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Research Article

CLINICAL RELEVANCE OF HIGH SENSITIVITY C-REACTIVE PROTEIN IN ACUTE MYOCARDIAL INFARCTION PATIENTS

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ABSTRACT

Objectives: Poor cardiovascular outcomes have been linked to high-sensitivity C-reaction protein (hs-CRP), a biomarker of residual inflammatory risk. Whether or not a patient has diabetes mellitus, evaluate the relationship among hs-CRP levels estimated at hospital admission and in-hospital consequences and death.

Methods: This prospective cohort study included 100 acute myocardial infarction (AMI) patients with both non-ST elevation myocardial infarction (STEMI) and STEMI who were admitted to the cardiac care critical care unit intensive therapy unit.

Results: Diabetics had a considerably higher incidence of hypertension (p=0.001) and dyslipidemia (p=0.001) compared to non-diabetics. Diabetics exhibited a significantly higher mean hs-CRP level (6.76±1.12 vs. 3.65±0.98 mg/dL; p=0.01) than non-diabetics. Meanwhile, compared to non-diabetics, diabetics utilized significantly more aspirin (p=0.001), beta-blockers (p=0.001), angiotensin receptor blockers (ARBs) (p=0.01), and statins (p=0.001). Furthermore, compared to those with hs-CRP <3 mg/L, those with hs-CRP ≥3 mg/dL had a significantly higher incidence of dyslipidemia (p=0.001) and hypertension (p=0.001).

Conclusion: The results of the current study demonstrated that hs-CRP upon admission is a valid predictor of hospital morbidity and death in patients with AMI who are diabetic or non-diabetic. Individuals with diabetes showed greater CRP levels than non-diabetic AMI patients did.

Keywords: Diabetes mellitus, High-sensitivity C-reactive protein, Acute myocardial infarction, Inflammation.

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INTRODUCTION

Cardiovascular disorder (CVD) is the most reported non-communicable disease worldwide and one of the major reasons for mortality, imposing a huge economic burden and reducing quality of life [1]. The CVD mortality rate showed a steady increase ranges with 12.1 million in 1990–18.6 million in 2019 [2]. In 2020, universally, cardiovascular disease-related mortality is around 19.1 million, and the mortality rate is higher in Eastern Europe and central Asia [3]. The major CVD-related mortality is mainly caused by coronary heart disease, which will affect 244.1 million people globally in 2020 [4].

One of the most commonly documented comorbidities with acute myocardial infarction (AMI) is Type 2 diabetes mellitus (T2DM), which is linked to an elevated threat of repeated cardiovascular happenings and greater in-hospital and long-standing mortality [5]. Atherosclerosis and T2DM have different etiological causes; yet, they are both characterized by inflammation [6]. Moreover, T2DM controls a modest degree of inflammation and is an independent threat factor for AMI. Conversely, compared to non-diabetic AMI, diabetic AMI is a more severe inflammatory disease [7,8]. Moreover, inflammation impedes the development of coronary atherosclerosis at every stage, including the rupture, thrombosis, and plaque progression that results in AMI [9]. Inflammation mediates a key role in tissue damage post-AMI and also progresses to cardiac remodeling and the eventual outcome [10].

During admission, C-reactive protein (CRP) is the extensively preferred inflammatory biomarker for the assessment of systemic inflammation among subjects with acute cardiac events [11]. Post-AMI and 6 h after the development of symptoms, there has been a substantial elevation in the circulating level of CRP [12]. Further, increased concentrations of CRP showed a positive association with the extent of the plague rupture and the size of the infarction [12]. The increased level of CRP during AMI is associated with many adverse events, such as cardiovascular related mortality, the development of chronic kidney disease, and overall mortality due to various causes. To evaluate the atherosclerotic risk, the majority of clinical settings employ the usage high-sensitivity CRP (hs-CRP) rather than routine CRP since it is raised during infections and other inflammatory conditions [13]. Mounting reports show that hs-CRP is more accurate and sensitive to predict outcome during an AMI attack as compared to traditional CRP assays [14,15], and even a slight elevation (≥2 mg/L) displays significant prognostic ability. Raised hs-CRP levels during AMI reflect the combination of the acute as well as the chronic inflammatory situation, namely, T2DM. Hence, hs-CRP has prognostic significance in AMI cases with diabetes as associated to non-diabetic AMI cases. Therefore, by comparing AMI cases with diabetes to cohorts deprived of diabetes, the study's primary goal was to evaluate the relationship among hs-CRP levels estimated at hospital admission and in-hospital consequences and death.

METHODS

Study subjects

This is a prospective cohort of one hundred cases with AMI in the Rajindra Hospital in Patia, Punjab, for the period from January 2022 to December 2023. The patients had been diagnosed with both ST elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI). The study was performed as getting the approval from the Institutional Ethical Committee, and the participants provided informed consent.

Inclusion criteria

Patients with STEMI and NSTEMI were recruited based on their previous histories and relevant investigations. Type 2 diabetic patients

were encompassed in the research plan if they informed the disease condition earlier or were on treatment with antidiabetic agents as per the American diabetes association criteria.

Exclusion criteria

Patients with renal damage, infections, malignancy, recent trauma, immunological disorders, hepatic diseases, and re-infarction were omitted from the study. Patients who had previous AMI, patients who had undergone thrombolysis therapy, and no previous hs-CRP assessment were also excluded from the study.

Study protocol

The detailed history of the patients was collected, and investigations such as electrocardiogram changes, lipid profile, and creatine phosphokinase-MB enzyme levels were measured using standard protocols. Hs-CRP was done by a particle-enhanced immunoturbidimetry assay [16]. A hs-CRP level >2 mg/L was measured as inflammation [17]. The AMI patients were distributed as 2 groups diabetic with 50 and non-diabetic with 50 subjects each.

Data analysis

For continuous variables, the data were shown as mean±SD. Frequency as well as percentage were used to depict the data for categorical variables. The students' t-test was assessed in comparing the groups with and without diabetes.

RESULTS

The demographics and clinical characteristics amid the diabetic and non-diabetic AMI cases are shown in Table 1. In this study, the incidence of hypertension (p=0.001) and dyslipidemia (p=0.001) was suggestively advanced in diabetics as compared to non-diabetics. The mean hs-CRP level was significantly advanced in diabetics as associated to non-diabetics (6.76±1.12 vs. 3.65±0.98 mg/dL; p=0.01). Meanwhile, the intake of statins (p=0.001), ARB (p=0.01), beta-blockers (p=0.001), and aspirin (p=0.001) was suggestively advanced in diabetics as associated to non-diabetics.

The demographics and clinical characteristics between the subjects with hs-CRP levels ≤3 mg/L and ≥3 mg/dL are shown in Table 2. In this study, the incidence of hypertension (p=0.001) and dyslipidemia (p=0.001) was suggestively advanced in cases with hs-CRP ≥3 mg/dL as compared to hs-CRP ≤3 mg/L. The mean hs-CRP level was considerably advanced in hs-CRP ≥3 mg/dL as compared to hs-CRP ≤3 mg/L (7.52±1.54 vs. 1.42±0.09 mg/L; p=0.001). Meanwhile, the intake of statins (p=0.001) and β-blockers (p=0.001) was significantly greater in hs-CRP ≥3 mg/dL as compared to hs-CRP ≤3 mg/L.

The in-hospital clinical endpoint based on the hs-CRP quartiles is shown in Table 3. When considering the overall population, the majority of the patients (40%) were present in the 4th hs-CRP quartile, and it was significant when compared to other quartiles (p=0.001). Meanwhile, the trend was similar in the case of diabetic and non-diabetic subjects, where the majority of the patients were present in the 4th hs-CRP quartile, and it was significant (p=0.001).

DISCUSSION

This study confirms other research that found hs-CRP, which is tested when AMI patients are admitted to the hospital, is a reliable indicator of both long-term mortality and in-hospital prognosis. It appears that this applies to both DM and non-DM patients.

It is widely recognized that inflammation shows a part in atherosclerosis as well as, by extension, AMI [8,18-20]. It is also well-documented that biomarker surrogates, like hs-CRP, can be used to predict the risk of death and recurrent episodes [21,22]. Furthermore, randomized and observational studies showed that lowering systemic inflammation increases the benefits to the cardiovascular system [23]. Specifically, the Aggrastat-to-Zocor experiment showed that lowering hs-CRP levels below 2 mg/L considerably improves the clinical prognosis of acute coronary syndromes subjects [17].

Table 1: Demographics, clinical characteristic, and hospital-related outcome between AMI diabetic and non-diabetic subjects

Variables	Diabetic (n=50)	Non-diabetic (n=50)	p-value
Age (years)	68.96±12.65	69.12±11.54	0.43
Gender			
Male (n, %)	26 (52)	28 (56)	0.28
Females (n, %)	24 (48)	22 (44)	
Body mass index (kg/m^2)	28.76±4.34	25.64±3.28	0.03*
Hypertension (n, %)	41 (82)	28 (56)	0.001*
Smokers (n, %)	35 (68)	24 (48)	0.001*
Dyslipidemia (n, %)	39 (78)	28 (56)	0.001*
STEMI (n, %)	32 (64)	24 (48)	0.001
hs-CRP (mg/L)	6.76±1.12	3.65±0.98	0.01*
Blood glucose (mg/dL)	204.76±72.34	128.12±43.98	0.001*
HbA1c (%)	7.6±1.2	5.6±0.8	0.002*
Serum creatinine (mg/dL)	1.05±0.04	0.78±0.01	0.001*
Medication treatment			
Statins (n, %)	35 (68)	24 (48)	0.001*
ARB (n, %)	32 (64)	28 (56)	0.01*
Beta blockers (n, %)	38 (76)	26 (52)	0.001*
Aspirin (n,%)	36 (72)	30 (60)	0.001*
Complications			
LV dysfunction (n, %)	8 (16)	5 (10)	0.01*
Cardiogenic shock (n, %)	10 (20)	6 (12)	0.003*
AV conduction block (n, %)	4 (8)	3 (6)	0.65
Arrythmias (n, %)	9 (18)	5 (10)	0.001*
Mortality	3 (6)	2 (4)	0.34

STEMI: ST elevation myocardial infarction, hs-CRP: High-sensitivity C-reaction protein, AMI: Acute myocardial infarction.*Denotes significant (p<0.05)

Chronically elevated levels of hs-CRP [19] are indicative of a condition of sub-clinical inflammation, which is a multifactorial metabolic illness associated with DM [8], according to mounting evidence. The more severe inflammatory state that patients with DM exhibit in AMI compared to those without DM [24] may account for, at least in part, their greater risk of short-term as well as long-term death [25,26]. There is on-going debate over the potential differences in prognostic significance between patients with diabetes and those without, with regard to hs-CRP during AMI. In fact, according to earlier research, CRP independently predicts death following AMI in patients with and without diabetes [27,28]. Martín-Timón *et al*. [24], however, did not discover any correlation between CRP.

However, Meisinger *et al*. [27] could not discover any correlation amid CRP and DM patients' long-term mortality (median 4 years) following AMI. These studies, though, were retrospective analyses of registry with older study populations (enrolled between 1998 and 2004). They also took into account patients who did not meet the current diagnosis of DM [27,28], and one research study [28] measured CRP according to the conventional method. More recently, CRP has been demonstrated to predict 3-year death in cases with AMI who have diabetes and those who do not [29]. However, the CRP median value (8.9 mg/L) used in this investigation to examine the predictive significance of CRP may include cases with the highest level of inflammation [29]. Therefore, it is unknown if hs-CRP in AMI cases with and without DM has a different predictive influence.

Through our investigation, we were able to verify that inflammation and DM status in AMI are closely related. In fact, compared to non-DM patients, DM patients had a higher median hs-CRP value and were further possible to have admission hs-CRP values ≥3 mg/L. Furthermore, even after accounting for significant covariates, inflammation and DM status were independently predictive of 2-year mortality and in-hospital outcome. Nevertheless, hs-CRP behaved differently in DM patients compared to non-DM cases when we looked into the connection between

Table 2: Demographics, clinical characteristic, and hospital-related outcome according to hs-CRP values

Variables	hs-CRP≥3 mg/dl (n=72)	hs-CRP≤3 mg/L (n=28)	p-value
Age (years)	71.28±11.98	67.52±10.87	0.001
Gender			
Male (n, %)	42 (58.3)	18 (64.3)	0.01*
Females (n, %)	30 (41.7)	10 (35.7)	
BMI (kg/m^2)	30.12±5.76	26.87±3.45	0.04*
Hypertension (n, %)	53 (73.6)	16 (57.1)	0.001*
T2DM (n, %)	38 (52.8)	12 (42.8)	0.001*
Smokers (n, %)	45 (62.5)	14 (50)	0.001*
Dyslipidemia (n, %)	52 (72.2)	15 (53.5)	0.001*
STEMI (n, %)	38 (52.7)	18 (64.2)	0.04*
hs-CRP (mg/L)	7.52±1.54	1.42±0.09	0.001*
Blood glucose (mg/dL)	185.12±42.87	156.87±38.92	0.001*
HbA1c (%)	6.8±1.1	5.8±0.9	0.000*
Serum creatinine (mg/dL)	1.01±0.02	0.95±0.009	0.007*
Medication treatment			
Statins (n, %)	48 (66.6)	11 (39.2%	0.001*
ARB (n, %)	44 (61.1)	16 (57.1)	0.05
β-blockers (n, %)	49 (68)	15 (53.5)	0.001*
Aspirin (n, %)	47 (65.2)	19 (67.8)	0.06
Complications			
LV dysfunction (n, %)	10 (14)	3 (10.7)	0.05
Cardiogenic shock (n, %)	13 (18)	6 (10.7)	0.001*
AV conduction block (n, %)	5 (7)	3 (7)	0.65
Arrythmias (n, %)	12 (16.6)	2 (7.1)	0.001*
Mortality	4 (5.5)	1 (3.6)	0.07

hs-CRP: High-sensitivity C-reaction protein, BMI: Body mass index, T2DM: Type 2 diabetes mellitus, STEMI: ST elevation myocardial infarction. *Denotes significant (p<0.05)

Table 3: In hospital clinical endpoint based on hs-CRP quartiles in overall , diabetic and non-diabetic populace

In-hospital clinical endpoint (n %)	Hs-CRP quartiles				p-value
	1st (1.5 mg/L)	2nd (1.5–3.4 mg/L)	3rd (3.5–12.5 mg/L)	4th (>12.5 mg/L)	
Overall population (n=100)	7 (7)	21 (21)	32 (32)	40 (40)	0.001*
Diabetics (n=50)	5 (10)	9 (18)	13 (26)	23 (46)	0.000*
Non-diabetics (n=50)	4 (8)	11 (22)	15 (30)	20 (40)	0.000

hs-CRP: High-sensitivity C-reaction protein, P-value and lt;0.05 is considered as statistically significant

inflammation and outcomes. Specifically, in both groups, the adjusted risk of the primary and secondary endpoints increased in tandem with the hs-CRP quartiles, with a more pronounced trend in patients without diabetes. Interestingly, a hs-CRP concentration >3 mg/L was linked to a nearly 2-fold amplified threat of both outcomes in the total group. When comparing DM patients to non-DM cases, the same risk was associated with advanced hs-CRP values. This suggests that the predictive significance of inflammation is still present in DM patients but is shifted in favor of advanced hs-CRP levels. This study seems to be a novel outcome that, if validated in subsequent research, may open the door to predictive classification and intervention techniques that are customized established on the existence or lack of diabetes.

The current analysis is not intended to address the causes behind the disparate prognostic behavior of hs-CRP in patients with DM and those without. On the other hand, the following theory is tenable: The admission hs-CRP level in AMI patients may be attributed to a fluctuating mix of acute and chronic inflammation. Therefore, elevated hs-CRP levels on hospital admission could not solely reflect the inflammatory reaction linked to the severity of AMI. The relationship between chronic inflammation and hs-CRP levels in AMI patients is well-established, and it may be more significant for DM patients than for non-DM patients due to the former's heightened inflammatory state.

CONCLUSION

The current study's findings showed that, in both diabetic and non-diabetic patients with AMI, hs-CRP at admission is a reliable indicator of hospital morbidity and mortality. When compared to patients with AMI who were not diabetic, those with diabetes had higher CRP levels. In patients with AMI, Hs-CRP may be used as a marker to predict hospital mortality. We conclude that elevated CRP levels in diabetics may be indicative of severe vascular endothelium damage, which may contribute to the development of cardiovascular events.

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AUTHORSHIP CONTRIBUTIONS

Dr. Kamaldeep Kaur and Dr. Deep Inder Singh – Design and Data collection or processing, editing of the manuscript. Dr. Amita and Dr. Kamaldeep Kaur- analysis or interpretation, literature search, manuscript writing and submission.

CONFLICTS OF INTEREST

Nil.

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