

Correlation between BISAP score and D-dimer level on their predictive ability to determine the severity of acute pancreatitis at 24-hours of hospital admission: an observational study



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ABSTRACT

Background: Early prediction of severity of acute pancreatitis (AP) is important for management of AP patients with escalation of care and aggressive therapy which can reduce complications. Bedside index of severity in AP (BISAP) score is helpful in early diagnosis of severe AP. D-dimer, a biomarker of secondary fibrinolysis may be helpful in predicting the severity of pancreatitis. **Aims and Objectives:** The objective of this study was to evaluate the two scoring systems - the BISAP score and D-dimer in early prediction (within 24 h) on the severity of AP and to analyze how D-dimer correlates with BISAP score. **Materials and Methods:** Seventy-five patients, aged 18–70 years, suffering from AP due to any cause were included for this prospective, observational study. Within 24 h of admission D-dimer was estimated and BISAP score was calculated. The severity was assessed based on D-dimer level and BISAP scoring systems within 24 h of hospital admission and data were tabulated for analysis. The D-dimer level > 2.5 mg/L was considered to be suggestive of severe pancreatitis. The BISAP score > 2 in first 24 h was defined as predictive of severe pancreatitis. Spearman rank correlation was used for an analysis of the association between two set of data (BISAP scores and d-dimer levels) and thus to measure the strength and direction of the relationship between the two variables. **Results:** In the present study, 37.3% of the patients had D-dimer ≤ 2.5 mg/L and 62.7% had D-dimer > 2.5 mg/L' on calculating the Pearson's correlation on the ranked values of the data (BISAP scores and D-dimer levels), the correlation coefficient (Spearman's Rho, designated as "rs") was found to be 0.406 which indicates about moderate positive correlation. **Conclusion:** D-dimer testing can be used as an alternative test to predict the severity of AP. It shows a moderate correlation with BISAP scoring.

Key words: Acute pancreatitis; BISAP score; Correlation coefficient; D-dimer; Severe acute pancreatitis

INTRODUCTION

Acute pancreatitis (AP) is a commonly encountered clinical problem with an incidence of around 2.3%.¹ Although most of the patients with AP are mild and recover without any sequelae, about 10–20% of patients may have a severe

attack of AP with necrosis and multi-organ failure. Patients with severe AP are associated with systemic inflammatory response syndrome (SIRS) and typically have a longer hospital stay. The management of severe pancreatitis is a challenge with a mortality of 20%.²⁻⁴ The management of AP depends on its severity.^{4,5} Therefore, it is necessary to

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stratify AP as early as possible and to predict the severity of the disease because early escalation of care and aggressive therapy may prevent complications and adverse outcomes of AP in high-risk patients.^{6,7}

Prior assessment of severity is one of the most important issues in the management of AP. Severe biochemical markers and complex scoring systems are in use to predict the severity of AP. Some scores such as Acute Physiology and Chronic Health Evaluation II scoring system are multifactorial and inconvenient or impractical for daily use.⁸ Although the Ranson's criteria are probably the most commonly used scoring system, it has the limitation that the evaluation cannot be completed until 48 h following admission. This may lead to missing the potential early treatment (critical hours) and thereby may increase mortality.⁸ Thus, each of these scoring systems has their own limitations such as complexity of the scoring system, low sensitivity or specificity, and inability to obtain a final score until 48 h after admission.⁸

The ideal scoring system should provide the advantage of simple, quick to calculate, early prediction of disease severity.⁹ Moreover, it should be accurate and reproducible.

In 2008, Wu et al.,¹⁰ proposed - Bedside Index of Severity in AP (BISAP), a new simplified scoring system for the early prediction of the severity of AP. BISAP scoring system contains data that can be evaluated at the time of admission in the bedside which are accurate in predicting patients' outcome within 24 h.¹¹ BISAP score help in early diagnosis of severe AP, preventing complications and overall mortality can be reduced. In AP, the release and activation of pro-inflammatory cytokines results in hypercoagulation and microvascular thrombosis and can lead to organ dysfunction.¹² D-dimer, a biomarker of coagulation and a specific indicator of secondary fibrinolysis, can be helpful in predicting the severity of pancreatitis.^{13,14}

Aims and objectives

The objective of this study was to evaluate the efficacy of the two scoring systems -- the BISAP score and D-dimer level in making prediction about the severity of acute pancreatitis at 24-hours of hospital admission and to determine the correlation between BISAP score and D-dimer.

MATERIALS AND METHODS

This was a hospital-based, prospective, and observational study conducted among patients admitted in surgical unit of Nil Ratan Sircar Medical College and Hospital, a Government Medical College. This study was conducted

after approval by the institutional Ethical committee and after obtaining written informed consent from patient or their legal guardian, depending on the situation.

Considering the average case load (as per the hospital records over past 3 years) and characteristics of the geographical location and population, we intended to have nonprobability sample by recruiting 75 patients with AP for the present study. It was a non-random purposive sampling to match the objective of the present study. The study spanned over around one and half year (approximately from the January 2021 to June 2022) till the sample size of 75 is reached. It was an observational study and, hence, no control was required.

Inclusion criteria

The study population (n=75) was patients aged 18–70 years, and diagnosed as suffering from AP, based on the presence of two of the following three features - (i) typical signs and symptoms including abdominal tension or specific peritonitis, (ii) levels up to 3 times higher than the upper limit of normal values of pancreatic amylase and lipase, and (iii) imaging showing characteristics findings of AP.

Exclusion criteria

The following criteria were excluded from the study:

- Pre-hospital interval more than 24 h
- Patients suffering from chronic pancreatitis and recurrent pancreatitis
- Age <18 years or more than 70 years
- Patients suffering from cancer, cirrhosis, or thrombotic disease
- Patients on anticoagulant drug use
- Patients having recent infection or any history of organ failure
- Pregnancy.

Study tools were: (i) History and clinical examination, (ii) laboratory investigations of amylase, lipase, D-dimer, BUN, leukocyte count, and (iii) radiological investigations: Chest X-ray, and CECT of abdomen. The severity of pancreatitis was assessed and the desired early treatment started and subsequently, the follow-up done.

Within 24 h of hospital admission, the BISAP score (Table 1) was calculated and the D-dimer level was estimated. The BISAP score >2 (score 3 or more) in first 24 h was considered as predictive of severe pancreatitis. The D-dimer level >2.5 mg/L was considered to be suggestive of severe pancreatitis. The BISAP scoring and the D-dimer level as documented within 24 h of hospital admission were tabulated for analysis to find out any correlation between them (Primary outcome).

BISAP scoring system comprises five variables which can be easily obtained and calculated within 24 h of admission: (i) Blood urea nitrogen >25 mg/dl, (ii) impaired mental status, (iii) SIRS, (iv) age more than 60 year, and (v) Pleural effusion on chest X-ray. Scoring point 1 is assigned to each variable if they are present within 24 h of presentation.

The altered or impaired mental status was defined as having disorientation, lethargy, somnolence, coma, or stupor on clinical examination. The presence of SIRS is diagnosed by presence of any two of criteria: (i) Temperature (<36°C or >38°C), (ii) pulse >90/min, (iii) respiratory rate >20 or PaCO₂ <32 mmHg, and (iv) WBC >12000/mm³ or <4000/mm³ or >10% bands.

Although, the variables were re-assessed after 72 h for treatment purpose, it was not considered for analysis. The study was designed mainly to analyze the two scoring systems- the BISAP and D-dimer to find any correlation. Reassessment also helped treatment purpose to decide whether the organ failure was transient (for <48 h) or persistent (lasting >48 h).

To access the organ failure in AP, modified Marshall scoring system was used (Table 2). In the 2012 revised Atlanta classification of AP, it is suggested that 3 organ systems such as respiratory, cardiovascular, and renal should be assessed to define organ failure.¹⁵ Using the modified Marshall scoring system, organ failure is defined as a score of ≥2 for one of these three organ systems.¹⁶

Statistical analysis

The data were tabulated in Microsoft excel and analyzed with SPSS version 22.0. Data had been summarized as count and proportions for categorical variables and mean±standard deviation for numerical variables. Spearman rank correlation was used for an analysis of

the association between two set of data (BISAP scores and d-dimer levels) and thus to measure the strength and direction of the relationship between the two variables. For this study, P≤0.05 was considered for statistically significant. The results have been presented with appropriate tables and diagrams.

RESULTS

The data from all 50 patients were available for analysis.

Majority of the patients were found to be of the age group 36–45 years and 56–65 years. More than two thirds of the patients diagnosed with pancreatitis were male patients and the rest were female. Of all the patients admitted with AP 40% had presence of gall stone disease (Table 3).

The clinical parameters and laboratory tests that were obtained after admission or after 48 h are presented in Table 4.

About 20% of patients had a BISAP score of 3 and more, which predicted the possibility of development of severe disease. About 37.3% of the patients had D-dimer ≤2.5 mg/L and 62.7% had D-dimer>2.5 mg/L (Table 5).

Out of all the patients diagnosed as suffering from AP ten patients had mild to severe hepatic dysfunction, nine patients developed renal dysfunction, five patients had pulmonary dysfunction and six patients had cardiac dysfunctions. Most of the patients with hepatic dysfunction had transient dysfunction and did not progress to persistent organ failure. In the present study, 64 patients (85.3%) did not suffer any complications. Only one patient developed pseudocyst formation and had to be operated later on and two patients developed recurrent attack of AP in the next 3 months following discharge and had to be readmitted for conservative management (Table 5).

On calculating the Pearson's correlation on the ranked values of the data (BISAP scores and D-dimer levels), the correlation coefficient (Spearman's Rho, henceforth, designated as "rs") was found to be 0.406 (P=0.0003, DF=73, n=75, t-statistics = 3.796). The value of "rs" measures the strength and direction of the relationship between two variables. It can vary from -1 (perfect negative

Table 1: BISAP scoring system

Parameters	Score 0	Score 1
Blood urea nitrogen	<25 mg/dl	>25 mg/dl
Impaired mental status	Absent	Present
SIRS	Absent	Present
Age	<60 years	>60 years
Pleural effusion	Absent	Present

SIRS: Systemic inflammatory response syndrome, BISAP: Bedside index of severity in acute pancreatitis

Table 2: Modified Marshal scoring system for organ dysfunction

System	Score 0	Score 1	Score 2	Score 3	Score 4
Respiratory (PaO ₂ /FiO ₂)	>400	301–400	201–300	101–200	≤100
Renal (Serum creatinine, mg/dl)	<1.4	1.4–1.8	1.9–3.6	3.6–4.9	>4.9
Cardiovascular (SBP, mm Hg)	>90	<90, responsive to fluids	<90, not responsive to fluids	<90, pH<7.3	<90, pH<7.2

Table 3: Demographic parameters

Characteristics	Category	Number (Proportion)
Sex (%)	Male	51 (68)
	Female	24 (32)
Male : Female ratio 2.1		
Age groups (%)	15–25	13 (17.33)
	26–35	14 (18.67)
	36–45	17 (22.67)
	46–55	14 (18.67)
	56–65	17 (22.67)
	Recurrent attack of pancreatitis	2 (2.7)

The data from total 75 patients were available for analysis. It is presented as number of patients (proportions). The mean age (years) was calculated as 41.88 ± 13.26

Table 4: Mean values of clinical parameters and laboratory tests

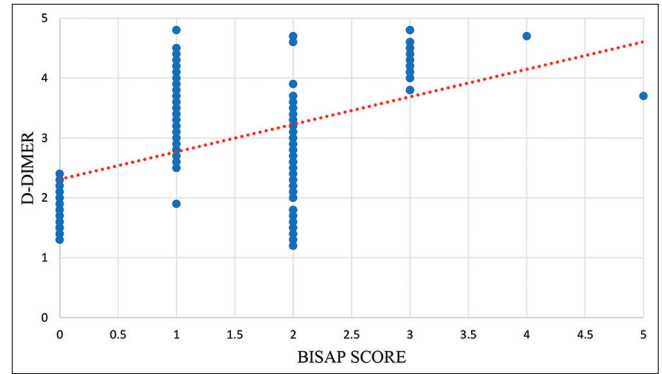
Parameters	Mean \pm SD
Blood urea nitrogen on admission (mg/dl)	26.8 \pm 9.1
Blood urea nitrogen after 48 h (mg/dl)	25.1 \pm 7.8
Mental status (GCS out of 15)	11.8 \pm 2.0
TLC (/mm ³)	16947.7 \pm 5325.2
LDH (U/L)	482.16 \pm 207.98
AST (U/L)	364.47 \pm 111.48
Random blood glucose (mg/dl)	295.61 \pm 120.34
Hematocrit drop (%)	8.39 \pm 2.35
Serum calcium (mg/dl)	8.27 \pm 0.97
PaO ₂ (%)	75.60 \pm 14.83
Base deficit (mEq/L)	4.07 \pm 1.13
Fluid loss (L)	5.79 \pm 1.76

Table 5: Clinical parameters - different scores and outcomes

Characteristics	Category	Number (proportion) (%)
Etiology	Gall stone disease	40
	Alcoholic	60
BISAP scores	0–2 (mild)	64 (85.3)
	3–5 (severe)	11 (14.7)
D-dimer level	\leq 2.5 mg/L	28 (37.3)
	$>$ 2.5 mg/L (severe)	47 (62.7)
Signs of SIRS	Pleural effusion	15 (20)
	Hepatic	9 (12)
	Renal	9 (12)
Organ dysfunction	Pulmonary	5 (6.7)
	Cardiac	6 (8)
	Pseudocyst formation	1 (1.3)
Complications	Recurrent attack of pancreatitis	2 (2.7)

The data from total 75 patients were available for analysis. It is presented as number of patients (proportions). The mean age (years) was calculated as 41.88 ± 13.26

correlation) through 0 (no correlation) to +1 (perfect positive correlation).¹⁷ Strong positive linear relationships have “rs” values closer to +1 and strong negative linear relationships have “rs” values closer to –1. In the present study, the $rs=0.406$, which indicates about moderate positive correlation.¹⁸

**Figure 1: The correlation between BISAP score and D-dimer**

The correlation between BISAP score and D-dimer is found to be positive and with moderate strength. When the observed data about BISAP score and D-dimer level was plotted graphically, neither a perfect linear relationship (strong correlation) exists between them nor they are diffusely scattered (No correlation). Moreover, they are not located at opposite poles with a wide dispersion. Hence, visual impression also indicates about a moderate correlation between them (Fig. 1).

DISCUSSION

AP is an inflammatory disease that varies from self-limiting condition to rapidly deteriorating disease and poses challenges in clinical practice. Most patients with AP have a mild form of the disease and respond to supportive treatment. However, approximately 20–30% patients suffer life-threatening disease with about 15% mortality rate.¹⁹ Accurate prediction of the disease severity early on in its course is important for prioritization of cases to offer timely escalation of therapy. Although this triage can reduce mortality and morbidity, remains to be a daunting task.²⁰ Local pancreatic complications and extra-pancreatic organ failure determine the severity of AP as per revised Atlanta classification.¹⁵ However, organ failure remains to be a stronger predictor of mortality than local complications (peri-pancreatic fluid collections and necrosis) and influences the length of hospital stay.^{15,21,22}

Multiple scoring systems have been developed based on clinical, biochemical, and imaging assessments in an attempt to predict the severity and prognosis of AP.^{20,23,24} Most of the models are based on data available from two points in time (i.e., at admission and 48 h), which makes them impractical to use in a triage setting. There is still no highly sensitive or specific test or severity scoring that can accurately measure the prognosis at admission. No scoring system has consistently proven to be superior than others.^{25–28} A lack of consensus still prevails as to which scoring system is the best at predicting the prognosis and

final outcome of AP.²⁸ This appears to be a never-ending quest.²⁰ The present study tries to evaluate about how BISAP score and D-dimer correlates about the predictive ability regarding prognosis and outcome in patients of AP.

In the present study, out of total 75 patients 14.7% developed severe AP (SAP) whereas 85.3% developed mild pancreatitis. The proportions of AP patients turning to severe course and requiring treatment in ICU is variedly reported in literature ranging from 5% to 10%^{7,28} to as high as 20–30%.¹⁹ Studies^{28–31} have shown highly variable incidence of organ failure in SAP ranging from 63.5 to 90.3 %, single organ failure in 24.7–37%, multiple organ failure in 27–65.6 %. Lapauw *et al.*,³¹ reported that in their study population (n=72), respiratory failure was the most common (56%), followed by cardiovascular failure (51%), renal failure (43%), hepatic failure (21%), and coagulopathy in 19% of patients. In another study (n=74), the intra-abdominal hypertension and acute compartment syndrome occurred in 59% and 27% of patients with AP.³² ACS is found to be one of the most important causes of significant morbidity and mortality in AP patients.³²

In the present study, the BISAP score >2 is used as cut of value to indicate about severity of pancreatitis. The BISAP score at a cut-off of ≥ 3 has been observed to have a moderate sensitivity and high specificity for predicting mortality and severe AP.³³ In comparison, at a cutoff of ≥ 2 , the sensitivity increased while the specificity is decreased.

In the present study, all patients who were predicted to develop severe pancreatitis due to persistence or progression of organ failure during 1st week actually developed severe pancreatitis later on. For this study, the BISAP score acted as an early marker for organ failure. Furthermore, all the patients who did not develop severe pancreatitis were correctly predicted as mild pancreatitis by the absence of persistent/progressive organ failure during 1st week. Resolution of organ failure that occurred within 48 h had a good prognosis. In contrast, progressively worsening and persistent organ dysfunction during the 1st week was associated with death in more than half of the patients and should be used as a marker for mortality and local complication.

In the present study, 37.3% of the patients had D-dimer ≤ 2.5 mg/L and 62.7% had D-dimer > 2.5 mg/L and a moderate positive correlation was found between BISAP score and D-dimer. In the present study, AP patients with high D-dimer levels had a higher incidence of pancreatic necrosis and organ failure than did patients with normal D-dimer levels. Wan *et al.*,¹⁴ in 2019, reported that assessing D-dimer levels at admission can be useful for risk stratification and prediction of outcomes in AP. In a

recent study,³⁴ the D-dimer level was found to be related with the triglyceride to high density lipoprotein-C ratio (TG/HDL-C). D-dimer and TG/HDL-C ratio could distinguish between mild and non-mild AP.³⁴

At the onset of AP, the abnormal activation of pancreatic enzymes results in inflammation, which induces thrombosis of the pancreas itself and further aggravates the injury.³⁵ The severity of AP bears a close association with degree of inflammation and thrombosis.³⁶ Besides the thrombosis involving the pancreas itself, the coronary venous thrombosis and splanchnic vein thrombosis has also been reported.³⁷ D-dimer, a marker fibrinolysis, can be useful in the rapid assessment of thrombotic activity. Thus, it may play an important role in the assessment of AP severity by monitoring pancreatic and extra-pancreatic thrombosis. It can safely exclude patients with suspected venous thromboembolism based on the clinical decision.^{38,39}

D-dimer has been widely used in clinical settings because it is convenient and stable. However, wide variation in the D-dimer operating characteristics and assay techniques translates in to the fact that the results of studies that used one assay cannot be extrapolated to studies that used another assay. This certainly limits the usefulness of multicenter studies. Much work remains to be done to standardize the performance and reporting of D-dimer assays. Caution should be exercised to translate the results of D-dimer studies into clinical practice.

Limitations of the study

The small sample size limits a more extensive evaluation of the ability of the BISAP score to predict organ failure and pancreatic necrosis using discrimination analysis. As the study was primarily designed to assess the two predictors at 24 h and to analyze correlation between them, the long-term assessment of morbidity and mortality could not be done. The Glasgow Coma Scale assessment used for the evaluation of impaired mental status is subject to inter-observer variation.

CONCLUSION

D-dimer level and BISAP score assessed at 24 h of hospital admission shows a moderate positive correlation between them regarding predictive capability. Along with BISAP scoring, measuring D-dimer level can act as an alternative test to predict the severity of AP.

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