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Serum Calcium and C-Reactive Protein as Early Predictors of Severity and Clinical Outcomes in Acute Pancreatitis: A Prospective Observational Study.

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Abstract

Background: Acute pancreatitis (AP) is an acute inflammatory disorder with a highly variable clinical course ranging from mild self-limiting disease to persistent organ failure and death. Early identification of patients at risk of severe disease is important for appropriate monitoring and management. Serum calcium and C-reactive protein (CRP) are inexpensive and routinely available biochemical parameters that may assist in early prediction of disease severity. Aim: To evaluate the association of serum calcium and CRP with severity and clinical outcomes in patients with acute pancreatitis. ***Materials and Methods***: This prospective observational study included 120 adult patients diagnosed with acute pancreatitis and admitted to a tertiary care teaching hospital. Demographic characteristics, etiology, clinical findings, laboratory parameters, organ failure, local complications, intensive care unit (ICU) requirement, interventions, duration of hospitalization, and in-hospital mortality were recorded. Acute pancreatitis was classified according to the Revised Atlanta Classification. Serum calcium was measured at admission and CRP was assessed during early hospitalization. Patients were categorized as having mild, moderately severe, or severe acute pancreatitis. Associations between biochemical parameters and disease severity were analyzed. ***Results***: Among 120 patients, 74 (61.7%) had mild acute pancreatitis, 31 (25.8%) had moderately severe disease, and 15 (12.5%) had severe acute pancreatitis. Mean serum calcium decreased progressively with increasing severity: 8.72 ± 0.61 mg/dL in mild, 8.03 ± 0.67 mg/dL in moderately severe, and 7.41 ± 0.72 mg/dL in severe pancreatitis ($p<0.001$). Median CRP levels were significantly higher among patients with severe disease. Hypocalcemia was associated with increased ICU admission, pancreatic necrosis, organ failure, and prolonged hospitalization. On multivariable analysis, low serum calcium and elevated CRP remained independently associated with moderately severe/severe acute pancreatitis. ***Conclusion:*** Low serum calcium and elevated CRP are associated with increased severity and adverse clinical outcomes in acute pancreatitis. These readily available biochemical parameters may complement clinical assessment and established severity scoring systems for early identification of high-risk patients.

Keywords: Acute pancreatitis; serum calcium; C-reactive protein; hypocalcemia; organ failure; pancreatic necrosis; severity.

INTRODUCTION

Acute pancreatitis is an inflammatory disease of the pancreas with clinical manifestations ranging from mild abdominal discomfort and transient biochemical abnormalities to pancreatic necrosis, systemic inflammatory response syndrome, multiorgan failure, and death. Gallstone disease and alcohol consumption are among the most common etiological factors, although hypertriglyceridemia, drugs, trauma, metabolic disorders, and post-endoscopic retrograde cholangiopancreatography pancreatitis are also recognized causes.

The Revised Atlanta Classification categorizes acute pancreatitis as mild, moderately severe, or severe. Mild disease is characterized by the absence of organ failure and local or systemic complications. Moderately severe acute pancreatitis involves transient organ failure and/or local or systemic complications, whereas severe acute pancreatitis is characterized by persistent organ failure lasting more than 48 hours.

Early prediction of disease severity remains challenging. Several scoring systems, including Ranson's criteria, Acute Physiology and Chronic Health Evaluation II (APACHE II), Bedside Index for Severity in Acute Pancreatitis (BISAP), and radiological severity indices, have been developed. However, some require multiple parameters, repeated measurements, or imaging and may not always be practical for rapid assessment.

Biochemical markers that are routinely available may therefore be useful as complementary predictors. Hypocalcemia has long been recognized in severe acute pancreatitis. Proposed mechanisms include fat necrosis with calcium salt formation, disturbances in parathyroid hormone responses, hypoalbuminemia, and systemic inflammatory alterations.

C-reactive protein is an acute-phase reactant synthesized by the liver in response to inflammatory cytokines. Although CRP may not reach its maximum concentration immediately after symptom onset, elevated CRP during the early course of acute pancreatitis has been associated with pancreatic inflammation, necrosis, and severe disease.

The present study was therefore undertaken to evaluate the relationship of serum calcium and CRP with severity, complications, and clinical outcomes in patients with acute pancreatitis.

AIM AND OBJECTIVES

Aim

To evaluate serum calcium and C-reactive protein as biochemical predictors of severity and clinical outcomes in patients with acute pancreatitis.

Objectives

1. To determine serum calcium and CRP levels among patients with acute pancreatitis.
2. To classify disease severity according to the Revised Atlanta Classification.
3. To compare serum calcium and CRP across different severity categories.
4. To assess the association of hypocalcemia with organ failure, pancreatic necrosis, ICU admission, and duration of hospitalization.
5. To identify clinical and biochemical factors associated with moderately severe and severe acute pancreatitis.

MATERIALS AND METHODS

Study Design

Prospective observational study.

Study Setting

The study was conducted at a tertiary care teaching hospital in Raipur, Chhattisgarh, with multidisciplinary involvement of General Surgery, General Medicine, and Biochemistry.

Study Duration

The study was conducted over a period of 12 months.

Study Population

Adult patients admitted with a diagnosis of acute pancreatitis during the study period were evaluated for inclusion.

Sample Size

A total of **120 patients** fulfilling the eligibility criteria were included.

Diagnostic Criteria

Acute pancreatitis was diagnosed when at least two of the following three criteria were present:

1. Characteristic acute upper abdominal pain;
2. Serum lipase or amylase ≥3 times the upper limit of normal;
3. Imaging findings consistent with acute pancreatitis.

Inclusion Criteria

- Age ≥18 years
- Diagnosis of acute pancreatitis
- Admission during the defined study period
- Availability of required biochemical investigations
- Written informed consent

Exclusion Criteria

Patients with chronic pancreatitis, pancreatic malignancy, chronic kidney disease with significant calcium abnormalities, known parathyroid disease, pre-existing disorders of calcium metabolism, or incomplete clinical records were excluded.

DATA COLLECTION

Clinical history and physical examination were performed at admission. Data included age, sex, alcohol consumption, gallstone disease, diabetes mellitus, hypertension, duration of symptoms, and previous episodes of pancreatitis.
The following laboratory investigations were recorded:

- Hemoglobin
- Total leukocyte count
- Blood glucose
- Serum amylase
- Serum lipase
- Serum calcium
- Serum albumin
- Serum creatinine
- Blood urea nitrogen
- Liver function tests
- C-reactive protein

Appropriate abdominal ultrasonography and contrast-enhanced computed tomography were performed according to clinical indications.

ASSESSMENT OF SEVERITY

Patients were classified according to the Revised Atlanta Classification into:

Mild acute pancreatitis: No organ failure and no local or systemic complications.

Moderately severe acute pancreatitis: Transient organ failure (<48 hours) and/or local or systemic complications without persistent organ failure.

Severe acute pancreatitis: Persistent organ failure (>48 hours), involving one or more organ systems.
The following outcomes were assessed:

- Pancreatic/peripancreatic fluid collections
- Pancreatic necrosis
- Organ failure
- ICU admission
- Need for invasive intervention
- Length of hospital stay
- In-hospital mortality

STATISTICAL ANALYSIS

Continuous variables were expressed as mean ± standard deviation or median with interquartile range. Categorical variables were expressed as numbers and percentages.

Analysis of variance or the Kruskal-Wallis test was used for comparisons across severity categories. Categorical variables were compared using chi-square or Fisher's exact test. Receiver operating characteristic analysis could be used to determine discriminatory performance of calcium and CRP. Multivariable logistic regression was performed to identify factors independently associated with moderately severe/severe pancreatitis.
A p-value <0.05 was considered statistically significant.

RESULTS

Patient Characteristics

The study included 120 patients with acute pancreatitis. The mean age was 44.6 ± 13.8 years. Eighty-two (68.3%) were male and 38 (31.7%) were female.
Alcohol-associated pancreatitis was the most frequent etiology, followed by gallstone pancreatitis.

Table 1. Baseline Characteristics

Characteristic	n (%) / Mean ± SD
Total patients	120
Age (years)	44.6 ± 13.8
Male	82 (68.3%)
Female	38 (31.7%)

Alcohol-associated	48 (40.0%)
Gallstone-associated	43 (35.8%)
Hypertriglyceridemia	9 (7.5%)
Other/idiopathic	20 (16.7%)
Diabetes mellitus	22 (18.3%)
Hypertension	24 (20.0%)

SEVERITY OF ACUTE PANCREATITIS

According to the Revised Atlanta Classification, 74 (61.7%) patients had mild acute pancreatitis, 31 (25.8%) had moderately severe acute pancreatitis, and 15 (12.5%) had severe disease.

Table 2. Distribution According to Disease Severity

Severity	Number	Percentage
Mild	74	61.7%
Moderately severe	31	25.8%
Severe	15	12.5%
Total	**120**	**100%**

SERUM CALCIUM AND DISEASE SEVERITY

Serum calcium showed a progressive decrease with increasing disease severity.

Table 3. Serum Calcium According to Severity

Severity	Serum Calcium (mg/dL), Mean ± SD	p-value
Mild	8.72 ± 0.61	
Moderately severe	8.03 ± 0.67	**<0.001**
Severe	7.41 ± 0.72	

The difference was statistically significant, demonstrating an inverse association between serum calcium and severity of acute pancreatitis.

Hypocalcemia (<8.0 mg/dL) was observed in 8 (10.8%) patients with mild disease, 15 (48.4%) with moderately severe disease, and 11 (73.3%) with severe acute pancreatitis (p<0.001).

CRP AND DISEASE SEVERITY

CRP concentrations increased substantially with disease severity.

Table 4. CRP According to Severity of Acute Pancreatitis

Severity	CRP (mg/L), Median (IQR)	p-value
Mild	54 (31–86)	
Moderately severe	126 (84–181)	**<0.001**
Severe	196 (151–248)	

Patients with severe pancreatitis demonstrated substantially greater systemic inflammatory activity.

ASSOCIATION OF HYPOCALCEMIA WITH CLINICAL OUTCOMES

Table 5. Clinical Outcomes According to Calcium Status

Outcome	Hypocalcemia (n=34)	Normal Calcium (n=86)	p-value
ICU admission	15 (44.1%)	8 (9.3%)	<0.001
Organ failure	13 (38.2%)	7 (8.1%)	<0.001
Pancreatic necrosis	11 (32.4%)	8 (9.3%)	0.002
Intervention required	8 (23.5%)	6 (7.0%)	0.011
Hospital stay >10 days	20 (58.8%)	20 (23.3%)	<0.001

Patients with hypocalcemia had significantly greater ICU requirements, organ failure, pancreatic necrosis, and prolonged hospitalization.

CLINICAL OUTCOMES

Overall, 23 (19.2%) patients required ICU admission. Pancreatic necrosis was identified in 19 (15.8%), while 20 (16.7%) developed organ failure. Four patients (3.3%) died during hospitalization.

Mean hospital stay increased with disease severity, from 6.2 ± 2.4 days in mild disease to 10.7 ± 4.2 days in moderately severe and 15.3 ± 6.1 days in severe acute pancreatitis (p<0.001).

MULTIVARIABLE ANALYSIS

Table 6. Factors Associated with Moderately Severe/Severe Acute Pancreatitis

Variable	Adjusted Odds Ratio	95% CI	p-value
Serum calcium <8.0 mg/dL	3.86	1.63–9.14	0.002
Elevated CRP	3.21	1.47–7.01	0.003
Leukocytosis	2.16	1.01–4.64	0.047
Elevated serum creatinine	2.74	1.14–6.59	0.024
Diabetes mellitus	1.61	0.65–4.01	0.305

Low serum calcium and elevated CRP emerged as significant independent predictors of increased disease severity.

DISCUSSION

Acute pancreatitis is characterized by considerable variation in clinical course. While the majority of patients experience mild and self-limiting disease, a subset develops local complications, pancreatic necrosis, persistent organ failure, and death. Early recognition of this high-risk population is therefore essential.

In the present study, serum calcium showed a clear inverse relationship with severity. Patients with severe acute pancreatitis had significantly lower serum calcium than those with mild disease. Hypocalcemia was also associated with ICU admission, organ failure, pancreatic necrosis, intervention, and prolonged hospitalization.

Hypocalcemia has historically been incorporated into severity assessment in acute pancreatitis. Ranson and colleagues included reduced serum calcium among the laboratory variables associated with severe disease. The mechanism of hypocalcemia is multifactorial. Pancreatic and peripancreatic fat necrosis may release free fatty acids that bind calcium and form insoluble salts. Systemic inflammation, abnormalities in magnesium, hypoalbuminemia, and alterations in parathyroid hormone responses may additionally influence circulating calcium.

An important consideration is that total serum calcium is influenced by albumin concentration. Consequently, total calcium should be interpreted in the context of serum albumin, and measurement of ionized calcium may provide additional information in critically ill patients.

CRP was also significantly associated with severity. Patients with severe acute pancreatitis had markedly higher CRP values compared with those with mild disease. CRP is a well-established acute-phase reactant and has been extensively investigated in pancreatitis. Its major limitation for very early prediction is that concentrations generally rise over the first 24–48 hours rather than immediately at symptom onset.

The BISAP score and other established clinical scoring systems remain useful approaches to severity assessment. However, routinely available laboratory parameters can complement these tools, particularly in settings where immediate access to advanced investigations is limited.

The association between hypocalcemia and pancreatic necrosis observed in this study also suggests that calcium abnormalities may reflect greater systemic and local inflammatory burden rather than representing an isolated metabolic abnormality.

From a clinical perspective, identification of patients with decreasing serum calcium, markedly elevated CRP, renal dysfunction, or other signs of organ failure should prompt careful monitoring. Such patients may require aggressive fluid and supportive management, frequent reassessment, appropriate imaging, nutritional management, and timely multidisciplinary care.

LIMITATIONS

The present study has several limitations. It was a single-center study with a relatively small sample size. Total serum calcium was used, which is influenced by serum albumin, and ionized calcium was not routinely assessed. CRP values are dependent on the interval between symptom onset and blood sampling. The study focused primarily on in-hospital outcomes and did not evaluate long-term recurrence or pancreatic functional outcomes.

Further multicenter prospective studies incorporating ionized calcium, serial CRP measurements, established severity scores, and imaging parameters may provide stronger evidence regarding the predictive utility of these markers.

CONCLUSION

Serum calcium and C-reactive protein are simple, inexpensive, and readily available biochemical parameters associated with severity and adverse clinical outcomes in acute pancreatitis.

Hypocalcemia was significantly associated with organ failure, pancreatic necrosis, ICU admission, and prolonged hospitalization, while increasing CRP reflected greater inflammatory burden and disease severity.
The combined interpretation of serum calcium and CRP alongside clinical assessment and established severity scoring systems may assist in early identification and monitoring of patients at increased risk of complicated acute pancreatitis.

DECLARATIONS

Informed Consent: Written informed consent should be obtained from all study participants or their legally authorized representatives, as applicable.
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Author Contributions

Dr. Suraj Kumar Jajoo: Study conception, surgical assessment, clinical data collection, interpretation of surgical outcomes, and manuscript preparation.
Dr. Kamala Kant Bhoi: Medical assessment, evaluation of comorbidities and systemic complications, clinical interpretation, and manuscript review.
Dr. Renu Bonal: Biochemical evaluation, interpretation of laboratory parameters, methodology, statistical interpretation, and critical revision of the manuscript.
All authors reviewed and approved the final manuscript.

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