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Original Research Article

Serum Procalcitonin Evaluation in Sepsis Patients

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Abstract:

Introduction: In the medical condition known as sepsis, the immune system works overtime to fight infection by releasing chemicals into the blood that cause widespread inflammation. The prohormone precursor of calcitonin known as procalcitonin (PCT) is largely synthesised in the C-cells of the thyroid gland and to a lesser extent in the neuroendocrine tissue of other organs like the lungs and intestines.

Method: In Bhubaneswar, Odisha's Apollo Hospitals (Tertiary Care Centre), a study was undertaken on patients in general medicine, emergency care, and intensive care units. It is situated in the eastern coastline region of Odisha's capital city. The iCHROMA II equipment was used for the serum procalcitonin assay.

Result: To investigate the role of serum PCT in the identification and prognosis of sepsis patients, we have 92 individuals. In the case group, Serum Procalcitonin (ng/mL) (Day 0) had a mean (SD) of 6.21 (5.43). In the control group, Serum Procalcitonin (ng/mL) (Day 0) had a mean (SD) of 0.37 (0.39).

Conclusion: One of the top causes of death in the globe is sepsis. To reduce morbidity and death in sepsis, early detection and prompt treatments are essential. The gold standard for diagnosing sepsis is microbiological culture, however it takes time and is not widely available. Serum PCT and CRP, two easily accessible biomarkers, have drawn a lot of interest in previous investigations. In this research, we assessed the roles of CRP and procalcitonin in the diagnosis and prognosis of sepsis patients.

Keyword: Sepsis, Serum PCT, Immune Inflammatory Response.

Introduction

Sepsis is defined as "a life-threatening organ dysfunction brought on by an abnormal host response to infection." [1] A condition known as sepsis occurs when the immune system overreacts to an infection and sends chemicals into the blood to fight it, causing widespread inflammation. The term "sepsis" was first used in a medical context more than 2700 years ago in Homer's poetry. The phrase's origins can be traced back to the Greek verb sepein, which means "to rot." [2] Sepsis continues to be the leading cause of death in critically ill patients despite the use of modern antibiotics and resuscitation methods. [3,4] The series of mechanisms that comprise the septic response are highly complex and also involve humoral and cellular responses, inflammatory and anti-inflammatory processes, and circulatory abnormalities. [5,6]

Epidemiologic data on sepsis differ depending on the type of database—community-based or hospital-based—and the technique of data collection—retrospective record review, discharge diagnosis, diagnosis on death certificates, or prospective observational research. [3] Data from India are few and largely focus on the epidemiology of infections (both acquired in hospitals and the community) as opposed to sepsis, which is the body's response to infection. [7] It is challenging to diagnose sepsis and determine how severe it is due to the condition's wide range of symptoms and lack of specificity. However, the early. To maximise the possibility of promptly executing a tailored treatment plan, it is essential to identify sepsis and classify its severity. [8,9], but it takes time and numerous cultures to evaluate if the results are clinically significant or simply contaminated. Microbiological culture is still the gold standard for diagnosing sepsis. Furthermore, a sizable percentage of sepsis patients still test negative for cultures. A few factors that could affect the outcomes of the culture include age, past medical conditions, immunological state, history of exposure, and the use of empiric antibiotic therapy that was initiated before collecting the samples. [10]

Procalcitonin (PCT) is the prohormone precursor of calcitonin, which is mostly expressed in the C-cells of the thyroid gland and to a lesser extent in the neuroendocrine tissue of other organs like the lungs and intestines. Because different cytokines and bacterial endotoxin impede the final step in the conversion of procalcitonin to calcitonin, large

quantities of these substances lead to an increase in PCT levels. Since bacterial infections are more specific, PCT is better. [11]

Calcitonin's 116 amino acid peptide precursor is called PCT. [11] It has been shown that PCT circulates in normal serum at a very low concentration; it is most likely created by the neuroendocrine cells in the thyroid and lungs. [12] Typically, it has plasma concentrations of low than 0.1 ng/ml.

The serum level of procalcitonin typically rises sharply in sepsis, peaking in less than 24 hours and reaching values that are tens, hundreds, or even thousands of times higher than normal levels. [13] These levels stay increased throughout the inflammatory process and are correlated with the severity of the illness. Notably, although they rarely overlap, the levels that result from systemic viral infection are often far lower than those from bacterial infection [14,15]

Although PCT is still one of the most promising sepsis indicators, there is still significant debate about its clinical applicability [16]. It is crucial for doctors to take into account the fact that the marker has been researched in a range of clinical settings and with various patient populations while treating patients at the bedside.

Materials and Methods

The study's participants were patients at Apollo Hospitals (Tertiary Care Centre), Bhubaneswar, Odisha, in the General Medicine, Emergency, and ICU departments. The capital city of Odisha's eastern shore is where it is located. All adults (over the age of 18) who met the criteria for Sepsis-3 as established by the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM) and who were admitted to the general medicine department, emergency room, or intensive care unit at tertiary care Apollo Hospitals, Bhubaneswar, with fever or a chronic inflammatory syndrome. For demographic, clinical, and laboratory data, the patients' medical records were mined.

Before beginning the use of empirical antibiotics, a blood sample was properly taken at the emergency room or intensive care unit and sent for bacterial culture. At Apollo Hospitals in Bhubaneswar, blood cultures were performed using the BACTEC 9120 (BD) and BAcTLERT 3D (BIOMERLEUX) machines. Microbiology department provided a blood culture report.

The iCHROMA II equipment was used for the serum procalcitonin assay. The procalcitonin test employs a sandwich immunodetection technique, in which the detector antibody in the buffer binds to the PCT in the serum sample and the antigen-antibody complex is captured to a different PCT antibody that has been immobilised on test strip as the sample combination migrates through the nitrocellulose matrix. As a result, more antigen-antibody complexes built up on the test strip the higher the concentration of PCT antigen in the serum. When processed to the QDxInstacheck Reader, the signal intensity of the fluorescence on the detector antibody reflects the quantity of antigen collected and displays the concentration of PCT in the specimen.

Statistical Analysis

Data tracking and coding were done in the MS Excel spreadsheet programme. Using the SPSS v23 tool from IBM Corp., the data were analysed. For continuous data, means, standard deviations, and medians were employed, and for categorical variables, frequencies and percentages. Data were visualised using column charts, pie charts for categorical data, and bar charts for continuous data whenever possible. applying the independent sample t test on data that were constantly distributed. The Wilcoxon test was the most appropriate non-parametric test for comparisons utilising data that were found to be non-normally distributed. The chi-squared test was applied to compare groups of categorical data. The expected frequency in the contingency tables was 5 for more than 25% of the cells, prompting the use of Fisher's Exact test.

Results

We split the 92 total patients, a case and control group of 46 each, to explore the effect of serum PCT in diagnosis and prognosis in sepsis patients. As previously mentioned, the case group consists of patients who meet the criteria for Sepsis-3, whereas the control group consists of healthy people who are similar in age and gender. Based on the primary outcome, which was 28-day mortality, the case group was further classified into survivors and non survivors. This chapter presents the analysis and interpretation.

Table1: Distribution of the cases in Terms of Gender (n = 46)

Gender	Frequency	Percentage	95% CI
Female	25	54.3%	39.2% - 68.8%
Male	21	45.7%	31.2% - 60.8%

Men made up 54.3% of the cases. There were 45.7% women overall.

Analyzing Diagnostic Performance of Pct

Table2: Comparison of the case and control groups of the Variable Sepsis in Terms

Serum Procalcitonin	Sepsis		Wilcoxon-Whitney	Mann U Test
(mg/L) (Day 0)	Present(case group)	Absent(control group)	W	p value
Mean (SD)	6.21 (5.43)	0.37 (0.39)		
Median (IQR)	3.65 (2.45-9.65)	0.3 (0.2-0.4)	2037.000	<0.001
Range	0.2 - 23	0.1 - 2.1		

In the case group, Serum Procalcitonin (ng/mL) (Day 0) had a mean (SD) of 6.21 (5.43). In the control group, Serum Procalcitonin (ng/mL) (Day 0) had a mean (SD) of 0.37 (0.39).

Serum Procalcitonin (ng/mL) (Day 0) varied significantly between the two groups (W = 2037.000, p = 0.001), with the case group having the highest median Serum Procalcitonin (ng/mL) (Day 0) value.

The means of Serum Procalcitonin (ng/mL) (Day 0) in the two separate groups are shown in the bar graph below.

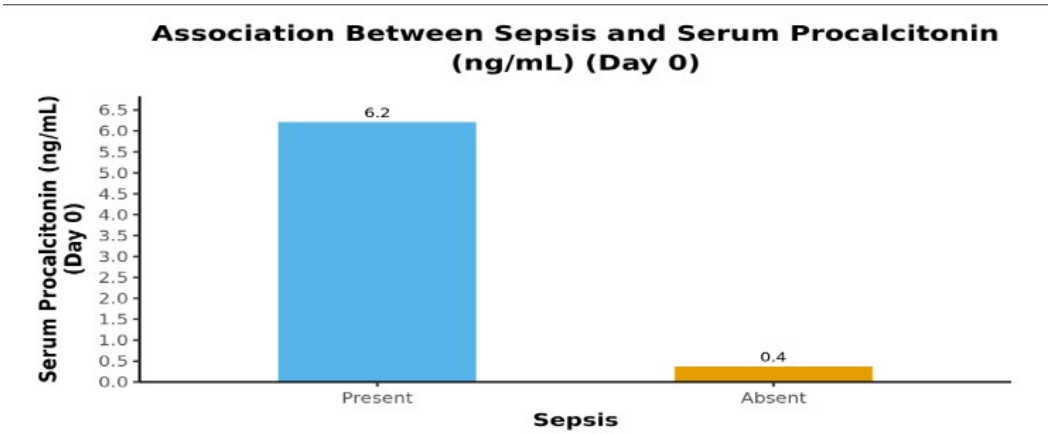
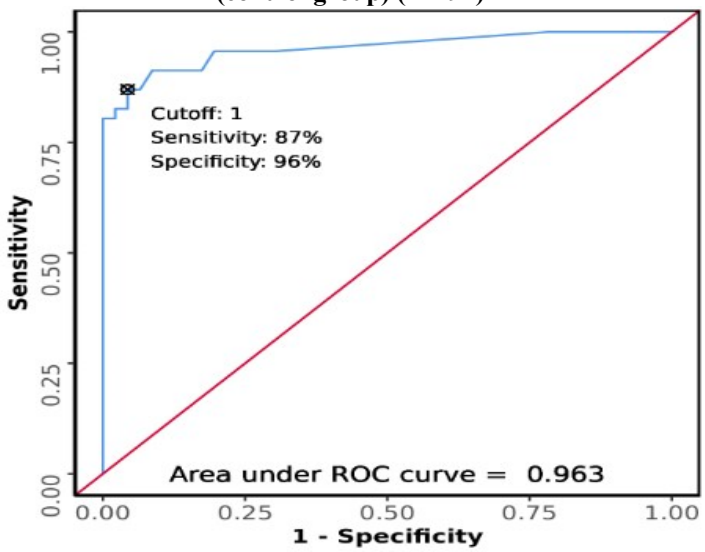


Table3: ROC Curve Analysis Showing Diagnostic Performance of Serum Procalcitonin(ng/mL) (Day 0) in Predicting Sepsis present (case group) vs Sepsis absent (control group) (n = 92)



Parameter	Value (95% CI)
Cutoff (p value)	≥ 1 (<0.001)
AUROC	0.963 (0.926 - 0.999)
Sensitivity	87.0% (74-95)
Specificity	95.7% (85-99)
Positive Predictive Value	95.2% (84-99)
Negative Predictive Value	88.0% (76-95)
Diagnostic Accuracy	91.3% (84-96)

Positive Likelihood Ratio	20 (5.13-77.93)
Negative Likelihood Ratio	0.14 (0.06-0.29)
Diagnostic Odds Ratio	146.67 (27.98-768.75)

Serum Procalcitonin (ng/mL) (Day 0) predicted Sepsis Present (case group) vs Sepsis Absent (control group) with an area under the ROC curve (AUROC) of 0.963 (95% CI: 0.926 - 0.999), indicating excellent diagnostic performance. With a p value of 0.001, it was statistically significant.

It predicts sepsis patients with a sensitivity of 87% and a specificity of 96% at a threshold of Serum Procalcitonin (ng/mL) (Day 0) 1.

The odds ratio (95% confidence interval) for sepsis was 122.57 (24.03-625.28) when serum procalcitonin (ng/mL) (Day 0) was 1. When serum procalcitonin (ng/mL) (Day 0) is 1, there is a 6.93 (3.68-14.01) percent (95% CI) relative risk for sepsis to be present**.**

Table4: Comparison of gender in survived and non survived group

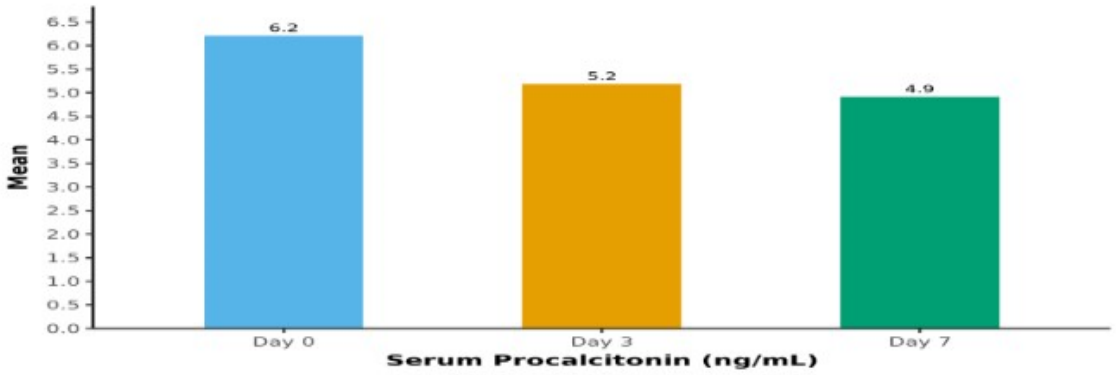
Gender	Outcome		Chi- Squared		Test
	Survived	Died	Total	χ2	P Value
Female	13 (38.2%)	8 (66.7%)	21 (45.7%)		
Male	21 (61.8%)	4 (33.3%)	25 (54.3%)	2.890	0.089
Total	34 (100.0%)	12 (100.0%)	46 (100.0%)		

There were 61.8% male participants and 38.2% female participants in the group that survived. 33.3% of the men and 66.7% of the women who did not survive belonged to this group. When it came to the distribution of, there was little difference between the different groups. Gender ($\chi2$= 2.890, p = 0.089).

Outcome Analysis Based on PCT

Table 5: Summary of Serum Procalcitonin (ng/mL)

Serum Procalcitonin (ng/mL)	Mean ± SD	Median (IQR)	Min - Max
Day 0	6.21 ± 5.43	3.65 (2.45-9.65)	0.2 - 23.0
Day 3	5.18 ± 4.88	3.60 (1.83-8.15)	0.1 - 21.2
Day 7	4.92 ± 6.70	1.80 (0.32-6.75)	0.1 - 28.0



On Day 0, the mean serum procalcitonin concentration (ng/mL) was 6.21 5.43.It was 5.18 ± 4.88 on Day 3. It was 4.92 6.70 on Day 7.

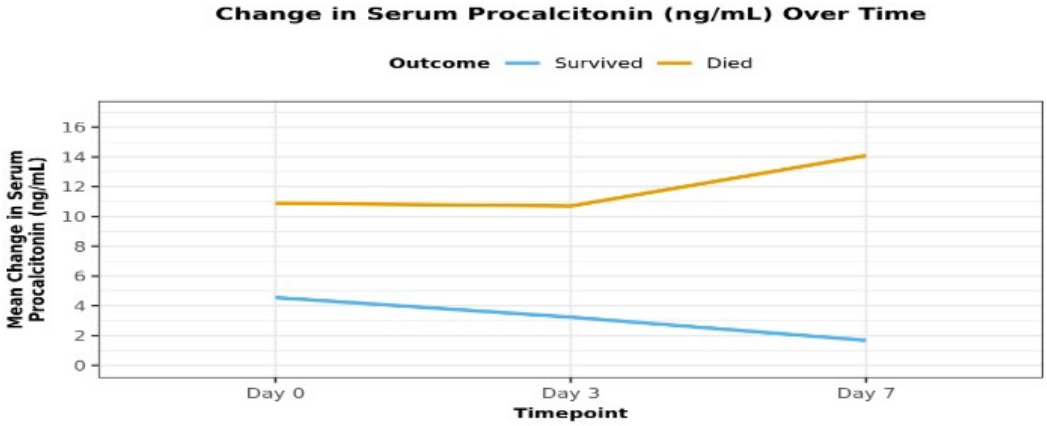
Table 6: Comparison of the Two Groups in Terms of change in PCT over time (n =46)

Serum	Outcome				P value
PCT(ng/mL)	Survived		Non Survived		
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Day 0	4.56 (4.25)	3.2 (1.97-5.72)	10.89 (5.84)	12.3 (6.72-14)	0.001
Day 3	3.24 (2.98)	2.05 (1.1-4.45)	10.70(5.10)	10.8(7.92-13.1)	<0.001
Day 7	1.68 (1.99)	1.2 (0.2-2.1)	14.09(6.91)	14.7 (11.78-18)	<0.001

The mean PCT for patients who survived dropped from a maximum of 4.56 on day 0 to a minimum of 1.68 on day 7. However, the mean PCT in the non-survivor group rose from 10.89 at day 0 to a

maximum of 14.09 at day 7. At days 0, 3, and 7, there was a sizable difference between the two groups in terms of serum PCT. There was no discernible difference between the two groups' mean changes in serum procalcitonin (ng/mL) throughout time.

Here is a line graph showing how the levels of serum procalcitonin in the two groups changed over time.



Discussion

For a better understanding of the study's findings, the data on how serum Procalcitonin and serum CRP levels function as diagnostic and prognostic markers in sepsis need to be corroborated with relevant literature and their clinical implications reviewed. This chapter specifically tries to do that.

Gender distribution:

46 patients with sepsis were used as the case group in the current study, while 46 healthy, normal people who were gender matched were used as the control group. The case group was then split into those who survived and those who didn't (died within 28 days of follow up). In our survey, there were 25 men (54.3%), and there were 21 women (45.7%). Participants in the survival group were split 61.8% male and 38.2% female. 33.3% of the non-survivors were men and 66.7% were women. In terms of gender distribution, there was no appreciable difference between groups that included survivors and those that did not. 47.9% of the participants in the study by Huang MY et al. (16) were men. Of those, 50.0% of the males were not survivors, and 47.5% of the males were survivors. Similar to our study, there was no discernible gender difference between the two groups (0.897).

The Area Under ROC Curve (AUROC) for PCT (Day 0) predicting patients with sepsis (case group) compared to patients without sepsis (control group) in our study was 0.963 (95% CI: 0.926 - 0.999), suggesting superior diagnostic performance. (p 0.001) It was statistically significant. With a sensitivity of 87% and a specificity of 96%, serum procalcitonin (ng/mL) (Day 0) 1 predicts patients with sepsis. When serum procalcitonin (ng/mL) (Day 0) is 1, the odds ratio (95% CI) for sepsis was 122.57 (24.03-625.28). When serum procalcitonin (ng/mL) (Day 0) is 1, the relative risk (95% CI) for sepsis was 6.93 (3.68-14.01).

In a prospective observational investigation, Tulzo Y et al. [17] found that the PCT had a sensitivity and specificity of 65% and 70%, respectively, at cut-off levels of 2 ng/ml.

Our research supports Muller et al. (13), who found that PCT is a potent diagnostic tool for identifying individuals with and without sepsis (at a cutoff value of 1ng/ml).

Table7: Comparison of diagnostics power of PCT with previous studies.

Study	Pct Cutoff Value	Sensitivity	Specificity
Muller et al. (37)	**1 ng/ml**	**89%**	**94%**
Tulzo Y et al. (56)	**2 ng/ml**	**65%**	**70%**
Ahmed et al. (51)	**0.5 ng/ml**	**93.8%**	**43.5%**
Our study	**1 ng/ml**	**87%**	**96%**

Conclusion

Based on our research, we came to the conclusion that both PCT are trustworthy indicators for correctly diagnosing sepsis patients. The diagnostic effectiveness of PCT did not significantly change. As a result, both PCT can be crucial for the early diagnosis of sepsis, which may allow for the quick start of antibiotic and other suitable treatments, perhaps improving the sepsis's unfavourable prognosis. At days 0, 3, and 7, there was a large difference in PCT between the survivors and non

survivors group. The trajectory of PCT over time showed no discernible difference between the groups of survivors and non-survivors.

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