

Original Article

Procalcitonin and C-reactive Protein as Outcome Predictors in Critically ill Patients with Sepsis

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Background : Procalcitonin (PCT) and C-reactive Protein (CRP) are the most frequently used biomarkers for critically ill patients. Changes in these biochemical markers may be useful in predicting therapeutic response and prognosis in septic patients. The aim of this study was to assess utility of CRP and PCT as predictors of outcome in critically ill patients with sepsis treated in ICU.

Materials and Methods : The study included 100 patients treated in ICU with sepsis. Data on Serum CRP and PCT level on day one and day seven were collected and compared with the outcome. Student 't' test, AUC and Pearson's correlation coefficient were applied to study its significance.

Results : The male female ratio was 61:39 with age group of 18 to 80 years. The mean CRP on day 1 was 54.5 ± 60.3 and on day 7 was 22.9 ± 34.7 ($p:0.0001$). The mean PCT on day 1 was 7.2 ± 3.6 and on day 7 was 1.7 ± 1.4 ($p:0.0021$). It was observed that both PCT (mean) and CRP (mean) decreased significantly on day 7 compared to day 1 amongst the survivors. The co-relation of outcome with CRP level was found to be more significant. The Pearson's correlation coefficient showed significant positive correlation with poor outcome of 28 patients (28%) in this study.

Conclusion : Changes in PCT and CRP concentrations were associated with outcome of critically ill patients with sepsis. The serum CRP was found to be a reliable biomarker for prediction of outcome in sepsis.

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Key words : Sepsis, Procalcitonin (PCT), C-reactive Protein (CRP), Morbidity, Mortality.

Sepsis is the systemic inflammatory response to microbial infection¹. An exaggerated immune response with overproduction of inflammatory mediators influence that results of diffuse injury of healthy tissues, major organs dysfunction and associated mortality². Procalcitonin (PCT) and C-reactive Protein (CRP) are the most frequently used biomarkers for critically ill patients with sepsis. If sepsis is well controlled, PCT and CRP may show decreasing patterns. A dynamic approach of assessing these biomarkers may provide more information on treatment outcome or modification of treatment in patients with sepsis. The aim of this study was to assess predictive values based on changes in PCT and CRP concentrations in patients with sepsis and to identify a single and cost-effective biomarker.

MATERIALS AND METHODS

This study was conducted on data collected from 100 consecutive patients treated in surgical ICU for sepsis of varied reasons in Gauhati Medical College & Hospital covering a period of six months. The

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Editor's Comment :

- PCT and CRP are two important biomarkers to prognosticate patients in sepsis.
- It can predict ICU requirements for these groups of patients and modulation of antibiotics during the course of treatment.

primary endpoint of this study was to determine the outcome of treatment on the basis of serum CRP and PCT level on day 1 and after 7 days from day of ICU admission. The laboratory data of serum PCT and CRP on day 1,2 and day 5,7. Serum PCT concentrations were measured using enzyme-linked fluorescent assays (Mini VIDAS method) with the lower reference limit was 0.05 ng/mL. Serum CRP concentrations were measured using latex agglutination principle and the lower reference limit was 10mg/L. The initial baseline PCT and CRP levels defined as peak levels from day1 to 2 and subsequent levels as minimal levels from days 5 to 7. PCT and CRP kinetics are expressed as Δ PCT and Δ CRP concentrations, which are the differences between baseline and subsequent measurements. All patients had clinical evidence of Sepsis according to the recently approved International Sepsis Consensus Conference definitions³.

Data were expressed as mean (SD) and $P < 0.05$ was considered statistically significant. Area under the ROC Curves were constructed according to Hanley and McNeil by plotting the sensitivity against

specificity⁴. An area under ROC Curve of 1 indicates a perfect predictive power and the closer the area under the ROC Curve to 1 indicate the greater discriminative power of the marker.

OBSERVATIONS AND RESULTS

There were 39 (39%) Female and 61 Male (61%) patients in the study population with mean age of 45.5 (Table 1).

The data showed improvement in results of treatment in 43 patients, stable in 29 patients and poor results (Deaths) in 28 patients after 7 days of treatment. The mean CRP on day 1 was 54.5±60.3 and on day 7 was 22.9±34.7 in survival group. The mean PCT on day 1 was 7.2±3.6 and on day 7 was 1.7±1.4 in same group of patients. It was observed that both PCT and CRP decreased significantly on day 7 compared to day 1 in survival group of patients (Table 2). The patients with stable and poor outcome on day 1 to day 7 showed no significant decline in serum concentration of CRP and PCT. In patients with poor outcome both CRP and PCT concentration were higher compared to survivors (Fig 1).

The Pearson’s correlation coefficient between outcome versus CRP and PCT at Day 1 and Day 7 showed significant positive correlation indicating that

with the increase of PCT and CRP on both Day 1 and 7 are associated with poor outcome (Table 3). The area under curve shows high predictive value in decreasing concentration of CRP and PCT on day 7 (Fig 2). It is observed that difference of concentration of CRP value on Day 1 and Day 7 is a better indicator in determination of outcome (Table 4).

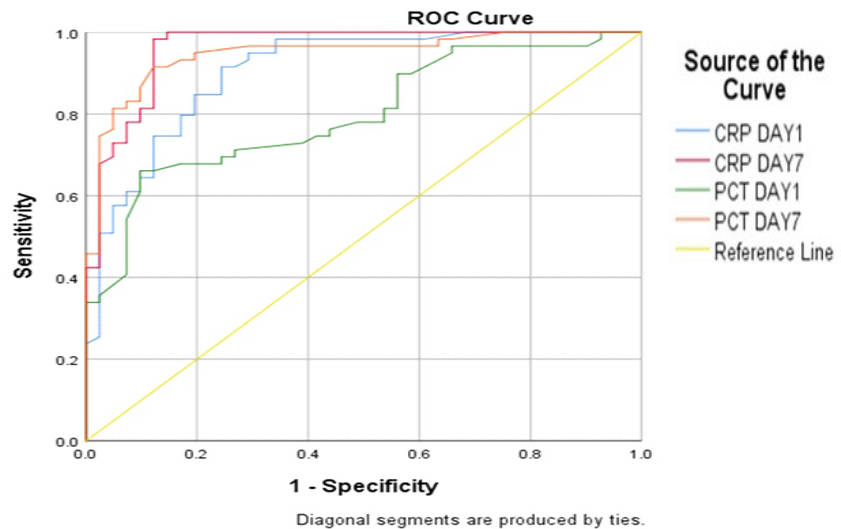


Fig 2 — ROC Curve between CRP and PCT versus Outcome

DISCUSSION

Biochemical markers help diagnose Sepsis and can predict patient outcome in severe Sepsis and Septic Shock^{1,5-7}. PCT, CRP are the most frequently used biomarker in clinical practice. PCT, CRP measurements are useful for monitoring the course of Sepsis in critically ill patients and may be used to indicate change in course of treatment and to measure its outcome^{8,9}. It could be a possible indicator of stopping antibiotics safely, sparing patients

SEX	N	%	Mean age
FEMALE	39	39.00%	41.9 ± 18.2
MALE	61	61.00%	47.6 ± 17
Grand Total	100	100.00%	45.5 ± 17.6

	DAY 1	DAY 7	P-VALUE
CRP	54.5 ± 60.3	22.9 ± 34.7	0.0001
PCT	7.2 ± 3.6	1.7 ± 1.4	0.0021

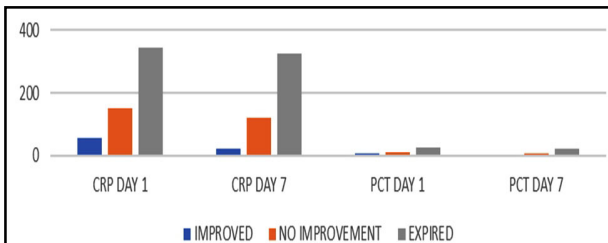


Fig 1 — Comparison of CRP and PCT with outcome

Correlations			
Outcome		CRP Change	PCT Change
	Pearson Correlation	0.417	0.377
	p-value	0.0001	0.0021
	N	100	100

Area Under the Curve for Prediction of Survival	
Test Result Variable(s)	Area
CRP DAY1	0.905
CRP DAY7	0.961
PCT DAY1	0.798
PCT DAY7	0.947

from drug toxicity, risk of resistance and even indicate possibility to stop ICU care. Although the diagnostic accuracy of PCT was higher than CRP in Sepsis (1-3) it was unclear which biomarker had more prognostic accuracy in septic patients. Several recent studies found CRP has higher prognostic value than that of PCT and that of both biochemical markers have similar predictive value for determining the outcome of septic patients¹⁰. In this present study CRP level was found to be reliable in predicting the outcome^{11,12}. In another study it was found that the changes in PCT and CRP at the onset and on the fourth day can predict survival of patients which is in conformation with the present study¹³. In one study it was described that a PCT-based protocol was not superior to a protocol based on serum CRP levels for reducing antibiotic use. Remarkably, the length of antibiotic therapy was shorter in the CRP group and less than the maximum therapy duration proposed¹². Recently, several studies it was found that CRP was as beneficial as PCT in predicting outcomes and reducing antibiotic use in septic patient^{8,9,11,13}. In addition, CRP is more cost effective than that of PCT. The CRP level indeed a better indicator in predicting outcome of treatment as compared to that of PCT.

CONCLUSIONS

The PCT and CRP concentrations can predict outcomes of critically ill septic patients. Changes in CRP concentrations were not inferior to changes in PCT concentrations in predicting treatment response and survival. It is as effective as both CRP, PCT concentrations in predicting the outcome in patients with severe Sepsis. In addition, CRP testing is more cost effective and readily available.

Limitations :

This study has several limitations. This is retrospective review of medical records in a single centre. The sample population was not large enough and time zero estimation was difficult to define because of the retrospective nature of the study. Never the less, the predictable power of PCT and CRP remains uninfluenced by the small sample size and the 7 day outcome and mortality are successfully indicated.

Conflict of Interest : None

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