

## Role of C-Reactive Protein in Predicting the Severity of Acute Pancreatitis

G Hemanth<sup>1</sup>, L Srinivas<sup>2</sup>

<sup>1</sup>Associate Professor, Department of General Surgery, Prathima Institute of Medical Sciences, Naganoor, Karimnagar, Telangana State.

<sup>2</sup>Associate Professor, Department of General Surgery, Prathima Institute of Medical Sciences, Naganoor, Karimnagar, Telangana State.

Received: 14-04-2023 / Revised: 19-05-2023 / Accepted: 21-06-2023

Corresponding author: Dr. L Srinivas

Conflict of interest: Nil

### Abstract:

**Background:** Intense abdominal pain is commonly caused by acute pancreatitis. The effectiveness of diagnostic markers such as pancreatic enzymes (such as amylase and lipase) in predicting outcomes has been disappointing. However, assessing C-reactive protein (CRP) offers a cost-effective and efficient alternative. In this study, we have investigated whether an early assessment of CRP levels can serve as a reliable predictor of morbidity and mortality in cases of acute pancreatitis.

**Methods:** The patients were selected based on the inclusion and exclusion criteria and the demographic profile of the cases was recorded based on a pre-structured proforma. A detailed clinical examination was carried out on the patients and findings were noted. Serum C-reactive protein (CRP) levels were measured serially at 24 hrs, 48 hrs, and 72 hours following admission. At the 72-hour mark, computed tomography (CT) scans were conducted using oral and intravenous contrast agents to determine the CT severity index, including Balthazar's and Ranson's scores, as well as assess the CT grade and necrosis grade.

**Results:** The comparison of CRP versus necrosis scores has been depicted in Figure 3. The sensitivity was 84.44% and Specificity was 80.53%. The correlation between the necrosis score in the CT severity index and serum CRP values was also determined. The duration of hospital admission was recorded as a marker of disease morbidity. A significant cutoff value of 100 mg/dl was used for CRP, although different studies cited in this research suggested different significant values (100 mg/dl and 150 mg/dl).

**Conclusion:** Elevated CRP values beyond the significant range positively correlate with the occurrence of necrosis in pancreatitis. This information can aid in deciding which patients require a contrast-enhanced CT scan (CECT), considering that this investigation is both expensive and not readily accessible.

**Keywords:** Acute pancreatitis, C Reactive Protein, CT severity score.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

### Introduction

Acute pancreatitis, characterized by acute inflammation of the pancreas, is a severe disease with varying degrees of severity, complications, and outcomes.

Unfortunately, there is limited available data on the epidemiology of this disease. However, international statistics provide some insights. In the UK, the incidence of

acute pancreatitis is reported to be 56 cases per 100000 persons per year [1], while in the US, there are over 220,000 hospital admissions attributed to acute pancreatitis annually [2]. A comprehensive epidemiological study using UK and European data demonstrated a rising incidence of all-cause acute pancreatitis [3]. Additionally, the incidence of acute pancreatitis was found to increase with age [3], with males having an incidence rate 10%-30% higher than females [4]. Among hospital admissions for acute pancreatitis, approximately 20%-30% of patients experience a severe course [1], with severe life-threatening complications occurring in 25% of these cases [4]. Mortality in severe acute pancreatitis can reach as high as 30% [2], while the overall estimated mortality rate for acute pancreatitis is around 5% [1].

The clinical presentation of acute pancreatitis can vary, and the majority of patients recover without complications. However, some patients experience severe complications such as pancreatic abscesses and pancreatic necrosis, leading to high morbidity and mortality rates [5]. Diagnostic markers, such as pancreatic enzymes like amylase and lipase, have not been successful as prognostic indicators. Other biochemical markers like CRP and pro-calcitonin are currently being evaluated for their prognostic value. CRP assessment is a cost-effective and reliable alternative [6]. CRP, also known as C-reactive protein, is the most commonly used marker, synthesized in the liver in response to the action of IL-6 and IL-1. Serum levels of CRP typically peak between 48-72 hours, and levels higher than 100-150 mg/dl are considered positive indicators [6]. In this study, we aimed to determine whether an early assessment of CRP levels alone can effectively differentiate between mild and severe acute pancreatitis, we aimed to evaluate the significance of serum C-reactive protein levels as a biochemical marker of disease severity, comparing it to

the standard Computed Tomography Severity Index (CTSI).

### **Material and methods**

This cross-sectional study was conducted in the Department of General Surgery, Prathima Institute of Medical Sciences, Naganoor, Karimnagar, Telangana State. Institutional Ethical approval was obtained for the study. Written permission was obtained from all the participants of the study.

#### ***Inclusion criteria***

1. Patients diagnosed with acute pancreatitis.
2. serum amylase (>4 times normal)
3. The radiological investigation includes the USG abdomen and CT abdomen with findings suggestive of pancreatitis.
4. Patients aged 20 years and above.

#### ***Exclusion criteria***

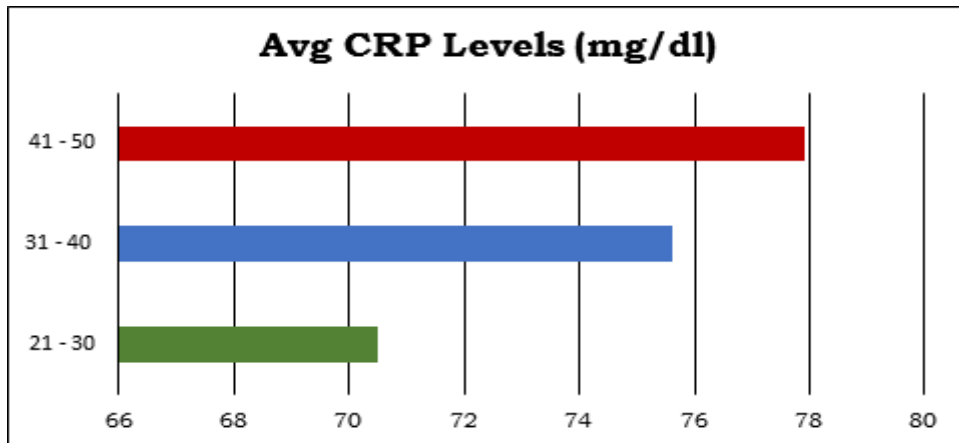
1. Patients with chronic pancreatitis.
2. Patients with acute pancreatitis with the presence of gallstones
3. Patients with disorders like Rheumatoid arthritis.
4. coronary artery disease, diabetes mellitus, and Obesity.

The patients were selected based on the inclusion and exclusion criteria and the demographic profile of the cases was recorded based on a pre-structured proforma. A detailed clinical examination was carried out on the patients and findings were noted. Serum C-reactive protein (CRP) levels were measured serially at 24 hrs, 48 hrs, and 72 hours following admission. At the 72-hour mark, computed tomography (CT) scans were conducted using oral and intravenous contrast agents to determine the CT severity index, including Balthazar's and Ranson's scores, as well as assess the CT grade and necrosis grade. Patients diagnosed with severe pancreatitis, according to the Atlanta classification, were closely monitored and treated in the surgical intensive care unit.

They received continuous cardiac and respiratory monitoring, along with regular biochemical investigations, including arterial blood gas analysis. On the other hand, patients with mild acute pancreatitis received treatment in our surgical ward.

**Results**

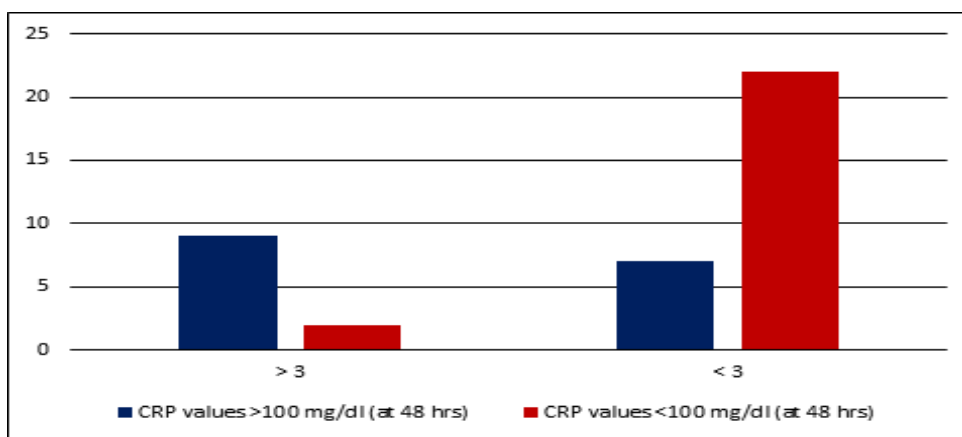
Out of the total n=40 cases, we found n=6(15%) patients in the age group of 21 – 30 years, n=24(52.5%) in the age group of 31 – 40 years, and n=10(25.0%) cases in the age group of 41 – 50 years all the cases included in the study were alcohol-induced pancreatitis and all the cases were male gender.



**Figure 1: Average CRP levels in (mg/dl) based on the age groups.**

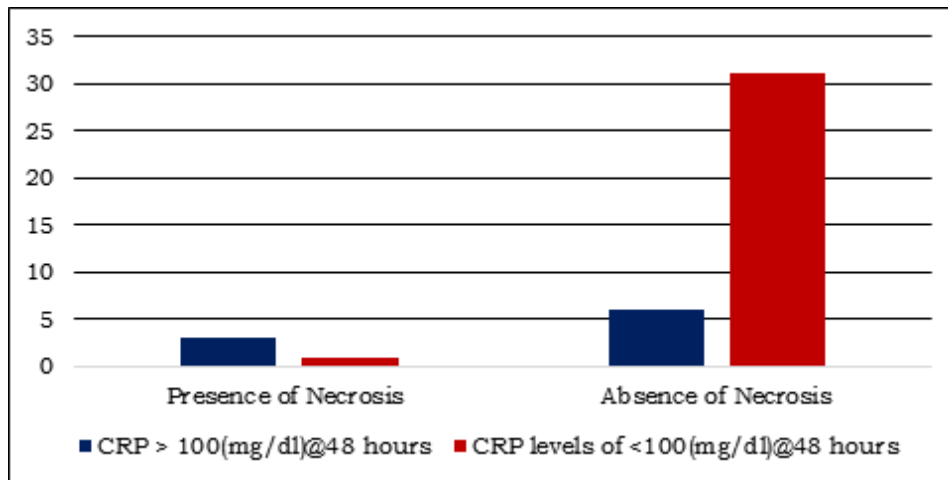
In our examination of n=40 patients, we observed that the mean CRP levels were increased based on the age of the patients. The CT scan indicated a greater severity of pancreatitis, and the CRP levels also consistently remained elevated. However, it is important to note that the observed p-value of >0.05 suggests clinical insignificance (figure 1). The duration of hospitalization ranged from 8 to 52 days among different patients, with a mean of 24 days. There is a correlation between the

number of days patients stayed in the hospital and their CRP values, specifically when comparing values above 100 mg/dl and values below 100 mg/dl. The mean duration of cases C-reactive protein (CRP) values were measured serially at 24 hours, 48 hours, and 72 hours after admission using a standard method. These values were then compared to the CT severity index, which was assessed through contrast-enhanced CT scans conducted 3-5 days after admission.



**Figure 2: Comparison of CRP values and CT severity index scores**

The sensitivity of the CRP with CT severity index was 85.12%, specificity was 78.30%, PPV was 58.20%, and NPV was 93.55%.



**Figure 3: Comparison of the number of patients with CRP value and presence or absence of necrosis.**

The comparison of CRP versus necrosis scores has been depicted in Figure 3. The sensitivity was 84.44% and Specificity was 80.53%. The correlation between the necrosis score in the CT severity index and serum CRP values was also determined. The duration of hospital admission was recorded as a marker of disease morbidity [7]. A significant cutoff value of 100 mg/dl was used for CRP, although different studies cited in this research suggested different significant values (100 mg/dl and 150 mg/dl). In this study, 100 mg/dl was chosen as significant because it was consistent with multiple studies and correlated with our study results. It is well established that peak levels of CRP are typically reached 48 hours after the onset of pain. Therefore, in this study, the CRP values at 48 hours were compared with the CT severity index. The CT severity index, assessed by contrast-enhanced CT with high sensitivity and specificity, is the current standard for evaluating disease severity and necrosis in patients with acute pancreatitis.

Therefore, it was used as the reference standard in this study to assess the value of CRP in this context. The CTSI value, which correlates with disease severity, is reported

in multiple studies as being equal to or greater than 3 (indicating the presence of necrosis or, if no necrosis is present, collections in and around the pancreas). This value is also considered indicative of severe disease in the Atlanta classification and was therefore used as significant to differentiate between mild and severe cases.

### Discussion

The fact that C-reactive protein (CRP) is an acute phase protein secreted by the liver in various inflammatory conditions and serves as a nonspecific marker is already established. This study aims to determine the usefulness of measuring serum CRP levels, which is a widely available and inexpensive inflammatory marker, in different aspects of acute pancreatitis. N=9 patients in the study were diagnosed with severe acute pancreatitis according to the Atlanta classification, with a CT severity index equal to or greater than 3. Therefore, using the CT severity index as a standard to compare CRP values is justified and is currently considered the standard approach based on multiple studies. Consistent with previous research, our study found that peak CRP levels were reached at 48 hours. Therefore, the statistical analysis compared

the CRP values at 48 hours with the CT severity index. Literature suggests that most therapeutic interventions for acute pancreatitis are effective only if initiated within 48 hours. [8, 9] While CRP levels can indicate the severity of the disease, they are not considered a highly reliable indicator in this context.

Different studies have reported varying significant values for CRP levels. [10, 11] However, we found that a CRP level greater than 100 mg/dl, as stated in the study by Meyer et al., [12] correlates with the values obtained in our study. Hence, we considered this value as the significant threshold for comparison. Due to the composition of our study group, we were unable to analyze the distribution of etiology in pancreatitis comprehensively, as it mainly consisted of young to middle-aged males. The average CRP values increased with each subsequent decade of life. In the 3rd decade, the average value was found to be 70.5 mg/dl, and in the 5th decade, it was 77.9 mg/dl (as shown in Chart 3). This observation aligns with the existing literature, which indicates that CRP values tend to rise with age, with elevated values commonly seen in older individuals. Among the patients diagnosed with severe disease, 7 patients had CRP values exceeding 100 mg/dl. The sensitivity was 84.44% and Specificity was 80.53%. The correlation between the necrosis score in the CT severity index and serum CRP values was also determined. These results establish CRP levels as a marker of severity in acute pancreatitis, demonstrating higher sensitivity and specificity compared to scoring systems (40-60%), as reported in the study by Gurleyik et al., [13]

Among the n=4 patients diagnosed with necrotizing pancreatitis and positive necrosis scores in the CT severity index (CTSI), n=3 patients had CRP values exceeding 100 mg/dl at 48 hours. Based on this data, it is confirmed that CRP levels can serve as an indicator for necrosis and aid in determining which patients with acute

pancreatitis require a contrast-enhanced CT (CECT) scan within 48-72 hours. This is particularly valuable considering that CECT is an expensive and limitedly available investigation. The duration of hospitalization ranged from 8 to 52 days among different patients, with a mean of 24 days. There is a correlation between the number of days patients stayed in the hospital and their CRP values, specifically when comparing values above 100 mg/dl and values below 100 mg/dl. This positive correlation between CRP levels and hospitalization duration confirms the use of CRP levels at 48 hours as a marker for the length of hospital stay and validates its utility as an indicator of morbidity. In previous studies, such as the one conducted by Meyer et al., [12] serial CRP measurements were performed for up to 7 days. These studies discovered that persistent elevation of serum CRP values are associated with a higher incidence of local complications (such as pseudocysts or abscesses) and an increased likelihood of requiring surgery during the course of the disease. Unfortunately, our study was limited to measuring CRP values only up to 72 hours from the onset of pain, preventing us from investigating the correlation between prolonged CRP elevation and the occurrence of local complications or the need for surgery.

### Conclusion

CRP, as commonly known, remains an acute phase reactant and a non-specific marker of inflammation, attributable to various underlying causes. Furthermore, CRP levels tend to rise with increasing age of the patient. Although CRP levels exhibit good sensitivity and specificity in identifying patients with severe acute pancreatitis, surpassing most clinical scoring systems in these measures, it proves to be an inadequate marker for timely intervention in this context. This inadequacy arises from the fact that peak CRP values are only reached after 48-72 hours, which coincides with the therapeutic

golden hour, the crucial timeframe for implementing effective treatments as emphasized in the literature.

However, according to the findings of this study, CRP can still offer utility in the following aspects:

1. Elevated CRP values beyond the significant range positively correlate with the occurrence of necrosis in pancreatitis. This information can aid in deciding which patients require a contrast-enhanced CT scan (CECT), considering that this investigation is both expensive and not readily accessible.
2. CRP levels positively correlate with the duration of the patient's hospital stay, indicating the morbidity associated with acute pancreatitis.

#### References

1. N.I.C.E. Pancreatitis, Diagnosis and Management Draft Scope for Consultation, National Institute for Clinical Excellence, London, UK, 2016.
2. D.C. Whitcomb, Acute pancreatitis, *N. Engl. J. Med.* 2006; 354 (20): 2142–2150.
3. D. Yadav, A.B. Lowenfels, Trends in the epidemiology of the first attack of acute pancreatitis, *Pancreas* 2006; 33 (4): 323–330.
4. J. Toouli, M. Brooke-Smith, C. Bassi, D. Carr-Locke, J. Telford, P. Freeny, et al., Guidelines for the management of acute pancreatitis, *J. Gastroenterol. Hepatol.* 2002; 17: 515–539.
5. Puolakkainen P, Valtonen V, Paananen A, Schröder T. C-reactive protein (CRP) and serum phospholipase A2 in the assessment of the severity of acute pancreatitis. *Gut.* 1987;28(6):764-71.
6. Mayer JM, Raraty M, Slavin J, Kemppainen E, Fitzpatrick J, Hietaranta A, et al. Serum amyloid A is a better early predictor of severity than C-reactive protein in acute pancreatitis. *Br J Surg.* 2002;89(2):163-71.
7. Vengadkrishnan K, Koushik AK. A study of the clinical profile of acute pancreatitis and its correlation with severity indices. *Int J Health Sci (Qassim).* 2015 Oct;9(4):410-17.
8. Mortelé KJ, Girshman J, Szejnfeld D, et al. CT-guided percutaneous catheter drainage of acute necrotizing pancreatitis: clinical experience and observations in patients with sterile and infected necrosis. *AJR Am J Roentgenol.* 2009; 192:110.
9. Chauhan S, Forsmark CE. The difficulty in predicting outcome in acute pancreatitis. *Am J Gastroenterol.* 2010; 105:443.
10. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. *Gut.* 2013; 62:102.
11. Singh VK, Bollen TL, Wu BU, et al. An assessment of the severity of interstitial pancreatitis. *Clin Gastroenterol Hepatol.* 2011; 9:1098.
12. Alberto Meyer, Márcia S Kubrusly, Vera M Salemi, Ana M de Mendonça Coelho et al. Severe Acute Pancreatitis: A Possible Role of Intramyocardial Cytokine Production. *JOP. J Pancreas (Online)* 2014 May 27; 15(3):237-242.