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Procalcitonin, C-Reactive Protein, and Neutrophil Ratio as Biomarkers for the Diagnosis and Prognosis of Severe Acute Pancreatitis

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ABSTRACT

Background: Severe acute pancreatitis (SAP) is a life-threatening condition associated with high mortality. Early identification of SAP is critical for timely, intensive intervention. This study evaluates the diagnostic and prognostic utility of procalcitonin (PCT), C-reactive protein (CRP), and the neutrophil ratio (N%) in acute pancreatitis (AP). **Methods**: A prospective, observational, cross-sectional study was conducted on 100 patients (50 with mild acute pancreatitis [MAP] and 50 with SAP) admitted to SMS Medical College, Jaipur. Biomarker levels were assessed within 24 hours of admission. **Results**: SAP patients demonstrated significantly higher mean levels of the neutrophil ratio (12.25 vs. 7.45), CRP (9.48 vs. 1.36), and PCT (15.29 ng/mL vs. 1.88 ng/mL) compared to MAP patients. Mortality was significantly higher in the SAP group (20%) compared to the MAP group (4%). Receiver Operating Characteristic (ROC) curve analysis for predicting mortality in SAP yielded an Area Under the Curve (AUC) of 0.768 for the neutrophil ratio, 0.715 for PCT, and 0.584 for CRP. **Conclusion**: PCT and the neutrophil ratio serve as highly effective early predictors of severity and mortality in AP, facilitating early triage and intervention.

Keywords: *Acute pancreatitis, CRP, Procalcitonin.*

INTRODUCTION

Acute pancreatitis is an inflammatory condition of the pancreas, most frequently triggered by excessive alcohol consumption or gallstones.[1] While the majority of cases are mild and resolve swiftly with supportive care, approximately 20–30% of patients develop a severe form of the disease.[2] Severe acute pancreatitis (SAP) is characterized by persistent organ failure lasting more than 48 hours, local complications such as pancreatic necrosis, and a mortality rate that can escalate to 30%.[3]

Because early intensive care is vital to improve patient outcomes, rapid and accurate assessment of disease severity is necessary upon hospital admission. Traditional multifactorial scoring systems, including APACHE II and Ranson's criteria, are frequently utilized.[4] however, their complexity makes them time-consuming and challenging to apply in daily clinical settings. Consequently, simple, accessible laboratory indicators like C-reactive protein (CRP), procalcitonin (PCT), and the neutrophil ratio have emerged as critical areas of research. This study aims to evaluate the combined diagnostic and prognostic significance of PCT, CRP, and the neutrophil ratio in predicting the severity and mortality of AP, particularly within the Indian population.[5,6]

METHODS:

A prospective, hospital-based, comparative, cross-sectional study was conducted in the Department of General Surgery at SMS Hospital, Jaipur, Rajasthan, over an 18-month period. The study cohort included 100 adult patients diagnosed with acute pancreatitis, categorized evenly into two groups based on the Revised Atlanta Classification: 50 patients with mild acute pancreatitis (MAP) and 50 patients with severe acute pancreatitis (SAP). Patients under 16 years of age, pregnant

women, and those with chronic pancreatitis, malignant pancreatic tumors, or multiple comorbidities (such as chronic renal failure) were excluded. Detailed clinical histories, physical examinations, and written informed consent were obtained from all participants. Routine laboratory investigations, including complete blood count with differential (to calculate the neutrophil ratio), serum PCT, CRP, amylase, lipase, renal and liver function tests, and serum calcium, were drawn within 24 hours of hospital admission.

Data were summarized using mean and standard deviation for continuous variables and proportions for qualitative data. Group differences were assessed utilizing Student's t-test and the chi-square test. Diagnostic accuracy was evaluated through sensitivity, specificity, ROC curves, and the calculation of the Area Under the Curve (AUC).

RESULTS:

The mean age of patients was higher in the SAP group (57.8 ± 25.12 years) compared to the MAP group (49.88 ± 21.61 years), with the highest incidence of SAP occurring in individuals over 67 years of age. A significantly higher proportion of females was observed in the SAP group (66%) compared to the MAP group (40%) (p=0.009). Mortality was significantly greater in the SAP cohort, recording 10 deaths (20%) compared to only 2 deaths (4%) in the MAP group.

Table 1: Mortality Rates in MAP and SAP Groups

Outcome	MAP	SAP
Survived	48 (96%)	40 (80%)
Deceased	2 (4%)	10 (20%)

Mortality was substantially higher in the SAP group (20% vs. 4%), showcasing the significant impact of disease severity on patient outcomes.

Biochemical evaluations demonstrated more extensive pancreatic pathology and multiorgan impact in the SAP cohort.

Table 2: Biochemical Marker Comparison Between MAP and SAP Groups

Variables	MAP (Mean ± SD)	SAP (Mean ± SD)	p-value
Albumin	3.6 ± 0.49	2.52 ± 0.5	<0.001
Amylase	405.64 ± 27.66	647.56 ± 38.84	<0.001
Lipase	454.32 ± 28.8	799.04 ± 40.86	<0.001

Elevated levels of these pancreatic enzymes reflect more extensive acinar cell damage and are significantly higher in the severe cohort. Similarly, SAP patients had higher serum creatinine (1.50 ± 0.28 vs. 0.96 ± 0.08) and lower serum calcium levels (6.94 ± 0.24 vs. 8.4 ± 0.49), reflecting a higher incidence of renal impairment and hypocalcemia.

The primary systemic inflammatory markers were significantly elevated in patients with SAP compared to MAP:

Table 3: Inflammatory Marker Comparison Between MAP and SAP Groups

Variables	MAP (Mean ± SD)	SAP (Mean ± SD)	p-value
Neutrophil Ratio	7.45 ± 1.43	12.25 ± 1.82	<0.001
WBC	9.26 ± 1.08	16.98 ± 1.86	<0.001
CRP	1.36 ± 0.48	9.48 ± 1.2	<0.001

These differences indicate a significantly stronger systemic inflammatory response in SAP patients. Mean serum PCT was also significantly elevated in patients with SAP (15.29 ± 4.44 ng/mL) compared to patients with MAP (1.88 ± 0.43 ng/mL). ROC curve analysis was performed to determine the accuracy of these biomarkers in predicting mortality among SAP patients.

Table 4: Diagnostic Accuracy (Area Under Curve) for Predicting Mortality in SAP

Variable	Area Under Curve (AUC)	95% Confidence Interval	p-value
Neutrophil Ratio	0.768	0.586 – 0.949	0.009
Procalcitonin (PCT)	0.715	0.532 – 0.898	0.037
CRP	0.584	0.337 – 0.830	0.417

- **Neutrophil Ratio:** Demonstrated the highest predictive accuracy (AUC = 0.768, p = 0.009). A cut-off value greater than 12.66 yielded 90% sensitivity and 60% specificity for predicting mortality.
- **Procalcitonin (PCT):** Showed moderate, statistically significant predictive capability (AUC = 0.715, p = 0.037). A PCT level greater than 17.65 ng/mL was associated with 90% sensitivity and 67.5% specificity.

- **C-Reactive Protein (CRP):** Yielded the lowest discriminatory power for mortality prediction (AUC = 0.584, p = 0.417). A threshold above 10.365 exhibited lower sensitivity (60%) and 77.5% specificity.

DISCUSSION:

In our study, it was noted that the most common age group in patients with SAP was above 67 years. In fact, 50% of SAP patients belonged to this age group, compared to 30% in the MAP group. Younger age groups were less represented in SAP, suggesting that severity increased with advancing age. ($p>0.05$). Kumar S et al[7] reported no significant differences in the distribution of age ($p = 0.714$) or sex ($p = 0.276$) between patients with mild and severe acute pancreatitis, indicating potential variability in demographic associations across different populations or settings. In the present study, notable differences were observed in the sex-wise distribution of patients across the MAP and SAP groups. While the MAP group comprised 30(60%) males and 20(40%) females, the SAP group had a higher proportion of females 33(66%) patients compared to 17(34%) males.

The severity of acute pancreatitis ranges from mild, self-limiting inflammation to severe, life-threatening necrosis and multiorgan failure. Because excessive activation of inflammatory mediators drives the pathogenesis of SAP, circulating biomarkers hold significant potential for early risk stratification.

This study demonstrates that the neutrophil ratio, CRP, and PCT are all significantly elevated within 24 hours of hospital admission in patients with SAP, affirming their utility in diagnosing the severe form of the disease. However, their prognostic capabilities regarding patient mortality differ. The neutrophil ratio reflects an imbalance in the immune response—specifically an overactive innate immune response driven by neutrophils and an underactive adaptive response—making it a highly sensitive marker of uninhibited systemic inflammation. Our analysis proved that the neutrophil ratio was the strongest predictor of mortality among the three markers.

Supporting this, Xu XY et al[8] demonstrated that CRP levels measured at hospital admission had predictive accuracy comparable to established scoring systems such as SOFA, BISAP, and the modified Marshall score in determining the clinical course of acute pancreatitis. Furthermore, it is well established that patients with milder forms of the disease generally exhibit lower CRP levels and fewer complications, whereas higher CRP values are typically associated with more severe disease and adverse outcome.[9] Reddy BJM et al[10] reported a significant difference in CRP levels between patients with mild and severe acute pancreatitis. In their study, the mean CRP level in patients with mild pancreatitis was 44.35 ± 53.04 mg/L, whereas patients with severe pancreatitis had a markedly higher mean CRP level of 174.80 ± 14.55 mg/L. These findings reinforce the utility of CRP as a reliable marker for distinguishing between mild and severe forms of the disease.

Procalcitonin is typically produced by the thyroid but is widely synthesized by multiple parenchymal tissues in response to bacterial infections and systemic inflammation driven by cytokines like IL-6 and TNF-α. Unlike CRP, PCT levels rise rapidly and specifically during intense inflammatory states, making it a highly reliable early prognosticator for multiorgan failure, sepsis, and mortality. Consistent with previous literature, our cohort showed a strong association between early PCT elevation (>17.65 ng/mL) and mortality.[11-13]

While CRP remains a well-established and highly utilized marker for acute-phase inflammation, its ability to predict mortality in this study cohort was limited. Although highly elevated CRP levels accurately distinguished SAP from MAP, CRP's non-specific nature regarding fatal outcomes resulted in poor overall discriminatory power for mortality (AUC = 0.584).

These findings differ notably from the results reported by Liang Y et al,[14] who found that CRP had superior diagnostic accuracy for SAP, with an AUC of 0.9754, a sensitivity of 100%, and specificity of 88%. In their study, CRP was highly reliable in identifying SAP, particularly due to its 100% negative predictive value (NPV), making it an excellent tool for ruling out severe disease. Procalcitonin also performed well in their cohort, with an AUC of 0.811, sensitivity and specificity of 81%, and an overall diagnostic accuracy of 81%, though it was less effective than CRP in predicting severe disease outcomes. Therefore, CRP emerged as a more reliable biomarker in identifying severe disease and guiding prognosis in patients with acute pancreatitis. A meta-analysis examining a subgroup of 8 studies using a PCT cut-off of 0.5 ng/mL reported pooled sensitivity and specificity of 73% and 87%, respectively, and an overall AUC of 0.880 for predicting progression to SAP.[15] This confirms the moderate to high predictive accuracy of PCT, especially when standardized cut-off values are applied.

Furthermore, Khanna AK et al[16] reported that procalcitonin had 100% sensitivity for predicting organ failure and mortality, and 86.4% sensitivity for predicting SAP. Similarly, Narayanaswamy T et al[17] reported that a serum PCT level ≥ 0.5 ng/mL at admission had 100% sensitivity and specificity for predicting progression to SAP, making it an exceptionally robust biomarker in their clinical setting.

CONCLUSION:

The early measurement of inflammatory biomarkers significantly improves the clinical evaluation of acute pancreatitis. The findings of this study provide strong evidence that serum procalcitonin (PCT) and the neutrophil ratio are valuable, highly sensitive prognostic indicators in the early stages of severe acute pancreatitis. Both PCT and the neutrophil ratio outperformed CRP in predicting mortality. Consequently, integrating PCT and the neutrophil ratio into routine initial assessments is highly recommended to enable timely identification, triage, and aggressive management of high-risk patients, ultimately improving survival outcomes.

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