ORIGINAL RESEARCH PAPER

Surgery

STUDY OF BISAP SCORE AS A PREDICTOR OF MORTALITY IN ACUTE PANCREATITIS OF ADULT PATIENTS

KEY WORDS:

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INTRODUCTION:

Moynihan described acute pancreatitis as ***"The most terrible of all the calamities that occur in connection with abdominal viscera"***

Acute pancreatitis is defined as an inflammatory process of the pancreas with possible peripancreatic tissue and multi-organ involvement inducing multi-organ dysfunction syndrome (MODS) with an increased mortality rate.The Incidence and etiology of AP varies with geographical location. In India most common etiology for AP is Alcohol followed by Gall stone [1,2]. Idiopathic Pancreatitis is third most common. The underlying mechanism of injury in pancreatitis is thought to be premature activation of pancreatic enzymes within the pancreas, leading to a process of auto digestion. Once the cellular injury has been initiated, the inflammatory process can lead to pancreatic edema, hemorrhage and, eventually necrosis. As inflammatory mediators are released into circulation, systemic complications can arise.

In most cases, AP is mild, self-limiting, and requires no special treatment; however, 20% to 30% of patients develop a severe disease that can progress to systemic inflammation and cause pancreatic necrosis, multi organ failure, prolonged hospital stay and potentially death[3]. Mortality in AP has a bimodal distribution [4].

PURPOSE OF MY STUDY:

Early, quick, and accurate risk stratification of AP patients would permit evidence-based early initiation of intensive care therapy for patients with severe Acute Pancreatitis (SAP) to prevent adverse outcomes and allow treatment of Mild Acute Pancreatitis (MAP) in the common ward.

Due to the risk of rapid deterioration in severe acute pancreatitis, the assessment of severity becomes crucial to a clinician, which will assist triage and the initiation of aggressive early treatment [5]. Therefore, a reliable risk stratification tool to predict the severity and prognoses of AP is of great clinical importance for the management of this disease. A series of severity scoring systems have been developed for the detection of SAP such as Ranson's score, APACHE II, modified Glasgow Score and CTSI (Balthazar score). However, they are very cumbersome and has its own limitations like low sensitivity and specificity, complexity of the scoring system as well as inability to obtain a final score until 48 hours after admission [8]. In 2008, the Bedside Index for Severity in Acute Pancreatitis (BISAP) score was proposed for the early recognition of patients at risk of mortality. This 5-point scoring system is comprised of five variables. Compared with traditional scoring systems, BISAP is more convenient to use with fewer items. Several studies have been conducted to validate the BISAP score. However, they differed in many aspects, such as population, cutoffs, and clinical endpoints, which result in a broad range of predictive accuracy.

Hence, we have performed this study to quantify the accuracy of BISAP score for predicting mortality and severity of patients with AP.

VARIABLES BISAP SCORE:

1. Blood urea nitrogen> 25mg/dl
2. Impaired mental status (Glasgow coma scale score< 15)
3. Systemic inflammatory response syndrome
   Presence of more than 2 of following criteria
   - Pulse >90 bpm
   - Respiration >20/min or PaCO2 < 32 mm Hg
   - Temperature >38 or < 36 degree Celsius
   - WBC count > 12000 or < 4000 cells/cubic mm or > 10% immature neutrophils
4. Age > 60 years
5. Pleural effusion (on CT scan or chest x- ray or USG)

Each variable on BISAP score is worth 1 point. Minimum score is '0' and maximum score will be '5'.There is steady increase in risk for mortality with the increasing number of points. Mortality ranged from <1% in the lowest risk group (score 0-2) to >20% in the highest risk group (score 3-5)[9].

AIMS AND OBJECTIVES:

It was a prospective observational study on acute pancreatitis cases admitted in the Department of General Surgery, Bankura Sammilani Medical College & Hospital from March 2018 to August 2019.

1. To evaluate the ability of BISAP score to predict mortality in patients with acute pancreatitis in our institution.
2. To study clinical, etiological and laboratory profiles of patients with acute pancreatitis.

REVIEW OF LITERATURE:

The ability to stratify patients early in their course is a major step to improving future management strategies in acute pancreatitis. Therefore, a reliable risk stratification tool to predict the severity and prognoses of AP is of great clinical importance for the management of this disease.

An ideal scoring system should promise an early, quick, simple, accurate, and reproducible description of disease severity. The earliest scoring system designed to evaluate the severity of AP was introduced by Ranson and colleagues in 1974.[10] Currently, a variety of scoring systems and Biochemical parameters are available to evaluate the severity of AP. However, all scoring systems have their own distinct pros and cons.

I) The Ranson's and modified Glasgow score contain data not routinely collected at the time of hospitalization. In addition both require 48hr to complete, missing a potentially valuable early therapeutic window [11].

ii) APACHE II was originally developed as an intensive care instrument. It has the advantage of allowing determination of disease severity on the day of admission

but requires the collection of a large number of parameters, some of which may not be relevant to prognosis in acute pancreatitis. Complexity is its major drawback [12].

iii) CTSI is calculated based on CT findings of local complications and cannot reflect the systemic inflammatory response [13, 14].

iv) CRP can also be used as an indicator of severity, that peaks 48-72 hours after the onset of pancreatitis. CRP level 150 mg/dl or higher defines severe acute pancreatitis. The major limitation is that it cannot be used on admission because sensitivity decreases if measured before 48 hours of onset of symptoms [4].

v) Other biochemical parameters like hematocrit, serum creatinine and BUN have been studied as prognostic indicator. The risk of pancreatic necrosis may increase with elevated hematocrit ≥ 44% at admission and a failure of admission hematocrit to decrease at 24 hours [15].Increased creatinine within 48 hours of admission has also been implicated in poor outcomes [16] and BUN > 20 mg/dl at admission or a rise within the first 24 hours is associated with a poor prognosis [17].

In 2008, Wu et al [18], using classification and regression tree (CART) analysis, a clinical scoring system was developed for prediction of in hospital mortality in acute pancreatitis. The scoring system was derived on data collected from 17,992 cases of acute pancreatitis from 212 hospitals in 2000-2001. The BISAP scoring system was validated on data collected from 18,256 acute pancreatitis cases from 177 hospitals in 2004-2005. The accuracy of the BISAP scoring system for prediction of mortality was measured by the area under the receiver operating characteristic curve (AUC). The performance of the new scoring system was further validated by comparing its predictive accuracy with that of APACHE II. A new mortality – based prognostic scoring system for use in acute pancreatitis has been derived and validated. The sensitivity and specificity for BISAP score is 75% and 97.5% [19].

Vikesh K. Singh et al[20], BISAP score was evaluated among 397 consecutive cases of acute pancreatitis admitted to their institution between June 2005 and December 2007. BISAP scores were calculated on all cases using data within 24h of presentation. The ability of the BISAP score to predict mortality was evaluated using trend and discrimination analysis. There was a statistically significant trend for increasing mortality ($p<0.0001$) with increasing BISAP score. The area under the receiver operating curve for mortality by BISAP score in the prospective cohort was 0.82(95% confidence interval: 0.70, 0.95), which was similar to that of the previously published validation cohort by B U Wu. BISAP score more or equal to 3 was associated with an increased risk of developing organ failure (odds ratio=7.4, 95% confidence interval: 2.8, 19.5), persistent organ failure (odds ratio=12.7, 95% confidence interval: 4.7, 33.9) and pancreatic necrosis (odds ratio=3.8, confidence interval: 1.8, 8.5). Thus the BISAP score represents a simple way to identify patients at risk of increased mortality within 24h of presentation.

In approximately 10-20% of patients no etiology is identified. Some of these patients may have microlithiasis and/or sphincter of oddi dysfunction (SOD) as the etiology of AP. With the increasing knowledge and understanding of the role of genetic abnormalities in hereditary and idiopathic chronic pancreatitis(CP), it is possible that these abnormalities will be implicated in idiopathic AP.

Clinically AP may be classified as mild or severe disease [21]. Severe AP (SAP) is associated with organ failure and/or local complications, such as necrosis, abscess or pseudo cyst of pancreas. Approximately 10-20% patients develop SAP. Mild AP is the more frequent presentation and is associated with interstitial edema, minimal or transient organ dysfunction and uneventful recovery.

Presence of pancreatic necrosis is the single best predictor of outcome during AP. Pancreatic necrosis is a diffuse or focal area of nonviable pancreatic parenchyma, typically associated with peri pancreatic fat necrosis, which is observed as non enhanced pancreatic parenchyma on CECT Abdomen. The degree of necrosis can predict the morbidity and mortality. Approximately 30% of patients with pancreatic necrosis develop infected necrosis with a mortality of 6-40% and morbidity of more than 80%.

MATERIALS AND METHODS:

STUDY DESIGN: It is a hospital based Prospective Observational study.

STUDY POPULATION: All patients diagnosed to have acute pancreatitis and admitted in In-Patient Department (IPD) of General Surgery, BSMC&H, Bankura.

Acute Pancreatitis was defined based on the 2012 revised Atlanta Criteria: i) mid epigastric pain radiating to back ii) elevation of serum lipase more than 3 times of the normal upper limit iii) CT scan reveling evidence of AP. Presence of any 2 out of 3 criteria is regarded as acute pancreatitis.

EXCLUSION CRITERIA: Acute Pancreatitis due to abdominal trauma, abdominal surgery and Pediatric age groups were excluded from the study.

PERIOD OF STUDY: The study was accomplished in a stipulated time frame of one and half year i.e. from March, 2018 to August, 2019.

METHODS OF DATA COLLECTION & SAMPLING: The study was carried out after obtaining permission from the WBUHS & Ethics Committee of Bankura Sammilani Medical College & Hospital. Informed consent was obtained from each patient prior to study enrollment. As per departmental records, average six to seven such cases got admitted in the IPD of General Surgery, BSMC&H i.e. more or less one case in each day/unit in a week. The data collection for the study was planned to be continued for a period of 8 months i.e.34 weeks (approximately). It was also decided that data collection would be conducted twice a week. These two days for data collection in each prospective week were chosen via simple random sampling technique using lottery method performed at the beginning of the week. Then eligible and willing case(s) attended on the selected days were included in the study. Thus the desired number of study subjects were enrolled in the study. BISAP score was calculated in all such patients based on data obtained within 24hrs of Hospitalization. Control(s) were not required for this study.

STUDY TOOLS:

1. Predesigned Pro forma.
2. Laboratory & Radiological investigation reports.
3. Thermometer

SAMPLE SIZE CALCULATION: Sample size(**n**) of my study was calculated based on a formula used for evaluating a Prognostic/Diagnostic test is:

$$\mathbf{n} = \frac{Z\alpha^2 \times Sn(1-Sn)}{L^2 \times P}$$

Where, $Z\alpha = 1.96$(Two tailed at 95% confidence interval), Sn = Sensitivity of the index test (75%), L = allowable error around the reported incidence which is assumed to be 0.2, P = Incidence of the disease (0.3/1000 population).

Considering of 10% non responders in the study, Final Sample Size is 66.

INVESTIGATIONS:

- WBC count, Hematocrit, BUN, Creatinine
- CXR (PA View)
- USG Abdomen, CECT Abdomen & MRCP(Selected Patient).
- Serum Amylase, Lipase, Triglyceride, LFT.
- Serum Na+, K+, Ca^{++}.

RESULTS & ANALYSIS:

A. BASELINE CHARACTERISTICS:

Table-1: Distribution of participants according to age category.

AGE GROUP(Year)	NUMBER	PERCENTAGE
< 20	01	1.52
20-40	45	**68.18**
41-60	16	24.24
> 60	04	6.06
TOTAL	**66**	**100**

Around 2/3rd , 45(68.18%) patients belonged to the age group of 20-40 year. Average age of the participants was estimated to be 38.37±11.50 (mean ± sd) with median of 36 years and a range of 54years.

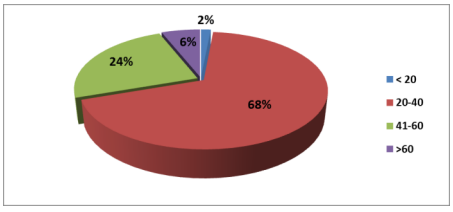


Fig.1: Distribution of participants according to age category.

Table-2: Distribution of participants according to Gender.

GENDER	NUMBER	PERCENTAGE
MALE	51	77.27
FEMALE	15	22.73
TOTAL	**66**	**100**

Among the participants majority 51(77.27%) were males with a Male to female ratio of **3.4:1.**

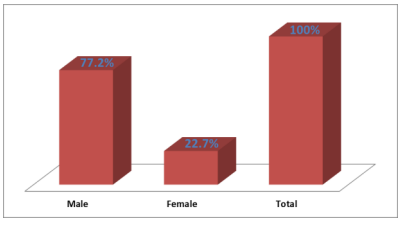


Fig.-2: Distribution of participants according to Gender.

Table-3: Distribution of participants according to etiology of acute pancreatitis.

ETIOLOGY	NUMBER	PERCENTAGE
ALCOHOL	32	48.48
GALLSTONE	18	27.27
HYPERTRIGLYCERIDEMIA	04	06.06
IDIOPATHIC	12	18.19
TOTAL	66	100

Most common etiology in this study was revealed to be **Alcohol 32(48.48%),** Followed by Gallstone 18 (27.27%). However, Idiopathic variety was found to be the 3rd most common.

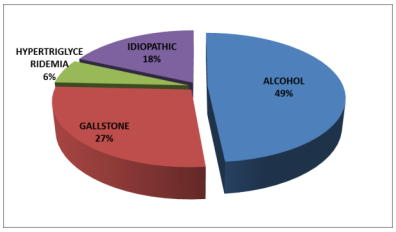


Fig. 3: Distribution of participants according to etiology

The severity of acute pancreatitis was defined on the basis of BISAP score.

Table 4: Distribution of participants according to severity of acute pancreatitis based on BISAP score, (<3 - mild, ≥ 3- severe).

BISAP SCORE	NUMBER	PERCENTAGE
SCORE < 3	56	**84.8**
SCORE ≥ 3	10	15.2
TOTAL	66	100

Out of 66 patients 56 patients **(84.8%)** were classified as **mild** acute pancreatitis.

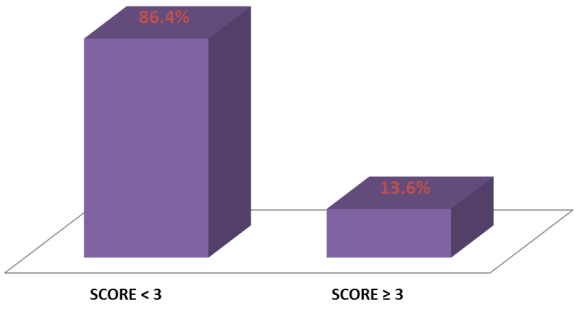


Fig. 4: Distribution of participants according to severity of acute pancreatitis.

Table-5: Distribution of participants according to their length of stay in hospital.

LENGTH OF STAY (day)	NUMBER	PERCENTAGE
< 7	43	**65.15**
≥ 7	23	34.85
TOTAL	66	100

Out of 66 patients, 43 patients (65.15%) were discharged within 6 days. Average, median and range of Length of stay were estimated to be 6.28±1.49 days (mean±sd), 3.89 days and 6 days, respectively. Analysis also revealed that there was a moderate correlation (r=0.49) between BISAP score and LOS.

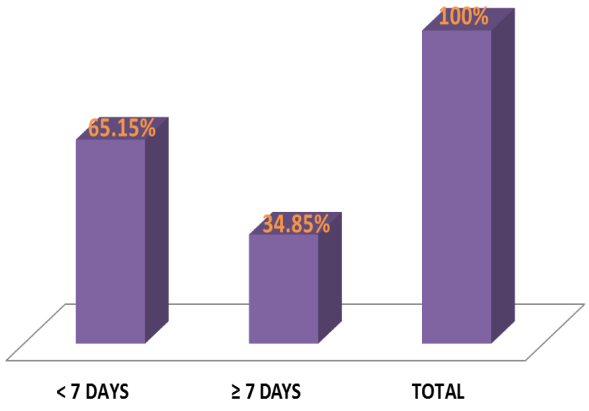


Fig.5: Distribution of participants according to hospital stay.

Table-6: Distribution of participants according to outcomes.

OUTCOME	NUMBER	PERCENTAGE
DEATH	08	12.1
DISCHARGED	58	87.9
Total	66	100

Among the 66 participants, 8 patients (12.1%) died in the course of disease. Out of these 8 patients, 2 had BISAP Score 4, 4 patients had score 3 and score 2 in 2 patient, number of

males were 5 and 3 female patients.

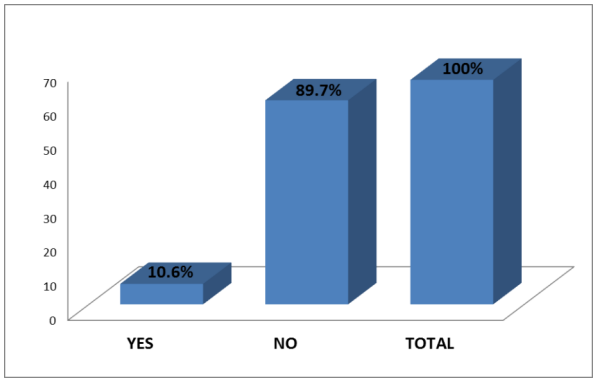


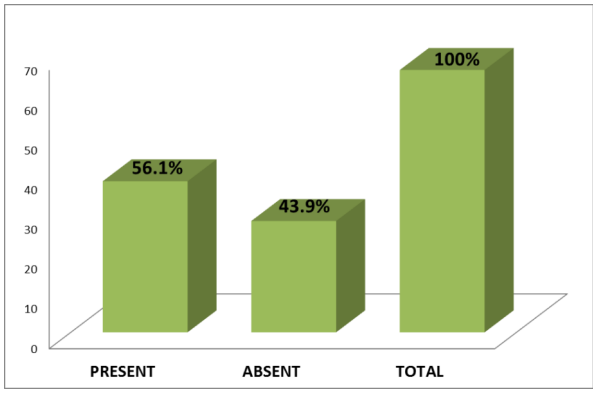
Fig. 6: Distribution of participants according to Outcomes.

Table 7: Distribution of participants according to presence pleural effusion.

PLEURAL EFFUSION	NUMBER	PERCENTAGE
Yes	37	56.1
No	29	43.9
TOTAL	66	100

Out of 66 patients 37 patients (56.1%) developed Pleural Effusion in one or both lungs.

Fig. 7: Distribution of participants according to pleural effusion



B.FINDINGS RELATED TO SPECIFIC OBJECTIVES

For Objective-1:

Table-8: Relationship between BISAP score and outcome of participants.

BISAP SCORE	DEATH No. (%)	DISCHARGE No. (%)	TOTAL No. (%)
SCORE ≥ 3	6 (9.1)[a=TP]	4 (6.1)[b=FP]	10 (15.2)
SCORE < 3	2 (3)[c=FN]	54 (81.8)[d=TN]	56 (84.8)
TOTAL	8 (12.1)	58(87.9)	66 (100)

TP=True positive, FP=False positive, TN=True negative, FN=False negative.

SENSISITIVITY=a/(a+c)×100=TP/(TP+FN)=75%
SPECIFICITY = d/(b+d)× 100 = 93.1%
POSITIVE PREDICTIVEVALUE = a/(a+b) × 100 = 60%
NEGETIVE PREDICTIVEVALUE = d/(c+d) × 100 = 96.4%
ACCURACY = (a+d)/(a+b+c+d) × 100 = 90.9%

DISCUSSION:

Acute pancreatitis (AP) remains a serious disease. It is defined as an inflammatory process of the pancreas with possible peri pancreatic tissue and multi-organ involvement. The majority of patients present with a mild disease, however approximately 10-20% run a severe course and require appropriate management in an intensive care unit. According to the Atlanta classification, severe acute pancreatitis (SAP) is defined as an AP associated with local and/or systemic complications.

Multi-organ dysfunction syndrome, extent of pancreatic necrosis, infection and sepsis are the major determinants of mortality in AP [6,7]. Pancreatic necrosis is considered as a potential risk for infection, which represents the primary cause of late mortality. Occurrence of acute respiratory, cardiovascular and renal failures (ARF) can predict the fatal outcome in SAP [9]. A wide range of mortality (20%-30%) has been reported in SAP [20,35]. Identification of patients at risk for mortality early in the course of acute pancreatitis is an important step in improving outcome. On account of differences in outcome between patients with mild and severe disease, it is important to define that group of patients who will develop severe pancreatitis, predicting which still represents challenge for the clinician.

Most patients of acute pancreatitis recover without complications, the overall mortality rate of this illness is between 2-5% [36,37]. Multiple risk stratification tools for acute pancreatitis have been developed, but their clinical usefulness is limited. Older measures such as, the Ranson's criteria and modified Glasgow score uses data that are not routinely collected at the time of hospitalization. In addition, both require 48hrs time period thereby missing potentially valuable early therapeutic window [11]. The APACHE II score is the most widely used prediction system currently but it requires the collection of large number of parameters, some of which may not be relevant to prognosis [12].

For this purpose a simple and accurate clinical scoring system that is bedside index for severity in acute pancreatitis (BISAP) scoring system [9] was developed in 2008. This scoring system used for stratifying patients according to their risk of hospital mortality and is able to identify patients at increased risk of mortality prior to the onset of organ failure. Data for BISAP score is collected within the first 24hr of hospitalization. The ability to stratify patients early in their course is a major step to improving management strategies in acute pancreatitis.

In this study, all patients were admitted with the chief complaint of abdominal pain, some patients had a history of nausea and vomiting. The severity of acute pancreatitis was defined on the basis of BISAP score and diagnosis of AP done based on the 2012 revised Atlanta criteria. In this study out of 66 patients, 10(15.2%) had severe pancreatitis, they had BISAP score more than or equal to 3 and 56(84.8%) were classified as having mild pancreatitis having BISAP score of less than 3. The disease was self-limiting in majority of the patients. Among the 66 patients in our study, 51(77.2%) were males and 15(22.8%) were females. Male to female ratio was 3.4:1. In mortality group, 5 were males and 3 females. Around 2/3rd, 45(68.18%) patients belonged to the age group of 20-40 years. Average age of the participants was estimated to be 38.37 ± 11.50 (mean ± sd) with median of 36 years and a range of 54 years. With respect to etiological factors of the acute pancreatitis, we found alcohol being the most common cause of acute pancreatitis, accounting for 48.5% of cases, gallstones being the second most common, accounting for 27.5% of cases. The proportion of two main causes greatly depends on the geographical and cultural variations. Alcohol is the main cause in the united states of America and finland [38], gallstones in southern Europe, whereas central and northern Europe sees a similar frequency of the two factors or a predominance of alcohol. Out 66 participants, pleural effusion developed in 37(56.1%) patients involving one or both lungs, as a complications of acute pancreatitis. In respect to length of hospital stay (excluding death in hospital), 41(69.5%) out of 58 patients were discharged from hospital within 7 days and 17(30.5%) patients after 7 days of

admission. Analysis also revealed that there was a moderate correlation (r=0.49) between BISAP score and Length of hospital stay. The mortality rates of patients with acute pancreatitis vary from 2 to 9 % while in severe cases, it is estimated at 30%. According to a recent study, the mortality rates among severe acute pancreatitis patients have decreased from 50-58% in 1978-1982 to 12-18% in 1993-1997. Also, early death of patients with acute pancreatitis were rare: nine out of ten deaths occur later than 3 weeks after disease onset. The total death in this study was 8 (**12.1%**).

Relationship between BISAP score and outcome of participants shows that BISAP scoring system is highly sensitive (sensitivity 75%) and specific (specificity 93.1%) to predict mortality in AP with a positive predictive value of 60% and negative predictive value 96.4%. These values are almost similar with the previous study done to validate BISAP scoring system [19] except low positive predictive value in this study.

LIMITATIONS:

Although the sample size of the present study was estimated using a suitable formula, But even then the findings seem to have less external validity, specially, in regard to formulating treatment guideline for an important surgical emergency like AP. It requires a larger multi-centric study suitable for generalization. Most of the Patients involved in the study belonged to the lower socio-economic status and thereby factors like malnutrition, addiction and delayed care seeking all come in to play for determining the morbidity and mortality among them. These factors weren't considered in the present study.

SUMMARY:

It was a prospective randomized observational study which was conducted under Department of General Surgery, BSMC&H, Bankura for a period of 18 months with the study population of General Surgery Department.

This study was done for evaluation of the BISAP score in assessing mortality and severity in an acute pancreatitis. The BISAP score was evaluated among 66 cases of acute pancreatitis admitted to our institution. BISAP scores were calculated in all cases using data within 24 hours of presentation. The study found that 15.2% patients had BISAP score more than or equal to 3 and 84.8% had BISAP score less than 3. Overall in our study group mortality was 12.1%. The most common etiological factor was chronic alcoholism and most commonly affected age group was 20-40 years. We also found that BISAP scores of ≥ 3 represent a simple way to identify patients at risk of increased mortality and the development of intermediate markers of severity within 24 hours of presentation.

Although most patients with acute pancreatitis recover without complications, the overall mortality rate of this illness is between 2% and 9%. Multiple risk stratification tools for acute pancreatitis have been developed, but their clinical usefulness is limited. Older measures, such as the Ranson's and modified Glasgow score, use data that are not routinely collected at the time of hospitalization, and these tools cannot be completed until 48 hours after admission. The APACHE II score is most widely used prediction system currently, but it requires the collection of a large number of parameters, some of which may not be relevant to prognosis.

Our study found that BISAP score was a simple, sensitive and specific tool to identify patients at risk of increased mortality and the development of intermediate markers of severity within 24 h of presentation.

CONCLUSION:

The BISAP score was a reliable tool to identify AP patients at high risk for unfavorable outcomes within 24 hours of presentation. It is also revealed that BISAP has the advantages of simplicity and speed over traditional scoring systems and performed similarly to other scoring systems in predicting SAP. So, BISAP may be helpful for the treating surgeon for taking decision regarding the effective management protocol of such group of patients.

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