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## Research article

### ETIOLOGY, CLINICAL PROFILE, SEVERITY AND OUTCOME OF ACUTE PANCREATITIS IN RELATION TO BED SIDE INDEX FOR SEVERITY OF ACUTE PANCREATITIS BISAP AND CT SEVERITY INDEX [CTSI] SCORES

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## ABSTRACT

**Background:** Acute pancreatitis is an inflammatory process of the pancreas with involvement of regional tissues or remote organ systems and with potentially devastating consequences. Early prediction of outcome of acute pancreatitis within 24 hrs by clinically based bed Side Index of Severity of Acute Pancreatitis [BISAP] Score and radiological based CT Severity Index [CTSI] later on being useful in initiation of early treatment, assessing severity, to prevent morbidity and mortality. In those who survive, it can progress to chronic pancreatitis resulting in malabsorption and permanent diabetes. **Aim:** The aim was to study aetiology, clinical profile, severity, outcome of acute pancreatitis in relation to BISAP Score and CTSI. **Materials and Methods:** This was an observational and prospective study. The present study enrolled 55 patients who were diagnosed as acute pancreatitis and patients with chronic pancreatitis were excluded from the study. Vital data like pulse rate, blood Pressure, temperature, respiratory rate, conscious level using Glasgow coma scale, serum amylase, lipase, Chest x-ray, US abdomen and CT abdomen [both CECT & NCCT] were done. BISAP Score was obtained at the time of presentation or within 24 hours of presentation and radiological based CT Severity Index [CTSI] was calculated using the Balthazar grading system and Necrosis Scoring system to assess the severity, morbidity and mortality. **The results:** In this study, the most common aetiology being alcohol intake followed by gall stones. BISAP Score < 2 predicted mild pancreatitis, Score > 3 had organ dysfunction and Score 4 had 100% mortality. The relation between CTSI score and Organ dysfunction showed increased organic dysfunction and higher mortality with higher CTSI Scores. p value < 0.0001 was calculated using Pearson Chi-square test and found to be statistically significant. **Conclusions:** Both BISAP and CTSI scores had positive correlation with morbidity and mortality.

**Key words:** Acute pancreatitis, BISAP Score, Balthazar Grading, CT Severity Index, Chronic pancreatitis

## INTRODUCTION

Acute pancreatitis is an inflammatory process of the pancreas with varying involvement of regional tissues or remote organ systems<sup>1-5</sup> and with potentially devastating consequences. The diagnosis of mild disease may be missed and death may occur before

diagnosis in 10% patients with severe disease. Acute pancreatitis runs a benign course in Asian countries and the aetiology is different from that of the western population. Gall stones and alcohol abuse account for 70% of cases of acute pancreatitis. The most common cause of acute pancreatitis is gallstones, including

microlithiasis, which accounts for 35 to 40 percent of cases with only 3 to 7 percent of patients developing gallstone pancreatitis<sup>6</sup>. The risk of developing acute pancreatitis in patients with gallstones is greater in men, but more women develop this disorder since gallstones occur with increased frequency in women. Alcohol may act by increasing the synthesis of enzymes by pancreatic acinar cells. Not all acute alcoholic pancreatitis patients progress to chronic pancreatitis, even with continued alcohol abuse. Triglyceride concentrations above 1000mg/dl can precipitate attacks of acute pancreatitis in 1.3 to 3.8%. Hypercalcemia can lead to acute pancreatitis due to deposition of calcium in the pancreatic duct and activation of trypsinogen within the pancreatic parenchyma. The incidence of acute pancreatitis increases with age.

The clinical features and the severity of acute pancreatitis are related to extrapancreatic organ failure secondary to the patient's systemic inflammatory response syndrome (SIRS) elicited by acinar cell injury.<sup>7</sup> The intrapancreatic release of active pancreatic enzymes leads to pancreatic autodigestion, setting up a vicious cycle of active enzymes damaging vascular endothelium, interstitium and acinar cells. The destruction spreads along the gland and into the peripancreatic tissues. The spectrum of acute pancreatitis ranges from interstitial pancreatitis, which is a mild and self limited disorder to necrotizing pancreatitis. Almost all patients with acute pancreatitis have acute upper abdominal pain at onset<sup>8</sup> are typically accompanied in approximately 90 percent of patients by nausea, vomiting, restlessness, agitation and relieves on bending forward. The warning signs of pancreatitis include fever suggesting infection, hypovolaemia due to fluid accumulation, Grey turner sign (flank discoloration) and Cullen's sign (periumbilical discoloration) suggesting haemorrhagic pancreatitis, visual loss due to retinopathy and tetany due to severe hypokalemia / fulminant pancreatitis. Fever is an important sign in patients with acute pancreatitis and is mediated by inflammatory cytokines in the first week. Fever in the second or third week is due to infection of the necrotic tissue and is much more significant. Patients with acute pancreatitis may be dyspnoeic due pleural effusion and may go into respiratory failure.

The diagnosis of acute pancreatitis is based on typical abdominal pain, 3 fold elevation in serum amylase or lipase level<sup>9</sup> and confirmatory findings on cross-sectional abdominal imaging. The sensitivity of serum lipase for the diagnosis of acute pancreatitis ranges from 85 to 100 percent in various reports.<sup>9-11</sup> Lipase measurements is more specific than serum amylase in patients with alcoholic pancreatitis presenting late to the physician. A diffusely enlarged, hypoechoic pancreas is the classic ultrasonographic finding in acute pancreatitis. Computerised Tomographic scan (CT scan) of abdomen is the most important in the diagnosis of acute pancreatitis, intra abdominal complications and for assessment of severity when results are combined with the Ranson score.<sup>12</sup> Contrast enhanced CT [CECT] distinguishes edematous from necrotizing pancreatitis. CT is more accurate than ultrasonography in the diagnosis of severe pancreatic necrosis 90 versus 73 percent in one report<sup>2</sup>. Patients with higher CTSI scores are likely to have a prolonged hospital course and higher mortality than patients with lower scores.<sup>3</sup> CT Severity Index is best evaluated three to five days into hospitalization because it may not be possible to distinguish interstitial from necrotizing pancreatitis on contrast enhanced CT scan on the day of admission. The likelihood of prolonged pancreatitis or a serious complication is negligible when the CTSI score is 1 or 2 and low with scores of 3-6 and with a score of 7-10 had a 92% morbidity rate and 17% mortality rate. CT Severity index<sup>4</sup> equals an unenhanced CT score plus necrosis score. Score 6 indicates severe disease. Magnetic resonance imaging [MRI] can distinguish the pancreatic necrosis seen on CT into necrotic pancreatic parenchyma, peripancreatic necrotic fluid collection, hemorrhagic foci, abscess, pseudocyst and pancreatic duct disruptions. MRI has greater sensitivity to detect mild acute pancreatitis compared to CT.

Routine clinical assessment identifies only 34 to 44 percent of patients with severe acute pancreatitis. With the exception of the APACHE II system, the other systems like Ranson, Glasgow, Banks, and Agarwal and Pitchumoni take 48 hours to complete, can be used only once, and do not have a high degree of sensitivity and specificity. The APACHE II has good negative value and modest positive predictive value for predicting severe acute pancreatitis and can be accurate at 24hrs. Clinical assessment for severe

pancreatitis by SIRS, BISAP score, Organ failure scoring systems within first 24 hours as accurate as most scoring systems. In SIRS four variables are taken each assigned one point. A SIRS score of 2 or more reliably predicted severe acute pancreatitis at the bedside and can be done daily.

Bedside Index of Severity in Acute Pancreatitis [BISAP] <sup>11</sup> a new scoring system was developed for bedside assessment of severity of acute pancreatitis. It consists of five variables, each assigned one point. The composite score of sum of all points is obtained within first 24 hours of admission. A BISAP score <sup>is</sup> simple to calculate requires only those vital signs, laboratories, and imaging that are commonly obtained at the time of presentation or within 24 hours of presentation. A score of  $\geq 3$  within 24 hours of presentation carry a 7.4 to 12.7 fold higher risk of developing organ failure and persistent organ failure respectively than those with scores  $< 3$ . Thus BISAP score could be used to stratify patients by risk within 24 hours of presentation for clinical care and to predict mortality. Organ failure was defined as a score of  $\geq 2$  in one or more of the three (respiratory, renal, and cardiovascular) out of the five organ systems. Organ failure is calculated during the first 72 hours of hospitalization based on the most extreme laboratory value or clinical measurement during each 24 hour period. Outcomes are worse in those with organ failure within 48 hours of presentation and in those  $> 48$  hours had a persistent organ failure.

Approximately 75% to 80% of patients with acute pancreatitis have a resolution of the disease process (interstitial pancreatitis) and in 25% of patients develop a more protracted course, often related to the necrotizing process (necrotizing pancreatitis) lasting weeks to months. Most of the deaths occur within the first or second week, usually of multiorgan failure due to associated pancreatic infection. In those who survive, severe pancreatic necrosis can scar the pancreas with subsequent obstructive chronic pancreatitis resulting in permanent diabetes and malabsorption. In this background, the present study has been undertaken to study the aetiology, clinical profile, severity and outcome of acute pancreatitis in relation to BISAP and CTSI.

#### Aim of study

The aim is to study aetiology, clinical profile, severity assessment using clinical criteria BISAP score,

radiological criteria CT Severity Index score and their correlation to the outcome of acute pancreatitis.

#### MATERIALS AND METHODS

This is prospective and observational study. Ethical clearance was obtained from the institutional ethics committee of Siddhartha Medical College. Informed consent was taken from the patients in their own language before collecting data. The present study enrolled 55 patients with acute abdomen who were diagnosed as acute pancreatitis based on elevated serum amylase, lipase levels and/or radiological evidence by ultrasound or CT scan abdomen. Patients with Chronic pancreatitis were excluded from the study. The duration of study was over a period of two years. Laboratory tests like serum amylase, lipase, haemogram, liver function tests, serum triglyceride, Blood Urea Nitrogen BUN, serum creatinine, blood glucose, lactate dehydrogenase, serum calcium, arterial blood gas analysis were done. BISAP Score <sup>11</sup> and Organ failure score were calculated using clinical parameters shown in Table:1&2

**Table 1: BISAP score**<sup>13</sup>

Parameter	Points given
Blood Urea Nitrogen $> 25$ mg/dl	1
Impaired mental status (Glasgow coma score $< 15$ )	1
Age $> 60$ years	1
Pleural effusion detected on imaging (chest radiograph / chest CT / Ultrasound chest)	1
SIRS <ul style="list-style-type: none"> <li>• Heart rate <math>&gt; 90</math> beats per min</li> <li>• Respiratory rate <math>&gt; 20</math> per min or <math>\text{PaCO}_2 &lt; 32</math> mm Hg</li> <li>• Temperature <math>&gt; 38^\circ\text{C}</math> or <math>&lt; 36^\circ\text{C}</math></li> <li>• White blood cell count <math>&gt; 12000/\text{cu. mm}</math> or <math>&lt; 4000/\text{cu. mm}</math> or Band forms <math>&gt; 10\%</math></li> </ul>	1 (at least any one of these)

**Table: 2 Criteria for organ failure based on Marshall scoring system**

Organ system	0	1	2	3	4
Respiratory ( $\text{PaO}_2/\text{FiO}_2$ )	$> 400$	301 - 400	201 - 300	101 - 200	$< 101$
Renal (S.creatinine(mg/dL))	1.5	$> 1.5 - 1.9$	$> 1.9 - 3.5$	$> 3.5 - 5.0$	$> 5.0$
Cardiovascular (systolic blood pressure, mm/Hg)	$> 90$	$< 90$ , fluid responsive	$< 90$ , fluid nonresponsive	$< 90$ , $\text{pH} < 7.3$	$< 90$ , $\text{pH} < 7.2$

CTSI Score<sup>3</sup> was calculated with Balthazar grading<sup>13</sup> and Necrosis score using NCCT and CECT abdomen findings given in Table:3&4.

**Table: 3 Balthazar grading<sup>13</sup> based upon unenhanced CT findings.**

Grade	Unenhanced ct findings	Score
A	Normal pancreas: normal size, sharply defined, smooth contour, homogenous enhancement, retroperitoneal Peri pancreatic fat without enhancement	0
B	Focal or Diffuse enlargement of the pancreas, contour may show irregularity, enhancement may be inhomogenous but there is no peripancreatic inflammation	1
C	Peripancreatic inflammation with intrinsic pancreatic abnormalities	2
D	Intrapancreatic or Extrapancreatic fluid collections	3
E	Two or more large collections of gas in the pancreas or retroperitoneum.	4

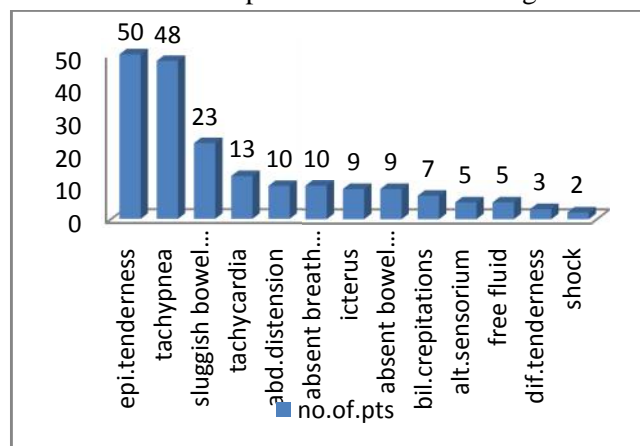
**Table 4: Necrosis score based on Contrast Enhanced CT scan findings**

Necrosis percent	SCORE
0	0
< 33	2
33 – 50	4
50	6

## RESULTS

A total of 55 patients with acute abdomen who were diagnosed as acute pancreatitis based on elevated serum amylase and/or lipase levels and radiological findings with ultrasound and CT abdomen were included in the study. BISAP and CTSI scores were calculated and independently checked for correlation with outcome of acute pancreatitis. Statistical analysis was done using Pearson's Chi-square test. (Pearson's chi square test is one of the several types of chi-squared tests. Here we used it to know whether the values are statistically significant or not.) P-value < 0.0001, p value is for comparison of outcome in the study with both BISAP and CTSI scores independently. Both Scores had statistically significant correlation to outcome.) was calculated which is highly significant. The results of this study are shown in the figures given below.

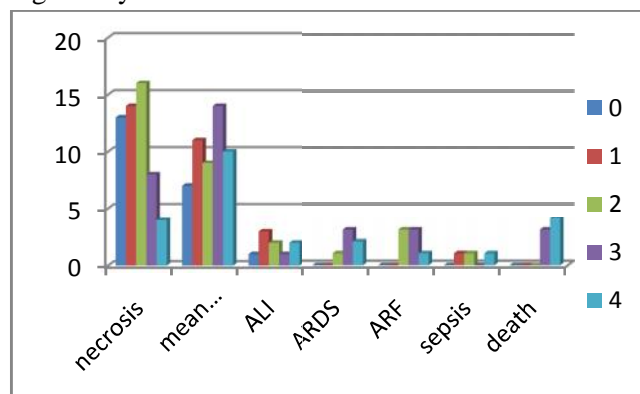
Out of the 55 patients in the study, males and females included are in the ratio 4.5:1 and the majority were in their fourth decade. Most common aetiology was alcoholic consumption by 51%, idiopathic in 49%, followed by gallstones in 16.4%. All the patients had abdominal pain at presentation with a characteristic feature radiation of the pain to the back (spine) was present in 43 (78%) of the patients, vomiting in 47 (85.45%) followed by fever in 20% of patients. Epigastric tenderness was the most common clinical finding in 50 patients (91%) followed by tachypnea in 48 patients (87%), sluggish bowel sounds (42%), tachycardia (23.60%), Pleural effusions in 18% of patients as shown in Fig:1.



**Fig 1: Clinical findings at the time of admission**

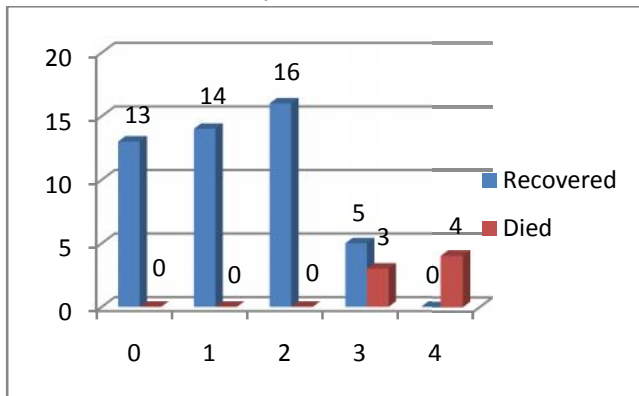
Serum amylase in 26 patients (47%) and serum lipase in 45 patients (82%) were elevated to greater than 3 times of upper limit of normal. Median value of amylase was 532 U/l and lipase was 988 U/l. Leukocytosis in 33 patients (60%) azotemia in 15 patients (25%).

BISAP Score and Organic failure score were calculated from their variables. **Fig:2** below shows positive correlation between BISAP Score and organic dysfunction.



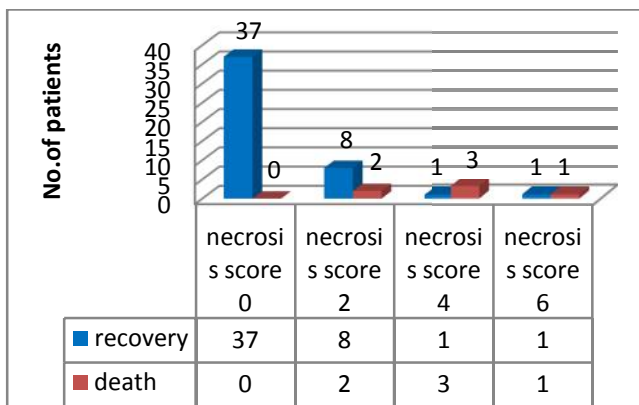
**Fig 2: Correlation of BISAP Score and organ failure in acute pancreatitis**

Fig 3 below shows positive correlation between BISAP Scores and outcome. In this study 48 (87.30%) recovered completely and 7 patients (12.70%) had mortality.



**Fig 3: Outcome of patients in relation to BISAP Score**

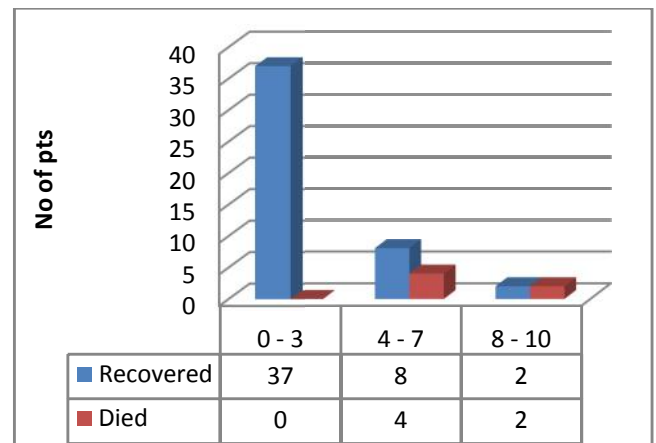
BISAP Score was independently checked for correlation with outcome. p value < 0.0001 was calculated using Pearson Chi-square test and found to be statistically significant. CT severity index [CTSI] was calculated using the Balthazar grading system and Necrosis Scoring system. Necrosis Scoring is based on CECT abdomen findings. Fig:4 below shows positive correlation between pancreatic necrosis and outcome.



**Fig4: Relation between pancreatic necrosis and outcome in acute pancreatitis**

The relation between CTSI and Organ dysfunction and outcome of patients was observed and it showed increased organic dysfunction and higher mortality with higher CTSI Scores as shown in Fig 5

CT Severity index was independently checked for correlation with outcome. p value < 0.0001 was calculated using Pearson Chi-square test and found to be statistically significant.



**Fig 5: Outcome in relation CT Severity Index [CTSI]**

## DISCUSSION

Acute pancreatitis is an inflammatory process of the pancreas with varying involvement of other regional tissues or remote organ systems<sup>1</sup> and with potentially devastating consequences. The spectrum of acute pancreatitis ranges from interstitial pancreatitis, which is mild and self limited disorder to necrotizing pancreatitis. Clinical assessment for severity of pancreatitis by SIRS, BISAP score and Organ failure scoring systems within first 24 hours are as accurate as most scoring systems. CT scan of abdomen is the most important imaging test for the diagnosis of acute pancreatitis, intra abdominal complications and for assessment of severity. CT is more accurate than ultrasonography in the diagnosis of severe pancreatic necrosis.<sup>2</sup> Contrast enhanced CT [CECT] distinguishes edematous from necrotizing pancreatitis. CT Severity index<sup>3</sup> equals an unenhanced CT score plus necrosis score. Necrosis Score is based on CECT Scan findings as per **Table:4.**

In this study the aetiology, clinical profile, severity and outcome of 55 patients with acute pancreatitis were studied. An attempt was made to assess the severity by clinical criteria like BISAP Score as per **Table:1** and radiological criteria like CTSI as per **Table: 3&4.** The disease is common in males when compared to females. Out of the 55 patients, 45 patients (81.8%) were males and 10 patients (18.2%) were females. The male: female ratio was 4.5:1 which is closely related to a study by Baig SJ, Abdur Rahed.<sup>4</sup> Majority of the patients were in their fourth decade (31%), followed by fifth decade (22%), third decade (20%), second decade (16%) and sixth decade

(9%) similar to a study by Garg PK, Khanna S, Bohidar NP.<sup>5</sup> In our study, the most common aetiology was alcohol intake (51%) followed by gall stones (16.4%) and in 27% of the patients, no aetiology could be identified. In studies by Garg PK, Khanna S, Bohidar NP<sup>5</sup> and by Gislason H, Horn A, Hoem A, Imsland AK et al<sup>7</sup> the proportion of gallstone pancreatitis was highest followed by alcoholic pancreatitis. In our study the numbers of female patients were less; this may be the cause for the smaller proportion of gallstone pancreatitis<sup>6</sup>. In a study done by SJ Baig et al<sup>4</sup> the aetiologies were similar to that of in our study. In this study abdominal pain<sup>8</sup> with radiation to the back was present in all 55 patients (100%) followed by epigastric pain in 31 patients. Vomitings were predominantly nonbilious in 47 patients (85.45%) and fever in 20% of the patients. Epigastric tenderness was the most common clinical finding in 50 patients (91%) followed by tachypnea in 48 patients (87%), sluggish bowel sounds (42%), tachycardia (23.60%), Pleural effusions in 18% of patients and altered sensorium in 5 patients as per Fig 1

Serum Amylase<sup>9, 10</sup> measurements were done at presentation to the hospital. In 47% of patients, it was elevated to > 3 times of upper limit of normal. Studies done previously show that the serum amylase values rise within 6 hours of onset and remain elevated for 3-5 days. In our study, the mean duration between symptom onset and presentation to hospital was 4.7 days and this may be the reason for serum amylase levels being in the normal range in the rest of the patients (53%). Lipase<sup>9,10</sup> is elevated in 82% of the patients at presentation making it a more sensitive test for diagnosing acute pancreatitis especially for patients presenting after a few days to the hospital.

In this study BISAP Score as per Table:1 and Organic failure score as per Table:2 were calculated from their variables and a positive correlation noted between them in acute pancreatitis as shown in Fig:2. Out of 55 patients included in the study, 48 patients (87.30%) recovered completely and 7 patients (12.70%) had a mortality as shown in Fig:3 In this study a BISAP score of 4 had 100% mortality and Score 3 predicted the development of organ dysfunction, persistent organ failure, necrosis and increased mortality and this correlated with a study done by Vikesh Singh; Beichen et al. CTSI calculated by using the Balthazar grading system<sup>13</sup> and Necrosis

Scoring system as per Tables 3&4. Necrosis Scoring was done based on CECT abdomen findings as per Table:4 Two patients were excluded as they had renal failure and CECT scan could not be done. Out of 53 patients, Necrosis Score 0% in 37 patients (69.80%) and all showed recovery (100%). Necrosis Score 2 was present in 10 patients, out of which 8 patients recovered and 2 patients died. Necrosis Score 4 was present in 4 patients and Necrosis Score 6 was present in 2 patients as shown in Fig:4 This study showed positive correlation between Necrosis Score and organic dysfunction and mortality as in study by Tenner S; Sica G; Hughes M: et al.<sup>14</sup> Fig:5 shows the outcome of acute pancreatitis in relation to CT severity index. Out of 53 patients, 37 (69.81%) patients had CTSI Score 0-3, 12 (22.64%) patients had score 4-7 and 4 patients had score 8-10. In this study, the CT severity index was found to be a good marker for assessing the prognosis and outcome of acute pancreatitis. Out of 53 patients, 47 patients (88.67%) recovered and 6 patients (11.32%) had mortality. Outcome results of this study were correlated with studies done by Simchuk EJ; Traverso LW; Nukui Y, et al<sup>3</sup> All the patients who had organ dysfunction had necrosis on CT. The relation between CTSI and Organ dysfunction was observed and it showed increased organic dysfunction 21%, 58%, 33% with CTSI Scores 0-3,4-7,8-10 respectively, and higher mortality with higher CTSI Scores which correlated with studies done by G Gurlyek; Emir S; Saglam A et al<sup>15</sup>. One drawback in the study was that CECT abdomen could not be done in patients who had acute renal failure and hence necrosis might have been missed, implying that the degree of correlation between necrosis and mortality/organ dysfunction might be still stronger.

## CONCLUSIONS

A composite of BISAP Score during the first 24 hours and CTSI Score after 72 hours of admission to the hospital predicted the outcome in terms of organ dysfunction and mortality in acute pancreatitis. These scores are helpful in initiation of early effective treatment and prevention of complications like chronic pancreatitis, malabsorption and permanent diabetes.

**Limitations of the study:** The limitation of present study includes smaller sample size, two patients were excluded as CECT abdomen could not be done as

they developed acute renal failure and hence necrosis might have been missed, implying that the degree of correlation between necrosis and mortality/ organ dysfunction might be still stronger.

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**Conflict of interest: Nil**

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