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Comparative Study Between BISAP Scoring System and C-Reactive Protein Analysis in Predicting Severity of Acute Pancreatitis

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Abstract

Introduction: Acute pancreatitis is one of the commonest conditions that presents as a surgical emergency worldwide.

Aim: The aim of the study was to compare BISAP scorings and serum levels of C-reactive protein in predicting severity of acute pancreatitis.

Materials and methods: Thirty patients got admitted from November 2012 to April 2014 in our hospital with acute pancreatitis were included in the study. C-reactive protein evaluated along with BISAP score at the time of admission. Patients assessed for severity by comparing both. Statistical analysis done by using Fischer's exact test, chi-square test and student *t*-test.

Results: 23.3% of patients had a BISAP score of 3, rest had a score of 1 or 2. 66.7% of patients had an elevated CRP. An elevated CRP level and an increased BISAP score was found to have a statistically significant relation ($p = 0.009$ and $p = 0.0002$ respectively) to length of patient's stay in hospital and hence the severity. BISAP and CRP levels had a positive correlation with a *p*-value of 0.064. Here, we found that BISAP scores had a statistically significant relationship with ICU stay (*p*-value: 0.014)

Conclusion: In conclusion, we found that BISAP is a better predictor of severity of acute pancreatitis compared to CRP levels. It is a useful means of predicting severity in acute pancreatitis. Larger studies will be needed to further consolidate our findings, but it is safe to say that BISAP has the advantage of simplicity and speed over more traditional scoring systems.

Keywords: Acute pancreatitis; Bisap scoring; C-reactive protein; Hospital stay.

Introduction

Acute pancreatitis (AP) is a sudden inflammation of the pancreas characterized by activation of pancreatic enzymes to cause self-digestion of the pancreas. According to the revision of Atlanta definition and classifications that was brought about by International consensus in 2012,[1] the diagnosis of acute pancreatitis requires two of the following three features.[1] Abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back);[2] serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal; and[3] characteristic findings of acute pancreatitis on contrast-enhanced computed tomography (CECT) and less commonly magnetic resonance imaging (MRI) or transabdominal ultrasonography.

Acute pancreatitis is one of the commonest conditions that presents as a surgical emergency. Worldwide, the incidence ranges between 5 and 80 per 100,000 population. The pathophysiology of acute pancreatitis is characterized by a loss of

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intracellular and extracellular compartmentation, by an obstruction of pancreatic secretory transport and by an activation of pancreatic enzymes. In biliary acute pancreatitis, outflow obstruction with pancreatic duct hypertension and a toxic effect of bile salts contribute to disruption of pancreatic ductules, with subsequent loss of extracellular compartmentation. Alcohol induces functional alterations of plasma membranes and alters the balance between proteolytic enzymes and protease inhibitors, thus triggering enzyme activation, autodigestion and cell destruction. Once the disease has been initiated, the appearance of interstitial edema and inflammatory infiltration are the basic features of acute pancreatitis. The accumulation of polymorphonuclear granulocytes in pancreatic and extrapancreatic tissue, and the release of leukocyte enzymes play an essential role in the further progression of the disease and in the development of systemic complications. Activation of different cascade systems by proteolytic activity, and consumption of alpha 2-macroglobulin further characterize the severe clinical course of acute pancreatitis.

Previously, acute pancreatitis was categorized as mild or severe with mild acute pancreatitis characterized by interstitial edema of the gland and minimal organ dysfunction whereas severe acute pancreatitis was characterized by pancreatic necrosis, severe systemic inflammatory response and often multiorgan failure.[2] The recent modifications[1] classify it into two broad categories of interstitial edematous pancreatitis and necrotising pancreatitis. Furthermore, acute pancreatitis has been graded as mild, moderately severe and severe types. Mild acute pancreatitis is characterized by the absence of organ failure and the absence of local or systemic complications. Moderately severe acute pancreatitis is characterized by the presence of transient organ failure or local or systemic complications in the absence of persistent organ failure. Severe acute pancreatitis is characterized by persistent organ failure.

While it is true that a majority of the patients have mild and self-limiting disease, 20% to 30% of patients develop a severe disease that can progress to systemic inflammation and cause pancreatic necrosis, multiorgan failure, and potentially death. Mortality varies from 1% in mild cases to 20% to 50% in severe disease. About one-third of deaths occur in the early phase of attack, from multiple organ failure, while deaths occurring after first week of onset are due to septic complications. Most patients of acute pancreatitis recover without complications, the overall mortality rate of this illness is between 2 and 5%.

Hence, early, quick, and accurate risk assessment of acute pancreatitis patients would permit evidence-based early initiation of intensive care therapy for patients with severe acute pancreatitis to prevent adverse outcomes and allow treatment of mild acute pancreatitis in the wards. Therefore, a reliable risk stratification tool to predict the severity and prognosis of acute pancreatitis is of great clinical importance for the management of this disease in view of reducing both morbidity and mortality.

An ideal scoring system should promise an early, quick, simple, accurate, and reproducible description of disease severity. At present, a variety of scoring systems are available to evaluate the severity of AP, including Ranson criteria,[3] acute physiology and chronic health evaluation (APACHE II),[4] and several others. It is safe to say that their advantages withstanding, all the scoring systems have limitations. For instance, the main limitation of the Ranson criteria is that the evaluation cannot be completed until 48 hours following admission, which may lead to missing an early therapeutic window and increased mortality.

In 2008, Wu et al.[5] retrospectively developed a new scoring system, the bedside index for severity in acute pancreatitis (BISAP), to estimate the risk of in-hospital mortality in patients with acute pancreatitis.

The BISAP incorporates 5 variables:

1. Blood urea nitrogen >25 mg/dL (BUN)
2. Impaired mental status (Glasgow Coma Scale Score <15)
3. Systemic inflammatory response syndrome (Presence of more than 2 of following criteria)
   - Pulse > 90 beats per minute
   - Respiration > 20/min or $PaCO_2$ <32 mmHg
   - Temperature < 36°C (96.8°F) or >38°C (100.4°F)
   - WBC count > 12000 or <4000 cells/cubic mm or >10% immature neutrophil/band
4. Age > 60 years
5. Pleural effusion (chest X- ray or USG)

Each point on BISAP score is worth 1-point. There is steady increase in risk for mortality with the increasing number of points.

BISAP score is an uncomplicated, quick and reasonably reliable for assessment of disease severity on admission. Also, data for BISAP score is collected within the first 24 hr of hospitalization. The ability to stratify patients early in their course is a major step to improving future management strategies in acute pancreatitis.

The present study was designed to assess acute pancreatitis using both BISAP and CRP levels and to compare the two in order to ascertain which is a more effective predictor of severity of the disease. We aim to find a reliable, simple and accurate means of stratifying patients with acute pancreatitis.

Objectives of Study

It was an observational prospective study including cases that came to Vydehi Institute of Medical Sciences and Research Centre from 2012 to 2014

1. The primary objective of this study is to compare the ability of BISAP score with C-reactive protein analysis to predict the severity of acute pancreatitis and prognosis of the disease.
2. To assess the severity of acute pancreatitis and to take decision for further management (ICU admission or conservative)

Materials and Methods

Period of Study

This was a prospective study conducted in Vydehi Institute of Medical Sciences and Research Centre from November 2012 to April 2014.

Source of Data

The study included all patients who presented to the Department of General Surgery, VIMS & RC (during the above-mentioned time period) with features suggestive of acute pancreatitis as well as patients referred from other departments.

Inclusion Criteria

All patients admitted to VIMS & RC with clinical features or ultrasound findings suggestive of acute pancreatitis

Exclusion Criteria

i. All patients admitted with acute pancreatitis but also diagnosed with other conditions

ii. All patients diagnosed to have complications of acute pancreatitis

Thirty patients were selected for the study based on these inclusion and exclusion criteria.

Methods

- Written informed consent was taken from each of the selected patients.
- Relevant demographic data and complete history was collected from each patient.
- Each patient underwent the following investigations:
  - Complete blood picture
  - Blood urea nitrogen
  - C-reactive protein
  - Chest X-ray
  - USG abdomen
  - Serum amylase and lipase
  - Serum electrolytes
  - Renal function tests
  - Liver function tests

BISAP score was calculated for each patient within 24 hours of admission, based on individual variables as follows:

- BUN >25 mg/dL
- Impaired mental status (Glasgow Coma Scale Score <15)
- SIRS is defined as two or more of the following:
  - Temperature of <36°C (96.8°F) or >38°C (100.4°F)
  - Respiratory rate >20 breaths/min or $PaCO_2$ <32 mm Hg
  - Pulse > 90 beats/min
  - WBC < 4,000 or >12,000 cells/mm^3 or >10% immature bands
- Age >60 years
- Pleural effusion detected on imaging

One point was attributed to each component and total BISAP score was computed and documented.

- CT scan was performed in 9 out of 30 patients due to inadequate information after ultrasound imaging.
- Each patient was monitored during hospital stay, and the duration of hospital stay as well as ICU stay was documented.

Statistical Analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. The following assumptions on data is made,

Assumptions:

1. Dependent variables should be normally distributed,
2. Samples drawn from the population should be random, cases of the samples should be independent.

Student *t*-test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

Chi-square/Fisher's exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant figures

+ Suggestive significance (p-value: $0.05 < p < 0.10$)

* Moderately significant (p-value: $0.01 < p \leq 0.05$)

** Strongly significant (p-value: $p \leq 0.01$)

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables, etc.

Results

Age Distribution

Half of our patients (50%) were between 31 and 40

Table 1: Age distribution

Age in years	Number	Percentage (%)
<20	1	3.3
21–30	5	16.7
31–40	15	50.0
41–50	7	23.3
>50	2	6.7
Total	30	100.0

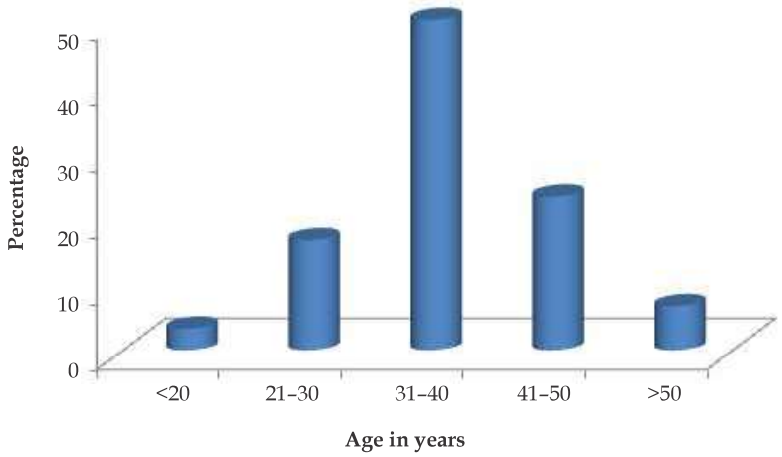

Fig. 1: Age distribution.

Table 2: Gender distribution

Gender	Number	Percentage (%)
Female	4	13.3
Male	26	86.7
Total	30	100.0

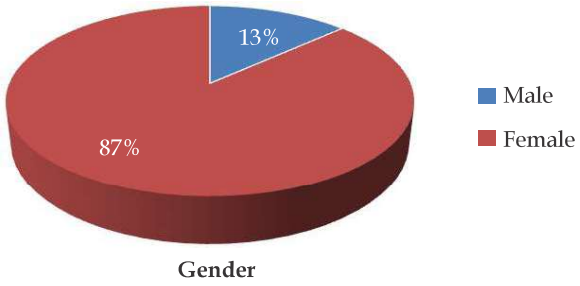

Fig. 2: Gender distribution.

years of age and only 3.35 were below 20. The mean age was 36.33 (SD ± 8.68) (Table 1 and Fig. 1).

Gender Distribution

We had 86.7% males and only 13.3% females in our study population (Table 2 and Fig. 2).

Symptomology of Patients

Out of the patients we studied, all (100%) presented with abdominal pain however only 60% complained of vomiting (Table 3).

Components of BISAP

As already mentioned, BISAP Score is calculated on the basis of following parameters (Table 4)

- Age above 60
- Blood urea nitrogen >25 mg/dL

Table 3: Symptomology of patients

Symptom	Present	Number	Absent	Number	Total
Pain	100%	30	0	0	100%
Vomiting	60%	18	40%	12	100%

Table 4: BISAP parameters

	Components	Number	Percentage (%)
AGE > 60 years	> 60 years	0	0.0
	< 60 years	30	100.0
BUN	>25 mg/dL	7	23.3
	<25 mg/dL	23	76.7
GCS	15/15	24	80.0
	<15/15	6	20.0
SIRS	Present	30	100.0
	Absent	0	0.0
Pleural effusion	Present	11	36.7
	Absent	19	63.3

- Altered mental status (GCS <15)
- Presence of pleural effusion
- Presence of SIRS having two criteria at least

BISAP Scores

BISAP scores computed were as follows (Table 5 and Fig. 3):

Table 5: BISAP scores

BISAP	Number	Percentage (%)
1–2	23	76.7
3	7	23.3
Total	30	100.0

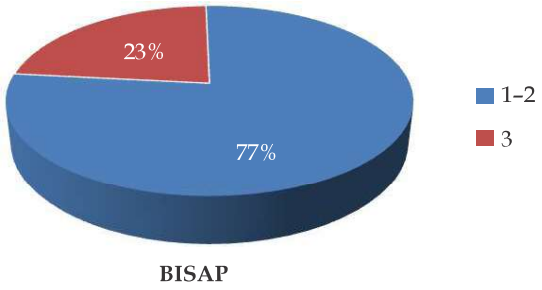

Fig. 3: BISAP scores.

Table 6: Amylase levels

Amylase (IN IU/L)	Number	Percentage (%)
<100	9	30.0
101–200	5	20.0
201–300	4	13.3
301–400	2	6.7
401–500	3	10.0
>500	6	20.0
Total	30	100.0

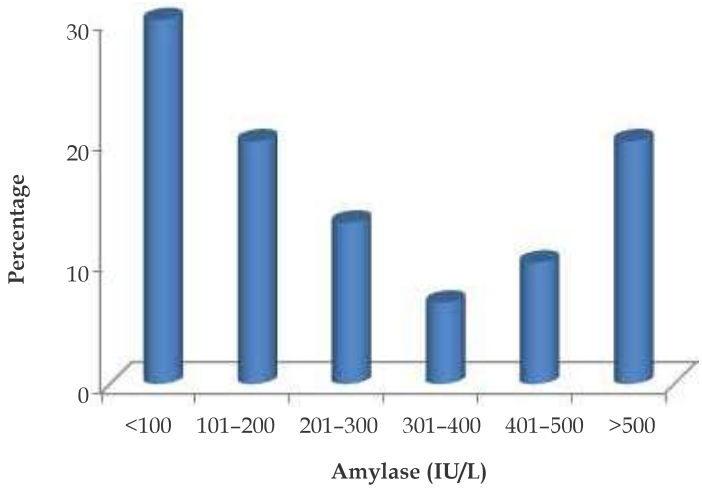

Fig. 4: Amylase levels.

Amylase Levels

The amylase levels had a Mean ± SD: of 391.33 ± 580.68. Thirty percent patients had serum amylase levels less than 100 IU/L (Table 6 and Fig. 4).

Lipase Levels

The lipase levels had a Mean ± SD: of 91.33 ± 580.68. About 43.3% patients had a low lipase level of below 100 IU/L (Table 7 and Fig. 5).

Table 7: Lipase levels

Lipase (IU/L)	Number	Percentage (%)
<100	13	43.3
101–500	9	30.0
>500	8	26.7
Total	30	100.0

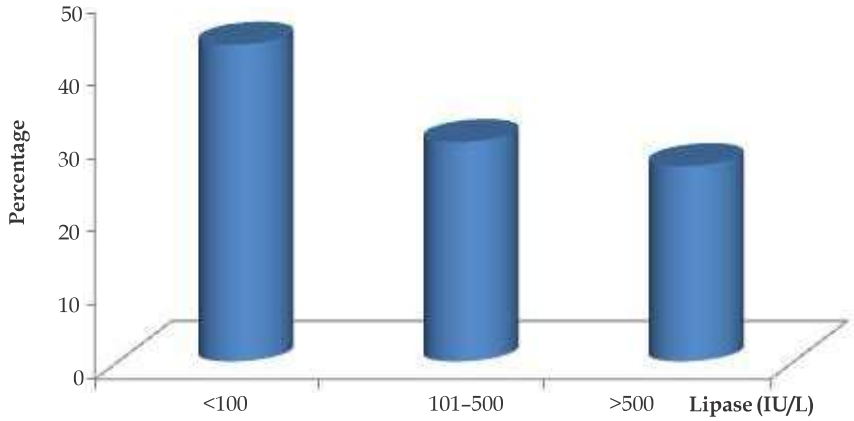

Fig. 5: Lipase levels.

Table 8: CRP Levels

CRP Levels (in mg/L)	Number	Percentage (%)
<150	10	33.3
>150	20	66.7
Total	30	100.0

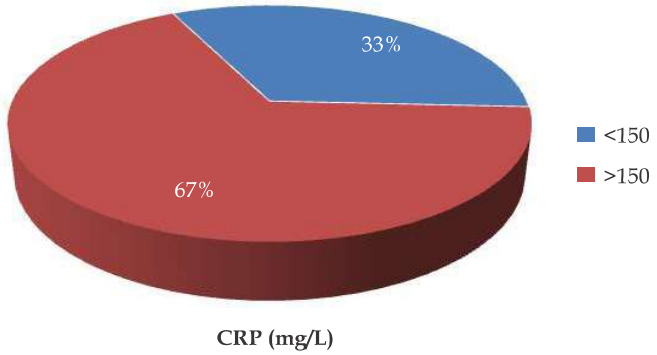

Fig 6: CRP levels.

CRP Levels

A CRP level of above 150 mg/L was considered significant. 66.7% of our patients had an elevated CRP (Table 8 and Fig. 6).

ICU Stay

Thirty percent of patients had severe disease which required stay in the intensive care unit (Fig. 7).

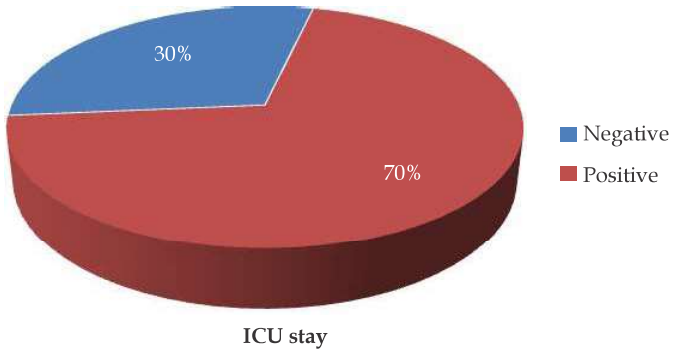

Fig. 7: ICU stay.

Table 9: Length of hospital stay

Hospital stay	Number	%
1–2	3	10.0
3–7	11	36.7
8–14	8	26.7
15–21	5	16.7
22–28	3	10.0
Total	30	100.0

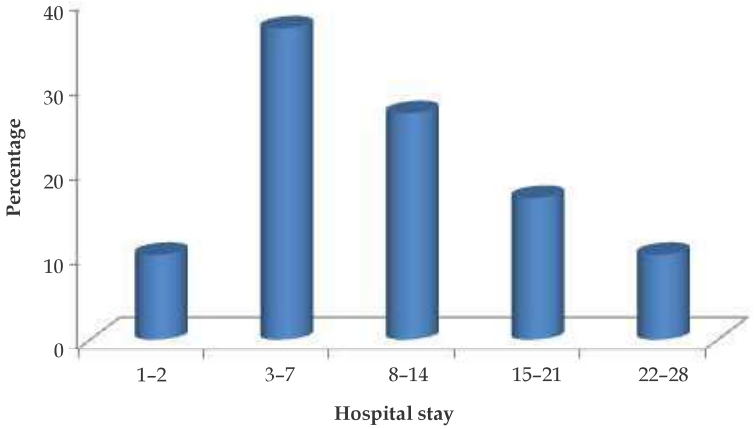

Fig. 8: Length of hospital stay.

Hospital Stay

The length of hospital stay among our patients varied from 1 day to 28 days. Mean duration of hospital stay was 10.10 days (with SD of 7.21) (Table 9 and Fig. 8).

Correlation of BISAP and CRP

While applying Fisher's exact test on BISAP scores and CRP levels, *p*-value was 0.064 which was significant. That is, a higher BISAP score was seen with elevated levels of CRP (Table 10).

Table 10: BISAP and CRP correlation

BISAP	(mg/L)		Total
	<150	>150	
1–2	100	65	76.7
3	0	35	23.3
	1–2	3	100.0
<150	100	0	p = 0.064 +, significant, Fisher's exact test
>150	65	35	

Table 11: Correlation of CRP levels with hospital stay

Hospital stay (days)	(mg/L)		Total
	<150	>150	
1–2	30	0	10.0
3–7	50	30	36.7
8–14	0	40	26.7
15–21	20	15	16.7
22–28	0	15	10.0
Total	100	100	100.0

p = 0.009**, significant, Fisher's exact test

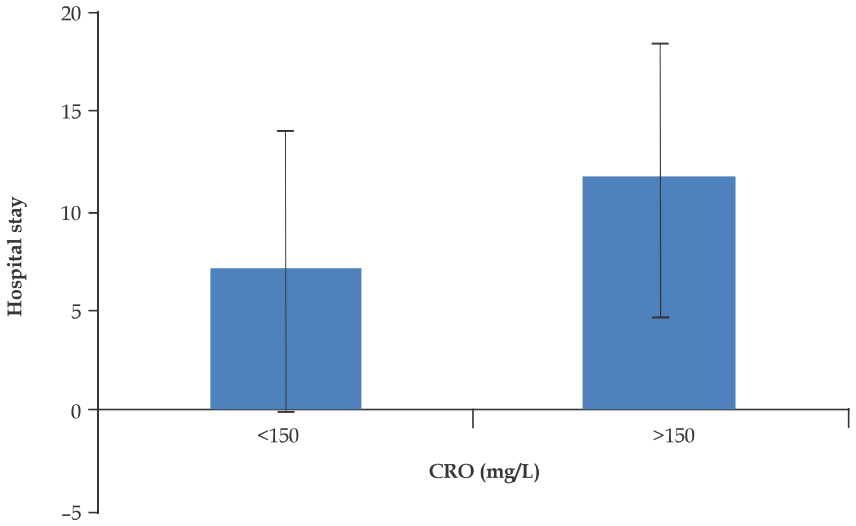

Fig. 9: Correlation of CRP levels with hospital stay.

CRP Levels and HospitaL Stay

An elevated CRP level was found to have a statistically significant relation (p = 0.009) to length of patient's stay in hospital. That is, a patient with elevated CRP was more likely to stay longer in the hospital than one with a normal CRP (Table 11 and Fig. 9).

CRP Levels and ICU Stay

The relationship between elevated CRP levels and ICU stay was not statistically significant (Table 12 and Fig.10).

Table 12: Correlation of CRP levels with ICU Stay

ICU stay	(mg/L)		Total		
	<150	>150		Negative	Positive
Negative	80	65	<150	80	20
Positive	20	35	>150	65	35
Total	100	100	100		

p = 0.675, Not significant, Fisher's exact test

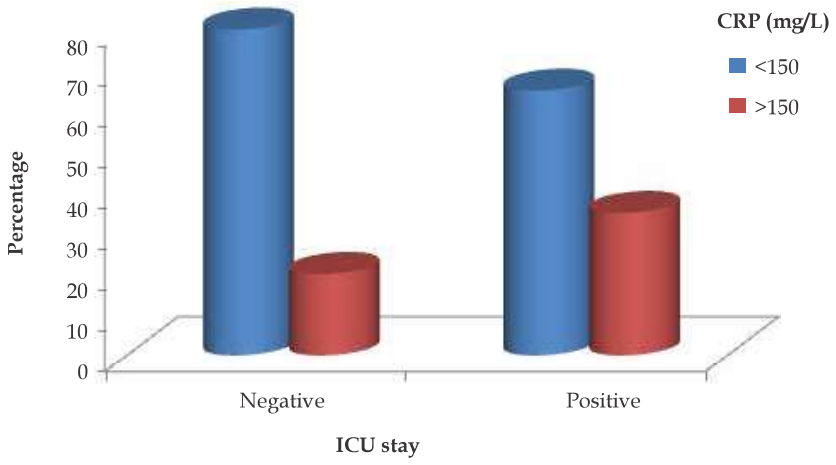

Fig. 10: Correlation of CRP levels with ICU stay.

Table 13: Correlation of BISAP scores with ICU stay

ICU stay	BISAP		Total
	Low BISAP	High BISAP	
Negative	82.6	28.6	70
Positive	17.4	71.4	30
	Negative	Positive	100
Low BISAP	82.6	17.4	
High BISAP	28.6	71.4	

$p = 0.014$*, significant, chi-square test

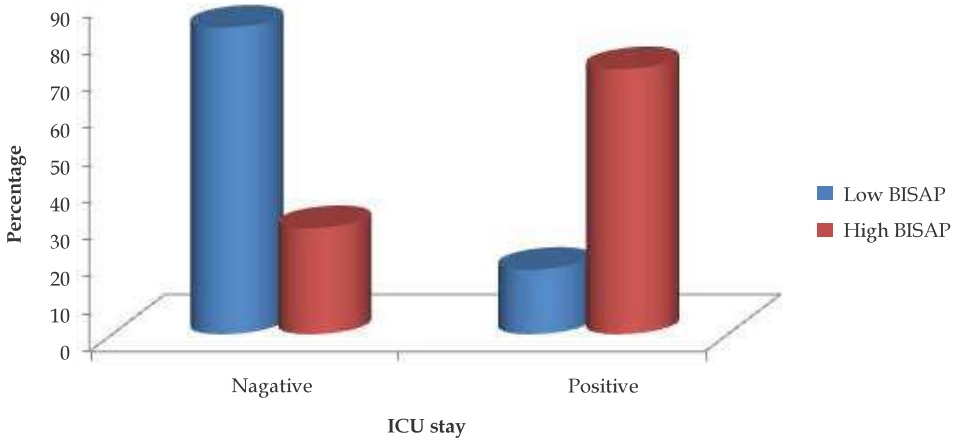

Fig. 11: Correlation of BISAP scores with ICU stay.

Table 14: Hospital stay with the grades of BISAP

Hospital stay	BISAP		Total
	Low BISAP	High BISAP	
1–2	3 (13%)	0 (0%)	3 (10%)
3–7	11 (47.8%)	0 (0%)	11 (36.7%)
8–14	5 (21.7%)	3 (42.9%)	8 (26.7%)
15–21	4 (17.4%)	1 (14.3%)	5 (16.7%)
22–28	0 (0%)	3 (42.9%)	3 (10%)
Total	23 (100%)	7 (100%)	30 (100%)

$p = 0.003$**, significant, Fisher's exact test

BISAP Scores and ICU Stay

When chi-square test was applied on collected data, we found that BISAP scores had a statistically significant relationship with ICU stay (p-value: 0.014). That is, patients with higher BISAP score were more likely to need ICU (Table 13 and Fig. 11).

On applying Student t test, it was found that BISAP score had a positive correlation with length of hospital stay ($p = 0.003$). That is, higher the BISAP score, longer was the stay in hospital (Table 14).

Discussion

We studied a total of 30 patients who presented with acute pancreatitis to our hospital during the period of study. In our study, 50% of the patients were between 31 and 40 years of age. The mean age was 36.33 (SD ± 8.68). Like other previous studies, it was seen that acute pancreatitis can affect people of all ages. Our study had 86.7% males and 13.3% females. This is in accordance to worldwide epidemiology in that pancreatitis is more common in males than in females.[6,7]

The main symptoms among our study population was pain abdomen (100%) which is a prerequisite for diagnosis of acute pancreatitis[1] and vomiting (in 60%).

All patients underwent tests to measure serum levels of pancreatic amylase and pancreatic lipase enzymes. The amylase levels had a Mean ± SD: of 391.33 ± 580.68. This mean was elevated but 30% patients had serum amylase levels less than 100 IU/L. This illustrates the fact that serum amylase can be normal in cases of pancreatitis and hence is not a reliable predictor of the disease. Similarly, the lipase levels had a Mean ± SD: of 91.33 ± 580.68. About 43.3% patients had a low lipase level of below 100 IU/L. Serum lipase is considered a more reliable diagnostic marker of acute pancreatitis than serum amylase. In patients with delayed presentation, its activity remains increased for longer periods (up to 8–14 days), and it has an increased sensitivity in acute alcoholic pancreatitis.

As there is no single laboratory test that can be used to diagnose acute pancreatitis, multiple scoring systems have been used to assess its severity. Commonest among these are Ranson's score, Glasgow Coma Scale and APACHE II score. As discussed earlier in detail earlier, these tests have their own disadvantages like delaying diagnosis to 48 hours beyond admission and complexity of the scoring itself.

BISAP score was chosen by us as it's a relatively new test and only limited data is available regarding its efficacy. It's easy to apply and can be used at the time of admission itself. Different cut-offs have been used with BISAP score with varying results. Vikesh Singh and colleagues[8] used a cut-off value at 3 that yielded a comparable sensitivity (38.6%), specificity (93.2%), PPV (59.1%), and NPV (85.6%). A study by Papachristou et al.[9] reported that with the cut-off value set at 3, BISAP score had a sensitivity of 37.5%, a specificity of 92.4%, a PPV of 57.7%, and an NPV of 84.3% in predicting SAP. However, the best cut-off value calculated using Youden index for BISAP was 2, and using this cut-off value yielded a sensitivity of 61.4%, a specificity of 83.1%, a PPV of 48.1%, and an NPV of 89.4%. We used a cut-off of 3 in our study. 23.3% of our patients had a score of 3. The rest had a score of 1 or 2. Wu et al.[5] who designed the scoring system predict a mortality of less than 3.6%, 1.6% and 0.4% for BISAP scores of 3, 2 and 1 respectively. The low scores of our patients and the absence of mortality in our study are thus in accordance with the previous study.

We also used C-reactive protein or CRP as a comparative index for assessing acute pancreatitis. A CRP level of above 150 mg/L was considered significant and 66.7% of our patients had an elevated CRP. Imamura et al.[10] studied levels of CRP in 20 patients and concluded that it is a useful indicator of severity of disease in early phase of acute pancreatitis.

On statistical analysis, we found a positive correlation between BISAP scores and CRP values (p-value 0.064). A patient with higher BISAP score had a higher value of CRP. Since in our search of literature, we found no similar study comparing these two indices, we cannot corroborate this finding.

All our patients had mild to moderate disease. There was no incidence of complications and no mortality during our study. We assessed severity of disease hence based on length of stay in hospital and the need for stay in the intensive care unit. The lengths of hospital stay among our patients varied from 1 day to 28 days. Mean duration of hospital stay was 10.10 days (with SD of 7.21). Bradley et al.[2] reported average length of hospital stay for uncomplicated pancreatitis to be 5–14 days.

We found that both an elevated CRP level and an increased BISAP score were found to have a statistically significant relation (p = 0.009 and p = 0.0002 respectively) to length of patient's stay in hospital. That is, a patient with elevated CRP or higher BISAP score was more likely to stay longer in the hospital.

We also studied correlation of the predictors to ICU stay. Thirty percent of our patients had disease severe enough to validate an ICU stay. Here, we found that BISAP scores had a statistically significant relationship with ICU stay (p-value: 0.014). However, CRP levels had no relationship with ICU stay. Again due to the novelty of our study, we have no previous reports to compare.

To conclude, BISAP score is a positive predictor of increased length of hospital stay as well as need for ICU care. However, CRP cannot be used to predict need of intensive care in acute pancreatitis. Hence, BISAP is a better predictor of severity of pancreatitis compared to CRP.

Limitations of our Study

- Due to paucity of time during this dissertation, we studied only a small sample size. Further studies with larger sample sizes need to be conducted in this area.
- We studied only uncomplicated cases of acute pancreatitis, studies including complications may yield varying results.

Summary and Conclusion

This was a prospective observational study of 30 cases of acute pancreatitis in Vydehi institute of medical college and research centre from November 2012 to April 2014. We aimed to compare BISAP score and CRP levels as indicators of severity of acute pancreatitis.

Among the 30 cases we studied, 4 (13.3%) were females and 26 (86.7%) were males. The ages ranged from 17 to 60 with a mean age of 36.33 (SD: 8.68). 23 patients (76.7%) had a BISAP score of 1 or 2 and the remaining 7 (13.3%) had a score of 3. Mean CRP level was 484.24 mg/L with 10 patients having normal and 20 (66.7%) having elevated CRP levels. Thirty percent patients required ICU stay and mean duration of hospital stay was 10.10 days (with SD of 7.21). BISAP and CRP levels had a positive correlation (p-value 0.064). Both BISAP and CRP levels had a positive correlation with length of hospital stay (p-0.001 and p–0.009 respectively). Only BISAP had a positive correlation with ICU stay (p–0.014).

In conclusion, the demographic data of age, sex and symptomatology in our study was comparable to other studies. We found that BISAP is a better predictor of severity of acute pancreatitis compared to CRP levels. Larger studies will be needed to further consolidate our findings, but it is safe to say that BISAP has the advantage of simplicity and speed over more traditional scoring systems. It is a useful means of predicting severity in acute pancreatitis in comparison to individual laboratory parameters like amylase, lipase and CRP levels. We confirm BISAP score to be an accurate means for risk stratification and prognostic prediction in our patients.

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