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Original Research Article

Evaluation of Serum C-Reactive Protein in Patients with Sepsis

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Abstract:

Introduction: According to the definition of sepsis, it is "a life-threatening condition of organ dysfunction brought on by an abnormal host response to infection." The acute stage of the protein known as C-reactive protein (CRP) is made in the liver. TNF-, IL-1, and IL-6 promote its production. It is heightened during an inflammatory immunological response, particularly when there is a bacterial infection. After the sickness has abated, the CRP levels rise and return to reference ranges more quickly.

Method: After ruling out exclusion criteria, patients who presented to the general medicine department, ER, or intensive care unit and met the Sepsis-3 criteria were taken with informed permission. The patients' medical records were mined for demographic, clinical, and laboratory information. The Mispa i2 machine was used to determine the serum C-reactive protein. The anti-human Creactive protein-coated latex fragments agglutinate when exposed to serum C-reactive protein (CRP). Turbidimetry can be used to measure the agglutination of the latex particles, which is proportional to the CRP concentrations.

Result: We have 46 patients to explore the function of serum PCT and CRP in the identification and prognosis of sepsis patients. Serum CRP (mg/L) (Day 0) in the case group had a mean (SD) of 39.91 (28.32). The control group's mean (SD) for serum CRP (mg/L) on Day 0 was 5.61 (4.86).

Conclusion: We came to the conclusion from our study that CRP might be regarded as dependable biomarkers for the precise diagnosis of sepsis patients. d Early detection of sepsis can be aided by CRP, which could speed the start of proper therapy with antibiotics and other factors, thereby improving the sepsis's unfavourable prognosis. Therefore, it is possible to regard CRP as reliable prognostic indicators in sepsis.

Keyword: Sepsis, Serum CRP, Immune Inflammatoru Response.

Introduction

According to the definition of sepsis, it is "a life-threatening organ dysfunction brought on by an abnormal host response to infection."[1] Sepsis is a disorder in which the immune system overreacts to an infection and releases chemicals into the blood to fight it, setting up widespread inflammation. More than 2700 years ago, Homer's poetry contained the first use of the word sepsis in a medical setting. The root of the phrase is the Greek word sepein, which means "to rot." [2] Despite the use of current antibiotics and resuscitation techniques, sepsis remains a primary cause of death in critically ill patients. [3,4] The chain of events that make up the septic response is incredibly complicated and includes inflammatory and anti-inflammatory processes, humoral and cellular reactions, and circulatory abnormalities. [5,6]

Depending on the source of the database—community-based or hospital-based—and the method of data collection—retrospective chart review, discharge diagnosis, diagnosis on death certificates, or prospective observational studies—epidemiologic statistics on sepsis vary. [3] Data from India are scarce and mostly pertain to the epidemiology of infections (both hospital and community acquired), as opposed to sepsis, which is the body's reaction to infection. [7] The highly diverse and non-specific nature of sepsis symptoms makes it difficult to diagnose the condition and gauge how severe it is. [8], but the early. It is crucial to diagnose sepsis and categorise its severity to increase the likelihood of implementing a targeted treatment plan quickly. [9,10] Microbiological culture is still the gold standard for diagnosing sepsis, but it takes time, requires multiple cultures to determine whether the results are clinically significant or just contamination. Additionally, a sizeable portion of sepsis patients continue to test negative for cultures. Age, previous illnesses, immunological condition, exposure history, and the use of empiric antibiotic therapy that was started before collecting the samples are just a few of the variables that may have an impact on the results of the culture. [11]

The acute phase protein known as C-reactive protein (CRP) is made in the liver. TNF-, IL-1, and IL-6 promote its production. It is heightened during an inflammatory immunological response, particularly when there is a bacterial infection. [12] After the sickness has abated, the CRP levels rise and return to reference ranges more quickly.

Sepsis has a well-established marker called CRP. The sera of pneumonia patients the ability to precipitate polysaccharide fractions from Streptococcus pneumonia, known as fraction C, in 1930. [13] This feature was not noticed in healthy volunteers and quickly vanished when patients healed. When a protein was found to be the root of this reaction, it was given the moniker CRP. The term "acute phase" was created to categorise infected patients with acute illness whose sera were CRP positive. Since that time, numerous other acute phase proteins have been identified.

CRP is primarily produced by the liver, much like many other acute phase proteins, mostly in reaction to IL-6. Aside from TNF and IL-1, other regulatory mediators of CRP production include them. [14] Within 4-6 hours of the stimulation, CRP secretion starts; it doubles every 8 hours; it peaks in 36-50 hours. The concentration of CRP can increase to above 500 mg/l, or more than 1000 times the value used as a reference, in response to a particularly strong stimulation. CRP has a half-life of 19 hours, therefore it declines quickly when the stimulus is gone or removed. However, if the underlying cause of the elevation persists, CRP can stay elevated even for very long times. [12,15]

Most invasive infections are associated with elevated serum CRP levels. [16] Even in patients with compromised immune systems, systemic fungal infections, acute Gram-positive and Gram-negative bacterial infections, and both generate substantial increases in CRP. In contrast, CRP levels are typically lower in the majority of acute viral infections. In addition to being used to diagnose sepsis, CRP has also been studied as a prognostic indicator. [17]

Materials and Methods:

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

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 Mispa i2 machine was used to determine the serum C-reactive protein. The anti-human Creactive protein-coated latex particles agglutinate when exposed to serum C-reactive protein (CRP). Turbidimetry can be used to measure the agglutination of the latex particles, which is proportional to the CRP concentration. 1x1 mL of CRP is the standard (BioSystems Cod. 31113).

Statistical Analysis:

In the MS Excel spreadsheet programme, data were coded and kept track of. To analyse the data, IBM Corp.'s SPSS v23 programme was employed. Means, standard deviations, and medians, for continuous data, and frequencies and percentages, for categorical variables, were used to elaborate descriptive statistics. Wherever possible, data were displayed graphically for data visualisation using column charts, and pie charts for categorical data and bar charts for continuous data. When continuously distributed data were made using the independent sample's t test. For comparisons using data that were determined to be non-normally distributed, the Wilcoxon test was the suitable non-parametric test. For categorical data group comparisons, the chi-squared test was employed. Fisher's Exact test was employed when it was discovered that the predicted frequency in the contingency tables was 5 for more than 25% of the cells.

Results:

We split the 92 total patients into two distinct categories, a case and control group with 46 each, to explore the effect of CRP in diagnosis and prognosis in sepsis patients. As previously stated, the case group consists of patients meeting Sepsis-3 criteria, whereas the control group includes of healthy people who are similar in age to the case group. Based on the primary result, or mortality after 28 days, the case group was further split into a survivor and non-survivor group. In this chapter, the analysis as well as interpretation are presented.

Table1: Distribution of the case group in Terms of Age (Years) (n = 46)

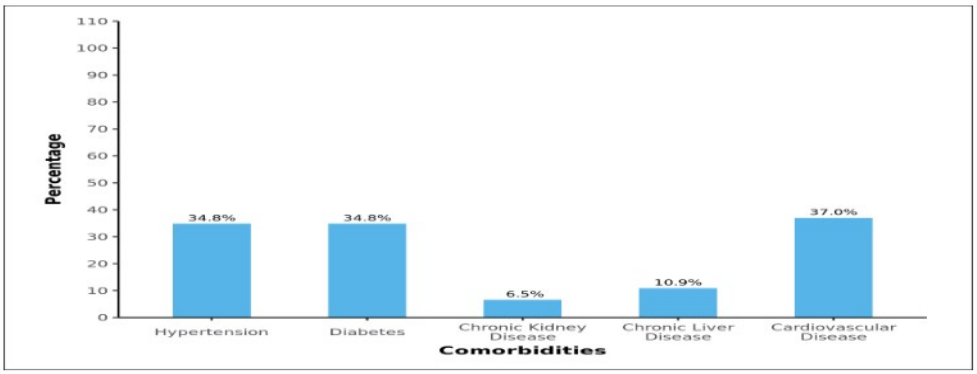
Age	
Mean (SD)	59.46 (16.06)
Median (IQR)	60 (48.25-73)
Range	26 - 88

Age (Years) has a regularly distributed distribution (Shapiro-Wilk test: p = 0.420). Age (Years) had a mean (SD) of 59.46 (16.06). Age (Years) median (IQR) was 60.00 (48.25-73). The range of ages (in years) was 26 to 88.(Table1)

Table 2: Comparison of the case and control groups of the Variable Sepsis in Terms of Serum CRP (mg/L) (Day 0) (n = 92)

Serum CRP	Sepsis		Wilcoxon-Whitney	Mann U Test
(mg/L) (Day 0)	Present(case group)	Absent(control group)	W	p value
Mean (SD)	39.91 (28.32)	5.61 (4.86)		
Median (IQR)	32 (22.25-53.75)	4 (3-6)	2008.500	<0.001
Range	4 - 112	1 - 25		

Serum CRP (mg/L) (Day 0) in the case group had a mean (SD) of 39.91 (28.32). The control group's mean (SD) for serum CRP (mg/L) on Day 0 was 5.61 (4.86). Serum CRP (mg/L) (Day 0) was significantly different between the two groups (W = 2008.500, p = 0.001), with the case group having the highest median Serum CRP (mg/L) (Day 0) value. (Table2)



Incidence of Comorbidities in Case Group::

Hypertension was present in 16 (34.8%) of the case group. Diabetes was present in 16 (34.8%). 3 (6.5%) of the case group had Chronic Kidney Disease. 5 (10.9%) of the participants had Chronic Liver Disease. Cardiovascular Disease was present in 17 (37.0%) of the case group.

Outcome Analysis in Case Group:

Table 3: Distribution of the Patients in Terms of Outcome (n = 46)

Outcome	Frequency	Percentage	95% CI
Survived	34	73.9%	58.6% - 85.2%
Died	12	26.1%	14.8% - 41.4%

34 patients—or 73.9%—of the total 46 patients in the case group—survived. 12 (or 26.1%) of the participants died.

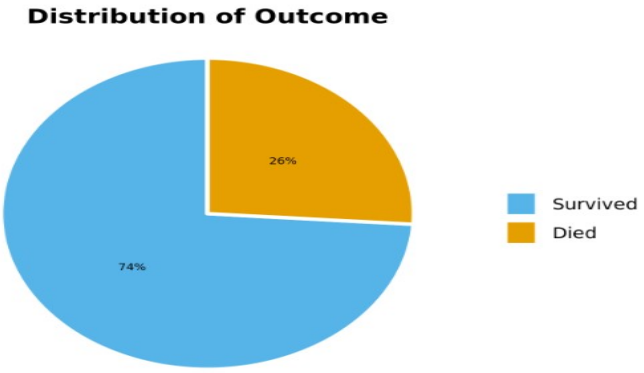


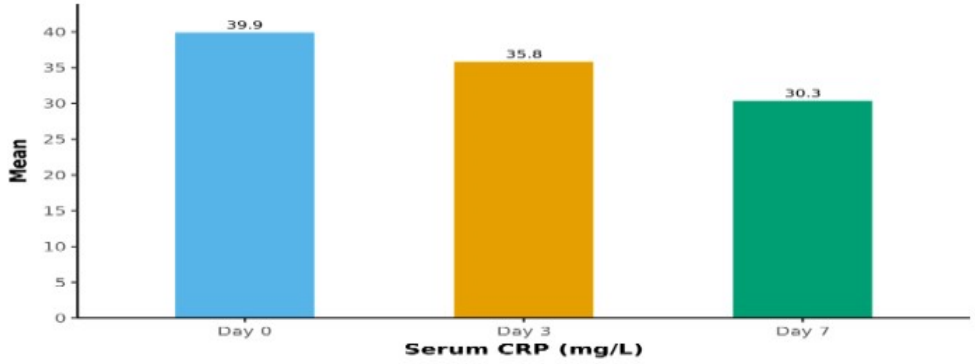
Table 4: Comparison of Age (Years) in survived and non survived group (n = 46)

Age (Years)	Outcome		Wilcoxon Whitney	Mann U Test
	Survived	Non Survived	W	p value
Mean (SD)	57.56 (15.48)	64.83 (17.14)		
Median (IQR)	58 (48.25-70.5)	66.5 (51.5-78)	161.000	0 .287
Range	26 - 83	39 - 88		

The average age (Years) of those who survived was 57.56 (SD: 15.48), while those who did not survive were 64.83 (SD: 17.14). In the group of people who survived, the median age (IQR) was 58 (48.25-70.5), while in the group of those who did not survive, it was 66.5 (51.5-78). Age (Years) did not significantly differ across the groups (W = 161.000, p = 0.287).

Table 5: Summary of Serum CRP (mg/L)

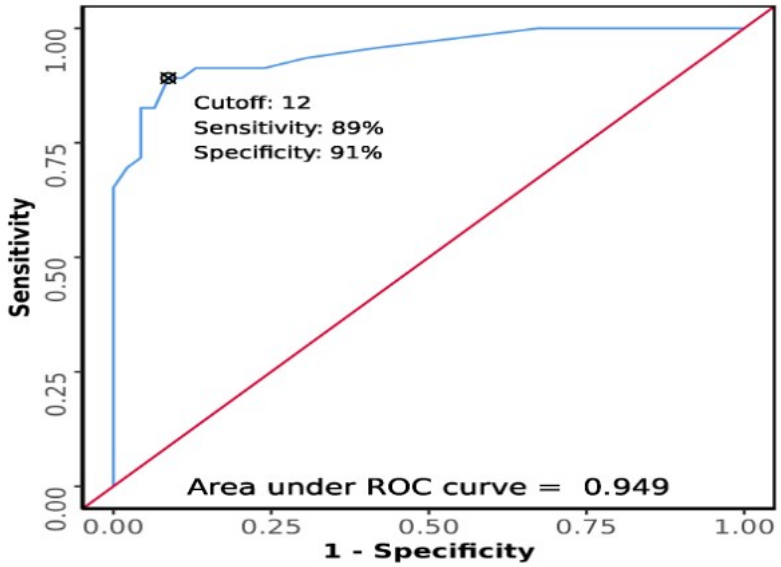
Serum CRP (mg/L)	Mean ± SD	Median (IQR)	Min - Max
Day 0	39.91 ± 28.32	32.00 (22.25-53.75)	4.0 - 112.0
Day 3	35.83 ± 27.62	30.00 (14.25-58.50)	3.0 - 104.0
Day 7	30.35 ± 31.81	16.00 (6.50-55.00)	2.0 - 108.0



Day 0's mean serum CRP value was 39.91 28.32 mg/L.was 35.83 27.62 on Day 3.Was 30.35 31.81 on Day 7.

Table 6: ROC Curve Analysis Showing Diagnostic Performance of Serum CRP (mg/L) (Day 0) in Predicting Sepsis present (case group) vs Sepsis absent (controlgroup) (n = 92)

Parameter	Value (95% CI)
Cutoff (p value)	≥ 12 (<0.001)
AUROC	0.949 (0.907 - 0.991)
Sensitivity	89.1% (76-96)
Specificity	91.3% (79-98)
Positive Predictive Value	91.1% (79-98)
Negative Predictive Value	89.4% (77-96)
Diagnostic Accuracy	90.2% (82-95)
Positive Likelihood Ratio	10.25 (4-26.29)
Negative Likelihood Ratio	0.12 (0.05-0.27)
Diagnostic Odds Ratio	86.1 (21.59-343.41)



The area under the ROC curve (AUROC) for Serum CRP (mg/L) (Day 0) predicting Sepsis Present (case group) vs Sepsis Absent (control group) was 0.949 (95% CI: 0.907 - 0.991), showing excellent diagnostic performance. According to statistics (p = 0.001), it was significant. With a sensitivity of 89% and a specificity of 91% at a cutoff of Serum CRP (mg/L) (Day 0) 12, it can identify patients who are sepsis-prone.

When serum CRP (mg/L) (Day 0) is 12, sepsis is more likely to be present, according to the odds ratio (95% CI), which was 68.08 (16.84-275.21). Serum CRP (mg/L) (Day 0) 12 is associated with a relative risk of 5.91 (3.28-11.4) for sepsis, according to the 95% confidence interval.

Discussion:

For a better understanding of the study's findings, the data on how serum CRP levels function as diagnostic and Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med [Internet]. 2017 Mar;43(3):304–77. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28101605 prognostic markers in sepsis need to be corroborated with relevant literature and their clinical implications reviewed. This chapter specifically tries to do that.

Age and Gender distribution:

The average age of the case group was 59.46±16.06 years, 57.56±15.48 years for the survivor group, and 64.83±17.14 years for the non-survivor group. Regarding age (years), there was no discernible difference between the two groups. In their investigation, which included 48 cases with a mean age of 74±12 years, Huang MY et al. [18] found that the mean age was 75±11 years for survivors and 70±14 years for non–survivors. Similar to our study, there was no discernible difference in age between the two groups (p = 0.355).

Study	Year Of Study	Mean(SD) of Age (Years)
Ibrahim et al. (48)	2014	28.8(9.3)
Young et al. (49)	2016	67.22(14.18)
Pradhan S et al. (58)	2018	43(19)
Yunus et al. (50)	2018	61.3(12.6)
Novita C et al. (61)	2019	47.4(14.02)
Our study	2021	57.56(15.48)

CRP as diagnostic tool for predicting sepsis:

The Area Under ROC Curve (AUROC) for Serum CRP (mg/L) (Day 0) predicting sepsis (case group) compared with patients without sepsis (control group) in our study was 0.949 (95% CI: 0.907 - 0.991), suggesting superior diagnostic performance. (p 0.001) It was statistically significant. Serum CRP (mg/L) (Day 0) 12 predicts sepsis in patients with an 89% sensitivity and 91% specificity cutoff. When serum CRP (mg/L) (Day 0) is 12, the odds ratio (95% CI) for sepsis was 68.08 (16.84-275.21). When serum CRP (mg/L) (Day 0) is 12, the relative risk (95% CI) for sepsis was 5.91 (3.28-11.4).

In terms of AUROC, specificity, positive predictive value, and diagnostic efficacy, the better parameter was Better parameter in terms of sensitivity and

negative predictive value was serum CRP (mg/L) (Day 0).

Sepsis was significantly predicted by serum CRP (mg/L) (Day 0). The diagnostic performance of Serum Procalcitonin (ng/mL) (Day 0) and Serum CRP (mg/L) (Day 0) did not differ significantly.

As a diagnostic predictor of sepsis, CRP exhibited a sensitivity and specificity of 84.3% and 53.8%, respectively, according to Pradhan S et al. [19]. Although it is not specific, CRP has been demonstrated to be a sensitive marker of sepsis.

In order to identify a sepsis marker, Póvoa P et al. (20) investigated CRP values at ICU admission. The sensitivity and specificity of CRP for the diagnosis of sepsis were 93.4 and 86.1%, respectively, with a threshold of 8.7 mg/L. Our study came to similar conclusions. CRP demonstrated sensitivity of 89% and specificity of 91% at the cutoff value of 12 mg/L.

Conclusion:

According to the results of our investigation, CRP can be regarded as a trustworthy biomarker for the precise diagnosis of sepsis patients. The diagnostic effectiveness of CRP showed no discernible variation. So, CRP can be crucial for the early detection of sepsis, which may permit the quick start of antibiotic and other suitable treatment, perhaps reducing the sepsis's unfavourable prognosis. When it came to CRP at days 0, 3, and 7, there was a considerable difference between the group of survivors and non survivors. The CRP trend over time between the survivor and non-survivor group did not significantly differ from one another.

The time spent in the intensive care unit, the time spent using a ventilator, and the time spent receiving vasopressor assistance all correlated favourably with CRP. Therefore, CRP is a reliable indicator of prognosis in sepsis.

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