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Original Research Article

Role of procalcitonin as a early predictive marker of infected pancreatic necrosis

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Abstract

Background: The aim of this study is to explore how procalcitonin can serve as a useful marker for predicting infected necrosis in acute pancreatitis. Acute pancreatitis is a major reason why people are hospitalized. This condition can vary from mild to severe. Although the modified CT Severity Index (CTSI) and FNAC are valuable tools, they have some drawbacks. They require advanced technical equipment and skilled personnel, and also carry a risk of complications, making them less accessible and affordable. Therefore, I believe that procalcitonin could be an important and cost-effective marker for assessing the severity of acute pancreatitis.
Materials and Methods: This study is a prospective observational study. The researchers measured procalcitonin levels in all patients diagnosed with acute pancreatitis when they were admitted and again 72 hours later. They also performed a Contrast Enhanced Computed Tomography (CECT) scan of the abdomen 72 hours after admission. The team compared the procalcitonin levels with the Computed Tomography Severity Index (CTSI) CT findings of presence of necrosis and gas. They considered a serum procalcitonin level of ≥0.5 ng/ml to be significant.
Results: Correlation of clinical severity with presence of pancreatic necrosis showed a positive correlation (p=0.001). Severe cases showed greater presence of infected pancreatic necrosis (IPN). Similarly serum procalcitonin (PCT) levels were also correlated with pancreatic necrosis. PCT levels both at admission and at 72hours showed a positive correlation with infected pancreatic necrosis with p-value being 0.002 and 0.004 respectively.
Conclusion: Thus, we may conclude that serum procalcitonin measurements are valuable in predicting disease severity in acute pancreatitis along with risk of developing infected pancreatic necrosis as it is a reliable indicator of the same.

Keywords: Acute pancreatitis, Severe pancreatitis, Infected pancreatic necrosis, Pancreatic necrosis, MCTSI (modified Computed tomography severity index, Serum procalcitonin, Revised Atlanta classification

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1. Introduction

Acute pancreatitis involves inflammation of pancreas and is amongst leading causes of hospitalization in gastrointestinal disorders. Common etiology being gall stones, alcohol and post ERCP. An attack may be precipitated by drug intake like (azathioprine, Corticosteroids etc.) or due to autoimmune disease. Premature activation of proenzymes is the main pathology behind inflammation which further leads to auto digestion of pancreas. Pancreatitis may also lead to superadded infection and systemic inflammatory response.

Acute pancreatitis ranges from mild to severe types that can be managed conservatively or may require active intervention respectively. The death rate varies from 3% for patients with mild swelling of the pancreas to as much as 20% for those with pancreatic necrosis.[1] Determining the disease severity and presence of tissue death is thus essential to predict the outcome.[2-3]

The updated Atlanta classification from 2012[4] sorts acute pancreatitis into three levels of severity: mild, moderate, and severe. Contrast-enhanced Computed Tomography (CECT) is the best imaging method for assessing acute pancreatitis because it helps determine severity, spot pancreatic necrosis, and show any local complications. The CT severity index (CTSI) was created in 1990 by Balthazar and had some limitations. It did not include complications outside the pancreas or those related to blood vessels, which caused differences in opinions among doctors when trying to measure the extent of necrosis, inflammation, and damage to the pancreas. Mortele and

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others suggested a new version of the CT severity index (mCTSI) to address these issues by considering complications that occur outside the pancreas.[1] In numerous studies, modified Mortele CTSI has showed a stronger correlation than the Balthazar index for detecting prognosis of patients with acute pancreatitis.[1-3,5-6]

Procalcitonin (PCT) is a 116-amino acid residue whose significance was first recognized in 1993 when a positive correlation between bacterial infection and sepsis with increased serum PCT levels was demonstrated.[5] It is challenging to tell the difference between bacterial and non-bacterial infections using other inflammatory markers like CRP, which lack specificity[3] whereas PCT shows a high specificity of 79%, and thus helps in accurately determining bacterial cause of SIRS.[6]

Diagnosing and starting treatment quickly is crucial for patients with infected necrosis and those who might develop further complications. Different methods, like Ranson and APACHE II, help determine how serious acute pancreatitis is, but they are not always completely reliable. Because of this, doctors also use certain blood tests, like CRP, and imaging scoring systems, such as CTSI, to assess the severity and spot any complications like necrosis or a septic foci. CRP is widely used clinically; however, it is less sensitive (47%) which is at par to clinical examination. Serum PCT assay overcomes this limitation in being cost effective with high sensitivity and accuracy.

Numerous studies have demonstrated advantages and higher sensitivity and specificity of serum PCT assay over other biomarkers such as CRP and clinical scoring systems like Ranson and APACHE II.[7-8] PCT levels are also significantly superior for identifying infected necrosis as compared to CRP levels along with identifying severe septic complications and death.[9] Thus though pancreatic necrosis can be well assessed on CECT it is not very sensitive or specific for detecting infected necrosis and FNAC followed by gram stain though very specific is rarely used due to requirement of high skill , increased risk of complications and being costly. Thus PCT can act as an early, cost -effective predictive marker of infected pancreatic necrosis as an adjunct to CECT.

2. Materials and Methods

2.1. Study design

This is a result of Prospective observational study conducted at Sri Guru Ram Das Hospital of Medical Sciences and Research, Vallah, Amritsar, Punjab from August 1, 2023 to February 28, 2025 on 60 patients.

2.2. Settings

This study included patients with acute pancreatitis who provided written informed consent and met the inclusion criteria. Conducted at Sri Guru Ram Das Institute of Medical Sciences and Research in Vallah, Amritsar, Punjab, this is a prospective observational hospital study. Doctors diagnosed patients with acute pancreatitis using the diagnostic criteria from the Atlanta guidelines for acute pancreatitis established in 2013. Researchers measured serum procalcitonin levels in all patients at the time of admission and again 72 hours later. They performed a Contrast Enhanced Computed Tomography (CECT) of the abdomen either at admission or within 72 hours. The team analyzed the relationship between procalcitonin levels and the Computed Tomography Severity Index (CTSI). They considered a serum procalcitonin level of ≥0.5 ng/ml to be significant.

2.3. Duration

Present study was conducted from August 1, 2023 to February 28, 2025 after taking approval from Institutional Research and Ethics Committee of Sri Guru Ram Das University of Medical Sciences, Amritsar.

2.4. Participants

Patients who were diagnosed as case of acute pancreatitis on basis of diagnostic criteria as per Atlanta criteria for acute pancreatitis from August 1 2023 to February 28, 2025 and gave written consent for same.

2.5. Inclusion criteria

1. Age more than 18 years.
2. Diagnosed cases of acute pancreatitis on basis of Atlanta 2013 guidelines.

2.6. Exclusion criteria

1. Co-infections like hepatitis B, C, and HIV infection.
2. Presence of any wound or septic foci which can lead to increase in serum Procalcitonin level.
3. Acute pancreatitis due to any intervention like surgery or Endoscopic retrograde cholangiopancreatography.
4. Traumatic pancreatitis.

2.7. Methodology

When patients who met the criteria for the study and agreed to participate were admitted to the hospital's emergency room, ward, or ICU, they were enrolled in the study. Those with pancreatitis received an explanation of the study and its goals through the Patient Information Proforma. After their enrollment, we collected demographic information and a detailed medical history. We conducted a thorough physical examination and took blood samples to check procalcitonin levels, along with other important tests like a complete blood count, serum electrolytes, renal function tests, liver function tests, amylase, lipase, and PTI. We measured procalcitonin levels at the time of admission and again 72 hours later using a Chemiluminescence Immunoassay. In healthy individuals, procalcitonin levels are usually very low (0.1 ng/ml), and we set the cutoff for diagnosing sepsis at ≥0.5 ng/ml.

We performed a CECT scan of the abdomen for all patients with acute pancreatitis either at admission or 72

hours after, but not before 72 hours from the start of their first symptoms. We determined the severity of acute pancreatitis using the modified CT Severity Index and compared it with the procalcitonin levels.

For our statistical analysis, we used the latest version of SPSS software, considering a P value of less than 0.05 to be significant for all tests. We calculated critical values for specific parameters using the receiver operating characteristic (ROC) function and evaluated them through a meta-analysis. A P value of less than 0.05 was considered statistically significant.

3. Results

The study included 60 patients with 38 males (63.3%) and 22 females (36.6%) with age ranging from 18 to 88 years and mean age being 41.78 yrs. Based on Atlanta's criteria, mild pancreatitis was documented in 15% subjects, moderate in 61.66% and severe pancreatitis in 23.33% patients. Our study found no strong link between the clinical severity of acute pancreatitis and the average age (p=0.633) or gender distribution. This is different from many other studies that show a positive relationship between higher BMI and more severe cases of acute pancreatitis. In our research, we did not find any significant connection (p=0.425).

In our study, alcoholism was the main cause of acute pancreatitis, with 27 cases. Gallstone disease came next with 15 cases, followed by unknown causes with 13 cases, and dyslipidemia with 3 cases. Gallstones were the second most common reason for all three grades of acute pancreatitis, after alcoholism. We found no link between the cause of the disease and how severe the acute pancreatitis was (p=0.279). Additionally, the severity of acute pancreatitis did not show any strong connection to other health issues like diabetes, hypertension, or hypothyroidism (p=0.096). We calculated the CTSI using the modified CT severity index by Mortele[1] in which the imaging findings were used to stratify the disease as mild (CTSI 0-2), moderate (CTSI 4-6) and severe (CTSI 8-10). Majority of the patients showed moderate acute pancreatitis (n=39) whereas 6 patients showed mild score (n=2) on CTSI and 15 patients showed a score of 8 or more.

Correlation of clinical severity with presence of pancreatic necrosis showed a positive correlation (p=0.001). Severe cases showed greater presence of infected pancreatic necrosis (IPN). Similarly serum procalcitonin (PCT) levels were also correlated with pancreatic necrosis. PCT levels both at admission and at 72hours showed a positive correlation with infected pancreatic necrosis with p-value being 0.002 and 0.004 respectively as shown in **Table 1** and **Figure 1**. Comparison between CTSI and serum PCT levels at admission showed a positive correlation (p=0.001) with mean PCT levels in severe pancreatitis (3.63 $\pm$ 2.38 ng/ml) significantly higher than in moderate (1.09 $\pm$ 1.19 ng/ml) and mild (0.45 $\pm$ 0.53 ng/ml) acute pancreatitis. Positive correlation was also seen between CTSI and serum PCT levels at 72hrs (p=0.001) with mean PCT levels in severe pancreatitis (4.89 $\pm$ 3.25 ng/ml) significantly higher than in moderate (1.64 $\pm$ 1.28 ng/ml) and mild (0.44 $\pm$ 0.54 ng/ml) acute pancreatitis. Therefore, PCT serves as a trustworthy early predictive marker for moderate (CTSI-6) and severe (CTSI 8-10) pancreatitis and as we saw that pancreatic necrosis is usually seen in severe pancreatitis thus we can also explain why PCT acts as a good indicator of presence of IPN as it acts as a reliable early predictive biochemical marker of both severe pancreatitis and infection.

Table 1: Comparison of serum PCT levels at admission and 72hrs with presence of pancreatic necrosis

Infected Pancreatic necrosis	PCT at admission(in ng/ml)		PCT at 72 hours(ng/ml)	
	<0.5	>0.5	<0.5	>0.5
Absent	21	13	22	12
Present	6	20	5	21
p-value	X^2: 8.91; p= 0.002		X^2: 12.31; p=0.004	

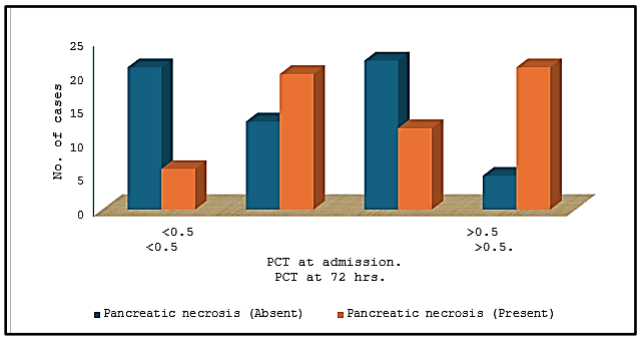

Figure 1: Comparison of serum PCT levels at admission and 72hrs with presence of pancreatic necrosis.

ROC analysis was carried out as shown in and demonstrated that area under curve of PCT at time of admission and after 72hrs was 0.923 and 0.851 (95% CI) respectively as shown in. **Figure 2**

Figure 2. The ROC demonstrated that the optimum cut-off value of serum PCT for predicting acute pancreatitis severity is 0.5ng/ml and since area under curve of PCT was above 0.5 both at admission (0.923) and 72 hours (0.851) it indeed shows Serum PCT to be a reliable indicator of presence of IPN (Infected Pancreatic Necrosis).

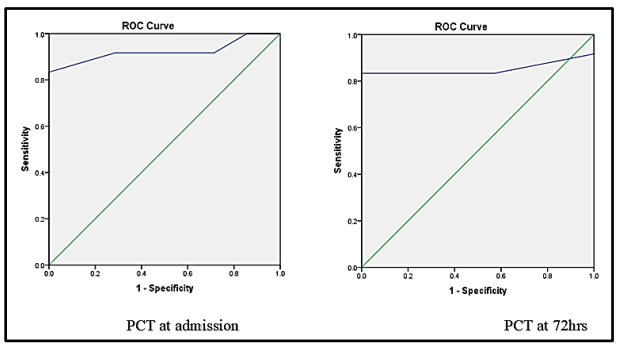

Figure 2: Roc analysis of infected necrotic pancreatitis with serum pct levels at admission and 72 hours.

4. Discussion

Acute pancreatitis is a major reason people end up in the hospital. Its severity can vary from mild cases that require simple treatment to severe and complicated cases that can lead to serious health issues and need active medical intervention. Severity prognostication is thus an important step in management of pancreatitis as the early recognition of severe pancreatitis in patients will help prevent morbidity and mortality associated with it.

Various markers along with multifactorial scoring system like Ranson, Glasgow, APACHE II and clinical data like age, etiology, obesity, Blood urea nitrogen, LDH, evidence of pancreatic necrosis, chronic health status and inflammatory markers have been analyzed to predict severity of pancreatitis, but they still can't tell if there is presence of sepsis. Presence of gas on CECT in case of pancreatitis is the most commonly used method of detecting septic foci however FNAC followed by gram stain is still the gold standard though rarely used. Henceforth there is a need for more readily available biomarker that is also cost-effective unlike CECT to help detect infection in pancreatitis.

This study included 60 patients with 38 males and 22 females with mean age of presentation being in the fourth decade (41.78yrs).Though, the world literature states 6th decade as the mean age as noted in study by Peter et al.[10] The difference can be explained due to higher consumption of alcohol in this part of world, especially by males in their 3rd and 4th decade. The male-to-female ratio of severe acute pancreatitis is 2.5:1 which is similar to data found in the studies of Uhl[11] and de Beaux et al[12] wherein the ratio was 1.6:1 and 1.85:1 respectively. The study showed that pancreatitis caused by gallstones happens more often in women, with a ratio of 3 to 1. In contrast, pancreatitis caused by alcohol is more frequent in men, with a ratio of 6 to 1. Most common etiology of pancreatitis was alcoholism which accounted for 27 cases followed by gallstone induced pancreatitis (15), idiopathic (13), dyslipidemia (3), autoimmune (1) and drug abuse related (1). There was no significant correlation between clinical severity of pancreatitis and etiology (p=0.279) which is consistent with study by Carr et al 2016 (70). PCT at admission (p=0.531) and at 72hrs (p=0.737) also did not show any positive correlation with the etiology of acute pancreatitis.

Mean BMI of patients detected with acute pancreatitis was 26.3 $\pm$ 3.51, with mild, moderate and severe pancreatitis having BMI of 27.36 $\pm$ 4.30, 25.92 $\pm$ 3.46 and 26.99 $\pm$ 3.12 respectively. There was no strong connection between the severity of acute pancreatitis and BMI, as shown by a p-value of 0. 425. However relative percentage of obese and overweight patients were highest in severe pancreatitis (78.58%) showing that high BMI acts as a risk factor for acute pancreatitis but is not a relevant parameter in detecting the severity. There was also no correlation seen between Serum PCT levels and BMI (p=0.974).[13]

In our research, we classified pancreatitis patients based on the updated Atlanta classification into three groups: Mild, Moderate, and Severe. Mild pancreatitis was seen in 15% subjects, moderate in 61.66% and severe pancreatitis was seen in 23.33% patients.

74.19% of severe acute pancreatitis also showed pleural effusions on x-rays. Which is comparable to the findings observed by Heller et al[14] who found abnormal chest radiograph in 84.2% of their patients in their study.

The average serum PCT levels at the time of admission were much higher in patients with severe pancreatitis (3.91±1.75 ng/ml) than in those with moderate (0.93±0.88 ng/ml) and mild pancreatitis (0.66±0.92 ng/ml), with a p-value of 0.001. After 72 hours, the PCT levels remained significantly elevated in the severe pancreatitis group (5.2±3.12 ng/ml) compared to moderate (1.44±1.03 ng/ml) and mild pancreatitis (0.45±0.92 ng/ml), also with a p-value of 0.001. Thus, serum PCT is a reliable marker in detecting the severity of acute pancreatitis early in the course of disease.

The presence of pancreatic necrosis was correlated with PCT at admission (p=0.002) and PCT at 72hrs (p=0.004) which showed it to be a reliable indicator of presence of necrosis. These results match what Mofidi et al[15] discovered, which also showed that serum PCT is helpful in predicting how serious acute pancreatitis is and the chance of getting infected pancreatic necrosis.

Modified CTSI showed a positive correlation with severity as is already seen in studies done by Dalal et al.[16] and Raghuwanshi et al.[17] Comparison between CTSI and serum PCT levels at admission and at 72hrs also showed a positive correlation (p=0.001) with mean PCT levels in severe pancreatitis (mCTSI grade 8-10) significantly higher than in moderate (mCTSI grade 4-6) and mild (mCTSI grade 0-2) acute pancreatitis which is 3.47 $\pm$ 2.47, 0.917 $\pm$ 0.9, 0.458 $\pm$ 0.538, respectively. This proves serum PCT can act as a comparable marker to mCTSI in detecting severity of acute pancreatitis.

ROC analysis was carried out and demonstrated that area under curve of PCT at time of admission and after 72hrs was 0.923 and 0.851 (95% CI) respectively. The ROC demonstrated that the optimum cut-off value of serum PCT for predicting acute pancreatitis severity is 0.5ng/ml and since area under curve of PCT was above 0.5 both at admission (0.923) and 72 hours (0.851) it indeed shows Serum PCT to be a reliable indicator of presence of IPN (Infected Pancreatic Necrosis).

The study had a few limitations like procalcitonin is not a specific marker and could be induced by many infected and non-infected factors. Some patients may have raised procalcitonin not because of acute pancreatitis progression, but due to other factors like trauma, bacterial infection,

surgery, sepsis. Even though the association of PCT is striking in this present study, other factors need to be comprehensively considered while studying PCT as a potential predictor of IPN. Another limitation was the small sample size (n=60). As the study was a prospective observational study over a fixed period of time, a limited number of patients could be enrolled for the study. Additional retrospective data could also be combined to increase the sample size for a better representation of the population. Also, this was a single center study. A multicenter randomized control trial would be more accurate in determining our findings.

5. Conclusion

Thus, we may conclude that serum procalcitonin measurements are valuable in predicting disease severity in acute pancreatitis along with risk of developing infected pancreatic necrosis as it is a reliable indicator of the same. As serum PCT level assessment at admission and 72hrs is comparable to CTSI in determining disease severity as well as predicting the prognosis, especially for moderate and severe pancreatitis, it can be a useful adjunct to conventional methods in severity stratification and detecting infection.

Thus, within its limitations, the study concludes that in subjects with acute pancreatitis, levels of serum Procalcitonin (PCT) helps in the accurate identification of subjects that have moderate to severe acute pancreatitis or will likely progress to severe form which gets complicated as infected pancreatic necrosis as is a reliable predictive indicator of disease severity and infection in acute pancreatitis. Its cost effectiveness and easy availability make it a reliable marker to be used in future.

6. Conflict of Interest

None.

7. Source of Interest

None.

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