU). For the assessment Complete Blood Count (CBC), Renal function, serum electrolytes, random blood glucose (RBS), lipid parameters, , hs-CRP, and high-sensitivity (hs)-troponin T were collected. In addition, the left ventricular ejection fraction (LVEF) was also evaluated through an echocardiographic within 24 hr. of admission in hospital. hs-CRP assays were conducted by following standard ELISA protocol with a detection limit ranging from 0.1 to 12.0 mg/dl.

Angiographic images of patients were evaluated by another team of cardiologists who were kept blinded to biochemical results of the patients to ascertain the degree of CAD and extents of coronary artery stenosis. Patients with the presence of greater than 50% stenosis in any left main artery or coronary artery (LMCA) were declared of having significant CAD. For every coronary angiogram (CAGs) a syntax score was calculated using an online algorithm version (2.28) (available at www.syntaxscore.com). Based on scoring, patients were classified into 3 groups: Group A (mild CAD; Syntax score: 0–22 points), Group B (moderate CAD; Syntax score: 23–31 points), and Group C (Severe CAD; Syntax score: ≥33 points). The 3 groups were compared for mean hs-CRP.

Data Analysis: Statistical analysis was performed using SPSS version 18. The student's t-test was used to compare continuous variables while the chi-square test was used for the comparison of categorical variables. For all the variables, a P-value less than 0.05 was considered statistically significant.

RESULTS

A total of 150 patients with STEMI were analyzed. The mean age of patients was 56.2 years (range: 20-75). Among the participants 110 (73.3%) were male and 40 (26.6%) were female where the mean body mass index (BMI) was 28.5 ± 5.1. The window period, the time between the onset of symptoms and reperfusion therapy, ranged between 0.5 to 24 hr (mean= 6 ± 2.4h).

Table – I: Clinical Characteristics of Patients (N=150)

Variables		N (%)	Mean hs-CRP, mg/dl (SD)	P-value
MI- type	AWAMI	87 (58%)	0.70 (± 0.54)	0.62
	AWMI + LWMI	9 (6%)	0.84 (± 1.13)	
	IWMI	21 (14%)	0.51 (± 0.72)	
	IWMI + PWMI	20 (13.3%)	0.87 (± 1.21)	
	IWMI + RWMI	8 (5.33%)	0.69 (± 0.84)	
	LWMI	5 (3.33%)	0.75 (± 1.01)	
Hypertension	Yes	57 (38%)	0.83(±0.53)	0.03
	No	93 (62%)	0.61(±0.45)	
Diabetes mellitus	Yes	71 (47.3%)	0.88(±0.64)	0.02
	No	79 (52.6%)	0.71(0.94)	
Smoking	Yes	50 (33.3%)	0.81(±0.74)	0.6
	No	100 (66.6%)	0.76(±0.84)	
Dyslipidemia	Yes	90 (60%)	0.61(±1.0)	0.04
	No	60 (40%)	0.79(±1.21)	
LVEF (%)	<30%	7 (4.6%)	0.82 (±0.56)	0.64
	>30%	143 (95.3%)	0.75(±0.65)	
Killip Class	Class I	121 (80.6%)	0.63(±0.72)	0.04
	Class II	19 (12.6%)	0.94(±1.3)	
	Class III	7 (4.6%)	1.4(±1.1)	
	Class IV	3 (2%)	0.98(±0.67)	

MI=myocardial infarction; AWMI=anterior wall MI; LWMI= lateral wall MI; IWMI= inferior wall MI; PWMI= posterior wall MI; RVMI=right ventricular MI; LVEF=left ventricular ejection fraction

Anterior Wall Myocardial Infarction (AWMI) is the commonly reported type of Myocardial Infarction among 87 (58%) patients while lateral wall MI (LWMI) was least reported in only 5 (3.3%) patients. Dyslipidemia, diagnosed when cholesterol level > 200mg; low-density lipoprotein (LDL) >130mg/dl; high-density lipoprotein (HDL) > 35mg/dl, and triglycerides were > 150mg/dl, was the most frequent coronary risk factor in 90 patients (60%) followed by type 2 diabetes mellitus (41%) and hypertension (38%). The correlation was established between hs-CRP and hypertension, total cholesterol, and smoking as mean hs-CRP values were observed elevated among these patients (Table I). No statistical difference was found between different types of MI in terms of hs-CRP values. Overall, half of the patients (50%) had elevated hs-CRP (greater than 0.5 mg/dl) while the remaining half were in the normal range (less than 0.5 mg/dl). Although no statistical difference was found between patients with different left ventricular ejection fractions (LVEF), in terms of hs-CRP, patients with LVEF less than 30% were having greater mean hs-CRP (0.82 mg/dl) (Table- I).

Table – II: Association between Coronary Angiogram Data and hs-CRP (n=102)

Parameter		n (%)	Mean hs-CRP (SD)	p-value
CAD	SVD	54 (52.9%)	0.62(±1.1)	0.2
	DVD	31 (30.3%)	0.71(±0.59)	
	TVD	10 (9.8%)	0.87(±0.62)	
	Insignificant CAD	7 (6.8%)	0.69(±0.71)	
LMCA	Unaffected	91 (89.2%)	0.59 (±0.72)	0.06
	Affected	11 (10.7%)	1.2 (±0.69)	
Thrombus	Absent	84 (82.3%)	0.65 (±0.73)	0.81
	Affected	18 (17.6%)	0.71 (±0.81)	
Calcification	Absent	73 (71.5%)	0.63(±0.57)	0.4
	Affected	29 (28.4%)	0.74(±0.89)	
Syntax score	Mild CAD	80 (78.4%)	0.53(±0.65)	0.06
	Moderate CAD	15 (14.7%)	0.91(±0.74)	
	Severe CAD	7 (6.8%)	1.2(±2.2)	

CAD= coronary artery disease; SVD=single vessel disease; DVD= double vessel disease; TVD= triple vessel disease; LMCA, left main coronary artery

Coronary angiography revealed single (SVD), double (DVD) and triple vessel (TVD) coronary artery disease in 54, 31, 10 patients, respectively (Table II). The relationship between hs-CRP and CAG findings is presented in Table III-V. No statistical significance was found between different CAD in terms of mean hs-CRP value. However, mean values for DVD and TVD were higher than SVD (SVD, 0.62 mg/dl; DVD, 0.71 mg/dl and TVD, 0.87 mg/ml). Table II shows mean hs-CRP values for three groups based on syntax score which was found to be directly related to syntax scores (Syntax score ≤22, 0.53 mg/ml; Syntax scores >22–32, 0.91 mg/ml, and syntax score >32, 1.2 mg/dl), however, the difference remained insignificant (Table II).

Table III represents the association of mortality rate with hs-CRP levels in the investigated patients. An insignificant difference was observed in hs-CRP values among patients with mortality or without mortality (Table-III)

Table – III: In-hospital and 30-days mortality rate of the patients (N=150)

Parameter		N (%)	Mean hs-CRP (SD)	P-value
In-hospital mortality	Absent	141 (94%)	0.71 (±0.83)	0.06
	Affected	9 (6%)	0.75 (±0.52)	
30-day mortality	Absent	149 (99.3%)	0.65 (±0.76)	0.07
	Affected	1 (66.6%)	0.87 (±0.45)	

Table – IV: Association of hs-CRP with Syntax Score and Number of Vessels Involved (N=150)

Variables	hs-CRP less than 0.5 mg/dl Mean (SD)	hs-CRP greater than/equal to 0.5 mg/dl Mean (SD)	p-value
No. of vessels	1.2 (±0.56)	2.5 (±1.3)	0.004
Syntax score	12.3 (±8.1)	16.4 (±6.5)	0.03

Grouped analyses have revealed that those with higher hs-CRP (≥0.5 mg/dl) were having significantly higher involvement of coronary arteries and a higher syntax score (Table- IV).

DISCUSSION

The literature has already established CRP as an indicative marker of ischemia in patients with acute coronary syndrome (ACS). The present study aimed to develop an association between hs-CRP and STEMI through a multi-analytical approach. The results found out mean hs-CRP values of greater than 0.5mg/dl in all the diagnosed types of MI. In this regard, Francassi et al reported that a CRP value of greater than 0.3mg/dl poses an 8-fold increased risk of repetitive ischemic events[11]. The mean age of the patients in our study was 56.2 years which indirectly indicates that older patients have raised CRP levels (≥0.5 mg/dl) and that age plays a role in the pathological value of CRP. A similar indication is reported in another study which has reported that the higher hs-CRP levels in elderly patients are significantly associated with a higher prevalence of cardiovascular disorders as compared with healthy subjects[12].

Moreover, the analysis in the present study found a significant relationship of hs-CRP with the diabetic status of the patients. This is consistent with the findings of Ebrahim et al who showed the inflammatory aspect of metabolic disorders by validating the elevation of hs-CRP in disorders such as dyslipidemia, hypertension, and type-II diabetes[13]. However, in our study, despite elevated levels, no significant difference can be found in terms of hs-CRP with the presence of smoking or LV dysfunction when contrasted with their absence. These results predict that these could be the possible risk factors of CAD as already discussed by previous studies[14, 15].

The Killip classification is based on symptom-based stratification of patients and is indicative of in-hospital mortality risks, the higher the class the more are the chances[16]. Our study has found a significant variation in the mean value of hs-CRP among various Killip classes which goes hand in hand with the previous

research done by Suleiman et al who found higher levels of CRP in older patients with more disturbed baseline functions[17].

In our study, 75 (50%) of patients had less than 0.5 mg/dl hs-CRP value and no significant difference existed among different types of MI. These findings are compliant with the results of the study conducted by Cristell et al who reported hs-CRP values less than 2 mg/dl in around 41% of patients, having a window period of less than 6 h. The authors couldn't justify the overlapping of hs-CRP with control values in their study[18].

The syntax scoring is based on lesion characteristics and coronary anatomy[19]. Our study has found a significant difference in mean values of hs-CRP among different groups based on syntax scoring (mild, moderate, and severe), and the relation between the two variables was found to be direct. This finding is also validated by Tanveer et al who showed a positive correlation between hs-CRP values and syntax scoring[20]. Whereas, Zebrack et al demonstrated a weak link between CAD score and CRP. The authors concluded that CRP could be suggestive of plaque properties while CAD score is well-predictive of the extent of diseases or plague[21]. Similarly, Rifai et al couldn't develop any relationship between CAD and inflammatory markers[22].

The study is limited in terms of its cross-sectional nature and small sample size. Therefore, it was not possible to determine causality and relationship with in-hospital consequences. It was also difficult to validate the results due to the dearth of similar studies in the literature. Therefore, it is suggested to conduct further studies in this research area while considering our study results as a hypothesis.

CONCLUSION

The study has found out hs-CRP is a potential candidate for navigating the development of ST-elevation myocardial infraction and predicting its prognosis. It has also developed an understanding related to the association of atherosclerosis and inflammatory pathways.

AUTHOR'S CONTRIBUTION

Niazi GZK: Manuscript writing, Data collection and analysis
Adnan F: Manuscript writing, Data analysis, Final critical review of manuscript
Bukhari SN: Conceived idea, Design methodology, Data collection, Data analysis, Literature review, Manuscript writing.
Taga MH: Manuscript writing, Data collection, Data analysis, Literature review.
Zaffar MZ: Manuscript writing, Literature review, Final critical review of manuscript
Kabir HA: Data collection and compilation, Literature review, Manuscript writing.

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