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Original Research Article

# A Study on the Role of C - reactive protein as a Severity Marker in Acute Pancreatitis

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**Conflict of interest: Nil**

**Abstract**

**Background**: Acute pancreatitis (AP) presents with highly variable clinical outcomes, necessitating early and effective severity assessment to guide management. C-reactive protein (CRP) has been investigated as a prognostic biomarker.

**Methods**: A prospective longitudinal cohort of 70 adult patients with AP was studied in the Department of Surgery and Medicine from September 2022 to March 2024. Serum CRP was assayed at 24, 48, and 72 hours post-admission. All patients underwent CECT abdomen after 72 hours for CTSI grading.

**Results**: Among the patients, 63% were male; mean age was 49.5 ± 10.3 years. Alcohol (59%) was the leading etiology, followed by biliary disease (21%). CTSI classified 35.7% as mild, 51.4% moderate, and 12.9% severe. On day 3, mean CRP values for mild, moderate, and severe AP were 44.1 ± 39.1, 140.9 ± 44.1, and 178.5 ± 54.6 mg/L, respectively, with a statistically significant difference ($p < 0.001$). ROC analysis identified a CRP cutoff of 155.5 mg/L (sensitivity 76.9%, specificity 89.5%, AUC 0.851).

**Conclusion**: CRP measured on day 3 is a reliable, accessible early predictor of AP severity, with high sensitivity and specificity compared to CTSI. A cutoff of 155.5 mg/L is suggested for triaging severe disease and identifying patients likely to require intensive management or imaging.

**Keywords**: Acute Pancreatitis, C - reactive protein, CT Severity Index, Inflammatory Marker, Disease Severity.
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## Introduction

Acute pancreatitis (AP) is a sudden-onset inflammatory condition of the pancreas that is associated with an overall mortality rate of 3–10%. However, the mortality rate of severe AP (SAP) increases to 36–50% [1,2]. The clinical presentation ranges from mild discomfort to life-threatening severe disease, making early and accurate risk stratification critically important for optimal management[1].

AP is diagnosed when at least two of three criteria are met: characteristic upper abdominal pain, elevated serum pancreatic enzymes (amylase or lipase) above three-fold normal, and suggestive imaging findings[1]. Severity assessment in AP is challenging in the early phase, yet essential for guiding supportive treatment intensity, predicting prognosis, and allocating resources like imaging or intensive care [1,3]. The revised 2012 Atlanta classification categorizes AP into mild, moderately severe, and severe forms based on the presence and duration of organ failure and local or systemic complications[1]. Unlike other acute abdominal conditions, AP has a notably unpredictable clinical course at presentation. Approximately two-thirds of patients recover with supportive care, but the remaining third may develop serious complications, including multiorgan failure and pancreatic necrosis [2]. Importantly, even initially mild AP (MAP) can progress to severe forms if not promptly managed [4,5].

Contrast-enhanced computed tomography (CECT) and scoring systems like the Balthazar CT Severity

Index (CTSI) are typically considered the gold standard for evaluating local complications and necrosis in AP. However, CT imaging is expensive, sometimes unsafe, and less sensitive within the first 48 hours [6,7].

This has prompted interest in laboratory markers, especially C-reactive protein (CRP), to differentiate MAP and SAP efficiently and cost-effectively [8,9]. Many recent studies have proposed CRP thresholds—commonly 150 mg/L at 48–72 hours—as significant predictors for SAP [10,11]. However, validation in regional settings remains necessary [12].

**Objective**

The objective of the study is to assess the value of C - reactive protein to differentiate Mild from Severe Acute Pancreatitis in comparison with Computed Tomography Severity Index (CTSI) as standard.

**Methods**

A prospective longitudinal study was conducted at the Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, India, involving the Departments of Surgery and Medicine from September 2022 to March 2024. Ethical approval was obtained from the Research Ethics Board, RIMS, Imphal (No. A/206/REB-Comm(SP)/RIMS/2015/752/94/2020).

**Inclusion criteria:** 1) Age ≥18 years; 2) Diagnosis of AP (≥2 of: characteristic pain, enzyme elevation >3x normal, imaging evidence).

**Exclusion criteria:** 1) Pregnant patients; 2) Connective tissue disorders; 3) Inability to undergo CT.

A sample size of 70 was calculated using the formula $N = [z(\alpha/2)^2 \times \text{sensitivity}(1\text{-sensitivity})] / d^2$, where sensitivity = 85.51% according to Mathew B et al. [13]. A convenient sampling method was used.

Serum CRP levels were measured at 24, 48, and 72 hours post-admission. A repeat CECT abdomen was performed at 72 hours to assess disease severity using the CTSI (Operational definition: 1–3 = Mild; 4–6 = Moderate; 7–10 = Severe). Data were analyzed using SPSS version 21. ANOVA was used to test associations; $p < 0.05$ was statistically significant.

**Results**

A total of 70 patients were included. Out of these, 42 (63%) were males and 28 (37%) were females. The majority were from the age group 46–60 years (35.8%), with a mean age of 49.5 ± 10.3 years (Table 1).

**Table 1: Baseline characteristics of patients with acute pancreatitis (N=70)**

| Characteristic | Sub-group | No. of Patients (%) |
|---|---|---|
| Gender | Male | 42 (63%) |
| | Female | 28 (37%) |
| Age group (years) | 18–30 | 8 (11.4%) |
| | 31–45 | 22 (31.4%) |
| | 46–60 | 25 (35.8%) |
| | >60 | 15 (21.4%) |
| | Mean ± SD | 49.5 ± 10.3 |
| Religion | Hindu | 40 (57%) |
| | Muslim | 18 (26%) |
| | Christian | 12 (17%) |

Nearly half (45.7%) had no comorbidities; among those with comorbidities, hypertension (22.9%) was most common. Alcohol consumption (59%) was the leading etiology, followed by biliary disease (21%) (Table 2).=

**Table 2: Distribution by comorbidities and etiology (N=70)**

| Variable | Category | No. of Patients (%) |
|---|---|---|
| Comorbidities | Hypertension | 16 (22.9%) |
| | Diabetes Mellitus | 8 (11.4%) |
| | Coronary Artery Disease | 5 (7.1%) |
| | Chronic Liver Disease | 5 (7.1%) |
| | Chronic Kidney Disease | 2(2.9%) |
| | COPD | 2(2.9%) |
| | None | 32 (45.7%) |
| Etiology | Alcohol consumption | 41 (59.0%) |
| | Biliary disease | 15 (21.0%) |
| | Hyperlipidemia | 12 (17.0%) |
| | Others | 2 (3%) |

**Table 3: Distribution by CT severity index and mortality (N=70)**

| Type of Pancreatitis | CTSI Score Range | No. of Patients (%) | Mortality n (%) |
|---|---|---|---|
| Mild | 1–3 | 25 (35.7%) | 0 (0%) |
| Moderate | 4–6 | 36 (51.4%) | 0 (0%) |
| Severe | 7–10 | 9 (12.9%) | 3 (33.3%) |
| Total | – | 70 (100%) | 3 (4.3%) |

One third of the patients (33.3%) in severe pancreatitis expired in the hospital. All the patients in the mild and moderate group recovered and discharged from the hospital.

**Table 4: Mean CRP level of mild, moderate and severe pancreatitis patients (N=70)**

| Type of pancreatitis | Mean CRP ± SD (mg/L) Day 1 | Mean CRP ± SD (mg/L) Day 2 | Mean CRP ± SD (mg/L) Day 3 |
|---|---|---|---|
| Mild | 35.2 ± 17.7 | 43.2 ± 17.1 | 44.1 ± 39.1 |
| Moderate | 43.1 ± 19.5 | 99.9 ± 20.6 | 140.9 ± 44.1 |
| Severe | 46.7 ± 20.4 | 116.1 ± 23.5 | 178.5 ± 54.6 |
| P value | 0.178 | < 0.001 | < 0.001 |

Mean CRP levels showed no significant difference on Day 1 ($p = 0.178$), but by Day 2 and Day 3, differences were highly significant ($p < 0.001$) (Table 4).

**Table 5: Distribution by duration of hospital stay (N=70)**

| No. of days | No. of patients | Percentages (%) |
|---|---|---|
| 0–10 days | 34 | 48.6 |
| 10–20 days | 25 | 35.7 |
| >20 days | 11 | 15.7 |

Almost half of the patients (48.6%) were discharged within 10 days of hospital stay. Very few patients (15.7%) stayed for more than 20 days in the hospital as shown in Table 5.

**Table 6: Sensitivity and specificity of CRP values on day 3**

| CRP values (mg/L) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| 150 | 76.9 | 84.2 | 52.6 | 94.1 |
| 155.5 | 76.9 | 89.5 | 60.0 | 94.4 |
| 160 | 69.2 | 89.5 | 60.0 | 92.7 |
| 170 | 61.5 | 89.5 | 57.1 | 91.1 |

**A CRP threshold of 155.5 mg/L provided the best balance for predicting severity.**

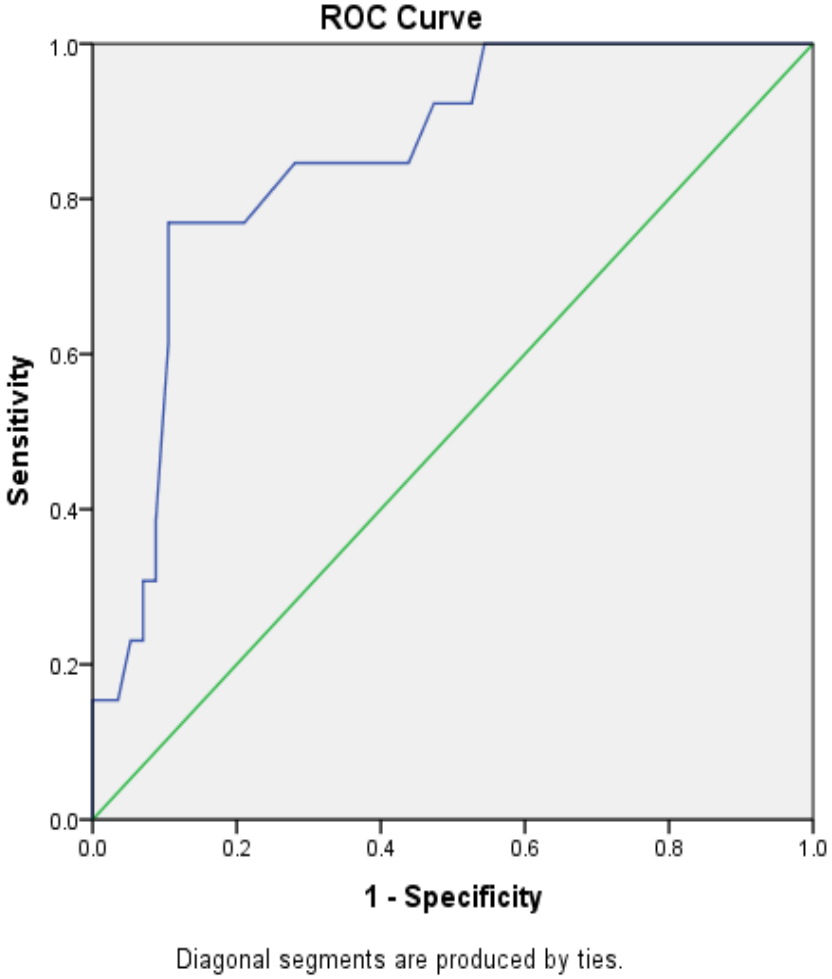


**Figure 1: ROC curve between sensitivity and 1-specificity of CRP. The area under the curve (AUC) was 0.851 (95% CI: 0.745–0.957, p < 0.001). At a cut-off of 155.5 mg/L, sensitivity was 76.9% and specificity was 89.5%.**

## Discussion

A total of 70 patients of acute pancreatitis were included in the study. Out of which 42 (63%) were males and remaining 28 (37%) were females. Párniczky A et al [14] reported in their study, 56% (n = 335) were male and 44% (n = 265) were female in their study population of acute pancreatitis. But Gurleyik G et al [15] reported in their study of 32.7% male population in their study population of acute pancreatitis. Similarly, Mayer AD et al [16] reported 45.5% of their study population to be male. Kaplan M et al [17] reported 62.5% female patients in their study population. Karabuğa B et al [18] reported in their study equivalent distribution of male (49.4%) and female (50.6%) in their study population of acute pancreatitis. Cardoso FS et al [19], Stirling AD et al [20] and Khanna AK et al [21] also reported 53.6%, 56% and 51.4% male patients respectively in their study population. Hämäläinen MT et al [22] reported in both study group of severe and mild acute pancreatitis, male predominated with 68.9% and 79.3% respectively in their study population. Joshi M et al [23] reported male predominance of 80% in their study population. Ćeranić DB et al [24], Kazmi SJ et al [25] and Deherkar JA et al [26] also reported 61.5%, 60% and 63% male predominance respectively in their study population which is in line to this study finding. Thus, in most studies male predominated the study population as in the current study. This observation may be attributed to the fact that,in developing countries like India, alcohol consumption is more common among males than females.

In this study, the overall mean age was 49.5± 10.3 years and the age group 46-60 years has the maximum number of patients with 35.8%. Minimum number of patients was seen in the group 18 to 30 years with 11.4%. Karabuğa B et al [18] reported the mean age of their patients to be 55.68 ± 18.30 years which is a little higher than this study population. Kazmi SJ et al [25] reported their study population were maximum at 40–50 years (27%) of age group which is similar to this study finding. But Deherkar JA et al [26] reported maximum patients in 31-40 years (32%) age group and the

mean age of the patients was 38.33±12.92 years which is a little lower than this study finding. Similarly, Stirling AD et al [20] also reported their average age of their patients to be 42 years. Kaplan M et al [17] reported the mean age of their patients to be 61.9±18.0 years which is a little higher than this study finding. Similarly Cardoso FS et al [19] and Yılmaz EM et al [27] reported 62 years and 59.97 years to be the mean age of their population respectively. Ćeranić DB et al [24] also found the mean age of 62.5 ± 16.8 years in their study population. On the other hand, Khanna AK et al [21] found the mean age of presentation for their patient to be 40.5 years. Elshal M et al [28] and Cho IR et al [29] reported the mean age of 46 years and 47.49 years for their study population respectively which is similar to this study finding. Irshad A et al [30] found that their study population were maximum at the age group of 46-60 years with 43.3%, which is also similar to this study finding. Thus, most of the patients were in their middle age when diagnosed with acute pancreatitis which in line with this study findings.

In this study more than half (57%) of the patients belong to the Hindu religion followed by Muslim (26%). Only 17% of the patients were Christian. It may be due to the fact that the catchment area of this hospital is a Hindu dominated area. Hypertension (22.9%) was the most common comorbidities present among the patient in this study followed by diabetes mellitus (11.4%), coronary artery disease (7.1%) and chronic liver disease (7.1%). Only 2.9% of the patient had chronic kidney disease and another 2.9% with COPD. Khanna AK et al [21] also reported hypertension and diabetes to be common comorbitities in their study. Kiyak M et al [31] found Hypertension, diabetes mellitus, coronary heart disease and COPD with 20.1%, 10.9%, 7.6% and 6.7% among their study population population which is similar to this study finding. Karabuğa B et al [18] also reported hypertension, diabetes mellitus, coronary artery disease and diabetes mellitus to be common comorbidities in their patients with incidences of 36.6%, 20.6% and 14.8% respectively. Thus most studies reported hypertension and diabetes mellitus to be common comorbidities among their study population which is similar to this study finding.

Out of 70 acute pancreatitis patients in this study, forty one patients had history of alcohol consumption which is 59% of the total population and was the most common cause of pancreatitis followed by biliary disease (21%) and hyperlipidemia (17%) but etiology of two patients were unknown. Párniczky A et al [14] reported in their study that biliary disease was the commonest etiology with 43.8% followed by alcohol abuse with 26.5%, idiopathic in 16.3% and hyperlipidaemia in 6.17%. Other studies also reported cholelithiasis as the commonest cause for acute pancreatitis followed by alcohol among their patients[26,17,19,24]. Similar finding has been reported by Kiyak M et al [31] that biliary cause is the commonest with 76.9% followed by hyperlipidaemia (8.8%) and alcohol (5.2%). Khanna AK et al [21] reported biliary (64%), alcoholic (13%), idiopathic (9%) and hypertriglyceridemia (2%) to be the causes of acute pancreatitis in their study. Cho IR et al [29] reported in their study that the commonest etiology of AP was alcoholic with 37.9% followed by biliary (32.0%), idiopathic (15.6%) and hypertriglyceridemia (8.7%). Stirling AD et al [20] also reported in their study that alcohol was the common etiology with 46.6% followed by biliary cause with 35.6% which is similar to this study finding. Thus, alcohol and gallstones were the commonest causes of acute pancreatitis in most of the studies which is in line with this study population. As alcohol has been consumed prevalently in this part of the country, it was found to be a major cause of acute pancreatitis in this study.

In this study, maximum of the patients were having moderate pancreatitis (51.4 %) followed by mild (35.7%) and severe (12.9%) according to CT severity index (CTSI). Similar finding has been reported by Mathew B et al [13] in their study that maximum of their study population had moderate pancreatitis (CTSI) with 47.8% followed by mild (35.6%) and severe (16.6%). In a study by Kazmi SJ et al [25] only 5.7% had mild pancreatitis, 52.8% had moderate pancreatitis and remaining 41.3% had severe pancreatitis.

Duration of hospital stay was less than 10 days for 48.6% of the study population in the current study. Very few patients (15.7%) stayed for more than 20 days in the hospital. One third of the patients (33.3%) in severe pancreatitis expired in the hospital. All the patients in the mild and moderate group recovered and were discharged from the hospital. Karabuğa B et al [18] reported 18.75% mortality among severe pancreatitis group of their patients. Párniczky A et al [14] and Silva-Vaz et al [2] reported that the mortality rate of acute pancreatitis was between 3% to 10%; however, this rate escalates to between 36% to 50% for cases of severe acute pancreatitis.

It was also found in this study that there was no significant difference in mean value of CRP on Day 1 between mild, moderate and severe pancreatitis. But there is significant difference on Day 2 and Day 3 between mild, moderate and severe pancreatitis. This observation showed that even though the CRP values are elevated in every case of acute pancreatitis, high value of CRP on the 2nd and 3rd day after the onset of symptoms suggest

that the patient has severe pancreatitis and has a high probability of progressing into other complications. While normal CRP value on admission hospital does not exclude life threatening acute pancreatitis [22].Párniczky A et al [14] also found in their study that the average CRP levels showed a significant difference between the mild and moderate, as well as the mild and severe AP groups. They also reported that the level of C-reactive protein (CRP) above 200 mg/L was associated with severe AP. Gurleyik G et al [15] also reported significant difference in mean CRP value at 48 hours between mild and severe pancreatitis along with CTSI mean score. Mayer AD et al [16] and Deherkar JA et al [26] also reported in their study that C reactive protein differentiated mild and severe attacks with greatest precision. Karabuğa B et al [18] also reported significant difference in the mean CRP between mild and severe pancreatitis. Similar finding has been reported by Cho IR et al [29] where mean CRP value at 48 hours were significantly different among mild, moderate and severe pancreatitis. Kiyak M et al [31] also reported significant difference in mean CRP between mild and severe AP. Stirling AD et al [20] also reported mean CRP to be different in mild, moderate and severe pancreatitis at 24 hours, 48 hours and 72 hours. Cardoso FS et al [19] reported in their study that CRP at 48 h after hospital admission had good discriminative and predictive abilities for severe acute pancreatitis, pancreatic necrosis and mortality than CRP measured at any other timing. Li Yet al32 also reported that high CRP > 110 mg/dl was an independent factor for predicting SAP in patients with AP. Khanna AK et al [21] reported CRP ≥ 150 mg/dl can predict severe acute pancreatitis with 86.2% sensitivity and 100% specificity.

Similarly Ćeranić DB et al [24] showed that CRP had a greater predictive value for the severity of AP in the follow-up and at a cut-off value of CRP at 48 hours as 152, the sensitivity was 0.81 and specificity was 0.69. Elshal M et al [28] also reported that the ROC CRP level greater than equal to 152 at 48 h after presentation would be suggestive of CTSI greater than equal to 4 thus, CRP level correspond to CTSI in severity of pancreatitis similar to this study finding. These findings are similar to the current study finding of ROC cut off CRP value of 155.5 with the sensitivity of 76.9% and specificity of 89.5% in predicting severe pancreatitis and area under the ROC curve was 0.851. High concentrations of C reactive protein seem to give a warning of severe local inflammation in the patient whose initial illness is relatively mild and whose clinical course is apparently benign. The magnitude of C reactive protein response is similar to that observed in patients with more overtly severe pancreatitis [16]. Therefore, CRP level is a useful tool in predicting severe pancreatitis like in many other studies.

Further CRP can be assessed at the early stage which is repeatable, easily accessible and inexpensive. Irshad A et al [30] has also showed in their study a strong positive correlation between CRP and CT severity index of acute pancreatitis. CRP and CT scan should be seen as an additional tool that aids clinical observation and physical examination, to predict complication and prognosis in acute pancreatitis and should not be used as single parameter.

**Limitation:** As the study was conducted in a single centre with a limited sample size, the findings may apply to the population studied and broader validation is needed. Despite these limitations, this study is one of very few done in India, and the findings will be a useful addition to the literature.

## Conclusion

CRP provides an effective, accessible, and reliable early marker for severity stratification in acute pancreatitis. A CRP level ≥155.5 mg/L at 72 hours after admission predicts severe disease with good sensitivity and specificity.

Routine CRP testing can help identify patients at risk for complications, enable timely escalation of care, and rationalize advanced imaging use.

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