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Serum Procalcitonin in adult sepsis patients: A cross sectional study

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Abstract:

Notwithstanding the progress made in sepsis diagnostic techniques, it continues to be a significant contributor to both morbidity and mortality. Diagnosing sepsis from other non-infectious disease states continues to be difficult. Although procalcitonin (PCT) is a valuable diagnostic tool for sepsis, its cut-off ranges differ across clinical settings. Establishing a correlation between PCT levels in serum and cultures, as well as determining the optimal PCT cutoff values with high sensitivity and specificity, was the objective of this study. **Materials & methods:** This prospective study comprised 150 patients recruited from various medical facilities. The patients

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were categorized into three groups: group I (constituting patients, n = 50), group II (culture-negative sepsis patients, n = 50), and group III (culture-positive sepsis patients, n = 50). A mean p-value less than 0.05 was deemed to be statistically significant. **Results:** The levels of PCT were considerably elevated in groups II and III in comparison to group I. PCT had the highest sensitivity of 78.26% and specificity of 88.40% at a concentration of 1.4 ng/ml in group II (area under curve: 0.87). Group III yielded the most optimal cut-off value of 2.31 ng/ml, which exhibited a sensitivity of 97.36% and specificity of 90.24% (AUC = 0.97). **Conclusion:** In conclusion, the ability of procalcitonin to effectively distinguish between culture-negative and culture-positive sepsis and non-infectious maladies establishes its potential as a biomarker in the diagnostic process of bacterial sepsis.

Keywords: Procalcitonin, Correlation; Diagnostic tool, Sepsis, Cultures, Medical Facilities.

Introduction:

Sepsis is a life-threatening condition that arises when the body's response to an infection injures its tissues and organs. Sepsis is a major cause of morbidity and mortality worldwide, and early recognition and treatment are crucial for improving outcomes. Procalcitonin (PCT) is a hormone secreted by C cells in the thyroid gland in response to bacterial infection, and its levels have been shown to be elevated in sepsis patients. Despite the potential utility of PCT as a biomarker for sepsis, its diagnostic value remains controversial, and more research is needed to clarify its role in the management of sepsis. The rationale and novelty of this study is to investigate the diagnostic value of serum PCT in adult sepsis patients and to identify factors that may influence its levels. The research question is what is the diagnostic value of serum PCT in adult sepsis patients, and what factors may influence its levels? Hence, the aim of the present study is to determine the diagnostic value of serum PCT in adult sepsis patients and to identify factors that may influence its

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levels. We hypothesize that serum PCT levels will be elevated in sepsis patients compared to non-sepsis patients, and factors such as age, gender, and severity of illness may influence its levels.

Materials & methods:

From …….to ……., we conducted a prospective observational study on 150 consecutive adult patients who were hospitalized and treated at our institute with sepsis of bacterial etiology. The study population consisted of individuals who were admitted from various medical departments. To aid in the computation of the Sequential Organ Failure Assessment Score (SOFA) score, a range of parameters were documented. In addition, demographic variables, clinical information, and additional fundamental characteristics of eligible patients were recorded. Initially, enrolled patients were categorized as non-infectious controls (group I) or those suspected of having sepsis based on clinical assessment. During subsequent follow-up, patients were further classified into the following groups, contingent upon the availability of microbiological culture results: Group I. Patients with non-infectious internal medicine morbidity comprised the control group. Acute renal failure, hypertensive cardiomyopathy, acute cerebrovascular disease, epilepsy, Crohn's disease, and neoplastic disease were the admission diagnoses of these patients.

Negative culture results support the clinical suspicion of infection in Group II (culture-negative sepsis group).

Patients who presented with culture-positive sepsis and had a microbiologically documented source of infection comprised Group III. At the time of analysis, we further subdivided Group III into group III (a) for gram-positive sepsis and group III (b) for gram-negative sepsis.

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The 2016 consensus definitions (Sepsis-3) jointly published by the Society of Critical Care Medicine (SCCM) and European Society of Intensive Care Medicine (ESICM) reclassify sepsis as an infection that results in a SOFA score increase of two or more points [18–21]. Two independent clinicians, blinded to the diagnosis, were required to confirm patient inclusion or exclusion from the sepsis cohort. There was no observed inconsistency between the two operators. Excluded were patients who had undergone recent surgery or transplantation, had a history of malignancy, had suspected or confirmed non-bacterial infections, or were being treated with immunosuppressant agents. Additionally, patients who were lost to follow-up were excluded; those who were followed up with until discharge or the occurrence of adverse events were continued.

The process involves identifying the infection and establishing diagnostic criteria: The International Sepsis Forum's consensus conference established the clinical diagnosis of infections by integrating imaging studies, laboratory results, clinical manifestations, and microbiological evidence [22]. The managing physicians identified the site of infection based on bacterial culture results and clinical impressions. In addition to intestinal abscesses, biliary tract infections, peritonitis, and enteritis, Brian also experienced intestinal infections. The identification of a urinary tract infection was based on suggestive signs and symptoms such as fever, dysuria, pyuria, frequency, a positive Gram stain, and suggested imaging. Urine cultures were considered positive if they contained more than 105 colony-forming units (cfu) per milliliter of microorganisms (or 103 cfu/mL in catheterized patients). Lung infections, such as pneumonia, necessitated a strong clinical suspicion in addition to the presence of lobar infiltrates on the chest X-ray. Patients who recovered etiologic agents from blood or pleural fluid were considered to have a positive culture result. On the contrary, we deemed semi-quantitative cultures of respiratory secretions favorable when they produced substantial to moderate proliferations of bacterial agents, as evidenced by the presence of only a few epithelial cells (10 per high power field) upon Gram stain examination. The

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identification of a primary bloodstream infection occurred when the isolated bacterial agent from the blood culture showed no association with a prior site-specific infection [23]. The Surviving Sepsis campaign established the standard institutional protocol, which the treating clinicians followed to supervise all sepsis patients [24].

Collection of specimens, laboratory analysis, and PCT measurement: Blood samples were collected simultaneously from each patient prior to initiating antibiotic therapy for the purposes of culture and PCT measurement. These samples were then transmitted to the microbiology laboratory for additional processing. In contrast, blood was only drawn from the control group upon admission. Per patient, two sets of anaerobic and aerobic broth flasks (BACTEC plus) were utilized for each blood culture. Five days were spent incubating blood culture containers in the BACTEC automated blood culture system (BD Biosciences, Maryland, USA). Subcultures were generated through the treatment of positive broths. Furthermore, microbiological analyses were conducted in accordance with the anatomical site of the infection. The specimens that were cultured in accordance with the request of the treating clinician comprised pleural or ascitic fluids, sputum/endotracheal aspirates, urine, pus, and various biological materials or fluids (such as those obtained from abdominal abscesses, peritonitis, and biliary infections). Standard laboratory procedures were utilized in order to identify the organisms present in the positive cultures.

Statistical analysis:

Qualitative variables were analyzed using the Fisher exact test, while quantitative variables were analyzed using a one-way ANOVA. To evaluate the diagnostic efficacy of PCT, receiver operating characteristic (ROC) curves were generated, and the area under the curve (AUC) was calculated. We then computed the Youden index, positive likelihood ratio, negative likelihood ratio, and PPV. Statistical

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significance was presumed for all tests when a null hypothesis could be refuted with a P value less than 0.05. All three groups underwent Kaplan-Meier survival analysis in accordance with the date of death or discharge. Statistical analyses were conducted using the SPSS program.

Results:

The technique divided the patients in the study into three categories. Half of the subjects were in the control group, half in the culture-negative sepsis group, and half in the culture-positive sepsis group. Compared to the control group, the septic patients had a substantially older mean age. The mean PCT value varied significantly between the three groups, with group III showing the greatest variation (19%). Sepsis was the cause of death in 28% of cases (n = 42).

Most clinically suspected bacterial infections were found in the respiratory tract (41%), followed by the abdomen (34%). The most common sites of infection in patients with culture-positive sepsis were the circulation (47%), urinary tract (26%), and respiratory tract (20%). There were 89 Gram-negative (GNB) infections and 61 Gram-positive (GPB) infections out of 150 patients, for a total of 59%. Of the 42 positive cultures, 8 were polymicrobial and the other 42 were monomicrobial, making up 85% of the total. After Escherichia coli (n = 11, 22%) with a mean PCT value of 19.2 ng/ml and Acinetobacter baumannii (n = 9, 18%) with a mean PCT value of 15.1 ng/ml, Klebsiella pneumoniae was the most frequent pathogen in Gram-negative cultures (n = 18, 36%). Despite its low prevalence (just 2 cultures), Citrobacter freundii outperformed E. coli and Acinetobacter baumannii in terms of mean PCT value (26.2 ng/ml). We observed that Gram-negative bacterial pathogens had the highest mean PCT values when comparing them to Gram-positive, polymicrobial, and non-specific isolates.

We used a PCT threshold value of 1.04 ng/ml with an 88% sensitivity, 79% specificity, and 82.93% NPV to predict bacterial sepsis. An NPV of 94%,

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sensitivity of 97%, and specificity of 90% at 2.31 ng/ml indicated culture-positive sepsis. Group II and III PCT values are very similar, which explains why culture negative sepsis is more specific than culture positive sepsis. The cutoff level of 2.60 ng/ml may differentiate between culture-negative and culture-positive sepsis with a sensitivity of 92.44%, even at this low variance; however, it can also predict false positives. The specificity of this cutoff, then, might or might not aid in distinguishing between the two. The levels of PCT were considerably elevated in groups II and III in comparison to group I. PCT had the highest sensitivity of 78.26% and specificity of 88.40% at a concentration of 1.4 ng/ml in group II (area under curve: 0.87). Group III yielded the most optimal cut-off value of 2.31 ng/ml, which exhibited a sensitivity of 97.36% and specificity of 90.24% (AUC = 0.97).

Discussion:

In this investigation, we highlight important data about the efficacy of PCT as a sepsis biomarker. This study is the first of its kind to assess the diagnostic accuracy of PCT across a range of risk thresholds in a diverse group of patients admitted to various medical units; the model encompasses both gram-negative and gram-positive sepsis, as well as culture-negative and culture-positive sepsis. Surgical and medical intensive care units, among other highly specialized settings, typically conducted prior research with a carefully selected patient group.
One of the main takeaways from this research is the cutoff for diagnosing culture-negative versus culture-positive sepsis. We also demonstrated a correlation between PCT levels and mortality across all three categories. Previous studies [6,7] have linked PCT levels with culture outcomes, as far as we are aware. Differentiating between the three groups, we found that PCT levels ranged from very low in the culture-negative sepsis group to very high in the culture-positive case. Statistical analysis has shown cutoff values for PCT, suggesting its potential use as a biomarker for sepsis diagnosis. We used a PCT threshold value of 1.04

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ng/ml with an 88% sensitivity, 79% specificity, and 82.93% NPV to predict bacterial sepsis.

An NPV of 94%, sensitivity of 97%, and specificity of 90% at 2.31 ng/ml indicated culture-positive sepsis. We determined these findings to be statistically significant, in line with previous research [6-10]. As a result of Group II and III PCT values are very similar, which explains why culture negative sepsis is more specific than culture positive sepsis. The cutoff level of 2.60 ng/ml may differentiate between culture-negative and culture-positive sepsis with a sensitivity of 92.44%, even at this low variance; however, it can also predict false positives. The specificity of this cutoff, then, might or might not aid in distinguishing between the two.

The cultures came back negative in 50 out of 50 septic individuals. This result is in line with previous research that has shown that 28–38% of patients with culture-negative sepsis have the condition [7,8,11]. For cases where culture results were negative, polymerase chain reaction (PCR) testing would have been an excellent option. Nevertheless, it is debatable if this method would have been useful in identifying and confirming a genuine bacterial infection.

Additional research is necessary to provide a comprehensive understanding of this occurrence. Despite the use of improved diagnostic algorithms for sepsis identification, the mortality rate is still significant. The reported death rates in several clinical trials range from 22% to 50% [9,10]. In our analysis, 40 deaths, or 28 %, were caused by sepsis. We observed a decreased hospital mortality rate (24 % vs. 30 %) for culture negative sepsis compared to culture positive sepsis. Previous research has corroborated this finding [12,13]. Despite this, some research has failed to find a link between culture and death rates [14,15]. Right now, we don't know what's causing these different results. It is highly unlikely that these latter investigations set out to do just that. Furthermore, distinguishing between Gram-positive and Gram-negative bacterial infections was achieved with a 76%

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sensitivity and 47% specificity at a PCT threshold of 3.12 ng/ml. A study conducted [16] examined clinical specimens and discovered that a PCT cut-off of 10.8 ng/ml could distinguish between Gram-negative and Gram-positive sepsis with an accuracy of 82.5%. Variations in population, research design, sample size, and randomization can explain why there is a wide range of cut-off values and specificities when comparing studies. Here, GNB was found to induce a higher PCT level elevation than GPB. Around one-third of people with Gram-negative

The etiological agents of Gram-negative sepsis were K. pneumoniae and E. coli, while MRSA was found in patients with Gram-positive sepsis, which is in line with a study [17]. Infections caused by non-fermenters, such as Acinetobacter baumannii, had an average PCT value of 15.1 ng/ml, whereas K. pneumoniae had the highest mean PCT value among the GNB, at 27 ng/ml. This confirms what a prior study found: that PCT levels are more elevated when Enterobacteriaceae are involved than when non-fermentative GNB is involved [18].
The significantly higher concentrations of PCT in the non-survivors compared to the survivors demonstrated its excellent capacity to predict septic patient mortality. Consistent with other research, this study adds weight to its findings [6,16-18]. Evidence from prior research demonstrating the biomarker's utility in prognostic stratification of critically ill patients with sepsis lends credence to this finding [1,3,4]. In fact, there is some evidence that certain subject groups are more likely to die if they have a culture-positive outlook [2,5,6]. Furthermore, it should be highlighted that clinicians' ability to distinguish between culture-negative and culture-positive sepsis only based on PCT levels is debatable. On the other hand, it could be useful for directing them in making early clinical decisions and other pertinent clinical data.

Conclusion:

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Serum PCT levels were found to be significantly higher in sepsis patients than controls, indicating its potential as a diagnostic biomarker. Incorporating PCT into diagnostic algorithms can aid in sepsis identification and clinical decision-making. Future studies should explore the utility of serum procalcitonin in various patient populations and settings and investigate its potential as a predictor of sepsis outcomes and treatment response.

Conflict of interest:

None.

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