

# Frequency of Raised C-Reactive Protein in Acute Heart Failure

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## ABSTRACT

**Objective:** To determine the C-reactive protein (CRP) levels in patients presenting with acute heart failure.

**Methodology:** This cross-sectional study was conducted at Punjab Institute of Cardiology, Lahore for a period of six months after approval from the Ethical Review Committee of the Institution. Three hundred and forty five patients were enrolled in this study by non-probability consecutive sampling technique. Patients of either gender having age 18-60 years who presented in the emergency department with acute heart failure within 12 hours were included in this study. After informed consent, their venous blood samples were drawn for the measurement of CRP levels. All the data was collected on a predefined proforma. The data was entered and analyzed in Statistical Package for the Social Sciences (SPSS) version 25.0.

**Results:** The mean age of patients was  $45.51 \pm 10.64$  years. There were 192 (55.7%) males and 153 (44.3%) females. The mean duration of heart failure was  $6.46 \pm 3.53$  hours. The mean CRP in the study patients was  $6.27 \pm 4.70$  mg/L. One hundred and ninety two (55.7%) patients had raised CRP while 153 (44.3%) patients had normal CRP levels.

**Conclusion:** Increased CRP levels were seen in a higher number of patients with acute heart failure. This may be established as a significant risk factor for in-hospital mortality due to heart failure.

**Keywords:** Heart failure. C-reactive protein. Inflammation.

## INTRODUCTION

Acute heart failure (AHF) is a clinical syndrome characterized by sudden worsening of shortness of breath (SOB) & fatigue. Patients usually present with signs of congestion, tachypnea, striving for more oxygen, and organ dysfunction due to hypoxic insult.<sup>1</sup>

Acute heart failure is a cardiac emergency that requires prompt attention and treatment. Despite a better understanding of underlying pathophysiology and advancements in the treatment, mortality remains in the range of 4 to 10%. One year mortality rate after discharge is also quite high and is up to 30%.<sup>2</sup> According to the Center for Disease Control and Prevention, 379,800 mortalities occurred due to heart failure in 2018 in the USA. The risk factors for cardiovascular illness have increased in the Asian population due to industrialization and organization. Hence, there is a corresponding increase in the incidence of diabetes, hypertension, and cardiovascular disease. Disease burden and mortality due to ischemic heart disease (IHD) and heart failure has also increased.<sup>3</sup> Inflammation plays an important role in the pathogenesis of heart failure. So, heart failure indicates low-grade inflammation in the body. Inflammatory

biomarkers are raised in patients presented with acute heart failure.<sup>4</sup>

C-reactive protein (CRP) is an acute phase reactant and an important inflammatory biomarker. It is synthesized in the liver in response to an inflammatory stimulus.<sup>5</sup> A significantly higher risk for developing acute heart failure was found in patients suffering from systemic sclerosis, systemic lupus erythematosus (SLE), and rheumatoid arthritis.<sup>6</sup> Certain biomarkers especially Natriuretic peptides i.e. (BNP), NT pro BNP, ANP, have been studied in the management of heart failure and have secured a place for themselves in the diagnosis and prognosis of HF patients. But these are still not readily available everywhere and are relatively costly too. Among the inflammatory markers, C-reactive protein (CRP) is a protein that has been found to have a consistent association with cardiovascular diseases including HF.<sup>7,8</sup>

The purpose of this study was to detect the frequency of elevated CRP in acute heart failure patients and to study the association of CRP patients' characteristics like age, gender, BMI, and duration of heart failure. It is a cost-effective and widely available test. It will be helpful for the physicians in the diagnosis and management of HF patients.

## METHODOLOGY

This cross-sectional study was conducted at Punjab Institute of Cardiology, Lahore from September 2018 to February 2019. After approval from the Ethical Review Committee of Institution (Letter No: RTPGME-Research/077, 09-03-2018), 345 patients were enrolled by non-probability consecutive sampling

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Received: November 5, 2021; Accepted: December 27, 2021

technique. Patients of either gender having age 18-60 years who presented with acute heart failure in the emergency department within 12 hours were included in this study. Patients with a history of acute infection, malignancy, recent trauma or surgery (<3 month), autoimmune disorders, and chronic obstructive pulmonary disease were excluded. After informed consent, their venous blood samples were drawn for the measurement of CRP levels. All the data was collected on a predefined proforma. After taking informed consent from the patients and without causing any delay in the provision of emergency treatment, all demographic and personal information was charted on a predefined proforma.

### STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) version 25.0 was used for data analysis. For qualitative variables like gender and BMI, frequency and percentages were calculated. Mean value and standard deviation was calculated for quantitative variables like age, CRP levels, and duration of heart failure. Data was stratified for age, gender, BMI, and duration of acute heart failure. Chi-square test was applied for data stratification and a p-value of  $\leq 0.05$  was taken as significant.

### RESULTS

A total of 345 patients were enrolled aged 18 to 60 years, with a mean age of  $45.51 \pm 10.64$  years. Total of 192(55.7%) were males while 153(44.3%) were females. Duration of heart failure at the time of presentation ranged from 1-12 hours. The mean duration of heart failure was  $6.46 \pm 3.53$  hours. C-reactive protein was elevated in 192(55.7%) patients

while 153(44.3%) had normal levels at presentation (Figure 1). The mean level of CRP was found to be  $6.27 \pm 4.70$  mg/L, with the lowest value being 0.1 mg/L and the highest value being 28 mg/L. One hundred and thirteen (58.9%) males and 79(51.6%) females had elevated CRP levels. No significant difference was found when CRP levels were compared according to the age groups, gender, BMI, and duration of heart failure (Table 1).

### DISCUSSION

C-reactive protein is an acute phase reactant and synthesized by the liver. Acute phase reactants are plasma proteins that show a change in their serum levels during the early phases of inflammation. This phenomenon is known as acute phase reaction because of its shorter half-life and its significance in determining acute flares in a chronic inflammatory condition is high. Though historically, these reactants have been associated with acute infections or autoimmune disorders, studies have suggested the association of CRP with ischemic heart disease and heart failure as well. The mechanism of its rise in acute heart failure is still unknown.<sup>7,9</sup> Literature shows that during hypoxic stress interleukin-6 is released from endothelial cells and monocytes, which leads to increased levels of CRP in the body.<sup>8</sup>

Our results showed that the mean level of CRP was  $6.27 \pm 4.70$  mg/L and CRP was raised in 192(55.7%) patients. Kausadikar et al. studied the role of CRP in ST-elevation myocardial infarction (STEMI) patients and found raised CRP levels in 34% patients with heart failure. They concluded that higher levels were associated with lower ejection fraction (EF) (i.e. <40%) and higher mortality.<sup>9</sup> Stumpf et al. studied the

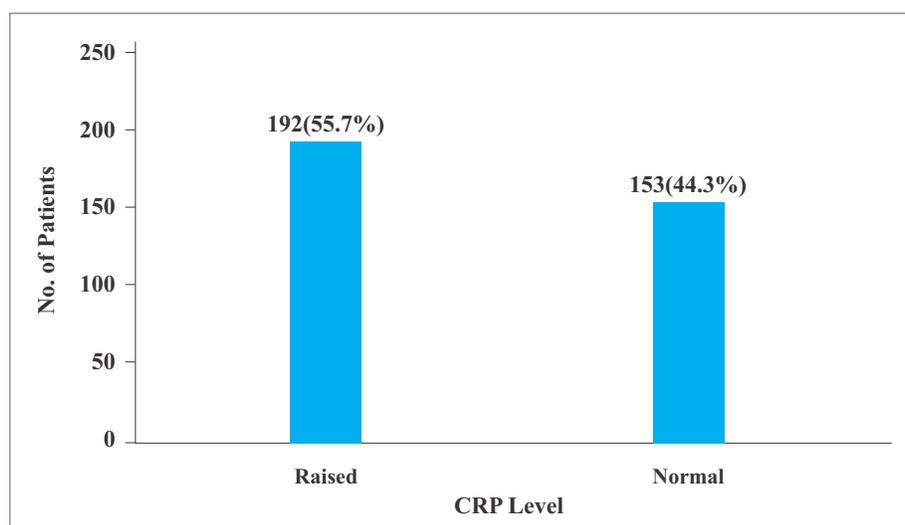


Figure 1: CRP Levels in Patients

**Table 1: Distribution of Raised CRP Patients in association with Age Groups, Gender, Duration of Heart Failure, and BMI**

Variables		Raised CRP		Total	p-value
		No	Yes		
Age Groups (Years)	18-40	48(40.7%)	70(59.3%)	118(34.2%)	0.323
	41-60	105(46.3%)	122(53.7%)	227(65.8%)	
Gender	Male	79(41.1%)	113(58.9%)	192(55.7%)	0.180
	Female	74(48.4%)	79(51.6%)	153(44.3%)	
Duration of Heart Failure	<6 hours	66(45.8%)	78(54.2%)	144(41.7%)	0.638
	6-12 hours	87(43.3%)	114(56.7%)	201(58.3%)	
BMI	Obese	66(39.3%)	102(60.7%)	168(48.7%)	0.065
	Non-Obese	87(49.2%)	90(50.8%)	177(51.3%)	

role of CRP as a predictor of heart failure in STEMI patients. They reported that the higher peak CRP level after 48 hours of the event is associated with a higher incidence of heart failure. It also showed higher cardiovascular mortality in the first year post-STEMI.<sup>10</sup> Another study by Al Aseri et al., in 2019 concluded that high-sensitivity C-reactive protein (hs-CRP) is associated with heart failure after STEMI.<sup>11</sup> The results of these studies strengthen the present study results. Polyakova et al. studied the role of CRP in acute myocardial infarction and found a linear correlation between it and infarct size. Also, higher CRP levels predicted a higher incidence of complications including recurrent acute coronary syndrome (ACS), arrhythmias, and heart failure.<sup>12</sup> Our study showed a higher trend of raised CRP in male patients (58.9%) as compared to females with acute HF (51.6%). Another study showed that higher CRP levels were found in males as compared to females.<sup>13</sup> Khera et al. studied the race and gender effect on CRP level and found that black ethnicity and females had higher levels of CRP as opposed to white ethnicity and men.<sup>14</sup> The association of gender with raised CRP is still controversial.

According to this study, CRP levels were raised in young patients aged between 41-60 years and no significant correlation was seen between BMI with raised CRP levels. In a study by DuBrock et al., in 2018, it was seen that the high CRP levels were associated with the middle age and higher body mass index.<sup>15</sup> These results are in contrast to the present study.

### CONCLUSION

C-reactive protein levels were found to be elevated in a

significant number of acute HF patients. This may be established as a significant risk factor for in-hospital mortality due to heart failure. Particular attention should be given to prior management in the presence of raised CRP levels in acute heart failure patients.

### LIMITATIONS & RECOMMENDATIONS

Our study was limited to the measurement of CRP levels merely at presentation. Future studies should focus on sequential CRP levels that will help to determine when the CRP levels peak in acute heart failure patients. Also, it would tell if a linear correlation exists between declining levels of CRP and clinical improvement so that recovery could be monitored using serial CRP levels. A multi-centered study with a higher number of patients should be conducted. After carefully excluding other possible causes of higher CRP via clinical history and examination, this marker can be used to detect HF patients who would require more intensive therapies during the hospital stay and also postdischarge. More studies are required to detect long-term prognostic implications of this marker in our population. Ultimately, this will lead to studies on the institution of drugs that would specifically target inflammatory markers in HF patients to improve survival.

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