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Acute pancreatitis: Comparison of Scoring Systems in Predicting its Severity

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ABSTRACT

Introduction: Acute pancreatitis (AP) is an acute inflammatory process of the pancreas. It has a highly variable clinical course. So an early, accurate and quick scoring system is necessary to stratify the patients according to their severity.

Objectives: To compare different scoring systems and their usefulness in predicting the severity in AP.

Methodology: This was a comparative cross-sectional observational study on 51 patients admitted with the diagnosis of AP. Ranson, Acute Physiology and Chronic Health Evaluation (APACHE) II, Bedside Index of Severity in Acute Pancreatitis (BISAP), Computed Tomography Severity Index (CTSI) of all patients were calculated. Similarly C-reactive protein (CRP) levels were measured at admission (CRPadm) and after 48 hours (CRP48). Result of these was compared with that of revised Atlanta classification. So using the receiver-operating curve (AUC) predictive accuracy of each scoring system was measured.

Results: Of 51 cases, 7 (13.7%) were graded as severe AP. The AUC for APACHE II was the highest for predicting severe acute pancreatitis 0.765 (95% CI: 0.578-0.951). CTSI had a high sensitivity for predicting severe AP 85.71 (95% CI: 42.13- 99.64) and CRP48 had a high specificity for predicting severe AP 90.91 (95% CI: 78.33- 97.47).

Conclusion: Similar predictive accuracy was shown by various scoring systems used in this study for severity of AP. To achieve further improvement in prognostic accuracy unique models are needed.

INTRODUCTION

Acute pancreatitis (AP) is an unforeseen inflammation of the pancreas, which is characterized by the activation of pancreatic enzymes which leads to self-digestion. It is an acute inflammatory process presenting as a mild pain with local inflammation to severe disease with multi-organ failure.[1] About 15 to 25 percent of all patients will develop moderately severe or severe AP.[2] The various tools to predict its severity can help identify patients at increased risk for morbidity and mortality, hence assisting in appropriate early triage to intensive care units and patients could be selected for specific interventions.[3]

A classification system which is clinically based for AP was established in the International Symposium on Acute Pancreatitis in Atlanta, Georgia in 1992.[3] However, the Atlanta severity classification system has been criticized because it was retrospective, the duration of organ failure was unspecified and local complications did not seem to increase mortality. In an international consensus in 2012, the Atlanta classification was revised which provided more clear definitions to classify AP using simple clinical and radiologic criteria. So, based on organ failure and severity was graded as mild, moderate and severe AP.[4]

There are multiple models to predict severity, which has been used since 1970s for assessment of the severity of AP, the most commonly used are Ranson's criteria[4] and APACHE-□scores[5]. The computerized tomography (CT) abdomen based Balthazar computed tomography severity index (CTSI) was developed in 1990.[6] These scoring systems have been established as an important tool for assessment of the severity.

The recent used tool, Bedside Index for Severity in Acute Pancreatitis (BISAP), has been proposed as an accurate and simple method for early identification of patients who are at risk of hospital mortality.[7] The organ failure is determined by the modified Marshall scoring system (MMS).[8] One of the earliest criteria is Ranson's criteria for detecting severity in AP.[9] It consists of 11 parameters for evaluating the prognosis of AP within the first 48 hours of an event. Five factors that are assessed at admission are age, leukocyte count, glycemia values, AST, and LDH. The six factors are assessed during the next 48 hours, which includes hematocrit, BUN, calcium, base deficit, PO2 and estimated fluid sequestration. For biliary pancreatitis a later modification included only 10 points. Hence, mortality increases with an increasing score.[10] So in patients with two or less criteria, the mortality rate is of 5%, 10% in those with 3-5 criteria, and 60% in patients with more than 6 criteria. [9] The APACHE II score has 12 physiologic measures and extra points based upon age and presence of chronic disease. The mortality is less than 4 percent with a score <8 and is 11 to 18 percent with a score >8.[11] BISAP score can identify patients early with increased mortality in hospitalized patients. The following five variables measured within the 1st 24 hours were found to be associated with increased mortality:

- Blood urea nitrogen (BUN) >25 mg/dl
- Impaired mental status
- Systemic inflammatory response syndrome (SIRS)
- Age >60 years
- Presence of a pleural effusion

Patients are assigned 1 point for each of the following during the first 24 hours: Patients with a score of zero had a mortality of less than one percent, whereas patients with a score of five had a mortality rate of 22 percent.[12] Based upon the degree of necrosis, inflammation and the presence of fluid collections, CT severity index- A CT severity score (the Balthazar score) has been developed.[6] C-reactive protein (CRP) is one of the acute phase reactants made by the liver in response to interleukin-1 and interleukin-6. It is a single biochemical marker widely accepted as a marker of the severity of AP. Though different cutoff values are proposed, levels of CRP above 150 mg/Liter at 48 hours differentiate severe from mild disease.[11]

There have been only few studies comparing these prognostic scoring systems based on the revised Atlanta classification in Nepal. This study was conducted for comparison of different scoring systems available in AP, such as Ranson's criteria, APACHE-II, BISAP, CTSI and one single laboratory parameter C-reactive protein (CRP) and their usefulness in predicting the severity in AP in a tertiary care center.

METHODOLOGY

This hospital-based comparative cross sectional observational study was conducted over a period of 6 months between June 2021 to December 2021 in the Department of Gastroenterology and Hepatology and Department of Surgery in ????????????? ??????????????????, which is a university hospital located in eastern part of Nepal. Approval from the Institutional Ethics committee was obtained (Reference number 633/077/078-IRC).

Sample size calculation: This study considered 95% CI and 80% power to estimate the sample size. In this regard the study considered 81% predicting rate of Acute physiology and chronic health evaluation II(APACHE-II) scoring system and 53% of CRP_{48} system in previous study,[13] which found to be of minimum difference. Now using two proportion formula, the sample size became 51.

$$n=\frac{2\,pq(Z_{a/2}+Z_{\beta})^2}{(P_1-P_2)^2}$$

Where, $p=\frac{P_1+P_2}{2}=80\%$

$q= 100-80=20\%$

$Z_{a/2}=1.96$ at 95% CI

$Z_{\beta}= 0.842$ at 80% power

Inclusion criteria

All patients more than 18 years of age with a diagnosis of AP were included in this study with following selection criteria based on the revised Atlanta classification of AP. Presence of at least two of the following three criteria:(i) Acute onset of persistent, severe, epigastric pain often radiating to the back, (ii) elevation in serum lipase or amylase to three times or greater than the upper limit of normal, (iii) characteristic findings of acute pancreatitis on imaging.[3]

Exclusion criteria

Patients who were diagnosed with chronic pancreatitis and pancreatic malignancy were excluded from the study.

Definitions

Grades of severity of AP were determined according to the revised Atlanta Classification. Mild AP was defined by the absence of organ failure and the absence of local or systemic complications. Moderately severe AP was defined by the presence of transient organ failure, local complications, or exacerbation of co-morbid diseases. Severe AP was defined by persistent organ failure for more than 48 hours.[13] Organ failure was defined as a score of 2 or more for one of the three systems (respiratory, cardiovascular, and renal) using the modified Marshall scoring system.[14]

After detailed history and physical examination, laboratory investigations were sent at the time of admission and at 48 hours after admission. All patients underwent abdominal ultrasonography at admission and contrast enhanced Computed tomography (CT) scan 72 hours after symptom onset. Patients were subsequently examined daily and laboratory investigations relevant to APACHE-II and BISAP scores were calculated using data from the first 24 hours after admission and the Ranson score using data from the first 48 hours. Serum CRP levels were measured at admission (CRP_{adm}) and after 48 hours (CRP_{48}). CTSI

was calculated in patients who underwent contrast enhanced computed tomography (CECT) within 72 hours after symptoms onset. For the prediction of severe AP the cutoff taken was as follows

- Ranson's Criteria: ≥3.
- APACHE-II score: ≥8.
- BISAP score: ≥3.
- CTSI score: ≥3.
- CRP: ≥150 mg / Liter

Statistical data analysis

Collected data were entered in MS Excel 2010 and analyzed using SPSS version 11.5 for statistical analysis. For descriptive analysis percentage, mean, standard deviation, median, IQR minimum and maximum were calculated and graphical and tabular presentations were made. For inferential statistics, X^2 one way ANOVA or Krushcal Walli's H test were applied to find out the significant difference between predicting factors and severity of AP at 95% CI where $p<0.05$. Sensitivity, specificity, positive predictive value and negative predictive value were calculated for each scoring system. ROC was applied to find out the cut off values in comparison to RA scoring system and others selected scoring system. Logistic regression was applied to find out the significant predicting factor for all scoring system at 95% CI where level of significance considered at $p<0.05$.

RESULTS

Patient characteristics

A total of fifty-one patients were included in the study. The age of the patients ranged from 23 to 83 years. The mean age was 46.4 years and among them 27 patients (52.9%) were male and 24 (47.1%) were female with male to female ratio of 1.1. The mean age of severe AP was 49.7 years. The most common etiology of AP was biliary 20 (39.2%) followed by idiopathic 15 (29.4%), alcoholic 14 (27.5%) and others were 2 (4%). Seven patients (13.7%) developed persistent organ failure for more than 48 hours and were classified as severe AP according to the Atlanta Classification. Nineteen patients (37.3%) were classified as moderately severe AP and 25 patients (49%) as mild AP. Severe AP was seen more in alcoholic etiology 4 (28.5%). (Table 1)

Most of patients admitted were during non-festival time 44 (86.3%) and 7 (13.7%) were during festival time. But severe AP was seen mostly during festival time (p=0.016), which was statistically significant. The most common comorbidity associated was Diabetes Mellitus 6 (11.8%) whereas 40 patients (78.4%) had no comorbidities. The most of severe AP was seen in those patients who had no comorbidities 6 (15%). The average day of pain relief was 3.3 days and average day of re feeding was 3.5 days. The average length of hospital stay in this study was 6.1 days whereas the length of stay for those graded, as having severe AP was 8.7 days. All patients were discharged in satisfactory condition after recovery. Table 1 shows the general characteristics of the study population.

Table 1: Patient characteristics (n=51)

Characteristics	Categories	Number (%)
Sex	Male	27 (52.9)
	Female	24 (47.1)
Mean Age (23-83)		46.4
Etiology	Biliary	20 (39.2)
	Alcohol	14 (27.5)
	Idiopathic	15 (29.4)
	Others	2 (4)
Average Total hospital stay (days)		6.1
Seasonal variation	Festival	7 (13.7)
	Non-festival	44 (86.3)
Average day of pain relief		3.3
Average day of refeeding		3.5
APACHE II	≥8	23 (45.1)
	<8	28 (54.9)
BISAP	≥3	23 (45.1)
	<3	28 (54.9)
Ranson's score	≥3	16 (31.4)
	<3	35 (68.6)
CTSI	≥3	42 (82.4)
	<3	9 (17.6)
CRP_{adm}	≥150	10 (19.6)
	<150	41 (80.4)
CRP_{48}	≥150	5 (9.8)
	<150	46 (90.2)
Revised Atlanta Classification	Mild	25 (49)
	Moderate	19 (37.5)
	Severe	7 (13.7)
Acute fluid collection		7(13.7)
Pseudocyst		5(9.8)
Acute necrotic collection		1 (2)
Walled off necrosis		1(2)
Mortality		0

Based on contrast enhanced CT findings, acute pancreatic fluid collections were noted in 7(13.7%), Pseudocyst in 5(9.8%), Acute necrotic collection 1 (2%) and walled off necrosis (WON) in 1(2%).

Table 2 showed that urea (41.43) and PCV (42.43±5.7) were high in severe AP group and calcium (8.1±0.9) was lower in severe AP group but none achieved statistically significance.

Table 2: Comparison of biochemical profile between mild to moderate AP with severe AP (n=51)

Categories	Mild to moderate AP (n=44)	Severe AP (n=7)	P value
Amylase in U/l	678.8	596.0	0.183
Lipase in U/l	533.7±238.2	443.3	0.358
LDH in U/l	466.7	575.4	0.948
Calcium in mg/dl	8.8±1.3	8.1±0.9	0.595
Urea in mg/dl	29.98	41.43	0.330
RBS in mg/dl	153.45±72.2	130.43±17.7	0.027
PCV in percentage	39.95±6.7	42.43±5.7	0.418
ALT in U/l	186.80	154.43	0.414
AST in U/l	217.70	157.43	0.373
Triglyceride in mg/dl	131.73±52.1	105.57±22.9	0.094

LDH: lactate dehydrogenase, ALT: alanine aminotransferase, AST: aspartate aminotransferase, RBS: Random blood sugar, PCV: packed cell volume

The sensitivity, specificity, PPV, and NPV of different scoring systems and CRP in prediction of severe AP using cutoff values of Ranson ≥ 3, BISAP ≥ 3, APACHE-II ≥ 8, CTSI ≥ 3, and CRP 48 ≥ 150 mg/ L are shown in Table 3.

Table 3: Sensitivity, specificity, positive predictive value, and negative predictive value of different scoring systems in prediction of severe acute pancreatitis

Categories	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
Ranson's score	71.43 (29.04- 96.3)	75.00 (59.7- 86.8)	31.25 (18.5- 47.6)	94.29 (83.48-98.18)	74.51 (60.4- 85.7)
APACHE-II	57.14 (18.4- 90.1)	56.82 (41.03-71.7)	17.39 (9.3-30.3)	89.29 (77.33-95.32)	56.86 (42.3-70.7)
BISAP	57.14 (18.4-90.1)	56.82 (41.03-71.7)	17.39 (9.3-30.3)	89.29 (77.33- 95.32)	56.86 (42.3-70.7)
CTSI	85.71 (42.1- 99.6)	18.18 (8.2-32.7)	14.29 (10.7- 18.9)	88.89 (53.98- 98.20)	27.45 (15.9- 41.7)
CRP_{48}	14.29 (0.36- 57.9)	90.91 (78.3- 97.5)	20.00 (3.2- 65.8)	86.96 (82.93- 90.15)	80.39 (66.9- 90.1)

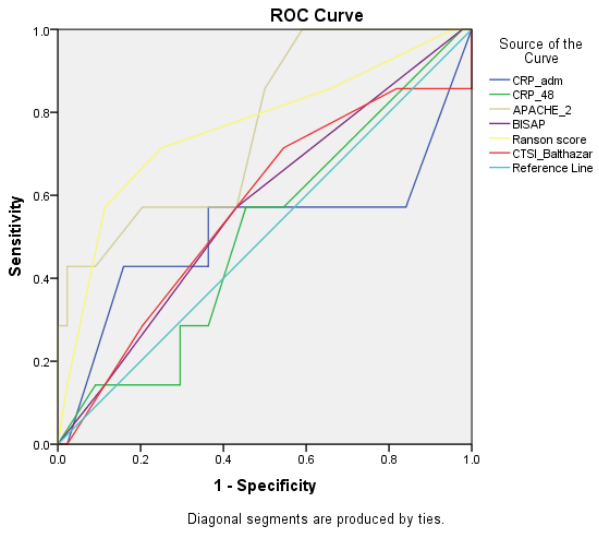

Figure 1 Receiver-operating characteristic (ROC) curves of different scoring systems and C-reactive protein in prediction of severe AP. BISAP: Bedside Index for Severity in Acute Pancreatitis; APACHE: Acute Physiology and Chronic Health Examination; CTSI: computed tomography severity index; CRP_{adm}: C-reactive protein measured at admission; CRP_{48}: C-reactive protein measured after 48 hours.

Comparison of scoring systems in prediction of severe AP

On the basis of the highest sensitivity and specificity values generated from the ROC curves, the following cutoffs were selected for prediction of severe AP: Ranson ≥ 3, BISAP ≥ 3, APACHE-II ≥ 8, CTSI ≥ 3, and CRP_{48} ≥ 150. The comparisons of ROC curves for severe AP among all scoring systems and CRP are shown in Figure 1. AUCs for Ranson, BISAP, APACHE-II, CTSI, CRP_{adm}, and CRP_{48} in predicting severe AP were 0.763 (95% CI: 0.547-0.979), 0.573 (95%CI: 0.348-0.799), 0.765 (95%CI: 0.578-0.951), 0.567 (95%CI: 0.326-0.807), 0.515 (95%CI: 0.219-0.810), and 0.508 (95%CI: 0.285-0.732), respectively. All scoring systems and CRP_{48} were found to be reliable in prediction of severe AP, except CRP_{adm}. The sensitivity, specificity, PPV, NPV and accuracy of different scoring systems and CRP in prediction of severe AP using cutoff values of Ranson ≥ 3, BISAP ≥ 3, APACHE-II ≥ 8, CTSI ≥ 3, and CRP_{48} ≥ 150 are shown in Table 3. APACHE-II score demonstrated the highest accuracy for prediction of severe AP (AUC = 0.765).

DISCUSSION

AP is a common and recurrent disorder, where inflammation of the pancreas with inconstant connection of other surrounding tissues or other organ systems.[15] Among the individuals with pancreatitis, identification of patients who are at risk of severe

disease and mortality is a crucial step for the purpose of effective management and prevention of mortality.

The mean age of the study population was 46.4 years with male predominance (52.9%) and the mean age of patient with severe AP was 49.7 years and severe AP was seen only in male patients (25.9%). Biliary AP (39.2%) followed by Idiopathic (29.4%) were the most common etiological factors in our study which is comparable to study done in India by Kumar et al. [15] and in South Korea by Cho JH et al.[13] This could be attributed to the higher prevalence of gall stone disease in this part. However, in this study, among the etiologies of AP, alcohol showed a significant association with patients with severe AP.

Based on revised Atlanta classification, 13.7% were classified as severe AP who developed persistent organ failure for more than 48 hours and predominant 49% was graded as mild AP. During the course of the study, there was no mortality recorded whereas in study by Cho JH et al.[9] 10% of patients died during hospitalization. Low death rate in our study could be due to predominant patients being mild AP. Most of patients admitted were during non-festival time (86.3%) but severe AP was seen mostly during festival time (p=0.016), which was statistically significant. This could be due to increased referral of sick patients in our hospital as most of the health workers could be on holidays in periphery hospitals.

In this study, accuracy of three clinical scoring systems, CTSI and one lab parameter CRP, in prediction of severe AP, were compared. The AUC for APACHE-II was the highest for all the five parameters considered as markers for severity of AP (AUC 0.765). In a similar study, Mounzer et al.[16], compared several prognostic scores and also found APACHE II to be more accurate as compared to Ranson's and BISAP. In this study, APACHE-II score appeared to be a more influential tool than other scoring systems. Considering process of calculating APACHE-II score was complex, it might be easier in the era of computerized calculation systems.

Ranson's score had high NPV 94.2%, PPV 31.2%, sensitivity 71.4% and specificity 75.0% in predicting severity in our study. The AUC for Ranson's score was just behind APACHE-II (AUC 0.763). This was comparable to a study done by Cho JH et al.[13] So our study showed that Ranson's score did a good job in predicting severity in AP.

BISAP was proposed to construct a simple and accurate clinical scoring system to estimate the mortality risk of AP at early stage. In our study, BISAP had high NPV 89.2% but low sensitivity 57.1% and specificity 56.8% for predicting severe AP. The AUC for BISAP was also behind APACHE-II and Ranson's score in predicting severity. So, BISAP performed poorer than APACHE-II and Ranson's score in predicting severity in this study. Whereas in a study done in India by Aggarwal et al.[17] BISAP score outperformed Ranson's score in terms of Sensitivity and specificity of prediction of severe AP.

In this study, using CTSI for prediction of severe AP, sensitivity and specificity were 85.7% and 18.1% respectively. The AUC was only fourth best in predicting severity in AP which is comparable to study by Cho JH et al.[13] The major limitation of CTSI is that pancreatic parenchymal necrosis may be unrecognized on an early CT performed within 24 h after admission and development of local complications, such as abscess or hemorrhage, usually occur late in the course of AP.[18]

In this study, the CRP_{48} was significantly higher in severe AP compared to mild to moderately severe AP. The sensitivity 14.2% and PPV 20.0% was low however specificity 90.9% and PPV 86.9% was comparable with other scoring systems. The AUC of CRP_{48} was only fifth best in predicting severity of AP. Despite the simplicity and easy availability of CRP in clinical practice, many studies have described limitation of clinical utility of CRP in the early phase of AP and revealed that usage of CRP alone was potentially failing to detect severe cases of AP at an earlier stage.[19]

CONCLUSION

This study demonstrates that the APACHE-II scoring system seems to have the highest accuracy in assessment of the severity in AP, although the predictive accuracy of APACHE-II was not significantly different compared to that of the other scoring systems.

LIMITATIONS OF THE STUDY

In this study, the number of patients with severe AP and mortalities was lower compared to other large-scale clinical studies; therefore, comparison of prognostic value of various scoring systems was difficult.

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CONFLICT OF INTEREST None

FINANCIAL DISCLOSURE None

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