

# Comparison Between Procalcitonin (Pct) Estimation and Contrast Enhanced Computed Tomography Findings for The Early Prediction of Severity and Morbidity in Acute Pancreatitis

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## Abstract

**Background:** Acute pancreatitis is an acute inflammation of the pancreas. It is one of the most common diseases of the gastrointestinal tract, leading to tremendous emotional, physical, and financial human burden. It can have severe complications and high mortality despite treatment. Objective: to comparison between procalcitonin (PCT) estimation and contrast enhanced computed tomography findings for the early prediction of severity and morbidity in acute pancreatitis. **Method:** The present prospective observational study was conducted on either sex of age group 18 to 65 years patients of acute pancreatitis admitted in department of General Surgery in emergency as well as OPD setting with pain in abdomen being diagnosed as a case of acute pancreatitis according to inclusion or exclusion criterion from January-2020 to June-2021 were enrolled in this study. **Results:** Out of a total 30 number of patients 20 (66.7%) were males and 10(33.3%) females. Mean age of patients was 37.77±11.1 years varied from 18- to 65 years. Etiology for the disease were Gallstone in majority of the cases 19(63.3%). 100% of patients presenting complaints of the disease were abdominal pain and vomiting Abdominal Tenderness as well as Bowel sound were common features in all patients. Mild pancreatitis was diagnosed in 24(80.0%) patients, it was Moderate in 6(20.0%) patients as noted as per CTSI scoring. The sensitivity & the specificity of Procalcitonin to diagnose severity of acute appendicitis (moderate) were 83.3% & 83.3% respectively, while it's over all accuracy, was 80.6% respectively, with a cut-off value of  $\geq 1.35$  ng/ml. **Conclusion:** Serum procalcitonin can be a new promising marker to predict the severity and outcome of acute pancreatitis. However, procalcitonin is a nonspecific marker of infection (bacterial/fungal) and sepsis and does not provide particulars about the underlying source of infection

**Keywords:** Serum procalcitonin, Enhanced Computed Tomography, Severity, Morbidity, Acute Pancreatitis.

## Introduction

Acute pancreatitis is classified into mild, moderate and severe on the basis of Atlanta classification. Mild cases of acute pancreatitis do not have any complication or organ failure and are often successfully treated with conservative measures, while severe cases have persistent organ failure, do require admission to the intensive care unit, antibiotics use or even surgery to deal with the complications.<sup>1</sup>

Annual incidence of Acute Pancreatitis (AP) ranges from 13-47/100,000 population. Annual incidence of Acute Pancreatitis (AP) ranges

from 13-47/100,000 population.<sup>2</sup> Severe acute pancreatitis (AP) is seen in approximately 10–20% of

patients with AP, and morbidity and mortality rates range from 30% to 50%.<sup>3</sup>

Nearly 60%–80% of all cases of AP in developed countries are attributable to either gallstone disease or alcohol abuse.<sup>4</sup> The incidence is similar in both sexes, although alcohol abuse is the more common cause in men and gallstones is the more common cause in women.<sup>5</sup> There is an upsurge in the incidence of AP over the last few decades, although the case fatality rate has remained unchanged.<sup>6</sup> This may either be due to increased incidence of gallstone disease or improvement in diagnostic modalities.<sup>7</sup>

The most common risk factors for acute pancreatitis are gallbladder disease (often caused by choledocholithiasis) and chronic alcohol consumption. Given newly

emerging diagnostic modalities, recent guidelines have recommended against the diagnosis of “idiopathic acute pancreatitis.”<sup>8</sup>

The Atlanta criteria use early prognostic signs, organ failure, and local complications to define disease severity.<sup>9</sup> Early prognostic signs include a Ranson score of 3 or greater, or an acute physiology and chronic health evaluation (APACHE II) score of 8 or greater.

The Ranson score evaluates 11 factors within 48 hours of hospital admission to predict severity of pancreatitis and risk of mortality. However, the sensitivity for predicting poor outcome is only 70%.<sup>10</sup> The APACHE II scoring system uses 12 criteria to predict the severity of pancreatitis, with the risk of death increasing as the score increases.<sup>11</sup>

Contrast-enhanced CT (CECT) has become the preferred assessment in the emergency department as the reference for both the diagnosis of AP and determination of the severity of AP in many centers. For the staging of acute pancreatitis, Balthazar et al.<sup>12</sup> developed a computed tomographic (CT)-based scoring system, in which severity of pancreatitis was graded from A to E on the basis of pancreatic enlargement and presence of peri-pancreatic fluid collections on un-enhanced CT scan. However, its main drawback was its inability to reliably depict pancreatic necrosis and, consequently, further define the risk of complications in patients with retroperitoneal fluid collections at the time of presentation.

Plasma procalcitonin (PCT) is a highly specific marker for the diagnosis of bacterial infection and sepsis. It is a peptide precursor of the hormone calcitonin, the latter being involved with calcium homeostasis. It is composed of 116 amino acid and is produced by para follicular (C cells) of the thyroid and by the neuroendocrine cells of the lungs and the intestine.<sup>1</sup> The level of Procalcitonin in the blood stream of healthy individuals is below the limit of detection (0.1 µg/L) of clinical assays.

Even the acute-phase reactant C-reactive protein (CRP), the most widely studied inflammatory marker in acute pancreatitis, is not practical as it takes 72 hours to become accurate.<sup>13</sup> CT or MRI imaging are also not much reliable early in the course of disease to determine severity of acute pancreatitis, as necrosis is usually not present at time of onset and it usually develop after 48-72 hr.<sup>14</sup> Due to this clinicians have been largely unable to predict who with acute pancreatitis will develop severe disease.

Present prospective observational study was aimed to comparison between procalcitonin (PCT) estimation and contrast enhanced computed tomography findings for the early prediction of severity and morbidity in acute pancreatitis.

## Materials and Methods

This prospective observational study was conducted in the Department of General Surgery in emergency as well as OPD setting on those patients who diagnosed pain in abdomen as a case of acute pancreatitis according to inclusion or exclusion criterion from January-2020 to June-2021 was considered for study at U.P.U.M.S, Saifai, Etawah (U.P). Sample size was minimum 30 patients

Sample size calculation: The sample was calculated on the basis of mean is of the study or data are on interval/ratio scale. Sample size was estimated using software Power analysis and sample size, version 8 (PASS-2008).

### Inclusion Criteria

1. Patients admitted in Emergency department with clinical diagnosis of acute pancreatitis.
2. History of pain in abdomen for 3 days or less along with 3 fold raised serum amylase & lipase levels with or without radiological evidence.

### Exclusion Criteria

1. Patient's serum Amylase and Lipase are within normal limit.
2. Pregnant patients
3. Presence of any other intra-abdominal mass
4. Patients not giving consent to be part of study
5. On further evaluation of patient, if a different final diagnosis is confirmed
6. Patients having conditions which cause elevated serum Procalcitonin levels.

### Screening/ Survey

A total of 33 patients were screened, 2 were rejected to participate in the study and 1 were not fit according to inclusion criteria and finally 30 patients were found fit according to inclusion criteria.

Local and English language was preferred to ask each patient's history and it was taken using a confidential questionnaire formulated by the staff members. The questionnaire included questions providing information on personal data, which were next properly encoded. The clinical data given by patients were then complemented with information on diagnosis of the disease, the treatment administered (present and/or past), adverse effects reported.

### Methodology

After obtaining approval from the Institutional Ethics Committee, Database collection included documentation of medical history, age, sex, prehospital interval, vital signs, abdominal signs, and drug history. A complete physical examination was performed and blood samples for procalcitonin with other relevant investigations were done.

The severity of acute pancreatitis was assessed by contrast-enhanced computed tomography (CECT). As per these criteria, the appropriateness of a particular

imaging modality in a given clinical setting is rated on a scale of 1 to 9. A rating of 1 means that a particular imaging modality is least appropriate and a rating of 9 suggests that the investigation is most appropriate in a given clinical scenario. For patients with suspected acute pancreatitis, rating for appropriateness of CT of the abdomen and pelvis is as follows: 15

1: Etiology unknown, first episode of pancreatitis (Rating=6);

2: Severe abdominal pain, elevated serum amylase and serum lipase, no fever or evidence of fluid loss at admission (Rating=7);

3: Severe abdominal pain, elevated serum amylase and serum lipase, 48 hours later assuming no improvement or degradation (assume no prior imaging) (Rating=8);

4: Severe abdominal pain, elevated serum amylase and serum lipase, fever and elevated white blood cell count (Rating=9);

5: Severe abdominal pain, elevated serum amylase and serum lipase, oliguria, tachycardia (Rating=9).

Abdominal CECT was done on a single-slice helical scanner Fxi-GE Medical System, typically 72 hours after admission when it was optimum to rule out pancreatic necrosis and properly delineate the areas of necrosis.

#### Statistical Methods

Data was recorded on a predesigned Performa and managed in a Microsoft Excel spreadsheet. The data were subjected to statistical analysis using software SPSS version 23.0. Continuous data are presented as means with standard deviations. Categorical data are presented as the percent frequency occurrence. Groups were compared using the Mann-Whitney U test for non-categorical data; Fisher's exact test was used to examine differences in the sex ratio, etiology, and death ratio. The

cutoff value of serum PCT, and other parameters were determined using receiver operating characteristic (ROC) curves. Sensitivity, specificity, positive, and negative predictive values, accuracy, and likelihood ratios were also calculated. Logistic regression analysis was used to establish the influence of the chosen parameters on the prognosis of AP. Fisher's exact. The P value of <0.05 was considered statistically significant.

#### Results

:Out of a total 30 number of patients drafted for study 20 (66.7%) were males and 10(33.3%) females .As for age, while mean age of patients was $37.77\pm 11.1$  years the same varied from 18-to 65 years. Maximum numbers of patients were between 31 -50 years of age.

Etiology for the disease were Gallstone in majority of the cases 19(63.3%) , followed by Alcohol in 8(26.7%)cases and Idiopathic 3(10.0%) cases.

Presenting complaints of the disease were abdominal pain as well as Vomiting. This was the complaint in all the 100% patients, besides abdominal distension was also reported in case of a few patients.

Past history, Alcohol users and tobacco users were the easy victims of the ailment. Among 30 patients under study 9 (30.0%) were Alcohol addicts and another 6(20.0%) were Tobacco users.

The observations as under were made while examination of the patients and the same were recorded in the table. While Abdominal Tenderness as well as Bowel sound were common features of all patients, Guarding 10 (33.3%), Distension 7(23.3%) and Free fluid 7(23.3%) were also the presenting features of a sizable number of patients as noted against each.

**Table No 1: Abdomen examination findings in studied patients**

Examination	Frequency (N=30)	Percentage (%)
Distension	7	23.3
Tenderness	30	100.0
Guarding	10	33.3
Rigidity	0	0.0
Hepatomegaly	3	10.0
Splenomegaly	0	0.0
Free fluid	7	23.3
Bowel sound	30	100.0

Blood examination of every patient was made and the findings of the blood analysis were computed in the

table below to compare the same with normal human blood composition.

**Table no. 2: Biochemical parameters**

Parameters	Mean±SD	Median	Range (Min-Max.)
Serum ALP (IU/L)	503.5±156.2	471	300-847
Serum amylase (U/L)	412.5±149.8	369.50	197-754
serum Lipase (U/L)	202.1±99.1	189	97-441
Blood urea (mg/dl)	48.9±16.5	46.5	23-80.6
Serum Creatinine (mg/dL)	1.1±0.4	0.97	0.47-1.97

<b>Serum Calcium (mg/dl)</b>	7.7±0.8	7.77	5.93-9.76
<b>Hemoglobin (g/dl)</b>	11.8±1.3	11.8	9.10-14.50
<b>Procalcitonin (ng/ml)</b>	1.2±0.4	1.2	0.3-1.8

Haemodynamic parameters of all the patients were recorded and noted in the table below. Mean Pulse rate (bpm) was 118.9±12.4 against the range of 98-146, mmHg, Mean systolic bp (mmHg) was 116.3±8.9 (mmHg) against the range of 104-132 mmHg, and mean Diastolic bp (mmHg) was 70.1±5.9 (mmHg) against the range of 56-84 mmHg.

#### CT findings

CT findings were recorded in the table as under. Enlarged pancreas as well as, Peri-pancreatic fat

stranding, were noted in every case and therefore recorded in the table below. Peri-pancreatic fluid collection was however, not seen in any one case as stated in the table. Necrosis was observed in 6 (20.0%) cases and pancreatic ascites in 7 (23.3%) patients. Emphysematous pancreatitis, Worm in pancreatic duct and Pleural effusion (left/right/bilateral) were also not seen in any one patient

**Table No. 3 CT findings of the studied patients**

CT findings	Frequency (N=30)	Percentage (%)
<b>Enlarged pancreas</b>	30	100.0
<b>Peripancreatic fat stranding</b>	30	100.0
<b>Peripancreatic fluid collection</b>	0	0.0
<b>Necrosis</b>	6	20.0
<b>Emphysematous pancreatitis</b>	0	0.0
<b>Pancreatic ascites</b>	7	23.3
<b>Worm in pancreatic duct</b>	0	0.0
<b>Pleural effusion (left/right/bilateral)</b>	0	0.0

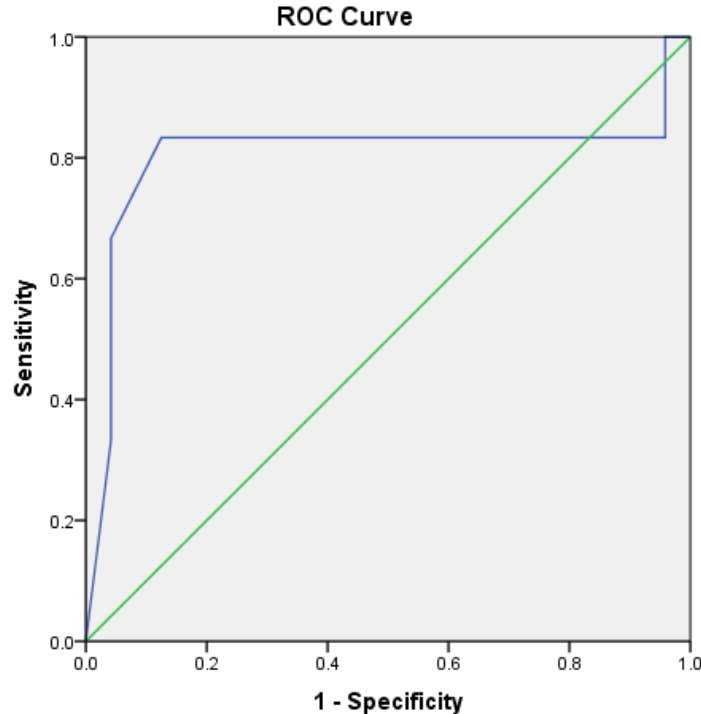
Distribution of severity of acute pancreatitis according to CTSI scoring was made and noted in the table. While Mild pancreatitis was diagnosed in 24 (80.0%) patients, it was Moderate in 6 (20.0%) patients as noted in the table. There was however, no case of severe pancreatitis among the patients studied.

The sensitivity & the specificity of Procalcitonin to diagnose severity of acute appendicitis (moderate) were 83.3% & 83.3% respectively, while its overall accuracy, was 80.6% respectively, with a cut-off value of  $\geq 1.35$  ng/ml.

**Table No. 4 ROC curve analysis**

Area Under the Curve	Std. Error <sup>a</sup>	Asymptotic Sig. <sup>b</sup>	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.806	0.143	0.023	0.525	1.000
The test result variable(s): Procalcitonin has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.				
a. Under the nonparametric assumption				
b. Null hypothesis: true area = 0.5				

#### Comparable tables between severities of acute pancreatitis



Diagonal segments are produced by ties.

Comparison of Procalcitonin and ICU stay between mild and moderate groups has been made in the table below. When Procalcitonin was  $1.12 \pm 0.3$  ICU stay was  $4.96 \pm 0.7$  days and when Procalcitonin was  $1.50 \pm 0.5$  ICU stay became more  $7.50 \pm 0.5$  days which indicates that any increases in the Procalcitonin brings about a significant difference in the number of days of hospital stay by the patient ( $P < 0.001$ ).

Comparison of biochemical parameters between mild and moderate groups has been made in the table below. Variation in the biochemical parameters between mild and moderate groups was more in respect of Serum ALP (IU/L) and Serum amylase (U/L) as P values in respect of these two were 0.039 and 0.181 respectively. In all others biochemical variation was not that acute

**Table no 5: Comparison biochemical parameters between mild and moderate group**

	Severity		P value
	Mild (N=24)	Moderate (N=6)	
<b>Serum ALP (IU/L)</b>	474.5±132.8	619.7±200.6	<b>0.039</b>
<b>Serum amylase (U/L)</b>	394.0±123.2	486.3±228.5	0.181
<b>serum Lipase (U/L)</b>	197.7±96.9	219±115.2	0.638
<b>Blood urea (mg/dl)</b>	48.1±5.6	51.8±21.0	0.628
<b>Serum Creatinine (mg/dL)</b>	1.1±0.4	1.1±0.5	0.775
<b>Serum Calcium (mg/dl)</b>	7.3±0.6	11.8±1.3	0.210
<b>Hemoglobin (g/dl)</b>	11.8±1.3	11.8±1.7	0.995

Comparison of hemodynamic parameters between mild and moderate groups has been made in the table below. Mild Pulse rate (bpm) was  $115.3 \pm 9.4$ , whereas Moderate Pulse rate (bpm) was  $133.3 \pm 13.1$ ,  $P = 0.001$ , which signifies that variation between the two was significant. Similarly Mild systolic BP (mmHg) was  $116.8 \pm 9.1$  (mmHg) and moderate

systolic BP (mmHg) was  $114.0 \pm 8.7$  mmHg and  $P = 0.497$ , which signifies that the difference was not significant. Likewise Mild Diastolic BP (mmHg) was  $70.3 \pm 6.3$  (mmHg) as against which Moderate Diastolic BP (mmHg) was  $69.3 \pm 4.3$  (mmHg) and  $P = 0.740$  which is also not significant.

## Discussion

In our study, out of the total patients, about two-thirds (66.7%) were males, and one-third (33.3%) were females; similar findings were observed by **Kaur K et al.**<sup>1</sup> (2020), where about two-thirds (68.3%) and one-third (31.6%) participants were males and females respectively.

In contrast, in the study conducted by **Kaur K et al.**<sup>1</sup> (2020), it was found that Alcohol was the precipitating factor for acute pancreatitis in a majority (56.6%) of the patients, while Gallstone was an etiological factor in less than half (43.3%) of the patients.

Abdominal pain and vomiting were the presenting complaints in 100 per cent of patients, besides abdominal distension was also reported in about one-fourth (23.3%) of the patients. **Shera IA et al.**<sup>16</sup> (2018) in a study showed that the most common complaint was non-radiating abdominal pain (73%), followed by vomiting (61.7%).

**Shera IA et al.**<sup>16</sup> (2018) in a study showed a little higher frequency of abdominal tenderness (47.5%) while comparatively lower frequency for guarding (22.6%).

The median blood urea level was 46.5 mg/dl, calcium level was 7.77 mg/dl, while procalcitonin level was 1.2 ng/ml. In a study conducted by **Woo SM et al.**<sup>17</sup> (2011), the median urea level was 19 mg/dl, total calcium was 8.6 mg/dl, and procalcitonin level was 1.66 ng/ml.

In this study, the mean amylase and lipase levels were 412.5 U/L and 202.1 U/L, respectively. **Swede H et al.**<sup>18</sup> (2017) showed a comparatively higher level of amylase and lipase, i.e., 623.23 U/L and 890.21 U/L, respectively.

## CT findings

In this study, enlarged pancreas and peri-pancreatic fat stranding were noted in every patient. The peri-pancreatic fluid collection was, however, not seen in anyone. Pancreatic ascites were noticed in about one-fourth (23.3%) of patients, and necrosis was observed in one-fifth (20.0%) patients. Emphysematous pancreatitis, Worm in the pancreatic duct and Pleural effusion (left/right/bilateral) were not seen in any patient. In contrast, **MIR MA et al.**<sup>19</sup> (2013) showed that the most common finding on CECT was that of peripancreatic fluid collection, noted in a majority (88%) of patients, and emphysematous pancreatitis was seen in a few (4%) patients.

According to CECT scoring, Mild pancreatitis was diagnosed in the majority (80.0%) of the patients, while moderate pancreatitis was present in one-fifth (20.0%) patients. However, **MIR MA et al.**<sup>19</sup> (2013) showed that less than half (44%) of the patients had moderate pancreatitis, about one-third (32%) had mild pancreatitis and about one-fourth (24%) had severe pancreatitis.

**Kumar S et al.**<sup>20</sup> Error! Bookmark not defined. (2017) conducted a study and showed that serum PCT at 0.9 ng/ml had a slightly higher sensitivity of 92.60 per cent and specificity was 80.30 per cent with an accuracy of 85.6 per cent.

In the present study, Area under the Curve (AUC) for PCT was 0.806, with a standard error of 0.143 (95 % CI 0.525—1.00) and a p-value of 0.023. **Kumar S et al.**<sup>20</sup> (2017) showed a similar AUC for PCT, which was 0.887, with a 95 % CI (0.825—0.928) and a p-value <0.001.

A comparison of Procalcitonin and ICU stay between mild and moderate groups revealed that when Procalcitonin was 1.12±0.3, ICU stay was 4.96±0.7 days, and when Procalcitonin was 1.50±0.5, ICU stay became more, i.e., 7.50±0.5 days which indicates that any increases in the Procalcitonin bring about a significant difference in the number of days of hospital stay. In their study, **Rau B et al.**<sup>21</sup> (2007) showed that the median length of stay was eight days in patients with severe pancreatitis.

This study revealed that in mild pancreatitis, mean serum ALP and serum amylase was 474.5 IU/L and 394 U/L, respectively; while in moderate pancreatitis, mean serum ALP and serum amylase was 619.7 IU/L and 486.3 U/L, respectively; Similarly, **Zerem D et al.**<sup>22</sup> (2017) in their study showed variation in the level of serum amylase, i.e., serum amylase level in mild pancreatitis was 938 IU/L while it was 1088 IU/L in severe pancreatitis (p >0.05). In their study,

We observed serum Lipase to be 197.7 U/L and 291 U/L in mild and moderate pancreatitis, respectively. **Cho JH et al.**<sup>23</sup> (2015) showed a higher serum lipase level of 1949.7 IU/L in mild to moderate pancreatitis and still a higher level of 2108.2 IU/L in severe pancreatitis.

We observed no difference in serum creatinine level (1.1 mg/dl) among mild and moderately severe pancreatitis. However, **Cho JH et al.**<sup>23</sup> (2015) showed that serum creatinine was 1.1 mg/dl in mild to moderate pancreatitis and 2.2 mg/dl in severe pancreatitis, which was statistically significant.

In mild pancreatitis, pulse rate (bpm) was 115.3, whereas, in moderate pancreatitis, pulse rate (bpm) was 133.3. Similarly, systolic BP was 116.8 mmHg in mild pancreatitis and 114.0 mmHg in moderate pancreatitis. Likewise, Diastolic BP was 70.3 mmHg in mild pancreatitis, as against which Diastolic BP was 69.3 mmHg in moderate pancreatitis. However, **Sternby H et al.**<sup>24</sup> (2017) observed lower systolic blood pressure (<90 mmHg) in severe pancreatitis.

## Conclusions

Increased serum levels of procalcitonin serve as a promising simple biomarker of prediction of severity of acute pancreatitis. It is a simple, inexpensive, routinely available and highly accurate. Hence, serum procalcitonin can be a new promising marker to predict the severity and outcome of acute pancreatitis. However,

procalcitonin is a nonspecific marker of infection (bacterial/fungal) and sepsis and does not provide particulars about the underlying source of infection.

The current study thus contributes to shed further light on the still existing controversies about the usefulness of procalcitonin in severity determination in acute pancreatitis. In this context, confusion arose from various studies, which comprised limited patient numbers and suffered from non-uniform definitions of complications

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