



# ACUTE CORONARY SYNDROME; CO-RELATION OF C-REACTIVE PROTEIN WITH CLINICAL OUTCOME OF PATIENTS

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**ABSTRACT... Introduction:** Atherosclerosis is intrinsically an inflammatory disease. Numerous studies has shown that elevated levels of C-reactive protein (CRP) are associated with increased cardiovascular risk. The objectives of this study was to determine the correlation of clinical outcome in terms of 30 day mortality with various level of C-reactive proteins among patients presenting with acute coronary syndrome **Study Design:** Descriptive. **Setting:** Department of Cardiology, Punjab Institute of Cardiology Lahore. **Period:** 06 months. **Material and Methods:** Total 250 patients presented in emergency department and diagnosed as cases of acute coronary syndrome base on history of chest pain, ECG and cardiac biochemical markers were included in the study. Management of ACS was continued while CRP levels of each patient were measured by latest Agglutination method. **Results:** Our study included 250 patients with acute coronary syndrome with a mean age of  $52.90 \pm 10.34$  years. Male patients were 220 (88%). Regarding the clinical presentation of patients, 20 (8%) had unstable angina, 95(38%) had NSTEMI and 135 (54%) had STEMI. CRP level were measured, 184(73.6%) patients had CRP levels  $< 22\text{mg/L}$  with mortality of 12 (6.5%) at 30 days and 66 (26.4%) patients had CRP levels  $> 22\text{mg/L}$  with mortality of which 13(19.6%) at 30 days. The mean CRP level was  $17.9 \pm 12.47$ ,  $18.08 \pm 15.73$  and  $22.38 \pm 17.92$  for patients with unstable angina, NSTEMI and STEMI respectively. The stratification of data for effect modifiers showed that 60(24%) patients had diabetes, 138 (55.2%) patients had hypertension and 65(26%) patients were smokers. **Conclusion:** Patients having higher CRP levels had higher risk of 30 day mortality.

**Key words:** C-reactive protein, Acute coronary syndrome.

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## INTRODUCTION

Coronary artery disease will likely to become major cause of death worldwide by the year 2020.<sup>1</sup> In Acute coronary syndromes underlying pathology is atheromatous plaque formation and its rupture. Inflammation plays a key role in the pathogenesis of atherosclerosis.<sup>2</sup> C - reactive protein is a plasma marker of atherothrombotic events.<sup>3</sup> C – reactive protein, which is used to describe acute reactions, has longer half life, more stable levels in blood and less circadian variability. In addition to conventional risk factors, C - reactive protein is an independent risk factor for cardiac events in patients with or without coronary artery disease.<sup>4</sup> Baseline C– reactive protein level is a power full independent predictor of both early and late mortality with acute coronary syndromes.<sup>5</sup> It helps in risk stratification in acute

coronary syndromes according to a study in which C-reactive protein levels were done in 1501 patients out of which 1106 had C-reactive protein  $< 22\text{mg/L}$  with mortality of 66 and 395 patients had C-reactive protein levels  $\geq 22\text{mg/L}$  with mortality of 78 patients.<sup>6</sup> However, there still is controversy regarding the use of C-reactive protein levels in clinical practice because some studies did not favor the CRP measurement for risk stratification in coronary artery disease.<sup>7</sup> No data is available regarding this issue in our country, the rationale of this study is to find out correlation of clinical outcome of acute coronary syndrome with C-reactive protein levels in our population.

## MATERIAL AND METHODS

Study design was descriptive, Sampling technique

was Non-probability purposive sampling and it was conducted for 6 months in the cardiology Department of Punjab Institute Of Cardiology Lahore. The objectives was to determine the correlation of clinical outcome in terms of 30 day mortality with various levels of C- reactive protein in acute coronary syndrome. The study included 250 patients of age between 20 to 70 years and either gender presented with ACS. Following patients were excluded from the study based on history and examination:

1. More than 12 hrs after the appearance of symptoms.
2. Infections.
3. Chronic inflammatory conditions.
4. Neoplastic diseases.
5. Trauma or surgery within last one week.

Patients fulfilling the inclusion and exclusion criteria were enrolled after informed consent. Acute coronary syndrome were managed according to standard guidelines. Blood sample were taken for routine investigations sent to Punjab Institute of Cardiology hospital laboratory where CRP level estimation was done. Data regarding age, gender, clinical presentation, C - reactive protein levels and in-hospital mortality was documented. Follow-up consultation was scheduled after one month.

Data was analysed using SPSS version 10. Mean  $\pm$  Standard deviation was calculated for quantitative variables like age. Frequency and percentage were calculated for the qualitative variables like gender. CRP levels will be divided in to two categories ( $<22\text{mg/L}$  and  $\geq 22\text{mg/L}$ ) and 30 day mortality in both groups were determined by calculating frequency/percentages. Data was stratified for diabetes, hypertension and smoking to address effect modifiers.

## RESULTS

Our study included 250 patients with ACS. Age was from 27 to 70 years with mean age of  $52.90 \pm 10.34$  years. Out of 250 patients 220(88%) were male and 30(12%) were females (Table-I). 20(8%) had unstable angina, 95(38%) had NSTEMI and 135 (54%) had STEMI (Table-II).

CRP levels was categoried in two categories, in 1<sup>st</sup> category of CRP levels  $< 22\text{mg/L}$ , there were 184 (73.6%) patients and in 2<sup>nd</sup> category of CRP levels  $> 22\text{mg/L}$ , there were 66 (24.6%) patients (Table-III). Table-IV presents mortality in both categories of CRP level. Table-IV presents mortality in various presentation of ACS. Table-V presents Effect Modifiers in the two categories of CRP level.

Gender	No.	Percentage
Male	220	88
Female	30	12

**Table-I. Gender distribution of study group (N=250)**

Type of ACS	No.	Percentage
USAP	20	8
NSTEMI	95	38
STEMI	135	54

**Table-II. Clinical Presentation (N=250)**

Category	No.	Percentage
CRP $< 22\text{mg/L}$	184	73.6
CRP $\geq 22\text{mg/L}$	66	26.4

**Table-III. Distribution by Categories of CRP levels(N=250)**

Category	No.	Mortality	Percentage
CRP $< 22\text{mg/L}$	184	12	6.5
CRP $\geq 22\text{mg/L}$	66	13	19.7
Total	250	25	10

**Table-IV. Distribution by mortality in different categories of CRP**

	No.	Diabetes	Hypertension	Smoking
CRP $< 22\text{mg/L}$	184	36	95	53
CRP $\geq 22\text{mg/L}$	66	24	43	12
Total	250	60	138	65

**Table-V. Stratification for effect modifiers**

## DISCUSSION

Coronary artery disease is one of the leading causes of death despite growing public awareness of the disease and major advances in its treatment. Several risk factors of coronary artery disease are identified.<sup>8</sup> However, many patients have no apparent clinical risk factors and normal cholesterol levels and this suggests the need for

the research of new marker for risk stratification of ischaemic patients.<sup>9</sup> Several inflammatory markers are related with cardiovascular risk. These include CRP, WBC count, ESR, plasma interleukin-6 (IL-6), IL-18, TNF alpha receptor 1, soluble intercellular adhesion molecule-1 (sICAM-1), P-selectin, soluble vascular cell adhesion molecule-1 (sVCAM-1), E-selectin, lipoprotein-associated phospholipase A2, and low serum albumin.<sup>10-30</sup> However C-reactive protein is considered as the “golden marker” of inflammation and it has been evaluated in many phases of ischaemic heart disease for risk stratification.

Several studies predicted the clinical outcome of ACS patients based on CRP. Pietila et al<sup>31</sup>, studied patients with acute myocardial infarction treated with fibrinolytic therapy and mortality at 6-month was related with peak CRP at presentation. Anzai et al and Tommasi et al documented that post-MI complications are related with peak CRP levels at first presentation.<sup>32-33</sup> The Thrombolysis in Myocardial Infarction (TIMI) 11, a study found that early detection of elevated troponin T and CRP increased the twofold risk of mortality.<sup>34</sup> Importantly, elevated CRP levels retained their predictive value even in patients with negative rapid troponin T, thus eliminating the contribution of myocardial necrosis from its prognostic strength. Biasucci et al<sup>35</sup> also confirmed the prognostic power of CRP levels at discharge in the patients of unstable angina without myonecrosis.

However the absolute CRP to predict cardiovascular risk in any clinical presentation is not known. In general, higher cardiovascular events occurred in patient with greater elevation of CRP. Instead, a high-sensitivity assay (hsCRP) can also be used in persons with clinical risk factors but CRP in the normal range. Similarly the optimal timing of measurement of CRP in patients with ACS is un-certain. However, in ACS it should be measured as early as possible along with serum troponins level because with time more myocardial necrosis can influence the CRP levels.<sup>36</sup> Similarly after myocardial infarction it should be measured after at least four to six weeks to permit resolution of the acute phase reaction.

Several pharmacologic agents are known to lower CRP, including statins and thiazolidinediones.

Local data on the subject are lacking. This study is an attempt to fill this gap. In our study patients with ACS, were mostly elderly, male and presented with ST elevation MI. We used the value of 22 mg/L of CRP to categorized the study group. We found the prognostic relationship of CRP in ACS patients. This study concluded that higher CRP levels are associated with higher 30 day mortality risk in ACS patients. This finding is similar to above mentioned international studies. However more studies on a larger scale are required in Pakistan to evaluate the role of CRP in prognostic stratification of patients with ACS. This study will set baseline data, regarding this internationally investigated fact. Here it has to be kept in mind that C-reactive protein levels are still not done routinely in patients of acute coronary syndromes in Pakistan, and in overburdened small number of cardiology hospitals this can be used as a tool to identify high risk patients.

## CONCLUSION

This study concluded that higher CRP levels are associated with higher 30 day mortality risk in patients presented with ACS so the CRP levels can be used to risk stratify these patients.

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*“There is not pillow so soft  
as a clear conscience.”*

**French Proverb**

#### AUTHORSHIP AND CONTRIBUTION DECLARATION

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1	Abubakar Maqbool	Data collection	
2	Naeem Asghar	Drafting & statistical analysis	
3	Shakeel Ahmad	Discussion	