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Comparing Procalcitonin v/s C-Reactive Protein and Total White Blood Cell Count as an Early Predictive Marker of Severity in Acute Pancreatitis and Guide to Initiate Antibiotic Therapy

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Abstract: ***Background: Early prediction of severity in acute pancreatitis is important as 20% of patient develops acute severe pancreatitis (ASP) which include multiple organ failure, local complications, pancreatic necrosis with 15-20% mortality. Sometimes clinical and regular markers of sepsis, such as WBC and CRP levels, mislead us to start unnecessary higher antibiotics which leads to emerging antibacterial resistance, increased cost and significant mortality. AIM: To evaluate the role of procalcitonin v/s c-reactive protein, white blood cell counts in early diagnosis of severity in acute pancreatitis and guide initiation of appropriate antibiotic therapy. Methods: This study was done in 30 patients admitted in Ballari Medical College and Research Center (BMCRC), Ballari for period of 3months, study design – prospective, comparative study. Procalcitonin levels checked for 50% of population and CRP, WBC counts for another 50% of population with Acute pancreatitis. Procalcitonin levels of <1ng/ml considered low risk and not started antibiotics, if 1to5ng/ml started with basic antibiotics and >10ng/ml started with higher antibiotics. High CRP, WBC counts started with higher antibiotics. Results: Our study demonstrating that PCT levels at admission accurately identify patients likely to progress to severe AP with better diagnostic accuracy of 91.9% compared to CRP and WBC count of 90.1% and 73.9% respectively. And guided to start appropriate antibiotics based on severity and reduced mortality with significant p value. Conclusion: This comparative study evaluates the effectiveness of procalcitonin PCT, C reactive protein CRP, and total white blood cell WBC count as early predictive markers of severity in acute pancreatitis AP. The study enrolled 30 patients with AP, dividing them into two groups for PCT or CRP/WBC guided group. Results showed that PCT had a diagnostic accuracy of 91.9%, compared to CRP 90.1% and WBC count 73.9%. Early PCT based antibiotic initiation led to reduced mortality and shorter hospital stays. These findings suggest that PCT is a superior marker for early diagnosis and effective treatment in severe AP cases.***

Keywords: Acute pancreatitis, procalcitonin, C reactive protein, white blood cell count, severity markers

1. Introduction

The incidence of acute pancreatitis varies from 5 to 80 per 1,00,000 throughout the world. Early prediction of severity in acute pancreatitis is important as 20% of patient develops acute severe pancreatitis (ASP) characterized by necrosis of pancreatic tissue which, with bacterial colonization, leads to infected necrosis, local complications, multiple organ failure, and severe sepsis with 15-20% mortality[1].

Various markers, including α1-antitrypsin, urinary trypsinogen activating peptide, amyloid A, and C-reactive protein (CRP), have been studied for diagnosis of severity in acute pancreatitis[4]. However, discriminating between pancreatic infection and inflammation is difficult, with neither clinical assessment nor commonly used markers of inflammation like WBC and CRP levels are specific and sensitive to bacterial infection.

CRP is the only clinically used marker but with its late peak of about 72hours and low sensitivity of 47% at hospital admission[6] and these markers may be high even in cases of pancreatitis due to viral and chemical causes.

Solely depending on these inflammatory markers may lead us to start unnecessary higher antibiotics which may contribute to emerging antibacterial resistance, antibiotic-related side effects, compromised treatment efficacy and unnecessary health care costs.

There is a need for a reliable and an ideal marker which should be simple, inexpensive, and highly accurate. However, Procalcitonin, a calcitonin propeptide (13 kDa, 116 amino acids), highly sensitive marker with its early rise in severe infection and inflammation compared with other biomarkers like CRP, White blood cell count. PCT values above 0.5 ng/ml considered abnormal[9].

2. Materials & Methods

1) Study Design: A Prospective, comparative, randomized study.

2) Study Setting and Duration
The study was conducted in the Department of General surgery at BMCRC, Ballari, spanning over 3 months beginning from 1st May 2023 to 31st July 2023.

3) Participants – All patient admitted in BMCRC with acute pancreatitis were included with inclusion and exclusion criteria being,

Inclusion criteria:
- Age more than 18 years.
- Valid informed consent.
- Patient diagnosed with acute pancreatitis.
- Patients not on steroids or NSAID'S.

Exclusion criteria:
- Patients in MODS (Multi Organ Dysfunction Syndrome).
- Patient who has already been started on antibiotic therapy before presentation.
- Comorbidities requiring prolonged antibiotic therapy.
- Immunocompromised patients.
- Patients on immunosuppressive therapy.

4) Study Sample Size: This study included 30 patients of acute pancreatitis admitted in BMCRC, Ballari.

5) Study Parameters
Demographic data such as age, gender, occupation and comorbidity were collected to understand the characteristics of the study population.

6) Study Procedure
After obtaining informed consent, a detailed history and examination were conducted to record demographic data and clinical parameters. Patients were randomly and sequentially assigned to either a PCT guided or a CRP, WBC guided groups and antibiotics assigned accordingly. Procalcitonin levels was checked for the 50% of patients and C reactive Protein, White blood cell count for another 50% of patients presenting with acute pancreatitis and antibiotics were started accordingly.

Grades	Procalcitonin Level (ng/L)	Antibiotics
Mild	0.05- 1 ng/ml	No Antibiotics started
Moderate	1- 5 ng/ml	Basic Antibiotics Started
High	>5 ng/ml	Higher Antibiotics Started

Grades	CRP Level	Antibiotics
Mild	6- 10 mg/L	No Antibiotics started
Moderate	10- 50 mg/L	1) Normal Total Counts- Basic Antibiotics Started 2) High Total Counts- Higher Antibiotics started
High	>50 mg/L	Higher Antibiotics Started

7) Study Data Collection
Data were meticulously collected during the course of hospital admission. Information was recorded in a structured format to ensure consistency and completeness. Based on levels of PCT and CRP, WBC levels patients were assigned antibiotics and response to antibiotics, duration of hospital stay were recorded.

8) Data Analysis
Statistical analysis was performed using SPSS software version 26 descriptive statistics like frequency table and percentages. Normal distribution of the data was checked before analysis. Unpaired t test and chi square test was used to analyze continuous and categorical variables respectively. Sensitivity, specificity, ROC curve analysis done, for all the statistical tests p value of less than 0.05 was taken as significant.

9) Ethical Considerations
The study was conducted in strict accordance with the ethical guidelines established by the Institutional Ethics Committee of BMCRC, Ballari. Prior to participation informed consent was obtained. Ethical approval was sought and obtained before the commencement of the study.

3. Results

1) Demographics and Risk Factors:
In our study there is no significant difference in outcomes between males and females (p-value = 0.931). The mean age of those who died is higher (42 years) compared to those who improved (34 years), but this difference is not statistically significant (p-value = 0.695). And no significant association with outcomes (p-values = 0.475 for both groups (alcohol and smoking).

2) Mean and Standard deviations of variables.
- WBC Count: Higher in the death group (mean = 23075) compared to the improved group (mean = 18118), but not significantly different (p-value = 0.246).
- CRP (C-Reactive Protein): Significantly higher in the death group (mean = 60.8) than in the improved group (mean = 33.9) with a p-value of 0.031, indicating a significant difference.
- Procalcitonin: Significantly higher in the death group (mean = 14.2) compared to the improved group (mean = 6.9), with a p-value of 0.001.
- Duration of Stay: Patients who died had a longer hospital stay (mean = 29.0 days) compared to those who improved (mean = 15.9 days), with a significant p-value of 0.035.

Table 3: Table depicting mean and Standard deviation of variables.

	OUTCOME				
	DEATH		IMPROVED		
	Mean	Standard Deviation	Mean	Standard Deviation	p-value
AGE	42	11	34	10	0.695
WBC COUNT	23075	6279	18118	7498	0.246
CRP	60.8	10.2	33.9	21.2	0.031
PROCALCITONIN	14.2	15.2	6.9	6.5	0.001
DURATION OF STAY	29	13.5	15.9	8	0.035

3) Procalcitonin and CRP, WBC Categories and outcome:
- Procalcitonin Category: No significant difference in outcome across different procalcitonin levels (p-value = 0.591).
- CRP Category: A significantly higher proportion of deaths occurred in the high-grade CRP category (p-value = 0.037).

Table 4: Table depicting Pct and CRP, WBC categories and outcome

		Outcome				P-Value
		Death		Improved		
		Count	Column N %	Count	Column N %	
CRP, WBC Category	Mild	0	0.00%	2	18.20%	0.037
	Moderate	1	25.00%	8	72.70%	
	High grade	3	75.00%	1	9.10%	
Procalcitonin Category	Normal	0	0.00%	2	16.70%	0.591
	Mild	0	0.00%	1	8.30%	
	Moderate	0	0.00%	3	25.00%	
	Moderately High	1	33.30%	3	25.00%	
	High grade	2	66.70%	3	25.00%	

4) Antibiotics Usage:

- There is no significant association between the type of antibiotics used (basic vs. higher) and patient outcomes (p-value = 0.198).

5) ROC Curve Analysis:

a) **Procalcitonin:** The AUC is 0.917, also indicating a high ability to distinguish outcomes. A level >7.8 is the best predictor of death, with 100% sensitivity and 75% specificity.

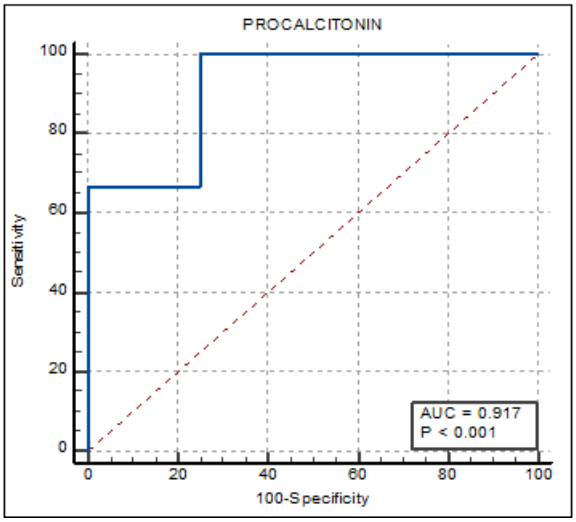

Figure 1: Graph depicting area under ROC curve of PCT group.

Area under the ROC curve (AUC) of PCT group

Area under the ROC curve (AUC)	0.917
Standard Error [a]	0.094
95% Confidence interval [b]	0.658 to 0.996
z statistic	4.432
Significance level P (Area=0.5)	<0.0001

[a] DeLong et al., 1988
[b] Binomial exact

b) **WBC Count:** The AUC is 0.739, which suggests a moderate ability to distinguish between outcomes. The optimal cut-off value for predicting death is a WBC count >17000, with 100% sensitivity and 54.55% specificity.

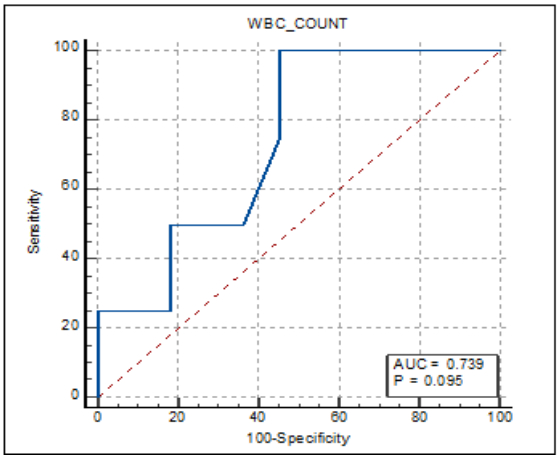

Figure 2: graph depicting area under ROC curve of WBC group.

Area under the ROC curve (AUC) of WBC group

Area under the ROC curve (AUC)	0.739
Standard Error [a]	0.143
95% Confidence interval [b]	0.454 to 0.925
z statistic	1.672
Significance level P (Area=0.5)	0.0945

[a] DeLong et al., 1988
[b] Binomial exact

c) **CRP:** The AUC is 0.909, indicating a high ability to distinguish between outcomes. A CRP level >47 is the best predictor of death, with 100% sensitivity and 90.91% specificity.

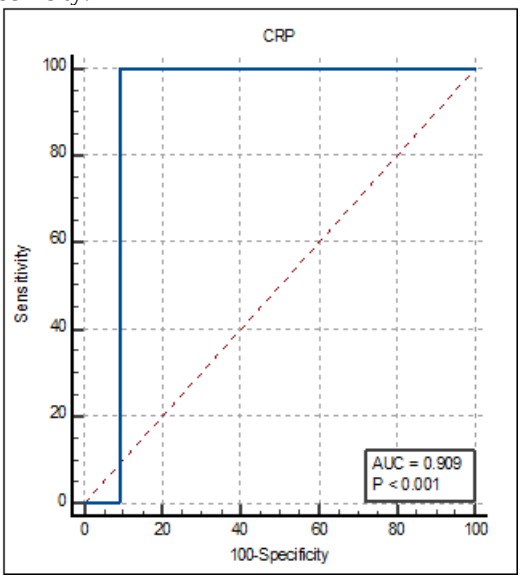

Figure 3: Graph depicting area under ROC curve of CRP group.

Area under the ROC curve (AUC) of CRP Group

Area under the ROC curve (AUC)	0.909
Standard Error [a]	0.0909
95% Confidence interval [b]	0.648 to 0.995
z statistic	4.5
Significance level P (Area=0.5)	<0.0001

[a] DeLong et al., 1988
[b] Binomial exact

4. Discussion

Acute pancreatitis (AP) is a potentially life-threatening condition characterized by inflammation of the pancreas. Early identification of patients at risk of severe AP is crucial for timely intervention and improved outcomes. Procalcitonin (PCT), a peptide precursor of calcitonin, has emerged as a promising biomarker in AP.

The study's significance lies in its potential to improve clinical outcomes in AP by identifying reliable biomarkers that guide early and appropriate antibiotic therapy, thereby reducing mortality and healthcare costs.

Current Evidence:
Numerous studies have demonstrated the utility of PCT in predicting the severity of AP, development of infected pancreatic necrosis, and overall prognosis.

A study by Rau et al. found that PCT levels correlated with the severity of AP and pancreatic infections[10]

A study by Olah et al. demonstrated the utility of PCT quick test in differentiating between sterile and infected forms of AP[11].

A meta-analysis by Mofidi et al. showed that PCT levels within 24 hours of admission accurately predicted the development of infected pancreatic necrosis and overall prognosis in severe AP[12].

Our study corroborates these findings, demonstrating that PCT levels at admission accurately identify patients likely to progress to severe AP with better diagnostic accuracy of 91.9% compared to CRP and WBC count of 90.1% and 73.9% respectively.

In our study based on Procalcitonin level we categorized the severity of disease, and the patient were started with antibiotics and reduced morbidity, mortality with significant p value of 0.01.

Recent studies have explored the combination of PCT with other biomarkers to enhance predictive accuracy. For instance, a study by Kylänpää-Bäck et al. (2001) found that combining PCT with soluble interleukin-2 receptor and soluble E-selectin improved predictive accuracy for severe AP. Future research should focus on:

1) Developing point-of-care PCT testing for rapid diagnosis and decision-making.
2) Investigating the role of PCT in guiding antibiotic therapy and reducing unnecessary antibiotic use.
3) Exploring the combination of PCT with other biomarkers and clinical scoring systems to enhance predictive accuracy.

5. Conclusion

Procalcitonin has proven to be a valuable biomarker for predicting the severity of acute pancreatitis, outperforming CRP and WBC count in terms of diagnostic accuracy. This study highlights the importance of early diagnosis using PCT, which leads to better targeted antibiotic therapy and improved patient outcomes. Future research should explore combining PCT with other biomarkers to further enhance predictive accuracy and treatment efficacy in AP.

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