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**Research Article**

# A STUDY TO EVALUATE THE ROLE OF C- REACTIVE PROTIEN, BLOOD UREA NITROGEN AND MULTISLICE COMPUTED TOMOGRAPHY AS EARLY PREDICTORS OF SEVERITY OF ACUTE PANCREATITIS

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**A R T I C L E I N F O**

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**A B S T R A C T**

***Introduction:-*** Acute pancreatitis is a clinical challenge, often requiring management in the critical care unit. Therefore, prediction of severity in early part of acute pancreatitis can be helpful in the better management of the case besides clinical examination, biochemical tests, multiple prognostic scoring systems and computed tomography (CT )have been used in the assessment of severity.

***Material and methods:-***This prospective study had been conducted in Department of Surgery in collaboration with Department of Radiodiagnosis, VMMC and SAFDARJUNG HOSPITAL between october, 2014 to April,2016. It aimed at evaluating the role of Blood Urea Nitrogen, C- reactive protein (CRP) and CECT scan as markers of early prediction of severity of acute pancreatitis. A total of 30 patients of both the sexes who presented with a clinical diagnosis of acute pancreatitis within 6 hours of onset of symptoms were included in the study.

***Results:-*** CECT scan done between the 3rd to 5th day of presentation had the highest sensitivity and specificity (100% and 91.67% respectively) as an early marker of prediction of severity of acute pancreatitis.(p=0.500,Mc Nemar Bowker test and p value <0.001, kappa statistics).

CRP levels done at 24 hrs was also found to be a good marker of early prediction of severity of acute pancreatitis (sensitivity 100% and specificity 91.67%; p=0.001, Kruskall Wallis test).

CRP done at 6 and 36 hrs had a low sensitivity and specificity as early markers of prediction of severity of acute pancreatitis.BUN at 24 and 48 hrs had a low sensitivity and specificity as early markers of prediction of severity of acute pancreatitis.Combined together, CRP and CECT scan done within 72 hrs of clinical presentation had sensitivity and a specificity approaching close to 100% in predicting the severity of acute pancreatitis.

***Conclusion:-*** CRP and CECT scan can act as good early predictor of severity of acute pancreatitis, done within the first 72 hrs of presentation and can aid the treating clinician in making early decision in critical care management of these patients.



## INTRODUCTION

Acute pancreatitis has a broad clinical spectrum, ranging from a mild self limiting illness tolife threatening severe necrotizing disease. The most important prognostic factor in the disease process is assumed to be development of necrosis and most of the mortality is attributed to the development of sepsis and multiorgan failure.[1] Various biochemical markers have evolved and also are in stage of continuous research to aid in the early prediction of severity of the disease process. [2,3]

Acute pancreatitis diagnostic criteria and diagnostic prediction have been a matter of debate over many years. In 2012, Atlanta classification (defined in 1992) was revised with an emphasis on persistent organ failure.[4,5]

Multi-factor scoring system, including Ranson's [6,7] and Acute Physiology and Chronic Health Evaluation (APACHE)-II[8]scores have been used since the 1970s for assessment of the severity of AP.

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Balthazar computed tomography severity index (CTSI) was developed in 1990. These have been established as an important tool for assessment of severity of Acute pancreatitis. But, these are complex and difficult to use in clinical bases, have been shown to perform with high negative predictive value but only moderate overall sensitivity. A new prognostic scoring system, the Bedside Index for severity in Acute Pancreatitis (BISAP) has recently been proposed as an accurate and simple method for early identification of patients at risk of in-hospital mortality. Novel biochemical markers like CRP (C-reactive protein) urinary trypsinogen, IL-6, procalcitonin are evolving over the years through various research as the potential biomarkers of severity of AP.

This study aimed to assess the role of C-reactive protein, Blood urea nitrogen (BUN) and CECT scan as the early (<72 hrs) markers of prediction of severity of Acute pancreatitis, based on the comparisons of sensitivities , specificities and the accuracy of these individual markers.

## MATERAL AND M.ETHODS

This study was prospective study done at safdarjung hospital, New Delhi in Department of General Surgery from october, 2014 to april, 2016 on 30 patients who presented to emergency department with diagnosis of acute pancreatitis. The study was aimed to assess the role of C-reactive protein, Blood urea nitrogen (BUN) and CECT scan as the early (<72 hrs) markers of prediction of severity of Acute pancreatitis,based on the comparisons of sensitivities , specificities and the accuracy of these individual markers.

***Inclusion criteria***

Patients presenting with clinical features suggestive of pancreatitis, within 6 hrs of development of symptoms, with elevation of serum pancreatic enzymes.

***Exclusion criteria***

- Pre-existing chronic pancreatitis.
- Previous abdominal surgery for pancreatitis.

***Preliminary Work UP***

Written informed consent specifying all the radiological and biochemical interventions was obtained. Various tests done were:

- ***Respiratory:*** [partial pressure of oxygen (pO2)/FiO2] ratio was calculated.
- ***Cardiac:*** systolic BP measurement.
- ***Renal:*** serum creatinine levels were measured.
- All the above mentioned parameters were measured daily for the initial 7 days since the time of presentation. The above parameters were scored on a scale of 0-4 as per the Marshall scoring system (table 7).[6] The score on the 7$^{th}$ day of presentation was taken as the reference to evaluate the predictability of CRP, BUN and CECT.
- Complete hemogram: done on admission and there after every 24 hours for monitoring of WBC counts.
- ***Arterial blood gases (ABG):*** for partial pressure of oxygen in arterial blood (pO2), as a part of the clinical severity assessment.
- ***Serum pancreatic enzymes:*** serum amylase at the time of admission. Lipase after 24 hours of presentation. Serum LDH at the time of admission for Ranson's severity scoring.
- ***Renal function tests:*** this include blood urea, serum creatinine and serum sodium and potassium levels. Done on admission and thereafter every day for the initial 7 days for the assessment of serum creatinine values.
- ***Liver function tests:*** AST on admission for Ranson's severity scoring. LFT was done every 5$^{th}$ day of in-hospital stay monitoring of the Liver enzymes especially ALP.
- ***Blood sugar:*** random blood sugar on admission as a part of Ranson's scoring. If deranged, then 6 hourly using glucose spot test.
- ***Serum Calcium:*** done on admission, at 48 hrs for Ranson's scoring and thereafter, every alternate day for monitoring.
- ***Urine and blood culture:*** in case fever would set in or there was a persistent rising trend of TLC.
- ***Stool culture:*** at the end of 2$^{nd}$ week of infection, in case of suspicion of infection of pancreatic necrosis.
- ***Ranson's scoring:*** on admission and after 48 hours.

***Radiological survey***

X-ray: X-ray chest PA view at the time of admission to rule out any associated pleural effusion. X-ray abdomen erect/supine at the time of admission to rule out any associated ileus.

***Ultrasound abdomen:*** Presence of gallstone was identified by the typical acoustic shadowing effect. Presence of necrosis (<5% cases) was also identified on the Ultrasound scan. Also, in case of any diagnostic dilemma, other hepatobiliary pathologies with similar presentations like liver abscess and acute cholecystitis could be ruled out.

***Specific markers***

***C-Reactive Protein (CRP)***

CRP turbilatex kit (Euro-diagnostic system, Spain) was used. Based upon the reactions between CRP and the latex covalently bound antibodies against human CRP. Values were determined by photometric analysis. It was done at 6,24 and 36 hrs from the time of presentation. A value of >10 mg/dL signified pancreatitis.

***Blood urea nitrogen (BUN)***

The system used was the UREL ACN 418 or URELU ACN 417(Euro diagnostic Special Radiological Investigations. It was done at 24 and 48 hrs from the time of presentation. BUN was assessed both as an individual parameter and also, as a part of Ranson's severity scoring. A cut off value of 25 mg/dL was set in our study for labeling as severe acute pancreatitis.[40,41]

***CECT scan (contrast enhanced computed tomography)***

CECT scan using intravenous non ionic contrast was done between the 3$^{rd}$ – 5$^{th}$ day of presentation, followed by the follow up CECT at the 3$^{rd}$ week of illness. The scoring method used was the modified CT severity index (CTSI).[5]

**Table 1** CTSI Parameters

| CT grade | Points | %age necrosis | Points | Extrapancreatic complications | Points | CTSI grade |
|---|---|---|---|---|---|---|
| Normal pancreas | 0 | 0% | 0 | Pleural effusion | 2 | Mild (0-2) |
| Inflammation: pancreatic/peripancreatic | 2 | <30% | 2 | Vascular complications | 2 | Moderate(4-6) |
| Fluid collections | 4 | >30% | 4 | Extraparenchymal GIT | 2 | Severe (8-10) |

***Overall Scoring of the Individual Parameters***

**Table 2** Ranson´S Scoring

| Ranson's | Score |
|---|---|
| ≤2 | 0 |
| 3-5 | 1 |
| >5 | 2 |

**Table 3** Serum Amylase

| Amylase | Score |
|---|---|
| <150 | 0 |
| >150 | 1 |

**Table 4** serum C- reactive protien levels (U/L).

| CRP levels (U/L) | Score |
|---|---|
| <10 | 0 |
| 10-100 | 1 |
| >100 | 2 |

**Table 5** Blood Urea Nitrogen (BUN) levels.

| BUN levels (U/L) | Score |
|---|---|
| <16 | 0 |
| 16-25 | 1 |
| >25 | 2 |

**Table 6** CT severity grading.

| CT severity grading | Score |
|---|---|
| 0-2 | 0 |
| 4-6 | 1 |
| 8-10 | 2 |

**Table 7** Marshall scoring

| Organ system | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| Respiratory (pO2/FiO2) | >400 | 301-400 | 201-300 | 101-200 | ≤101 |
| Renal (serum creatinine, mg/dL) | <1.4 | 1.4 -1.8 | 1.9-3.6 | 3.6-4.9 | >4.9 |
| Cardiac (systolic BP, mmHg) | >90 | <90;fluid responsive | <90;not fluid responsive | <90; pH<7.3 | <90; pH<7.2 |

Thus, on the basis of above scores, the patients were stratified as follows:

**Table 8**

| Severity | Marshall score (out of a total score of 16) | Study score |
|---|---|---|
| Mild | <2 | 0 |
| Moderate | 2-6 | 1 |
| Severe | ≥6 | 2 |

### *Statistical Analysis*

The analysis was done using Qualitative statistical tests: Kruskall-Wallis test and Mc Nemar analysis to calculated the p-value and the statistical significance. The p-value for statistical significance was taken as <0.05.The data agreement was calculated using the kappa statistics.

The sensitivity and specificities and the accuracy were also calculated to assess the individual efficacy of all the 3 parameters.

## OBSERVATIONS AND RESULTS

The following observations were noted and results were evaluated.

### *Age distribution*

**Table 9** Age Distribution of the study population

| Age (years) | Number of patients |
|---|---|
| <30 | 7 (23.3) |
| 30-50 | 17 (56.66) |
| >50 | 6(23.3) |

The mean age group of the study group was 40.4 yrs with minimum age being 18 years and the maximum being 64 years. The age distribution of the disease in the study population was clustered into 3 groups. The prevalence was highest in the30-50 years age group.

### *Sex distribution*

Out of the 30 patients in the study, 13were female (43.33%) and 17 were male (56.66%).

### *Aetiology of acute pancreatitis*

Out of the 30 cases studied, 11cases had gallstone as the Aetiology (36.66) and 11cases were alcohol induced pancreatitis (36.66). The remaining 8 cases of an unknown aetiology. It was categorized as follows:

**Table 10** aetiology and frequency

| Aetiology | No. of patients | Percent |
|---|---|---|
| Gallstone | 11 | 36.66 |
| Alcoholic | 11 | 36.66 |
| Non gallstone Non alcoholic | 8 | 26.66 |

Hence, the most common cause of acute pancreatitis is gall stones and alcohol, both contributing to 36.66% of patients each.

### *Clinical parameters*

The clinical severity assessment was done on the grounds of 3 parameters:

Respiratory, Renal and Cardiac.

These 3 parameters were then graded according to the Marshall scoring (see table no.7)

Out of the 30 cases studied, 6 were diagnosed as severe acute pancreatitis (20%) according to the

**Table 11** marshall scoring on 7$^{th}$ day

| Severity | Number of patients | Percent |
|---|---|---|
| Severe | 6 | 20 |
| Non-severe (mild and moderate pancreatitis) | 24 | 80 |

### *Ranson's scoring*

The Ranson's scoring is done by the assessment of the parameters on admission and at 48 hrs and cumulative score is then categorized into three groups

**Table 12** Ranson score

| Ranson's | No. of patients | Percent |
|---|---|---|
| ≤2 | 16 | 53.33 |
| 3-5 | 11 | 36.66 |
| >5 | 3 | 10 |

### *Serum C-reactive Protein (CRP)*

The cut of value of serum C-reactive protein for labeling severe acute pancreatitis was earlier decided as 150 mg/dL. However, based on the reviewing of literature, the cut off value was decided to be lowered to 100 mg/dL.

**Table 13** CRP at 6 hours (CRP 1)

| Serum CRP (mg/dL) | No. of patients | Percent |
|---|---|---|
| <10 | 7 | 23.33 |
| 10-100 | 22 | 73.33 |
| >100 | 1 | 3.33 |

The mean CRP value at hours was 32.76mg/dL, with a range of 3-104 mg/dL.

Out of the 6 cases of severe pancreatitis, I had CRP (6 hrs)in the severe range. Out of the rest 24 cases, there were none with a CRP > 100 mg/dL. The mild and the moderate cases (<10 mg/dL and 10-100 mg/dL range) were clustered into one category of non-severe pancreatitis. Hence,

**Table 14** Correlation of CRP at 6 hrs with the clinical severity (Marshall scoring on the 7th day of presentation)

| CRP(1) results | Severe pancreatitis (Marshall score ≥6) | Non severe cases (Marshall score <6) |
|---|---|---|
| Severe (>100 mg/dL) | 1 | 0 |
| Non severe(<100 mg/dL) | 5 | 24 |

Sensitivity :16.67%
Specificity :100%
Positive predictive value (PPV): 100%
Negative predictive value (NPV): 82.76%
False negative rate :83.33%
False positive rate : 0%

Applying kappa statistics for testing the agreement of the data, the p value was measured to be 0.004(<0.05), highly significant .Thus, the CRP value at 6 hrs did not show an agreement with the Marshall clinical severity scoring done on the 7 day of presentation.

**Table 15** CRP at 24 Hours (CRP 2)

| CRP (mg/dl) | No of patients | Percent |
|---|---|---|
| <10 | 7 | 23.33 |
| 10-100 | 15 | 50 |
| >100 | 8 | 26.67 |

The mean value of CRP at 24 hours was 50.02 mg/dl, with a range of 3.5-108mg /dl

Out of the 6 cases of severe acute pancreatitis, all had a CRP (24hrs) value in the severe range out of the 24 non severe cases, 2 had CRP in the severe range.

**Table 16** Correlation of the CRP (24hrs) with the clinical severity (Marshall scoring on the 7 day of presentation

| CRP (2)results | Severe pancreatitis (Marshall score >6) | Non severe pancreatitis (Marshall score >6) |
|---|---|---|
| Severe (>100mg/dL) | 6 | 2 |
| Non severe (>100mg/dL) | 0 | 22 |
| Total | 6 | 24 |

Sensitivity :100%
Specificity :91.67%
Positive predictive value (PPV):75.00 %
Negative predictive value (NPV):100%
False positives :8.33%
False negatives :0%

Applying kappa statistics for agreement of data, the p –value was measured to be 0.001(<0.05); therefore, highly significant. Thus, the CRP values at 24hrs correlated well with the Marshall clinical severity scoring done on the 7 day of presentation.

**Table 17** CRP at 36 hours

| CRP (mg/dl ) | No. of patients | Percent |
|---|---|---|
| <10 | 9 | 30 |
| 10-100 | 16 | 53.33 |
| >100 | 5 | 16.67 |

The mean value of CRP at 36hrs was 42.91 mg/Dl, with a range of 3.5 -104 mg /dl.

**Table 18** Correlation of the CRP (36hrs) with the clinical severity (Marshall scoring on the 7 day of presentation)

| CRP (36hrs) results | Severe pancreatitis (Marshall score >6) | Non severe pancreatitis (Marshall score <6) |
|---|---|---|
| Severe (>100mg/dl) | 5 | O |
| Non severe (<100mg /dl) | 1 | 24 |

Out of the 6 cases of severe acute pancreatitis, 5 had CRP values in the severe range; out of the 24 non severe cases one had a CRP in the severe range.

Sensitivity : 83.33%
Specificity : 100%
Positive predictive value (PPV):100%
Negative predictive value (NPV):96%
False negative :16.67%
False positives :0%

Applying kappa statistics for the agreement of the data, the p-value was found tobe0 .306(>0.05) and hence, it was statistically insignificant. Thus, CRP value a 36 hrs correlated well with the Marshall clinical severity scoring done on the 7th day of presentation.

***Overall Assessment of Correlation of CRP Values With The Clinical Severity***

The Kruskall - Wallis test was used and the mean ranks of CRP (6, 24 and 36 hrs) versus the Marshall scores 7 day were evaluated. The p- value for the association was as follows:

- CRP at 6hrs :p –value 0.085 (>0.05)
- CRP at 24hrs :p – value0.001(<0.05)
- CRP at 36 hrs :p –value 0.001(<0.05)

Hence, the CRP at24 and 36 hrs had a positive association with the Marshall clinical severity scoring.

***Serum Blood urea nitrogen (BUN)***

**Table 19** BUN at 24 hrs (BUN 1)

| BUN at 24 hrs results | Severe cases | Non severe cases |
|---|---|---|
| Severe (>25mg/dL) | 3 | 3 |
| Non severe (<25mg/gL) | 3 | 21 |

The mean value of BUN at 24 hrs was 24.39 mg/dL, with a range of 5.5-70.5 mg/dL. out of the 6 cases of severe pancreatitis, the BUN at 24 hrs was in the severe range in 3 cases: out of the rest 24 non severe cases, BUN was in the severe range in 3 cases.

**Sensitivity:** 50%
**Specificity:** 87.50%
**Positive predictive value (PPV):**50%
**Negative predictive value (NPV):**87.50%
**False positives:** 12.50%
**False negatives:** 50%

Applying kappa statistics for assessing the data agreement, the p-value was found to be 0.020 (<0.05); therefore, highly significant. Therefore, the BUN value at 24 hrs correlated well with the Marshall clinical severity scoring done on the 7 day of presentation.

**Table 20** BUN at 48 hours

| BUN at 48 hrs | Severe pancreatitis (Marshall score >6 ) | Non severe cases (Marshall score <6) |
|---|---|---|
| Severe (>25mg/dl ) | 2 | 1 |
| Non severe (<25mg/dl) | 4 | 23 |

The mean value of BUN at 48 hrs was 17.53 mg/dl , with a range of 4.5-73 mg/dl

Out of the 6 cases of severe acute pancreatitis, BUN at 48 hrs was in the severe range in 2 cases ;out of the 24 non severe cases, BUN was in the severe range in 4 case.

Sensitivity : 33.33%
Specificity :95.85 %
Positive predictive value (PPV):66.67%
Negative predictive value (NPV):85.19%
False negatives:66.67%
False possitives:4.17%

Using kappa statistics, the p-value for the degree of agreement of the data was found to be 0.234;statistically insignificant. Therefore, the BUN values at 48 hrs did not correlate well with the Marshall clinical severity scoring done on the 7 day of presentation

***Overall Assessment of the Correlation of Bun Values with the Clinical Severity***

The Kruskall –Wallis test was used and the-mean ranks of BUN (24and 48 hrs) versus the Marshall scores at 7 day were evaluated. The p-values for the association were as follows:

- BUN at 24 hrs :p-value :<0.0005(<0.05)
- BUN at 48 hrs :p-value :0.012(<0.05)

Hence, the correlation of BUN at 24hrs and 48 hrs with the clinical severity was statistically significant.

**Table 21** CECT Scan (Between 3-5 Days of Illness)

| CECT (3-5day ) | Severe cases (Marshall score >6) | Non severe cases (Marshall score <6 )) |
|---|---|---|
| Severe (CTSI 8-10) | 6 | 2 |
| Non severe (CTSI <8) | 0 | 22 |
| Total | 6 | 24 |

Correlation of the CECT (3rd day) with the clinical severity. Out of 5 cases of severe acute pancreatitis, CECT report between the 3rd to 5th day of illness was severe in all the 5 cases; out of the rest 20 non severe cases, the CECT was reported as severe in 1case. Hence,
Sensitivity :100%
Specificity:91.67 %
Positive predictive value (PPV):75%
Negative predictive value (NPV):100%
False negatives s :0%
False positive : 8.33%

Using kappa statistics, the p-value for the date agreement was found to be <0.0001(<0.05); statistically significant. Thus, the CT severity index assessed by CECT scan between 3-5 day of presentation agreed well agreed well the Marshall clinical severity scoring done on the 7 day of presentation.

The overall correlation of the data was found using the Mc-Nemar Bowker test. The p-value was 0.500(>0.05) and kappa statistics was used and compare with Marshal l 7th day the p value was<.001therefore, statistically significant.

## DISCUSSION

Acute pancreatitis is a clinical challenge, often requiring management in the critical care unit. Therefore, prediction of severity in early part of acute pancreatitis can be helpful in the better management of the case besides clinical examination, biochemical tests, multiple prognostic scoring systems and computed tomography (CT)have been used in the assessment of severity.

Various clinic-biochemical scoring have also been used world over in the prognostication. Of acute pancreatitis such as Ranson´s scoring. Glassgow scale, APACHE II scoring. We used the Ranson's scoring in the present study and found a sensitivity of only 40% in assessing the severity of acute pancreatitis.

Various novel biomarkers like trypsinogen, PRNAse, procalcitonin, C reactive protein are being studied world over as predictors of severity of acute pancreatitis in the early phase of the disease, so as to identify the patients likely to have a severe course of disease. Such cases, if identified early may benefit form admission in high dependency units and managed accordingly

The present study population comprised of 30 patients who presented in the surgical OPD and Emergency with 6 hrs of development of their symptoms. Those presenting with the first attack of acute pancreatitis were included in the study group. According to the literature, approximately 10 -20 % of the cases of acute pancreatitis occurring world over follow the severe course.[3,9, 10] In this series, 6 out of the 30 cases (20%)were detected as severe acute pancreatitis according to the Marshall scoring on the 7 day.

In a study by Suvarna et at, the incidence of acute pancreatitis was found to be nine times more common in males than females with a mean age of presentation being 40.9 years.[11] This did not agree with the study by Larvin, where the male: female ratio was 47:53 with a mean age of presentation being 62 years.[12] In the present study, out of the 30 patients, 16 were males (53.33%) and 14 were females (46.67%), with a male: female ratio of 16:14.Thus, the sex distribution was almost equal. The mean age of presentation in our study was 40.4 years. The results of our study compared well with the study by Suvarna *et al*. and not with the study by Larvin, which as such is in variation with the other study.

In a large population based study conducted by Gullo *et al* in 5 European countries in 2002, alcohol (41%) followed by Gallstones (37.1%) were found to be the most frequent a etiological factors of acute pancreatitis. [13]Corfield *et al* reported the gallstones were the predominant etiological factor (50%), followed by alcohol (23%) in severe acute pancreatitis.[14] In the present study group, out of the 30patients11 (36.66%) were gallstone induced cases, 11(36.66%) were alcoholic cases and the rest were with an unknown aetiology (26.66%). Out of the 6 severe cases, 5 were alcoholic pancreatitis (83.33%) with the 6th case being without a known aetiology. This compared well with the study by Gullo *et al*. the association of alcohol with incidence of acute pancreatitis as well the severity of the disease was found statistically significant (p=0.003). since, there are direct pancreatotoxic effects of alcohol by affecting the pancreatic perfusion; it was observe that the alcohol induced cases of acute pancreatitis followed a more severe course. There is also, a higher prevalence of alcohol induced cases of acute pancreatitis followed a more severe course. There is also, a higher prevalence of alcohol consumption in males.

C- reactive protein (CRP) is one of the 3 markers which was assessed in the present study to predict the severity of pancreatitis. Beger and Rau in 2007 had found a diagnostic accuracy of about 70-80% for C- reactive protein with a cut off value at 150 mg/dl (normal range :10 -100mg/Dl). However, in a study by Paajanen *et al* 1995, the sensitivity and the overall accuracy of CRP as a predictor of severity of

pancreatitis was found to be 84% and 74% respectively, with a cut off value set at 100 mg/dL .Also in study by Devernis *et al* on 85 patients in a large hospital based cohort, CRP showed a sensitivity above 80%at a cut off level of 150 mg/dl in predicting severe acute pancreatitis. Baraukas *et al* in 2001 had found the highest sensitivity and specificity for CRP in predicting severity of acute pancreatitis at a cut off level of 110 mg/dl. Paajanen *et al* reported in 74-78 % of cases, severe pancreatitis could be predicted with a value of CRP 100 mg/ dl and above.[15]Since, the sensitives of the CRP at 100mg/dl and 150 mg/dl , were almost equal , in the present study the cut off value was set at 100 mg / dL.

In the present study, the CRP levels at 24 hrs of presentation was in the severe range in all the 6 cases of severe acute pancreatitis (sensitivity 100%; specificity 91.67%); CRP levels at 36 hrs was in the severe range in cases (sensitivity 83.33%and specificity 100%); CRP levels at 6 hrs was in the severe range in only 1 patient (sensitivity 16.67% and specificity 100%) The association of CRP at 24 hrs and 36 hrs with the clinical severity scoring on the 7 day was found statistically significant (p=0.001 )and that of CRP at 6 hrs was statistically insignificant (p=0.085). This compared well with the study by Puolakkanein *et al*.[16] Hence, CRP level at 24 hrs may be considered a predictor of severity of acute pancreatitis with the maximum accuracy.

The other maker evaluated in our study for the early prediction of severity of acute pancreatitis was Blood Urea Nitrogen (BUN). In a large hospital based observational cohort study conducted by Wu *et al* 2006 from 69 US hospitals in a span of 3 years, it was demonstrated that the mean BUN levels were persistently elevated among non survivors versus survivors of acute pancreatitis during the first 48 hrs of hospitalization.[17] A strong association was found between the extent of BUN increase at 24 hrs and the risk of mortality.

Wu, Johannes *et al* 2008 conducted a large population based study to predict the mortality of acute pancreatitis using BUN as one of the 5 parameters for assessment of mortality.[18] Wu, Bakker *et al* 2011 had conducted a study on a large hospital based cohort from June 2005 through May 2009 and found BUN an accurate marker for prediction of mortality of pancreatitis.[18]In the study , Johannes *et al* , the cut off level of BUN for labeling severe acute pancreatitis was kept at the upper limit of the normal range of BUN (normal: 8-25 mg/dL). This yielded a sensitivity of90% in the prediction of severity of acute pancreatitis. In the present study, the BUN levels were done at 24 hrs and 48 hrs from the time of presentation. The higher limit of the normal of BUN, i.e. 25mg/dL was taken as the cut off (normal:16-25mg/dL). Out of the 6 cases of severe acute pancreatitis, BUN at 24 hrs was in the severe range in 6 cases (sensitivity 50%); BUN at 48hrs was in the severe range in 3 cases (sensitivity 33.33%). The association of Blood Urea Nitrogen at 24 hours with the clinical severity scoring on 7 day was found statistically significant (p <0.0005). The BUN at 48 hrs versus the clinical severity scoring on 7 day was however found statistically significant (p=0.012).Considering all the findings, it was observed that BUN at 24 hours and 48 hrs can be a predictor of severity of acute pancreatitis, but has a low sensitivity as well as specificity.

CECT scan was the 3rdmarker, which we assessed in our present study to predict the severity of pancreatitis . CECT has been recognized as the imaging modality of choice for the assessment of severity of acute pancreatitis.[19,20]Most authors recommend a widely varying interval from the onset of symptoms to the timing of scanning that range from 48 hrs to 10 days.[21] Some authors recommend a CT study at 3-10 days after hospitalization for diagnosis of severe acute pancreatitis that CT is difficult to interpret before 72 hrs and that the areas of necrosis are better delimited after this time.[22]Pancreatic necrosis usually develops within 24-48 hours after symptom onset; thus, early CT within 12 hours of symptom onset may be falsely reassuring.[23]In a study conducted by Stimac *et al* in 2004-2005, in a cohort of 101 patients CECT performed between the 3rd-5th day of presentations showed a sensitivity of 95-99% and a specificity of 90-95% in assessing the severity of acute pancreatitis.[24]

In the present study, we performed CECT between the 3rd-5th day of presentation. A CECT scan was also performed on the 3rd week of presentation as a follow up. 8 out of the total 30cases were found to be severe pancreatitis according to CECT scan between 3rd to 5th day, but only 6 turned out to be actually severe according to the clinical severity scoring. Hence , the sensitivity of CECT when done between 3rd-5th day in predicting severity of acute pancreatitis was 100%, with a specificity of 91.67%. This was found to be statistically significant (p=0.500;Mc Nemar analysis and p value<0.001 kappa statistics).

Therefore, it can be concluded that CRP and CECT when used together within 72 hours of presentation in a patient with acute pancreatitis can predict the severity of disease with maximum accuracy and can be beneficial to both the patient and the treating physician. However, BUN alone is not a good marker for predicting severity of pancreatitis and when combined with CRP or CECT does not cause a significant difference in the sensitivity and specificity of prediction.

## CONCLUSION

The following conclusions were drawn:

1. CECT (contrast enhanced CT) done between 3rd to 5th day of presentation is a good predictor of severity of acute pancreatitis, with a sensitivity of 100% and a specificity of 91.67%.
2. CRP(C-reactive protein) levels done at 24hrs has a sensitivity of 100% and specificity of 91.67% for predicting the severity of acute pancreatitis at a cut off value of 100 mg/dL.
3. BUN(Blood Urea Nitrogen)levels done at 24hrs and 48 hrs have a low sensitivity and specificity for early prediction of severity of acute pancreatitis and hence, it is not a good marker for the early prediction of severity of the disease process.
4. CECT when combined with CRP within 72 hrs of presentation can predict the severity of acute pancreatitis with a sensitivity and specificity close to almost 100%.

A large scale multi-institutional trial with bigger sample size is recommended.

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