

Comparison of Various Severity Scores in Predicting the Outcome in Acute Pancreatitis - A Single Centre Observational Study

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ABSTRACT

Background: Acute pancreatitis (AP) is a potentially fatal disease that can range from mild and self-limiting to rapidly progressive, leading to multiple organ failure and death. Aim: This study aimed to compare various severity scores in predicting outcomes in AP.

Methods: This is an observational cross-sectional study conducted from June 2018 to December 2019. Adults diagnosed with AP were included in the study.

Results: A total of 57 patients were included, with mean age of patients were 40.07 years. Among them, 36.84% had mild, 35.08% had moderately severe, and 28.07% had severe AP (SAP), with a 10.52% mortality rate in the SAP. Alcohol was the most common cause (59.64%), and abdominal pain was the most frequent symptom (100%). In predicting severity, APACHE II at 48 hours had the highest AUROC of 0.980, with a cut-off score of ≥ 9 offering the best sensitivity and specificity compared to other scores. For predicting mortality, APACHE II at 48 hours also had the highest AUROC of 0.992, with a cut-off score of ≥ 16 providing the best predictive accuracy.

Conclusion: The APACHE II at 48 hours is the best predictor of SAP and mortality and CRP is a reliable parameter, not a score in predicting severity but is an inferior parameter in predicting mortality.

Keywords: acute pancreatitis, severity scores, APACHE II

INTRODUCTION

Acute pancreatitis (AP) is a rapid-onset inflammation of the pancreas characterized by the early activation of pancreatic enzymes, which causes the pancreas to begin digesting its own tissue. This condition has a general mortality rate of 3-5%. (1-3). In most cases, AP is mild and resolves on its own without complications. However, approximately 20 % of AP patients experience moderate or severe disease characterized by local complications (pancreatic necrosis, fluid collections, splanchnic vein thrombosis, and pseudoaneurysms) and organ failure (respiratory, cardiovascular, and renal). Multi-organ failure (MOF) involving <2 organ systems and persistent (<48 h) organ failure (POF) are associated with a higher risk of death and local complications, especially pancreatic necrosis (4).

Severe AP is associated with mortality rates ranging from 20-40% (3,5,6).

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Although AP is a common clinical condition, there is a lack of prevalence data from India (3). In contrast, the incidence of AP has been reported to be higher in countries such as the USA, Finland, and Scotland, with rates of 49.3, 46.6, and 41.9 per 100,000 population, respectively (7). In the last ten years, the mortality rate linked to severe AP has not increased despite the rising number of AP cases. This is likely due to improvements such as earlier detection of severe cases, reduced use of invasive procedures early on, implementation of enteral nutrition, and better intensive care management (5). As a result, promptly identifying patients at risk for severe AP is crucial to ensure they receive appropriate care and timely intervention (8-10).

Although numerous prognostic scoring systems have been introduced since the 1970s to forecast severe AP, their clinical usefulness remains limited, as they typically yield low positive predictive values (PPV) between 11% and 23% (11). These scoring systems often require more than 24 hours for a complete assessment of disease severity, potentially delaying appropriate care. Additionally, many of these scoring systems were initially developed to predict mortality, not organ failure. However, with the decline in AP-related mortality over the past decade, organ failure has emerged as a more clinically relevant outcome for assessing disease severity (12).

Initial assessment of AP severity should include an evaluation of fluid status, organ failure (such as cardiovascular, respiratory, or renal), and the calculation of the acute physiology and chronic health evaluation (APACHE II) score and systemic inflammatory response syndrome (SIRS) score (13,14). While the measurement of amylase and lipase levels is useful for diagnosing pancreatitis, serial measurements do not help in predicting disease severity, prognosis, or guiding management (15). Early recognition of cases that may progress to severe pancreatitis is crucial for initiating timely and appropriate treatment (16-18). Although several classification systems, including SIRS, Glasgow, Ranson, and APACHE II, are available for assessing the severity of AP, they are not well-validated for predicting mortality. Early organ failure remains a strong predictor of disease severity and the need for intensive care treatment (16-18).

In light of these challenges, this study aimed to compare various scoring systems in predicting the severity and mortality of AP and to assess the

correlation between C-reactive protein (CRP) levels and the severity of the disease.

MATERIALS AND METHODS

Study Design and Ethical Consideration

This is an observational cross-sectional study conducted over 18 months, from June 2018 to December 2019. The study design and methodology received approval from the institutional ethics committee and review board. Written informed consent was obtained from all the patients prior to the commencement of the study.

Inclusion Criteria and Exclusion Criteria

Patients of either sex, above 18 years of age, diagnosed with AP were included in the study. Patients with a history of chronic pancreatitis (characterized by chronic abdominal pain, maldigestion with weight loss, or radiological evidence of the condition) and those who are immunocompromised were excluded from the study.

Data Collection

Data was collected from patients, including their demographic profile (age and sex), duration of illness, symptoms at presentation, co-morbid conditions, medications, past history of AP, and history of alcohol use or smoking.

Study Endpoints

The study endpoints were to investigate the etiology and clinical profile of patients with AP, and to assess and analyze different severity scores and their correlation with patient outcomes.

Evaluation of Severity Scores

To evaluate the performance of different severity scores, the area under the receiver operating characteristics (AUROC) curve was computed for each score. The AUROC provides a measure of the ability of the score to discriminate between patients with different outcomes (e.g., survivors vs. non-survivors). Optimal cut-off scores were determined based on the AUROC analysis. From these cut-off points, the positive predictive value (PPV), negative

predictive value (NPV), sensitivity, and specificity of each score were calculated.

Statistical Analysis

Data were analyzed using SPSS V20 software. Descriptive analysis of the continuous variables was done. The mean values of variables among Mild/moderate pancreatitis were compared with those of severe pancreatitis, non-survivors were compared with those of survivors and the results were expressed as mean (SD). Comparison of two independent variables with normal distribution was performed using Students test (t) test. Independent variables with non-normal distribution was performed using Mann Whitney U test. Multivariate analysis of the variables was performed to know the importance of each variable in predicting the outcome. $p < 0.05$ was considered statistically significant. Area under receiver operating characteristics (AUROC) curve was computed to determine optimal cut-off scores for analyzing the performance of different scores.

RESULTS

A total of 57 patients were included in the study, with mean (SD) age of the patients were 40.07 (12.18) years. Patients in this study had age between 18-70 years, of which 71.93% were male and 28.07% were female. Among the study population, 36.84% patients had mild, 35.08% had moderately severe and 28.07% patients had severe pancreatitis, 10.52% patients with severe pancreatitis expired. The mean (SD) age of patients was 41.98 (12.401) years (Range: 18- 70 years) among mild/moderately severe pancreatitis and 35.19 (10.41) years (Range: 20-59 years) among severe pancreatitis.

Alcohol (59.64%) was the most common etiology in patients, followed by biliary (21.05%), hypertriglyceridemia (5.26%), idiopathic etiology (10.52%), and hypercalcemia (1.75%) (fig. 1). Pain in abdomen (100.00%) was the commonest symptom at presentation seen in all the patients followed by vomiting (71.9%), constipation/obstipation (47.4%), shortness of breath (31.6%), fever (19.3%), jaundice (14.0%), oliguria (9.8%), and altered sensorium (5.3%) (fig. 2). The mean respiratory rate was significantly higher in severe compared to mild/moderately severe (32.31 (6.36) cpm vs 21.66 (4.07) cpm, $p < 0.001$) and non-survivor group compared to survivor 30.67 (3.50) cpm vs 23.94 (6.74) cpm, $p = 0.002$). The laboratory parameter including hemoglobin, hematocrit, total leucocyte count, platelet

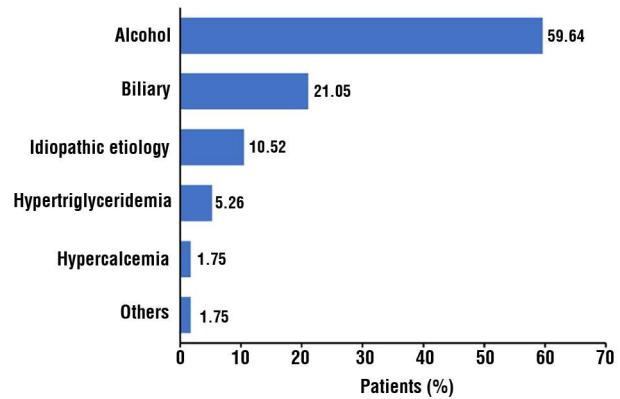


Figure 1 - Etiological factors according to the severity

count, blood urea on day 0, serum creatinine on day 0, serum LDH levels, serum calcium levels were found to be statistically significant between mild/moderate pancreatitis and severe pancreatitis groups (table 1). Among study population, 28.07% patients had persistent organ failure. Respiratory failure (43.75%) was most common, followed by combined renal, respiratory and cardiovascular failure (25%), combined renal and respiratory failure (18.75%), and isolated renal failure (12.5%) (fig. 3).

At the end of 8 weeks, pseudocyst was seen in 2 patients, WON in 8 patients, new onset diabetes mellitus in 1 patient, splenic and portal vein thrombosis in 1 patient and death in 6 patients. endoscopic interventions were done in 2 patients of WON. The mean (SD) of bedside index of severity in acute pancreatitis (BISAP) (2.63 (0.806) vs 1.39 (0.703), $p < 0.001$), Ranson score (4.75 (1.80) vs 1.98 (1.129), $p < 0.001$), APACHE II score at 48 hours (15.71 (5.26) vs 4.85 (2.83), $p < 0.001$), Imrie score (3.80 (1.014) vs 1.87 (1.105), $p < 0.001$), CRP at 48 hours (104.13 (39.75) vs

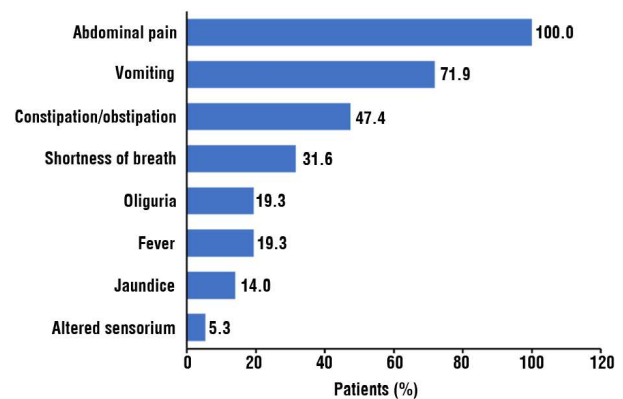


Figure 2 - Distribution of symptoms at presentation

Table 1 - Lab parameters according to severity of pancreatitis

Lab parameters	Mild/Moderate (N=41)	Severe (N=16)	p value	Survivors (N=51)	Non-survivors (N=6)	p -value
Hemoglobin (gm/dL)	14.11 (3.12)	16.16 (3.22)	0.032	14.41 (3.01)	17.06 (4.51)	0.059
Hematocrit (%)	41.50 (8.10)	48.23 (8.69)	0.008	42.70 (7.98)	49.28 (13.11)	0.081
TLC (cells/mm ³)	13911.71 (4049.44)	18271 (5795.80)	0.002	14718.46 (4634.61)	18683.33 (6635.18)	0.063
Platelet count (lakh/mm ³)	2.41 (1.19)	1.57 (0.44)	0.008	2.27 (1.11)	1.31 (0.44)	0.043
INR	1.07 (0.107)	1.13 (0.133)	0.097	1.09 (0.12)	1.05 (0.04)	0.407
RBS (mg/dL)	155.63 (49.49)	169.44 (62.93)	0.38	157.55 (50.94)	176.17 (74.78)	0.424
Blood urea at day 0 (mg/dL)	33.58 (18.60)	55.00 (31.98)	0.003	33.58 (18.60)	55.00 (31.98)	0.003
Blood urea at 48 hours. (mg/dL)	29.27 (13.35)	63.13 (44.62)	<0.001	31.90 (18.55)	97.17 (45.10)	<0.001
Serum creatinine at day 0 (mg/dL)	0.917 (0.467)	1.79 (1.54)	0.02	0.937 (0.47)	3.08 (1.84)	<0.001
Serum creatinine at day 48 hours (mg/dL)	0.805 (0.37)	2.06 (1.81)	<0.001	0.845 (0.47)	3.81 (1.67)	<0.001
Serum sodium (meq/L)	134.02 (4.49)	135.5 (8.33)	0.392	134.02 (5.69)	138.0 (5.762)	0.112
Serum potassium (meq/L)	4.12 (0.65)	4.15 (1.10)	0.906	4.03 (0.74)	4.91 (0.85)	0.009
Serum Amylase (U/L)	798.54 (637.03)	608.63 (408.13)	0.274	749.63 (599.60)	707.83 (481.74)	0.870
Serum Lipase (U/L)	866.37 (1293.93)	273.68 (252.01)	0.076	744.88 (1187.74)	301.55 (269.54)	0.367
LDH (IU/L)	496.76 (217.11)	739.88 (528.24)	0.016	542.39 (313.00)	757.17 (566.59)	0.154
SGOT	71.07 (94.91)	85.69 (62.17)	0.572	71.24 (87.60)	108.67 (76.81)	0.321
SGPT	60.85 (81.59)	63.06 (56.01)	0.921	57.12 (74.94)	98.50 (68.41)	0.203
Serum calcium	9.05 (0.71)	7.66 (0.80)	0.00	8.82 (0.87)	7.35 (0.71)	<0.001

Data presented as mean (SD). INR, international normalized ratio; LDH: lactate dehydrogenase; RBC: red blood cell; SGOT: serum glutamic-oxaloacetic transaminase; SGPT: serum glutamic pyruvic transaminase; TLC: total leukocyte count.

64.69 (62.35), p=0.027) were significantly higher among patients with severe pancreatitis compared to mild/moderate group (table 2).

The mean score of BISAP (2.67 (1.03) vs. 1.63(0.848), p=0.007), ranson (5.33 (1.86) vs. 2.45 (1.59), p<0.001)

APACHE II at 48 hours (21.75(3.86) vs. 6.51 (4.48), p<0.001), imrie (4.60(1.14) vs. 2.18 (1.20), p<0.001) were significantly higher non- survivors compared to survivors (table 2). The APACHE II at 48 hours has the highest AUROC compared to BISAP, ranson, imrie severity scores (0.980 vs 0.861 vs. 0.880 vs. 0.908). The APACHE II at 48 at score ≥9 has comparable sensitivity and specificity in predicting severity better than other scores. C-reactive protein had very low AUROC and hence is not a good predictor of severity (table 3).

The APACHE II score at 48 hours, with a cutoff of ≥16, had the highest AUROC of 0.988, demonstrating the best predictive accuracy for mortality with a sensitivity of 100% and specificity of 95%. The imrie score, at a cutoff of ≥ 3, had an AUROC of 0.928, with sensitivity and specificity of 100% and 59%, respectively. Ranson's score, at a cutoff of ≥ 3, had an AUROC of 0.873, with 83% sensitivity and 63% specificity. The BISAP score, at a cutoff of ≥ 2, had an AUROC of 0.783, with sensitivity and specificity of 83% and 44% respectively. C-reactive protein at 48 hours, with a cutoff of ≥ 88, had an AUROC of 0.724, with sensitivity and specificity of 100% and 66%, but was not a strong predictor of mortality due to its lower AUROC compared to the other scores (table 4).

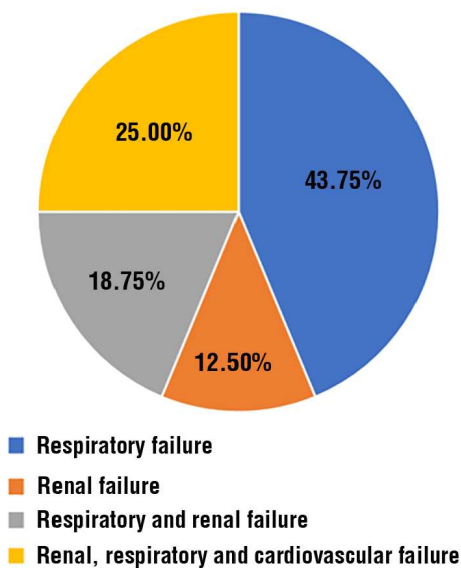


Figure 3 - Distribution of organ failure

Table 2 - Comparison of severity scores and CRP levels in patients with AP

Scores	Mild/Moderate (N=41)	Severe (N=16)	p value	Survivors (N=51)	Non-survivors (N=6)	p value
BISAP	1.39 (0.703)	2.63 (0.806)		1.63 (0.848)	2.67 (1.03)	0.007
Ranson's	1.98 (1.129)	4.75 (1.80)	<0.001	2.45 (1.59)	5.33 (1.86)	<0.001
APACHEII (admission)	5.54 (3.001)	15.56 (5.561)	<0.001	7.08 (4.78)	19.17 (3.251)	<0.001
APACHEII (at 48hours)	4.85 (2.83)	15.71 (5.26)	<0.001	6.51 (4.48)	21.75 (3.86)	<0.001
Imrie's score	1.87 (1.105)	3.80 (1.014)	<0.001	2.18 (1.20)	4.60 (1.14)	<0.001
CRP (on admission) (mg/L)	28.12 (42.38)	68.3 (78.6)	0.016	36.51 (54.0)	64.0 (81.6)	0.269
CRP (at 48 hours) (mg/L)	64.69 (62.35)	104.13 (39.75)	0.027	73.27 (61.92)	97.2 (7.4)	0.396

Data presented as mean (SD).

APACHE II: Acute Physiologic Assessment and Chronic Health Evaluation; BISAP: Bedside Index of Severity in Acute Pancreatitis; CRP: C-reactive Protein.

Table 3 - Comparison of BISAP, Ranson Score, APACHE II score (on admission & at 48 hours), Imrie's score, CRP level (on admission and at 48 hours) in predicting severity.

	Cutoff	Sensitivity %	Specificity %	PPV%	NPV%	AUROC
BISAP	≥ 2	93%	54%	42.4	91.6	0.861
Ranson's	≥ 3	81%	73%	54.16	90.90	0.880
APACHE II (admission)	≥ 7	93%	59%	53.8	93.5	0.930
APACHE II (at 48 hours)	≥ 9	93%	93%	77.7	94.8	0.980
Imrie's score	≥ 3	100%	73%	60	96.8	0.908
CRP (on admission) (mg/L)	≥ 24	93%	66%	52.38	86.1	0.800
CRP (at 48 hours) (mg/L)	≥ 70	93%	73%	60	96.88	0.778

Data presented as %.

APACHE II: Acute Physiologic Assessment and Chronic Health Evaluation; AUROC: area under receiver operating characteristics;

BISAP: Bedside Index of Severity in Acute Pancreatitis; CRP: C-reactive Protein; PPV: Positive Predictive Value; NPV: Negative Predictive Value.

Table 4 - Comparison of BISAP, Ranson Score, APACHE II score (on admission & at 48 hours), Imrie's score, CRP level (on admission and at 48 hours) in predicting mortality.

	Cutoff	Sensitivity	Specificity	PPV	NPV	AUROC
BISAP	≥ 2	83	44	15.15	95.8	0.783
Ranson's	≥ 3	83	63	20.8	96.96	0.873
APACHE II (on admission)	≥ 13	100	89	50	100	0.966
APACHE II (at 48 hours)	≥ 16	100	95	66.6	100	0.992
Imrie's score	≥ 3	100	59	20	96.8	0.928
CRP (on admission) (mg/L)	≥ 24	83	53	14.28	91.6	0.628
CRP (at 48 hours) (mg/L)	≥ 88	100	66	26.09	100	0.724

Data presented as %.

AUROC: Area Under Receiver Operating Characteristics; APACHE II: Acute Physiologic Assessment and Chronic Health Evaluation;

BISAP: Bedside Index of Severity in Acute Pancreatitis; CRP: C-reactive Protein; PPV: Positive Predictive Value; NPV: Negative Predictive Value.

DISCUSSION

Acute pancreatitis was an inflammatory condition of the pancreas and may have a variable severity. Most of the patients have mild disease with minimal morbidity, and the rest of the patients have 10%-20% of mortality in severe AP (19). In this study, APACHE II at 48 hours is the best predictor of severe AP and mortality. The BISAP being simple bedside score, is still a reliable predictor of

severity compared to other severity scores. The CRP is a reliable marker in predicting severity but is an inferior marker in predicting mortality.

In present study, majority patients were the males. Similar finding demonstrated by Robert et al. and Shakya P et al. (20,21), incidence of AP overall was significantly higher among men than women. In contrast to this, retrospective study showed that there was predominance of AP in females compared to males

(22). This might be due increased prevalence of biliary pancreatitis in females.

In current study, alcohol was the most common etiology followed by biliary, hypertriglyceridemia, idiopathic etiology, and hypercalcemia. In line with current study, Mukherjee D et al, reported alcohol as the commonest etiology, followed by idiopathic causes, and obstructive causes (23). In contrast, one study showed that gallstones were the most common cause of AP, followed by alcohol, idiopathic, post- endoscopic retrograde cholangiopancreatography, and miscellaneous causes (24). Another study reported that biliary was the commonest cause, followed by alcoholism, hypertriglyceridemia, and the others (25). The most frequent cause of pancreatitis, according to a comparable study by Robert et al., was gallstones. Other prevalent causes were alcohol, hyperlipidemia, abdominal trauma, hypercalcemia, starvation, pancreatic cancers, and cystic fibrosis (20).

Pain in abdomen was the commonest symptom at presentation seen in all the patients followed by vomiting, constipation/obstipation, shortness of breath, fever, jaundice. Other studies (22,26-28) also corroborate that the most common presentation was abdominal pain followed by vomiting, abdominal distension, fever and jaundice.

The present study revealed that 36.84% patients had mild, 35.08% had moderately severe and 28.07% patients had severe pancreatitis, 10.52% patients with severe pancreatitis expired. In contrast, the recent study found that the majority of patients (71.20%) had mild pancreatitis, 23.71% had moderate pancreatitis, and 5.09% had severe pancreatitis (29). Another study reported that 63.7% patients were mild, 25.8% were moderate and 11.0 % severe (30).

Organ failure is the main determinant of severity and a major cause of early mortality. In the present study, 36.06% patients developed persistent organ failure, of which respiratory failure was most common, followed by combined renal, respiratory and cardiovascular failure then by combined renal and respiratory failure, isolated renal failure found in of patients. In line with current study reported 49.6% patients had severe AP, respiratory failure (59%) was the most common organ failure followed by respiratory failure with renal failure (31%) and respiratory and renal with cardiac failure (10%) (24). In contrast to the present study, the other study found that respiratory plus cardiac failure was more common, followed by respiratory and renal failure, and then respiratory, renal, and cardiovascular failure (33).

In predicting severity, APACHE II at 48 hours had the

highest AUROC with a cut-off of ≥ 9 compared to other severity scores. Similarly, Larvin et al. found that the APACHE II score had higher predictive accuracy for severe AP than the Ranson score and could be calculated at any time point (34). In current study, APACHE II (at 48 hours) score had superior predictive value of mortality with an AUROC of 0.988 followed by APACHE II (on admission), Imrie score, Ranson's score, BISAP and CRP 48 hours & on admission. Similarly, a study by Khanna et al showed that APACHE II was more accurate in predicting mortality in AP with AUC- 0.86 (35). Similarly, one study (36) reported that APACHE II is a useful prognostic scoring system for predicting the severity of AP. In contrast to this, an observational study found that changes in serum procalcitonin levels and APACHE II scores between admission and 48 hours are closely correlated and can effectively predict mortality in acute pancreatitis. Notably, the change in serum procalcitonin levels was a more reliable indicator than the change in APACHE II scores among survivors (37).

C-reactive protein on admission and at 48 hours were a poor predictor of mortality. The calculated AUROC for CRP on admission and at 48 hours for predicting was 0.628 and 0.724 respectively & hence was a poor marker in predicting outcome in AP. Similarly, Aaron D. Stirling et al showed that a CRP rise of >90 mg/dL from admission or an absolute value of >190 mg/dL at 48 h predicts severe disease with the greatest accuracy (38). In line with study, Khanna et al demonstrated that CRP was a good predictor of severity (AUC-0.91) but not a good predictor of mortality (AUC-0.75) (35). Similarly, other studies reported the showed that CRP levels were not statistically significant in non- survivors compared to survivors (39,40).

Limitations

A limitation of study was the small sample size, as it was conducted at a single center. A similar multi-center study would provide a larger sample size, allowing for a better determination of the cut-off values for various severity scores in estimating how severe acute pancreatitis may become and its associated mortality risk. Additionally, other parameters that need to be evaluated include inflammatory markers such as IL-6, which could not assess in this study due to financial constraints and limited resources.

CONCLUSION

Blood urea, serum creatinine, and serum calcium levels are key indicators to evaluate disease severity

and mortality outcomes in AP. Respiratory failure is the most frequent organ failure observed in AP. While CRP is a dependable marker for assessing the severity of the condition, it is less effective in predicting mortality. Scoring systems such as BISAP, Ranson's criteria, APACHE II (both on admission and at 48 hours), and Imrie scores are significantly higher in patients with severe AP and those who do not survive. Of these, APACHE II at 48 hours is the most accurate for predicting both severity and mortality, with BISAP also being a reliable and simple bedside tool for these predictions.

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Conflict of Interest

All authors declare no conflicts of interest.

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