

Evaluation of Procalcitonin and C- Reactive Protein to Predict Blood Culture Positivity in Sepsis

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ABSTRACT

Background- Sepsis is one of the most important cause of death in hospital setup. Blood culture is the most important and definite tool for diagnosis of sepsis but it take 48-72 hours, in this condition biomarkers procalcitonin and CRP play important role in early diagnosis of sepsis. PCT is more specific marker than CRP. Our study revealed that there is an association between PCT value and blood culture positivity. High PCT value ($>10\text{ng/ml}$) independently linked with gram negative bacteraemia particularly Enterobacteriaceae. **Aim-** To study the comparison between procalcitonin and CRP to predict blood culture positivity in bacterial sepsis.

Methods- This is prospective observational study with duration 2 years. during the study who met the inclusion criteria were included in the study after taking inform consent.

Result- Our study revealed That ROC curve of procalcitonin level in predicting culture positivity (both gram -ve and +ve) showed an area under the curve of 0.67 with 95% CI of -0.74 . The association is highly statistically significant (p value <0.001) while curve of CRP level in predicting culture positivity (both gram -ve and + ve) showed an area under the curve of 0.519 with 95% CI of $0.43 - 0.60$. The association was not statistically significant (p value = 0.653). PCT is better predictor of blood culture report than CRP in sepsis patients. PCT levels correlate with Gram negative bacteria specially enterobacteriaceae. Higher (>10) PCT values independently associated with enterobacteriaceae in blood culture.

Keywords- Sepsis, Procalcitonin, CRP, blood culture.

INTRODUCTION

In hospital setup sepsis is one of the most important cause of death. Recently sepsis is redefined as an abnormally regulated host response to a infection which result in life threatening multiple organ dysfunction.¹

In normal condition when a pathogen enters in to body then it activates various immune cells. These immune cells release numerous proinflammatory and anti- inflammatory mediators in to blood in a balanced manner to counter act invasive agent. Sometime this delicate balance between proinflammatory and anti-inflammatory mediators become disturbed and proinflammatory mediators show predominant action which results in abnormal and dysregulated immune response and lead to multiple organ dysfunction which result in increase mortality.² In sepsis mortality significantly reduced if early and rapid diagnosis and treatment given. new advance clinical criteria and some important biomarkers such as procalcitonin and CRP play important role in

early and rapid diagnosis of sepsis. Among PCT and CRP, PCT is more specific marker than CRP. In sepsis, measurement of PCT concentration can provides more information about severity and course of disease than CRP and there is strong relationship between PCT concentration and multiple organ dysfunction. Our study revealed that there is an association between PCT value and blood culture positivity. High PCT value independently linked with gram negative bacteraemia particularly enterobacteriaceae.³ our study aim is the comparison between procalcitonin and CRP to predict blood culture positivity in bacterial sepsis patients.

MATERIALS AND METHODS\Study Site: IMS & SUM HOSPITAL BHUBANESWAR.

The study was an prospective observational study having Patients with sepsis admitted in our tertiary care hospital over the duration of two years have been included in this study. Patients who will be provisionally diagnosed as a case of sepsis obliging the below mentioned inclusion criteria who would be admitted under the Post Graduate Department of Medicine at Institute of Medical Sciences and SUM Hospital will be included in the study. A total of 200 patients admitted at IMS & SUM HOSPITAL during the period of study who met the inclusion criteria were included in the study under guidance of my guide.

INCLUSION CRITERIA:

1. All septicaemia patients.
2. Age >18 years & <80 years.
3. Suspected Sepsis cases who will be fulfilling the criteria of Sepsis as described in SOFA criteria / APACHE II criteria.

B) EXCLUSION CRITERIA:

1. Age <18 years & >80 years.
2. Pregnant Women

The study will be conducted on at least 200 patients who would be admitted at IMS & SUM Hospital and who meet the inclusion criteria & give their written/ informed consent for being a part of the study. Ethical clearance will be obtained from Ethical Committee of IMS & SUM Hospital and an informed/ written consent will be taken from the patients and/or, their relatives, after thoroughly explaining the process. A sample of 5 ml venous blood will be collected to study the following parameters:

- 1) Total Leucocyte Count (TLC)
- 2) Serum C-reactive Protein (CRP)
- 3) Serum Procalcitonin
- 4) Blood Culture and Sensitivity

A sample of 10 ml urine sample will be collected to study the following parameters:

- 5) Urine Routine & Microscopy

6) Urine Culture & Sensitivity

An appropriate specimen of throat swab/ wound swab/ pus will be collected and that will be cultured for bacterial infection.

STATISTICAL ANALYSIS

Data were collected and entered in the Microsoft excel and analyzed in the SPSS version 20. The categorical variables were expressed in terms of frequency and percentages. The continuous variables were expressed in terms of mean and standard deviations. Association between the two categorical variables was determined by Chi-squared test. Receiver operating characteristics curve was used to determine the predictive ability of laboratory parameters with the culture positivity and outcome. The ROC curves were expressed in terms of area under the curve (AUC) and 95% confidence interval (CI). P value less than 0.05 was considered statistically significant.

Results

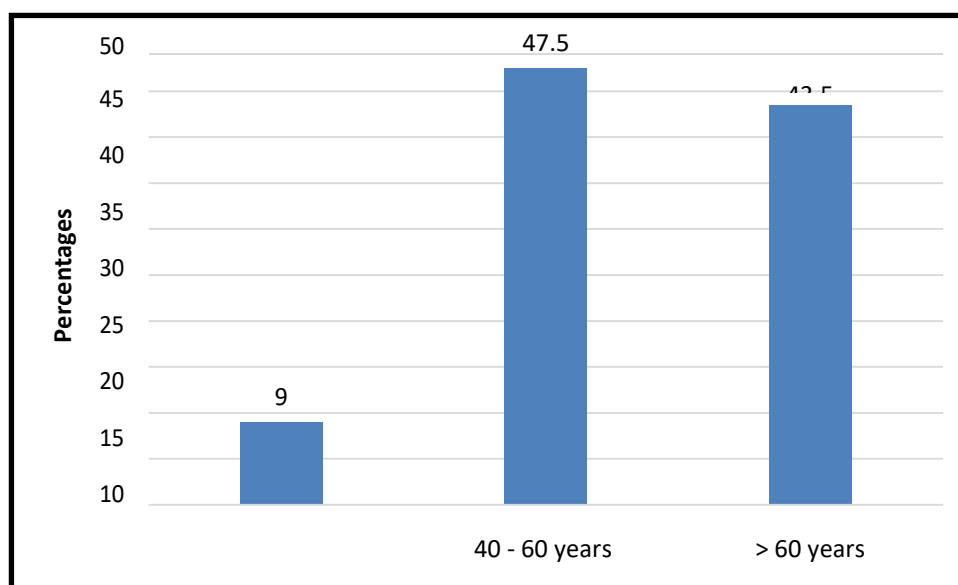
The mean age of the study participants was 56.84 years with a standard deviation of 11.39 years.

Table 1: Age groupwise distribution of the study participants

Age Category	Frequency	Percentages
< 40 years	18	9.0
40 - 60 years	95	47.5
> 60 years	87	43.5

The mean age of the study participants was 56.84 years with a standard deviation of 11.39 years.

Figure 1: Age group wise distribution of the study participants

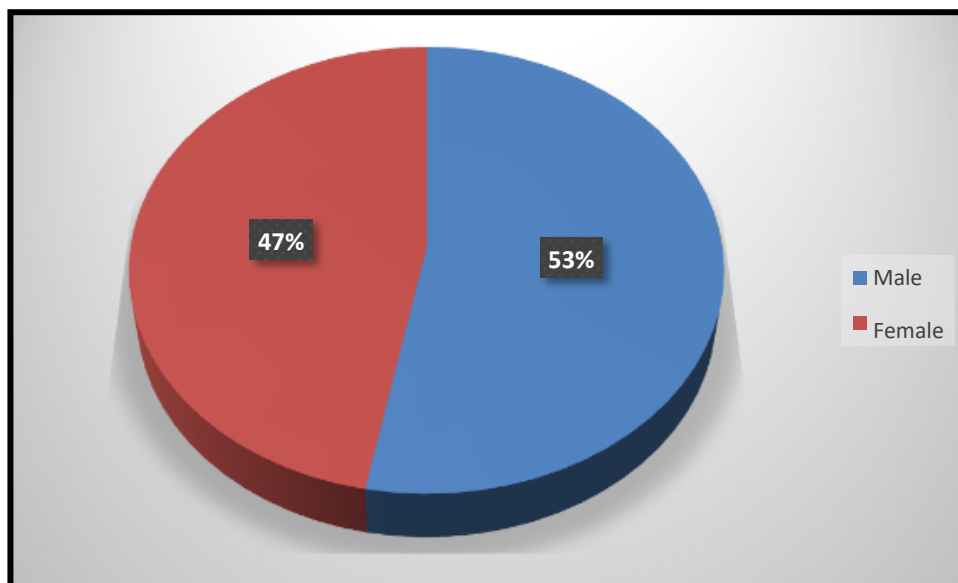


The above Bar diagram shows that the maximum no. of patients (47.5%) were in 40-60 years age group followed by 43.5% patients in age group >60 years.

Table 2: Gender distribution of the study participants

Gender	Frequency	Percentages
Male	106	53
Female	94	47

Figure 2: Gender distribution of the study participants

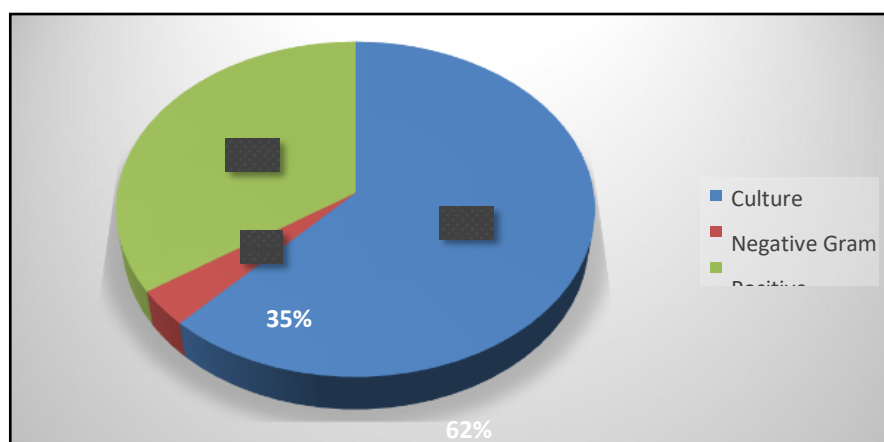


The above pie chart shows male predominance over females in study subjects. 53% (106/200) were males while 47% (94/200) were females.

Table 3: culture sensitivity of the patients suffering from sepsis

Culture reports	Frequency	Percentages
Culture Negative	124	62.0
Gram Positive	7	3.5
Gram Negative	69	34.5

Figure 3: culture sensitivity of the patients suffering from sepsis

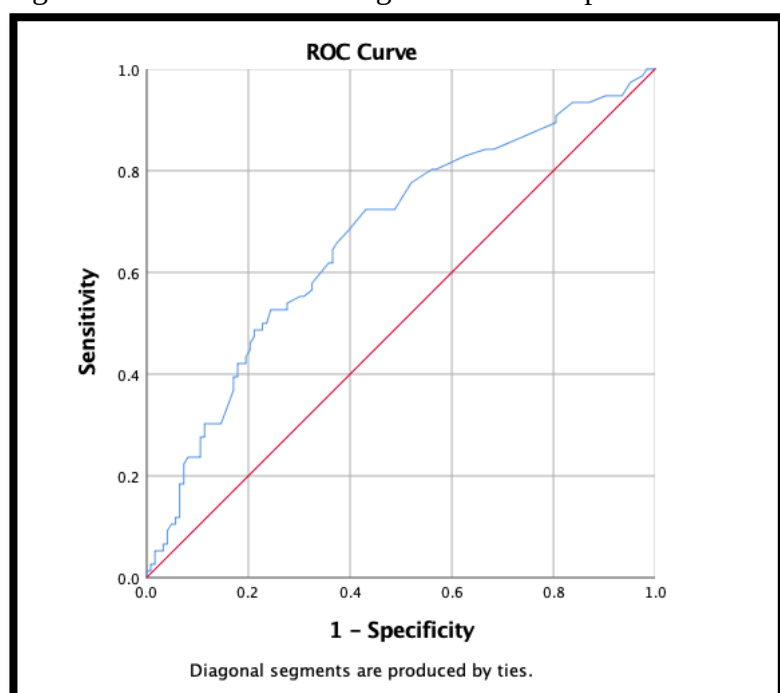


Above table and pie chart shows 62%(124/200)sepsis patients was culture egative,38%(76/200) was culture positive, among culture positive cases 34.5% (70/200) was contained Gram negative organism while 3.5%(7/200) contained Gram positive organism.

Table 4: Laboratory parameters of the study participants

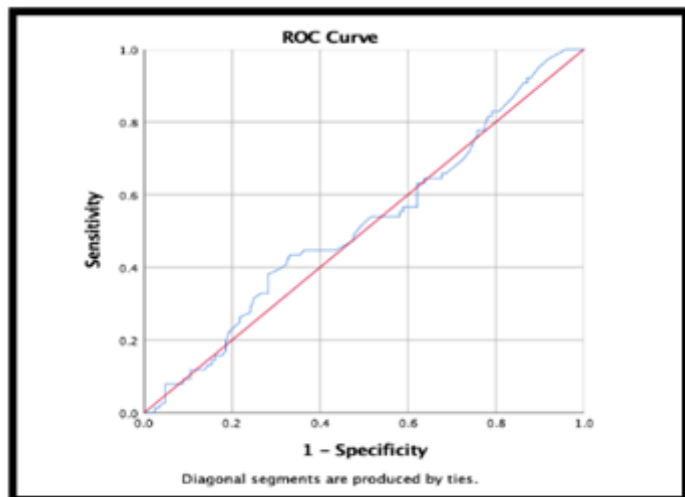
Parameters	Mean	SD
Procalcitonin	9.72	19.18
CRP	10.35	9.96
TLC	18187.0	7964.0

Figure 4: ROC curve showing association of procalcitonin level with culture positivity



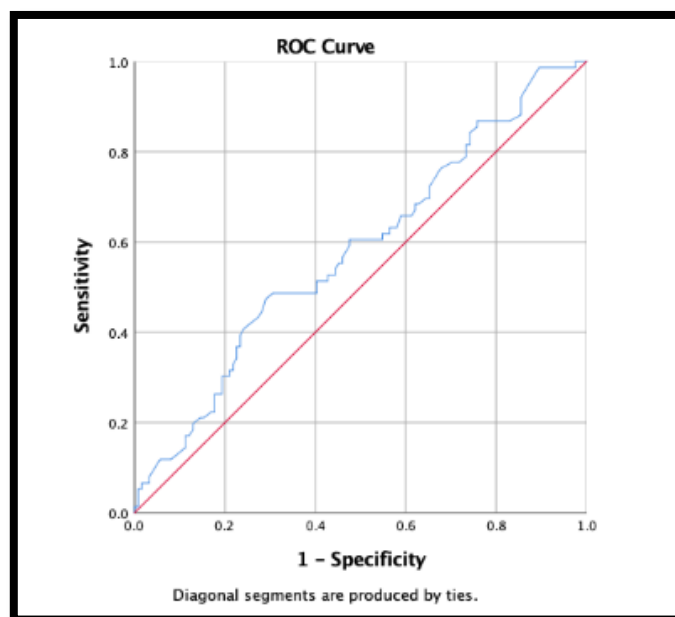
The ROC curve of procalcitonin level in predicting culture positivity (both gram -ve and +ve) showed an area under the curve of 0.67 with 95% CI of 0.59 –0.74. The association is highly statistically significant (p value <0.001).

Figure 5: ROC curve showing association of CRP level with culture positivity



The ROC curve of CRP level in predicting culture positivity (both gram -ve and + ve) showed an area under the curve of 0.519 with 95% CI of 0.43 –0.60. The association was not statistically significant (p value = 0.653).

Figure 6: ROC curve showing association of TLC count with culture positivity



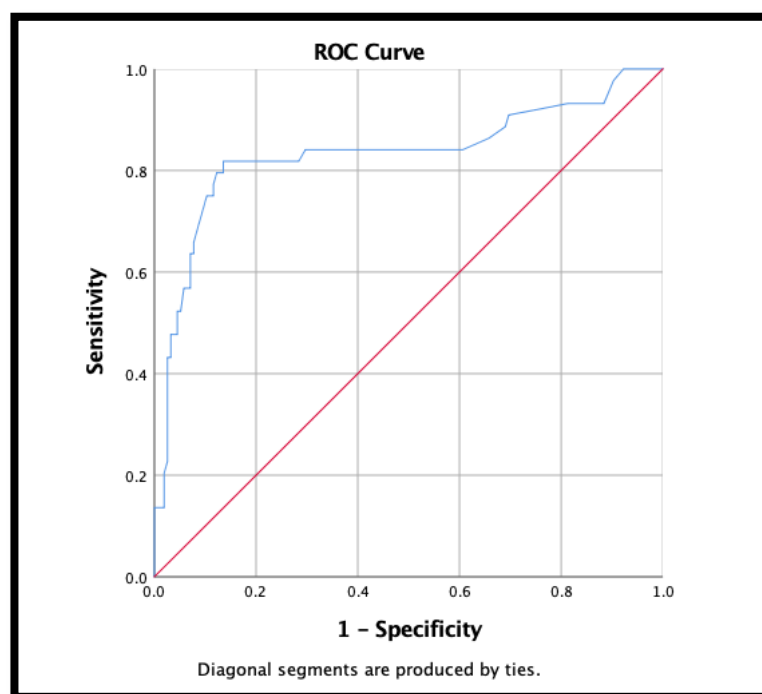
The ROC curve of TLC level in predicting culture positivity (both gram -ve and + ve) showed an area under the curve of 0.58 with 95% CI of 0.49 – 0.66. The association was not statistically significant (p value = 0.055).

Table 5: Association of procalcitonin level at cutoff of 10 with culture positivity

Culture	Procalcitonin level	p value
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	< 10	> 10	
Gram positive			
Yes	3 (42.9)	4 (57.1)	0.004
No	105 (85.4)	18 (14.6)	
Gram negative			
Yes	50 (72.4)	19 (27.6)	0.001
No	105 (85.4)	18 (14.6)	
Gram positive or gram negative			
Yes	53 (69.7)	23 (30.3)	0.008
No	105 (85.4)	18 (14.6)	

Figure 7: ROC curve showing procalcitonin level predicting mortality



The ROC curve of procalcitonin level in predicting mortality showed an area under the curve of 0.83 with 95% CI of 0.74 – 0.91. The association was highly statistically significant (p value<0.001)

Discussion

In this study the mean age of the study participants was 56.84 years with a standard deviation of 11.39 years. The maximum no.of patients (47.5%) were in 40-60 years age group followed by 43.5% patients in age group >60 years and 9% were in <40. In 2001 Angus DC et al⁴ conducted a study that observed mean age was seen to be 63 years. In 2010 Todi et al⁵ conducted a study that observed the mean age of population was 58.17 years. In 2013 Menezes BM et al⁶ conducted a study in that study mean age was 59 years and standard deviation was +/16. In this study gender

distribution shows male predominance over females in study subjects. 53% (106/200) were males while 47% (94/200) were females. A study conducted by Padkin et al⁷ in 2003 that shown almost same distribution that is male predominance (53%) over females (47%). In 2010 Todi et al. conducted a study that observed male involvement greater than female. Along with this our study also revealed the ROC curve of CRP level in predicting mortality showed an area under the curve of 0.57 with 95% CI of 0.48 – 0.66. The association was not statistically significant (p value = 0.134). Observed mortality rate increased with higher PCT values such that mortality 0.5% (1/200) was seen in subjects with normal PCT values and 16.5% (33/200) mortality was seen in subjects with values >10 ng/ml. Thus, high PCT level was associated with increased mortality risk. The ROC curve of procalcitonin level in predicting mortality showed an area under the curve of 0.83 with 95% CI of 0.74 – 0.91. The association between 28-day mortality and PCT level was found to be highly statistically significant (p value <0.001). Therefore above study revealed PCT is better predictor than CRP of mortality in sepsis patients. In our study blood culture and sensitivity done in 200 patients. Out of 200 individuals 38% (76/200) was culture positive and 62% (124/200) was culture negative, among culture positive cases 69 cases was Gram –ve mainly enterobacteriaceae and 7 was Gram +ve mainly cocci. S.R. Nannan Panday in 2019 had been conducted a study which shown culture positivity in sepsis associated with high mortality.⁸ Mitul Patel conducted a study in Birmingham UK on utility of blood culture in sepsis diagnosis and treatment.⁹ In our study we have analysed association between PCT and blood culture. In this study, PCT and blood culture was done in 200 subjects, out of 200 patients in 38% (76/200) patient's blood culture was positive. PCT concentration was <0.5 with 1% enterobacteriaceae, 0.5-2.0 with 6% enterobacteriaceae, 2.0-10 with 8% enterobacteriaceae, >10 with 7.5% enterobacteriaceae. For 0.5% Gram negative bacteria <0.5, 0.5-2.0 for 4% Gram –ve bacteria, 2-10 for 3% Gram –ve bacteria, >10 for 4.5% Gram –ve bacteria. <0.5 for 0% Gram +ve cocci, 0.5-2.0 with 0.5% Gram +ve cocci, 2-10 with 0.5% Gram +ve cocci and >10 for 2.5% Gram +ve cocci. Our study revealed PCT levels correct with Gram negative bacteria specially enterobacteriaceae. Higher (>10) PCT values independently associated with enterobacteriaceae in blood culture. The ROC curve of procalcitonin level in predicting culture positivity (both gram -ve and +ve) showed an area under the curve of 0.67 with 95% CI of 0.59 – 0.74. The association is highly statistically significant (p value <0.001). In 2019 Matteo Bassetti et al³ had been conducted a retrospective case control study in Italy which revealed almost similar result about relationship between PCT and blood culture. Liyinglai et al¹⁰ had been conducted a study which shown PCT has ability to predict blood culture report. Our study revealed PCT is a significant predictor of blood culture report. CRP is an important biomarker for early diagnosis of sepsis. Its levels may be vary with severity of sepsis. This study have been analysed association between CRP and blood culture. In this study, blood culture and CRP was done in 200 subjects, out of 200 patients in 38% (76/200) patient's blood culture was positive. CRP concentration was <0.5 with 5% enterobacteriaceae, 0.5-2.0 with 6% enterobacteriaceae, 2.0-10 with 6% enterobacteriaceae, >10 with 3.5% enterobacteriaceae. For 3% Gram negative bacteria <0.5, 0.5-2.0 for 1% Gram –ve bacteria, 2-10 for 4% Gram –ve bacteria, >10 for 4% Gram –ve bacteria. <0.5 for 0% Gram +ve cocci, 0.5-2.0 with 1.5% Gram +ve cocci, 2-10 with 0.5% Gram +ve cocci and >10 for 1.5% Gram +ve cocci. Our study revealed that CRP was not able to predict blood culture report. The ROC curve of CRP level in predicting culture positivity (both gram -ve and +ve) showed an area under the curve of 0.519 with 95% CI of 0.43 – 0.60. The association was not statistically significant (p value =

0.653). Liyinglai et al had been conducted a study in 2019 which shown that PCT has better ability than CRP to predict blood culture report. In 2019 Matteo Bassetti et al had been conducted a retrospective case control study in Italy which revealed that CRP was not able to predict blood culture report. That is role of CRP to predict blood culture report is not significant. Our study has been shown PCT is better predictor of blood culture report than CRP in sepsis patients.

Conclusion

PCT is better predictor of blood culture report than CRP in sepsis patients. PCT levels correlate with Gram negative bacteria specially enterobacteriaceae. Higher (>10) PCT values independently associated with enterobacteriaceae in blood culture. In sepsis WBC count may be raised, normal or decreased. Mortality increases with increase WBC count. There is an independent association between blood culture report and TLC count which is not significant. In blood culture of sepsis patients Gram -ve bacteria more commonly present. PCT is better predictor of mortality than CRP in sepsis patients. Male predominance over females in sepsis patients. More commonly involve adult >40 year.

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