

# Relevance of High Sensitivity C-Reactive Protein (hs-CRP) Level in Patients with Acute Coronary Syndrome (ACS) and Short Term Outcome

Gul Hassan Brohi<sup>1</sup>, Shahzeb Rasool Memon<sup>2</sup>, Shahbaz Ali Shaikh<sup>3</sup>, Kamran Ali Shahani<sup>4</sup>, Sarfraz Hussain Sahito<sup>3</sup> and Mukhtiar Abro<sup>5</sup>

## ABSTRACT

**Objective:** To evaluate the relevance of High Sensitivity C-Reactive Protein (hs CRP) level in patients with acute coronary syndrome (ACS) and short term outcome.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** This study was conducted at the Department of Cardiology, Liaquat University Hospital Hyderabad for six months from 15<sup>th</sup> March 2018 to 14<sup>th</sup> September 2018.

**Materials and Methods:** The ACS (ST elevated MI, non-ST elevated MI, and Unstable Angina) patients were confirmed based on clinical history, ECG, Cardiac Enzymes, cardiac markers (Troponins), and further evaluated for hs-C-reactive protein levels. The data were analyzed in SPSS version 16.

**Results:** A total of 60 patients with acute coronary syndrome were recruited i.e. 40(66.7%) STEMI, 14(23.3%) NSTEMI, and 6(10%) unstable angina. The mean CRP level of intermediate-risk was  $2.51 \pm 0.51$ ,  $p < 0.001$ , high-risk  $10.95 \pm 7.7$ ,  $pp < 0.001$ , and low risk  $0.862 \pm 0.51$ . There are significant values ( $< 0.05$ ), and 2(9.5%) died in the low-risk group. Six (85.7%) alive and 14 (43.75%) die in a high-risk group, 4 (19%) in the low-risk group, 1(14.3%) in the intermediate-risk group, and 8(25%) high-risk group were hospitalized within three months. The mean  $\pm$  SD of CRP with STEMI, NSTEMI, and UA was  $6.82 \pm 8.0$ ,  $5.11 \pm 5.9$ , and  $4.63 \pm 8.2$  ( $p = 0.05$ ).

**Conclusion:** Serum hs-CRP levels show a significant correlation with the acute coronary syndrome. Measurement of C-reactive protein may have clinical significance in the management of patients hospitalized for the confirmed acute coronary syndrome.

**Key Words:** C-reactive protein, acute coronary syndrome, short-term outcome, high sensitivity.

**Citation of article:** Brohi GH, Memon SR, Shaikh SA, Shahani KA, Sahito SH, Abro M. Relevance of High Sensitivity C-Reactive Protein (hs-CRP) Level in Patients with Acute Coronary Syndrome (ACS) and Short Term Outcome. Med Forum 2020;31(12):191-195.

## INTRODUCTION

Cardiovascular diseases remain the leading cause of death worldwide, making it essential to realize the

<sup>1</sup>. Department of Cardiology, Liaquat University of Medical & Health Sciences, Jamshoro.

<sup>2</sup>. Department of Cardiology & Acute Medicine, Sunderland Royal Hospital, United Kingdom.

<sup>3</sup>. Department of Cardiology, NICVD, Karachi.

<sup>4</sup>. Department of Pediatrics, Khairpur Medical College Khairpur Mir's, Sindh.

<sup>5</sup>. Department of Medicine, Peoples University of Medical & Health Sciences for Women Shaheed Benazirabad (SBA).

Correspondence: Dr. Mukhtiar Abro, Assistant Professor of Medicine, Peoples University of Medical & Health Sciences for Women Shaheed Benazirabad (SBA).

Contact No: 0300-3023832

Email: farooq346@gmail.com

Received: March, 2020

Accepted: August, 2020

Printed: December, 2020

causes, pathogenesis of these diseases, and improve their diagnostic and treatment capabilities as well as prophylactic programs.<sup>1</sup> Numerous research has shown the correlation of pro-inflammatory biomarkers with recurrent hypertension, cardiovascular, coronary artery (CAD) disorder (ACS), peripheral artery disease, stroke and repeated coronary and cerebrovascular disorders, with the investigator (checked-case and prospective cohort) as well as with randomized controlled trials (RCTs).<sup>2</sup>

A meta-analysis of such measurement trials has found that the high-quartile hsCRP levels are 1.5 in contrast to the lowest quartile has, after the modification of the established risk factors for significant cardiovascular events.<sup>2</sup>

C-reactive protein (c-reactive protein CRP) is a much better indicator of outcome than CRP through conventional assays, which is separately correlated with cardiovascular events in all low-density cholesterol lipoprotein types.<sup>2</sup>

People of land- Asian origin have one of the highest susceptibilities to Coronary artery disease (CAD) in the world,<sup>1,2</sup> and it is therefore not surprising that CAD is

now the leading cause of death in the Indo-Pakistan subcontinent.<sup>3</sup>

C reactive protein is an acute phase reactant synthesized in the liver. It is a predictor of mortality and morbidity independent of LDL cholesterol levels.<sup>3</sup> Elevated CRP level indicated the consequences of the active coronary atherosclerotic lesion in inflammation or tissue injury.<sup>4</sup> CRP is considered as a cardiovascular predictor when a baseline of more than 10 mg suggests a non-cardiogenic vascular source of inflammation such as infection, or a chronic inflammatory state. Its clinical diagnosis based on the history of chest pain, ECG showing with or without ST-segment changes. Non-ST EMI myocardial infarction is based on whether an elevation in myocardial protein such as creatinine kinase/Troponins.<sup>5</sup> The research dealt with the pertinence of high-sensitivity C-reactive protein (hs CRP) levels in acute syndrome patients and short-term effects.

## MATERIALS AND METHODS

This cross-sectional study was carried out on 60 consecutive patients confirmed as Acute Coronary Syndrome in the Department of Cardiology Liaquat University Hospital Hyderabad for six months from 15<sup>th</sup> March 2018 to 14<sup>th</sup> September 2018). All patients presenting as ACS, diagnosed based on clinical history, ECG, Cardiac Enzymes, Cardiac markers were included in the study while all those patients who do not fulfill the inclusion criteria and atypical chest pain were excluded from the study.

Informed written consent was taken from all patients for participation in the study. All such patients were further evaluated for their hs-CRP levels and divided into three groups based on the level of hs-CRP i.e. low risk, intermediate-risk, and high risk. Data was collected on pre-designed proforma, a high standard of Medical ethics was observed.

**Data Analysis:** The data was evaluated using program SPSS version 22.0. The chi-square test was applied among the categorical parameters at 95% confidence interval and the p-value < 0.05 was considered statistically significant.

## RESULTS

A total of 60 patients were included in the study. The mean CRP levels were found to be 10.95 mg/L in the total no. of patients with acute coronary syndrome included. There was no significant correlation between age and CRP level ( $r=0.11$ ,  $p<0.05$ ) in total subjects meaning that there is no influence of age on elevated c-reactive protein in acute. The total subjects were divided into three groups based on CRP, of low risk consists of 21 patients whole 7 patients were included in the intermediate-risk group. A high-risk Group comprised of 32 patents. The mean CRP levels of intermediate risk  $(2.51) \pm 0.51$ ,  $p < 0.001$ , and high

risk  $(10.59 \pm 7.7)$   $p < 0.001$  are significantly higher as compared to low risk  $(0.862 \pm 0.51)$ . Table: 05, there is a significant relationship between mortality rate and three groups based on the risk of CRP levels. It means that high levels of CRP in ACS patients have been proved to be a good mortality predictor in this study. and Table: 06 shows a comparison of 3 months' pre-hospitalization among total patients in three groups. There is no significant relation between pre-hospitalization and the three groups based on CRP levels. When three groups were compared based on risk factors, Table: 05 shows the comparison of the groups based on no risk while Table: 07 shows the mean values of CRP along with standard error of the mean. There is a significant difference between CRP levels of both groups of low risk and high risk ( $p=0.04$ ). CRP levels are significantly higher in high-risk groups as compared to low-risk groups ( $p < 0.001$ ) showing that smoking has a great influence on CRP levels, there is no significant difference between the levels of CRP in the three groups divided based on diabetes mellitus ( $p=0.11$ ). It is suggested on this basis that Diabetes mellitus has no independent effect on CRP levels in these three groups. Hyperlipidemia was not found in three groups. Statistical analysis shows a significant association between the three groups and two combined risks ( $p < 0.05$ ) but due to variation and sample size in three groups, CRP levels are not found significantly higher with the increase in high risk when groups were compared based on two risk factors.

**Table No.1: Baseline characteristics of the patients (n = 60)**

	Number	%age	Mean±SD
Age in years	-	-	55.2 ± 11.4 years
Gender:			
Male	50	83 %	-
Female	10	17 %	-
Risk factors:			
Smoker	28	47 %	-
Diabetes mellitus	06	10 %	-
Hypertension	06	10 %	-
Dyslipidaemia	Nil	Nil	-
CRP levels	-	-	10.95 ± 7.78 mg/L

**Table No.2: C-Reactive protein levels in three groups**

	Mean CRP ±SEM	Mean Age ± SEM
1. Low risk (hs CRP <2Mg/L)	0.862±8.81	52.23±8.81
2. Intermediate Risk (hs CRP=23 mg/L)	2.51 0.51***	51.85±6.51
3. High Risk (hs CRP<3v mg/L)	10.95 ± 7.7 ***	55.2±11.4

\*\*\* $p < 0.001$  with respect to the low-risk group.

The diabetic hypertensive patients of intermediate-risk groups have significantly higher CRP values (p = 0.048) when compared with diabetic hypertensive patients of low-risk groups, but the high-risk group has non-significant higher CRP levels when compared with a low-risk group (p= 0.499). Whereas the smoking hypertensive patients of intermediate-risk groups have significantly higher CRP values (p=0.031) when compared with smoking hypertensive patients with the low-risk group. The high-risk group in smoking

hypertensive has a significantly higher CRP level when compared with the low-risk group (p=0.008). This study shows mean values of CRP in three groups divided based on the type of ACS i.e. STEMI, NSTEMI, and UA. There is a significant association between mortality rate and type of ACS (p=0.05). The present study also found that increased CRP levels were associated with increased risk for death in three months follow-up.

**Table No.3: The outcome of patients based on mortality, re-hospitalization, and risk factors (n = 60)**

	Low risk (hs CRP<2 mg/L) n = 21 (%)	Intermediate Risk (hs CRP=2-3) n = 7 (%)	High Risk (hs CRP<3 Mg/L) n=32(%)	X <sup>2</sup> value	df	P value
<b>Mortality</b>						
Alive	19(60.5%)	6(85.7%)	18(56.25%)	151.5	2	0.0001
Died	2(9.5%)	1(14.3%)	14(43.75%)			
<b>Re-hospitalization</b>						
Re- Hospitalization	04(19%)	01(14.3%)	08(25%)	5.695	01	(<0.05)
<b>Risk factors</b>						
Smoker	07(33.4%)	01(14.3%)	10(32%)	28.86	04	(<0.05)
Diabetes mellitus	04(19%)	0(0.0%)	02(6.25%)			
Hypertension	0(0.0%)	02(28.6%)	04(12.5%)			
<b>Combined risk factors</b>						
HTN + DM	02(9.5%)	02(28.6%)	03(9.4%)	90.537	04	(<0.05)
HTN + Smoker	06(28.6%)	01(14.3%)	06(18.75%)			
Smoker + DM	0(0.0%)	01(14.3%)	02(6.25%)			

**Table No.4: CRP levels among three groups based on no risk**

	No of Patients	Percentage	Mean CRP levels
Low risk (hs CRP<2 mg/L)	-	-	-
Intermediate Risk (hs CRP=2-3mg/L)	01	14.3	2.67±0.42
High Risk (hs CRP<3 Mg/L)	08	25	12.04±7.82 - P=0.046

**Table No.5: Comparison of CRP levels Ahree groups based on one risk factor**

	Smoker	Diabetes Mellitus	Hypertension	Dyslipidaemia
Low risk (hs CRP<2 mg/L)	1.09±0.564	0.85± 0.436	Nil	Nil
Intermediate Risk (hs CRP=2-3mg/L)	2.1± 0.00 Non-significant	Nil	2.45± 0.07	Nil
High Risk (hs CRP<3 Mg/L)	8.14± 4.92*** P<0.01	23.4± 2.5 P=0.11	11.5± 85** P<0.01	Nil

**Table No.6: Comparison of CRP Levels Among Three Groups On the Basis of Tow Risk Factors**

	HTN/DM	HTN/SMOKER	HTN/SYSLIPIDAEMIA	SMOKER/DM
1. Low risk (hs CPR<2MG/l)	1.20	0.85 0.436	Nil	Nil
2. Intermediate Risk (hs CRP=2-3mg/L)	2.35 0.05 P=0.048*	2.30 0.01 P=0.031	Nil	2.9 0.0
3. High Risk (hs CRP >3 mg/L)	10.33 9.67 P=0.499	8.8 3.45 P=0.008	Nil	10.65 3.04 P=0.27

**Table No.7: Comparison of CRP levels among three groups on the basis of type of ACS**

	Mean value of CRP ± SEM
1. STEMI	6.82 ± 8.0
2. NSTEMI	5.11 ± 5.9
3. UA	4.63 ± 8.2

**Table No. 8: Outcome of patients on the basis mortality rate in three types of ACE**

	STEMI	NSTEMI	UA	X <sup>2</sup> value	df	P-value
Mortality						
Alive	29(72.5%)	10(71.43%)	4(66.7%)	12.45	01	(p<0.05)
Died	11(27.5%)	4(28.5%)	2(33.3%)			

## DISCUSSION

The present study includes a group of 60 patients with acute coronary syndrome, including 50(83%) males and 10(17%) females. This age group analysis showing the youngest patient in the study was 34 years and the oldest patient was 78 years with the mean age group of 56.1 which is consistent with the study of Vythilin gam KT.<sup>4</sup> PrashanthPanduranga's study also shows a mean age group of 51.28 years in coronary artery disease patients.<sup>5</sup> The gender analysis shows a male predominance in the current study, which resembles the Nadogome study.<sup>6</sup> HRT may be cardio protective since it impacts female cell procoagulants.<sup>7</sup> In this study, the group analyses show 06(10%) cases to be hypertensive, 06(10) cases suffering from diabetes mellitus, 28(47%) were smokers. Morrow et al study showed an association of risk factors like hypertension (64%). Diabetes(44%) in CAD.<sup>8</sup> In current study group, 47% of patients are smokers and a population-based survey found a high prevalence of smoking in both urban and rural populations among CAD.<sup>9</sup> In the present study, all the patients with CAD diagnosis of stable and unstable angina were confirmed both clinically as well as with relevant investigation.<sup>9</sup>

The elevated incidence of stroke, acute ischaemic attack, fever, peripheral artery disease, and accidental coronary failure has also been linked with higher hs-CRP.<sup>10,11</sup>

The hs-CRP values do not correlate explicitly on the simulated tomographic or authentic plaque pressure with the rate of the coronary artery calcification. 1229 Kaptoge et al. meta-analysis.<sup>9</sup>

Hs-CRP applies a statistical benefit to certain cardiovascular risk factors, including obesity and cholesterol, to nearly all of the research to date.<sup>10,12</sup>

The chances for coronary heart disease is roughly 1.5 in Danesh et al.<sup>13</sup> in the patients with the largest tertilehs-CRP, as opposed to the patients with The Tertile Lowest.

Specific prognostic details will be given by applying the High Sensitivity C-Reactive Protein to the Framingham danger ranking.<sup>13-15</sup>

Cushman et al.<sup>16</sup> Women over 65 with hs-CRP > 3mg / L and 10-year frequency framing ham> 20% had 31% coronary heart disease compared to 16% with hs-CRP The Reynolds Hazard Assessment ranks all men and females for cardiovascular risk more reliably, according to previous research.<sup>6,15</sup>

Ridker et al.<sup>12</sup> have found that the Reynolds Risk Rating scale is Either higher or lower than 40% of the

sample women's health (age < 45 years of age) and about 20% of the sample women's health doctors were classified as being at interim risk for cardiovascular problems in their health survey (aged > 50 years).

These instructions were however written in 2003, while they followed the outcomes of the reasoning for utilizing rosuvastatin (JUPITER)trial.<sup>16</sup>

Current recommendations taking into account JUPITER results such as those released by the Canadian Cardiovascular Society in 2009 allow for hs-CRP assessment across all intermediate-risk individuals.<sup>16</sup>

Patients with higher hs-CRP coronary artery disease anticipate potential harmful medical conditions, like MI, premature mortality, and Cardiac Failure<sup>17</sup> equivalent, are more prone to suffer negative consequences including Mi and mortality of patients receiving low hs-CRP treatments.<sup>17</sup>

In patients with coronary artery bypassing grafting of hs- > mg / L (15 of 59 patients), Milazzo et Al.<sup>17</sup> have been finding a 25% potential for repeated ischemic attacks, relative to a 4% frequency (1 of 27 patients) in patients with a hs- < 3 mg / L.

Milazzo and Al.<sup>17</sup> observed a 25% risk for frequent ischemic attacks for patients with coronary artery bypassing hs- > mg / L (15 out of 59 patients), contrasted with the 4% incidence (1 out of 27 patients), in patients with hs-<3 mg / L..

## CONCLUSION

This study showed the persistent elevation of CRP in unstable angina which indicates further continuing inflammation. Serum hs-CRP levels show a significant correlation with the acute coronary syndrome.

### Author's Contribution:

Concept & Design of Study: Gul Hassan Brohi  
Drafting: Shahzeb Rasool Memon, Shahbaz Ali Shaikh

Data Analysis: Kamran Ali Shahani, Sarfraz Hussain Sahito, Mukhtiar Abro

Revisiting Critically: Gul Hassan Brohi, Shahzeb Rasool Memon

Final Approval of version: Gul Hassan Brohi

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Adukauskiene D, Čiginskienė A, Adukauskaitė A, Pentiokinienė D, Šlapikas R, Čeponienė I. Clinical

- relevance of high sensitivity C-reactive protein in cardiology. *Medicina (B Aires)* 2016;52(1):1–10.
2. Kamath D, Xavier D, Sigamani A, Pais P. High sensitivity C-reactive protein (hs-CRP) & cardiovascular disease: An Indian perspective. *Ind J Med Res* 2015;142(3):261.
  3. Mani P, Puri R, Schwartz GG, Nissen SE, Shao M, Kastelein JJP, et al. Association of Initial and Serial C-Reactive Protein Levels With Adverse Cardiovascular Events and Death After Acute Coronary Syndrome. *JAMA Cardiol* 2019;4(4):314.
  4. Vytilingham KI. The Incidence and Epidemiology of Coronary Heart Disease in South India. *J Assoc Physicians Ind* 1966;14(5):289–300.
  5. Panduranga P, Riyami AA, Sulaiman KJ, Mukhaini M. C-reactive protein in unstable angina: clinical and angiographic correlation. *Heart Asia* 2010;2(1):140–4.
  6. Malhotra P, Kumari S, Kumar R, Jain S, Sharma B. Prevalence and determinants of hypertension in an un-industrialized rural population of North India. *J Hum Hypertens* 1999;13(7):467–72.
  7. Nakagomi A, Freedman S Ben, Geczy CL. Interferon- $\gamma$  and Lipopolysaccharide Potentiate Monocyte Tissue Factor Induction by C-Reactive Protein. *Circulation* 2000;101(15):1785–91.
  8. Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, Cannon CP, et al. C-Reactive Protein Is a Potent Predictor of Mortality Independently of and in Combination With Troponin T in Acute Coronary Syndromes: A TIMI 11A Substudy. *J Am Coll Cardiol* 1998;31(7):1460–5.
  9. Kaptoge S, Di Angelantonio E, Lowe G, Pepys MB, Thompson SG, Collins R, et al. C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: An individual participant meta-analysis. *Lancet* 2010;375(9709):132–40.
  10. Blake GJ, Rifai N, Buring JE, Ridker PM. Blood Pressure, C-Reactive Protein, and Risk of Future Cardiovascular Events. *Circulation* 2003;108(24):2993–9.
  11. Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO, Criqui M, et al. Markers of Inflammation and Cardiovascular Disease. *Circulation* 2003;107(3):499–511.
  12. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-Reactive Protein and Other Markers of Inflammation in the Prediction of Cardiovascular Disease in Women. *N Engl J Med* 2000;342(12):836–43.
  13. Danesh J, Wheeler JG, Hirschfield GM, Eda S, Eiriksdottir G, Rumley A, et al. C-Reactive Protein and Other Circulating Markers of Inflammation in the Prediction of Coronary Heart Disease. *N Engl J Med* 2004;350(14):1387–97.
  14. Ridker PM, Buring JE, Rifai N, Cook NR. Development and Validation of Improved Algorithms for the Assessment of Global Cardiovascular Risk in Women. *JAMA* 2007;297(6):611.
  15. Ridker PM, Paynter NP, Rifai N, Gaziano JM, Cook NR. C-Reactive Protein and Parental History Improve Global Cardiovascular Risk Prediction. *Circulation* 2008;118(22):2243–51.
  16. Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM, Kastelein JJ, et al. Reduction in C-reactive protein and LDL cholesterol and cardiovascular event rates after initiation of rosuvastatin: a prospective study of the JUPITER trial. *Lancet* 2009;373(9670):1175–82.
  17. Milazzo D, Biasucci LM, Luciani N, Martinelli L, Canosa C, Schiavello R, et al. Elevated levels of C-reactive protein before coronary artery bypass grafting predict recurrence of ischemic events. *Am J Cardiol* 1999;84(4):459–61.