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THE DIAGNOSTIC VALUE OF SERUM C-REACTIVE PROTEIN, PROCALCITONIN, INTERLEUKIN-6 AND LACTATE DEHYDROGENASE IN PATIENTS WITH ACUTE PANCREATITIS

Original Research

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ABSTRACT

Background: Acute pancreatitis is an inflammatory condition of the pancreas that varies in clinical severity, ranging from mild self-limiting episodes to life-threatening systemic involvement. Timely identification of severe disease is critical to guide appropriate management and improve patient outcomes. Several biomarkers have emerged as promising tools for early diagnosis and risk stratification. This study evaluates the diagnostic significance of C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6), and lactate dehydrogenase (LDH) in patients with acute pancreatitis.

Objective: To determine the diagnostic value of serum CRP, procalcitonin, interleukin-6, and LDH in patients diagnosed with acute pancreatitis.

Methods: This cross-sectional observational study was conducted over six months (February to August 2023) at the Department of Medicine, PEMH Rawalpindi. A total of 200 patients diagnosed w ith acute pancreatitis, based on serum lipase levels elevated 2–3 times the normal, were included. Blood samples were drawn at admission, 48 hours, and 72 hours. CRP, PCT, and LDH levels were analyzed using Beckman Coulter, while IL-6 was measured via ELISA. Patients were stratified into mild (n=94), moderate (n=74), and severe (n=32) based on clinical severity.

Results: Among the 200 patients, 145 (72.5%) were male and 55 (27.5%) females. In the mild group, mean CRP reduced from 90 ± 5 mg/L to 65 ± 2 mg/L, and PCT from 0.08 ± 0.02 to 0.065 ± 0.01 ng/ml. In moderate cases, CRP increased from 120 ± 7 to 141 ± 3 mg/L, and PCT from 0.10 ± 0.02 to 0.14 ± 0.01 ng/ml. In severe AP, CRP rose from 200 ± 10 to 246 ± 4 mg/L and PCT from 0.20 ± 0.02 to 0.25 ± 0.03 ng/mL by 72 hours (all p=0.05).

Conclusion: CRP and procalcitonin showed strong diagnostic relevance in assessing the severity of acute pancreatitis and monitoring disease progression. Interleukin-6 also demonstrated potential as a supportive biomarker.

Keywords: Acute Pancreatitis, Biomarkers, C-Reactive Protein, Diagnosis, Interleukin-6, Lactate Dehydrogenase, Procalcitonin.

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INTRODUCTION

Acute pancreatitis (AP) is a sudden inflammatory condition of the pancreas that presents with a broad spectrum of clinical manifestations, ranging from mild, self-limiting symptoms to life-threatening complications involving multiple organ systems. This disease represents a significant global healthcare burden, with an estimated incidence of 34 cases per 100,000 individuals annually, although this rate may vary between 5 and 80 cases per 100,000 depending on geographic and socioeconomic factors (1). The predominant etiologies of AP include gallstone migration, excessive alcohol intake, and metabolic disorders such as hypertriglyceridemia (1,2). Early identification of severe disease is essential to guide therapeutic strategies and improve patient outcomes, yet predicting the course of AP remains a clinical challenge. In recent years, several biomarkers have gained attention for their potential utility in stratifying disease severity in the early stages of AP. Among them, C-reactive protein (CRP), a well-established acute-phase reactant, plays a central role in the systemic inflammatory response. Although CRP levels at admission have limited prognostic value, a concentration exceeding 150 mg/L within 48 hours of symptom onset has demonstrated a strong correlation with severe disease evolution (3,4). Similarly, procalcitonin (PCT), a precursor of the hormone calcitonin, has emerged as a valuable biomarker in distinguishing bacterial infections, particularly in the context of sepsis. Its utility in AP lies in its ability to identify infectious complications and gauge the severity of inflammation, especially when levels rise beyond the physiological threshold of <0.1 ng/mL in healthy individuals (5).

Interleukin-6 (IL-6), a pleiotropic cytokine involved in immune modulation, is another promising marker under investigation. It plays a pivotal role in initiating and amplifying the inflammatory cascade, beginning with pancreatic injury and extending to systemic involvement and multiorgan dysfunction (6). Elevated IL-6 levels within the early phase of AP have been closely associated with poor prognosis and serve as a reliable predictor of disease severity (7). Additionally, lactate dehydrogenase (LDH), an intracellular enzyme released during tissue injury, has been linked to organ damage in AP and may provide supplementary insight into the risk of mortality and prolonged hospitalization (8,9). Despite advancements in diagnostic imaging and scoring systems, clinicians continue to rely on timely, accurate biomarkers for early risk stratification and prognosis in acute pancreatitis (10). However, a unified approach integrating these markers for clinical decision-making is yet to be established. Therefore, this review aims to evaluate and synthesize current evidence regarding the prognostic value of CRP, PCT, IL-6, and LDH in acute pancreatitis, with the objective of clarifying their individual and combined roles in predicting disease severity and guiding early management strategies.

METHODS

After receiving approval from the Institutional Ethical Review Committee, this cross-sectional study was carried out at a tertiary care hospital in Rawalpindi over a six-month period, from February 2023 to August 2023. Informed written consent was obtained from all participants prior to their inclusion in the study. The primary objective was to evaluate the prognostic significance of selected inflammatory biomarkers in patients diagnosed with acute pancreatitis. A total of 200 patients were enrolled, with the sample size determined using the WHO sample size calculator based on a 95% confidence interval, 5% margin of error, and an estimated population proportion of 60%. Participants were selected according to defined inclusion and exclusion criteria. Eligible patients were adults over the age of 20 years, presenting with clinical symptoms of acute pancreatitis and elevated serum lipase levels (2–3 times above the normal range), with symptom onset reportedly within six hours prior to presentation. Patients with a history of recurrent or chronic pancreatitis, pancreatic pseudocysts, subacute onset of symptoms, or who had undergone ERCP within the preceding 24 hours were excluded. Individuals unwilling to participate were also excluded from the study (11,12).

Comprehensive demographic data were collected, including age, sex, educational background, occupation, marital status, and history of smoking or substance use. Each participant underwent a detailed physical and systemic examination, with special attention to abdominal findings. The diagnosis of acute pancreatitis was established based on clinical presentation and confirmed by elevated serum lipase levels (13). Upon admission, blood samples were drawn to measure the levels of C-reactive protein (CRP), lactate dehydrogenase (LDH), procalcitonin, and interleukin-6 (IL-6). A 10 mL venous blood sample was collected in a gold-top serum separator vial (14), centrifuged at 4°C, and allowed to rest for 30 minutes before analysis. CRP, procalcitonin, and LDH were quantified using the Beckman Coulter automated analyzer (15), while IL-6 levels were assessed via enzyme-linked immunosorbent assay (ELISA), though the specific kit and

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manufacturer details were not documented. All biomarker levels were measured at three intervals: at the time of admission, 48 hours, and 72 hours post-admission to observe temporal changes and associations with disease severity. Data analysis was performed using SPSS version 25. The chi-square test was applied to examine associations between categorical variables, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

Out of a total of 200 patients diagnosed with acute pancreatitis, 145 (72.5%) were male while 55 (27.5%) were female. The cohort was stratified based on disease severity into three groups: mild (n=94, 47%), moderate (n=74, 37%), and severe (n=32, 16%), using serum lipase levels as the defining criterion. Demographically, the study population was predominantly male (72.5%), and 59.4% of patients with severe acute pancreatitis were above the age of 55, indicating a potential age-related predisposition to more severe disease. In the mild group, inflammatory markers showed a declining trend over the 72-hour monitoring period. C-reactive protein (CRP) levels were 90 ± 5 mg/L at admission, 78 ± 3 mg/L at 48 hours, and 65 ± 2 mg/L at 72 hours (p=0.05). Procalcitonin (PCT) values were 0.08 ± 0.02 ng/mL, 0.07 ± 0.01 ng/mL, and 0.065 ± 0.01 ng/mL, respectively (p=0.05). Lactate dehydrogenase (LDH) levels were 160 ± 3 IU/L at baseline, increased slightly to 165 ± 2 IU/L at 48 hours, and decreased again to 159 ± 3 IU/L by 72 hours (p=0.04). Interleukin-6 (IL-6) levels were measured at 48.2 ± 2 pg/mL on admission, 51 ± 1 pg/mL at 48 hours, and 46 ± 2 pg/mL at 72 hours (p=0.05).
In the moderate group, inflammatory markers generally exhibited a rising pattern over time. CRP values were 120 ± 7 mg/L, 136 ± 3 mg/L, and 141 ± 3 mg/L at the three respective time points (p=0.04). PCT levels rose from 0.10 ± 0.02 ng/mL on admission to 0.11 ± 0.03 ng/mL at 48 hours and 0.14 ± 0.01 ng/mL at 72 hours (p=0.05). LDH levels were 189 ± 3 IU/L at admission, 195 ± 3 IU/L at 48 hours, and 191 ± 3 IU/L at 72 hours (p=0.05). IL-6 values showed a modest but consistent increase: 54.5 ± 3 pg/mL, 55.3 ± 1 pg/mL, and 57 ± 2 pg/mL, respectively (p=0.05). In the severe group, biomarker levels were substantially higher and demonstrated a marked upward trend. CRP was 200 ± 10 mg/L at admission, 220 ± 3 mg/L at 48 hours, and 246 ± 4 mg/L at 72 hours (p=0.05). PCT values were 0.20 ± 0.02 ng/mL on admission, 0.19 ± 0.03 ng/mL at 48 hours, and peaked at 0.25 ± 0.03 ng/mL at 72 hours (p=0.04). LDH levels increased from 194 ± 4 IU/L to 221 ± 3 IU/L at 48 hours and further to 230 ± 3 IU/L by 72 hours (p=0.05). IL-6 was 60.2 ± 4 pg/mL at baseline, 63 ± 2 pg/mL at 48 hours, and 66.6 ± 2 pg/mL at 72 hours (p=0.05). Among patients in the severe AP group, 19 out of 32 individuals (59.4%) were over the age of 55 years, indicating a potential association between advanced age and disease severity. Inter-group analysis revealed statistically and clinically significant differences in biomarker levels across mild, moderate, and severe categories of acute pancreatitis. Patients in the severe group consistently exhibited markedly elevated levels of inflammatory markers compared to the moderate and mild groups. The mean CRP concentration increased progressively with disease severity, from 77.7 ± 10.2 mg/L in mild cases to 222 ± 13.4 mg/L in severe cases. Similarly, procalcitonin levels were substantially higher in the severe group (0.213 ± 0.03 ng/mL) compared to moderate (0.116 ± 0.02 ng/mL) and mild (0.072 ± 0.01 ng/mL) groups. LDH and IL-6 followed comparable trends, with severe AP cases demonstrating higher mean levels (LDH: 215 ± 4.5 IU/L; IL-6: 63.3 ± 3.2 pg/mL) than moderate (191.7 ± 3.1 IU/L and 55.6 ± 2.1 pg/mL) and mild (161.3 ± 2.6 IU/L and 48.4 ± 2.5 pg/mL) groups, respectively.

Table 1: Patient Demographics

Demographic Variable	Count	Percentage
Total Patients	200	100%
Male	145	72.50%
Female	55	27.50%
Age > 55 in Severe Group	19	59.4% (of severe group)

Table 2: Biomarker Trends Over Time

Biomarker / Timepoint	Mild	Moderate	Severe
CRP Admission	90	120	200
CRP 48h	78	136	220
CRP 72h	65	141	246
PCT Admission	0.08	0.1	0.2
PCT 48h	0.07	0.11	0.19

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Biomarker / Timepoint	Mild	Moderate	Severe
PCT 72h	0.065	0.14	0.25
LDH Admission	160	189	194
LDH 48h	165	195	221
LDH 72h	159	191	230
IL-6 Admission	48.2	54.5	60.2
IL-6 48h	51	55.3	63
IL-6 72h	46	57	66.6

Table 3: Inter-Group Biomarker Analysis

Biomarker	Mild (Mean ± SD)	Moderate (Mean ± SD)	Severe (Mean ± SD)
CRP (mg/L)	77.7 ± 10.2	132.3 ± 11.2	222 ± 13.4
Procalcitonin (ng/mL)	0.072 ± 0.01	0.116 ± 0.02	0.213 ± 0.03
LDH (IU/L)	161.3 ± 2.6	191.7 ± 3.1	215 ± 4.5
IL-6 (pg/mL)	48.4 ± 2.5	55.6 ± 2.1	63.3 ± 3.2

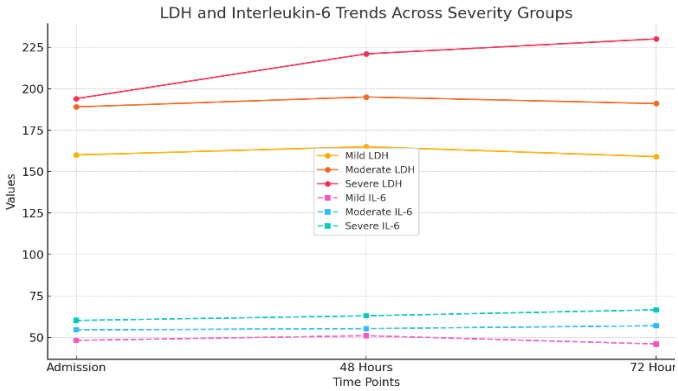


Figure 1 LDH and Interleukin-6 Trends Across Severity Groups

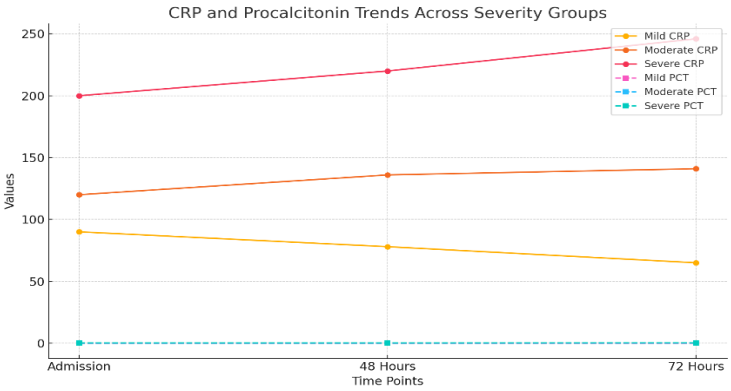


Figure 2 CPR and Procalcitonin Trends Across Severity Groups

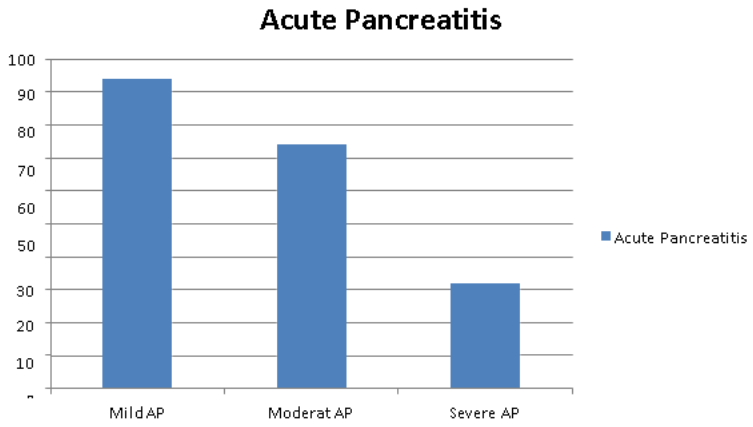


Figure 1 Acute Pancreatitis

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DISCUSSION

Acute pancreatitis remains a prevalent gastrointestinal emergency with a wide clinical spectrum, ranging from self-limiting mild inflammation to rapidly progressing severe disease marked by systemic complications and high mortality. The results of this study highlight the utility of inflammatory biomarkers—namely C-reactive protein (CRP), procalcitonin (PCT), lactate dehydrogenase (LDH), and interleukin-6 (IL-6)—in stratifying disease severity within the first 72 hours of admission. These findings are consistent with existing literature, affirming the role of these markers in early prognostication and guiding clinical decisions (13). CRP levels demonstrated a significant elevation in patients with severe acute pancreatitis, aligning with prior evidence indicating that CRP levels measured at 48 hours possess strong prognostic accuracy for predicting pancreatic necrosis and in-hospital mortality, particularly at cutoff values between 170 and 190 mg/L (14). The consistent trend of elevated CRP in this study across increasing severity categories strengthens its role as a dependable early-phase biomarker. Moreover, PCT levels showed significant elevation in severe cases, reinforcing its value in identifying bacterial complications and guiding severity assessment, as supported by previous large-cohort studies that established PCT as a highly sensitive marker for infection-associated worsening of acute pancreatitis (15,16).

The role of LDH in the context of acute pancreatitis remains partially elucidated. In this study, although LDH levels were higher in severe cases, the trend appeared more static with minimal intergroup variation compared to CRP and PCT. This plateau effect may reflect LDH's generalized association with tissue damage rather than a specific correlation with inflammatory burden (17). In contrast, IL-6 exhibited a progressive rise from mild to severe categories, reinforcing its role as an early and sensitive cytokine in the inflammatory cascade of acute pancreatitis. Its elevation during the first 48 hours has previously been documented as a potential predictor of systemic complications and multisystem involvement (18). However, its limited application in routine clinical practice due to cost constraints remains a recognized barrier, despite its high predictive value. The distribution of cases across the severity spectrum in the present study (47% mild, 37% moderate, and 16% severe) reflects the natural epidemiological trend of acute pancreatitis, where a majority of cases remain self-limiting. Notably, more than half of the patients in the severe group were over the age of 55, indicating a possible age-related predisposition to severe disease progression. This finding aligns with broader clinical observations that older age contributes to immune dysregulation and poorer outcomes in acute inflammatory states (19).

The major strength of this study lies in its prospective design, serial measurement of biomarkers, and stratified analysis across severity groups. These elements allowed for a dynamic assessment of biomarker trajectories and their temporal relevance to clinical deterioration. However, the study is not without limitations. The single-center design and relatively small sample size limit the generalizability of findings. In addition, key clinical outcomes such as duration of hospital stay, requirement for intensive care, organ failure, and mortality were not evaluated. The exclusion of these parameters restricts the ability to correlate biochemical findings with tangible clinical endpoints, which are essential for validating the utility of biomarkers in prognostic models. The lack of data on treatment interventions and their influence on biomarker levels also leaves a gap in understanding the full clinical context. In future research, a multicenter design with larger sample size, integration of clinical severity scores, and longitudinal follow-up to include outcomes such as mortality, complications, and length of stay would provide a more robust framework for evaluating the prognostic role of inflammatory markers. Incorporating cost-benefit analyses, especially for high-cost assays like IL-6, would also enhance the clinical applicability of findings (20). Despite limitations, the present study adds to the growing body of evidence that supports the use of early-phase inflammatory markers, particularly CRP, PCT, and IL-6, in stratifying disease severity and potentially guiding early therapeutic interventions in acute pancreatitis.

CONCLUSION

Acute pancreatitis remains a clinically significant condition due to its potential for high morbidity and mortality, particularly in severe forms. This study highlights the valuable role of inflammatory biomarkers—especially C-reactive protein and procalcitonin—in diagnosing and assessing the severity of the disease. Their consistent elevation in more severe cases supports their use not only for early stratification but also for monitoring disease progression and therapeutic response. Interleukin-6, while less commonly used in daily clinical settings, demonstrated strong diagnostic potential and may serve as a reliable tool in future practice for predicting disease severity. Overall, the findings reinforce the practical utility of these biomarkers in enhancing early clinical decision-making and improving patient outcomes in acute pancreatitis.

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Author Contribution

Author	Contribution
Bilal Ahmed Kayani*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muhammad Sohail Khan	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Qasir Sajid	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Nashwah Waheed	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Furqan Shahid	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Breid Hamza	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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