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Prognostic Significance of Procalcitonin and C-reactive Protein: Usefulness as Biomarker of Sepsis in ICU Patient

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ABSTRACT
Early diagnosis and appropriate therapy of sepsis is a daily challenge in intensive care units (ICUs) despite the advances in critical care medicine. Procalcitonin (PCT); an innovative laboratory marker, has been recently proven valuable worldwide in this regard. This study was undertaken to evaluate the utility of PCT in a resource constrained country like ours when compared to the traditional inflammatory markers like C - reactive protein (CRP) to introduce PCT as a routine biochemical tool in regional hospitals. It was a comparative study. This study was conducted one year. At the department of General Medicine at Murshidabad Medical College.73 patients were included in this study. The clinical presentation of 75% cases revealed a range of systemic inflammatory responses (SIRS). The diagnostic accuracy of PCT was higher (75%) with greater specificity (72%), sensitivity (76%), positive and negative predictive values (89% and 50%), positive likelihood ratio (2.75) as well as the smaller negative likelihood ratio (0.33). Both serum PCT and CRP values in cases with sepsis, severe sepsis and septic shock were significantly higher from that of the cases with SIRS and no SIRS ($p<0.01$). PCT is reported to be more accurate than CRP in identifying and assessing the severity of sepsis, despite the fact that both markers cannot differentiate between infectious and noninfectious clinical syndromes.

INTRODUCTION

Despite significant investments in critical care resources, severe sepsis fatality rates range from 28% to 50% or more. Furthermore, cases of severe sepsis are predicted to rise in the future for various reasons, including increased knowledge and sensitivity for the diagnosis; increasing numbers of immunocompromised individuals; broader usage of invasive procedures; more resistant germs; and an aging population[1]. The ACCP/SCCM Consensus Conference developed definitions for the terms "SIRS", "sepsis", "severe sepsis" and "septic shock" in 1992, which are now commonly used. Systemic inflammatory response syndrome (SIRS) refers to a wide range of complex results caused by systemic activation of the innate immune response. The clinical parameters include two or more the following: Symptoms include fever (>38°C) or hypothermia (<36°C), elevated heart rate (>90 beats/min), tachypnea (>20 breaths/min), hyperventilation (PaCO2 < 32mmHg) and abnormal white blood cell count (>12,000 cells/mm^3 or <4000 cells/mm^3) or presence of more than 10% immature neutrophils. Sepsis is defined as SIRS caused by infection, whether bacterial, viral, fungal, or parasitic in nature. Severe sepsis causes at least one acute organ failure, hypoperfusion, or hypotension[2,3].

Traditional indicators of systemic inflammation, such as CRP, erythrocyte sedimentation rate (ESR) and white blood cell count (WBC), have also shown limited value in such individuals due to their low sensitivity and specificity for bacterial infection. Furthermore, microbiological cultures, the traditional gold standard diagnostic approach for sepsis, are time-consuming, do not represent the host's reaction to systemic inflammation or the start of organ dysfunction and can be misleading with false positive or false negative results. These inadequacies in culture and existing blood tests have prompted researchers to seek out more sensitive and specific markers. In recent years, PCT has received great attention as a particular and early marker for systemic inflammation, infection and sepsis, both in children and adults[3,4].

Procalcitonin is a prohormone of calcitonin that is released by several types of cells in many organs in response to proinflammatory stimulation, notably bacterial stimulation; calcitonin is exclusively generated in the C cells of the thyroid gland in response to hormonal stimulation[5]. Depending on the clinical context, a PCT concentration more than 0.1 ng/mL indicates a clinically significant bacterial infection necessitating antibiotic treatment[6]. A PCT concentration of more than 0.5 ng/mL indicates that a patient is at risk of developing severe sepsis or septic shock[7,8].

Hyperprocalcitoninemia develops within 2-4 hours of systemic inflammation or infection, typically reaches peak concentrations in 8-24 hours and lasts as long as the inflammatory process continues. PCT has a half-life of around 24 hours, therefore concentrations return to normal rather rapidly when the patient recovers. In comparison, CRP takes 12-24 hours to rise and can stay elevated for up to 3-7 days. Because PCT concentrations rise quicker and return to normal faster than CRP, they have the potential to aid in illness diagnosis and monitoring[9]. Furthermore, a number of studies have found that the systematic use of PCT for sepsis diagnosis and monitoring may have a beneficial influence on antibiotic (AB) treatment reduction, allowing for a shorter stay in the ICU and lower expenditures per case. This will also help to battle the spread of antibiotic-resistant microorganisms, which is mostly caused by the overuse of antibiotics[10]. Additionally, researchers found a ≥30% decrease in PCT levels between days 2 and 3 to be an independent predictor of survival in ICU patients[11].

Thus, procalcitonin has been identified as a promising biomarker that may add value to the clinical decision-making process by assisting in diagnosis, prognosis assessment and treatment selection and monitoring. This biomarker is currently widely used in Europe and it has just been approved by the FDA in the United States for the diagnosis and monitoring of sepsis, as well as the evaluation of the systemic inflammatory response in clinical settings[12]. PCT is now commercially available in Bangladesh for the first time and it is being used as a biomarker at Apollo Hospital in Dhaka. So far as we know, this is the first PCT study on the Bangladeshi population. This study was conducted to identify and analyze the amount of PCT in comparison to other traditional methods such as CRP, with the goal of establishing PCT as a standard tool for sepsis therapy in our nation.

MATERIALS AND METHODS

Study Design: This study was a comparative study designed to assess the prognostic significance of Procalcitonin (PCT) and C - reactive protein (CRP) levels in patients diagnosed.

Study Population: The study population for the research titled "Prognostic Significance of Procalcitonin and C-Reactive Protein: Usefulness as Biomarkers of Sepsis in ICU Patients" consists of adult patients aged 18 years or older who are admitted to the Intensive Care Unit (ICU) with a diagnosis of sepsis, suspected sepsis, or septic shock. These patients must have had Procalcitonin (PCT) and C - reactive protein (CRP) levels measured as part of their diagnostic or therapeutic protocol.

Study Duration: 1 year.

Study Place: Murshidabad Medical College and Hospital, West Bengal 742101.

Inclusion Criteria:

- Adult patients (≥18 years old) admitted to the ICU with suspected or confirmed sepsis.
- Elevated Procalcitonin (PCT) and/or C - reactive protein (CRP) levels on admission or during ICU stay.
- Patients with a clinically confirmed diagnosis of sepsis, following international sepsis guidelines (e.g., Sepsis-3 definition).
- Patients with complete medical records and access to biomarker data (PCT and CRP levels).
- ICU patients with documented organ dysfunction related to infection (e.g., respiratory, renal, or cardiovascular failure).
- Patients willing or able to provide informed consent (if applicable).
- ICU stay of at least 48 hours, allowing enough time for observation of biomarker trends.

Exclusion Criteria:

- Patients under 18 years of age.
- Patients with non-infectious causes of systemic inflammation (e.g., trauma, post-surgery, autoimmune diseases) not related to sepsis.
- Patients with chronic inflammatory diseases (e.g., rheumatoid arthritis) that may interfere with PCT and CRP interpretation.
- ICU patients with a known malignancy or receiving immunosuppressive therapy, which may affect biomarker expression.
- Patients with end-stage renal or liver disease, as altered organ function may skew biomarker levels.
- Pregnant patients, due to altered immune and biomarker responses.
- Patients with insufficient biomarker data (missing PCT or CRP levels).
- Patients transferred from other ICUs with ongoing sepsis treatment.

Sample Size: 73

RESULTS

This study included a total of 73 cases; 46 (63%) males and 27 (37%) females. The mean age was 28.8±9.3 years. A total of 39 (53.4%) culture positive isolates were discovered from 73 clinical specimens. Blood (45.2%), urine (17.8%), wound swabs (10.9%), pus (5.4%), ulcer exudates (6.8%) and tracheal aspirates (4.1%) were the clinical specimens used for microbiology culture. Escherichia coli was the most prevalent isolate (35.8%). Mixed infection was discovered in 7 (9.5%), with Pseudomonas, Acinetobacter and other microbes being the most prevalent (Table 1).

Table 1: Group by Clinical Diagnosis

Group by Clinical Diagnosis	Number of Cases (%)	Mean±SD Serum PCT (ng/ml)	Mean±SD Serum CRP (mg/l)
No SIRS	18 (24.7)	0.8±1.90	20.2±20.03
SIRS	27 (37.0)	1.7±2.57	30.4±27.92
Sepsis	15 (20.5)	11.9±8.82	41.6±8.79
Severe Sepsis	7 (9.6)	26.2±9.99	48.0±9.72
Septic Shock	6 (8.2)	40.4±13.83	49.5±15.19

Table 2: Group by clinical diagnosis

Group by clinical diagnosis	P values for PCT	P values for CRP
No SIRS vs SIRS	0.703	0.937
Sepsis	0.002(1)	0.004 (1)
Severe sepsis	0.003(1)	0.000(+)
Shock	0.006(1)	0.001(1)
SIRS vs No SIRS	0.703	0.937
Sepsis	0.004(1)	0.005(1)
Severe sepsis	0.003(1)	0.000(1)
Shock	0.007(1)	0.002(1)
Sepsis vs Severe sepsis	0.05	0.4
Shock	0.020(*)	0.436
Severe sepsis vs Shock	0.325	0.997

Table 3: Validity Tests

Validity Tests	PCT (High to Any Possibilities of Sepsis %)	CRP (High to Any Possibilities of Sepsis %)
Sensitivity	76.36 (62.98-86.7)	85.45 (73.3-93.5)
Specificity	72.2 (46.52-90.31)	33.3 (13.34-59)
(+ve LR)	2.75 (1.29-5.87)	1.28 (0.91-1.81)
(-ve LR)	0.33 (0.19-0.57)	0.44 (0.17-1.09)
PPV	89.36 (76.9-96.45)	79.66 (67.1-89)
NPV	50 (29.93-70.07)	42.86 (17.6-71.1)
Accuracy	75.34	72.6

The average PCT level was 9.19±13.9 ng/ml (range: 0.03-60 ng/ml), whereas CRP was 31.4±19.6 mg/l (range: 0.11-63 mg/l). Culture-positive patients had average PCT and CRP levels of 10.9±14.6 ng/ml and 34.2±17.8 mg/l, while culture-negative patients had values of 7.1±12.8 ng/ml and 28.2±21.3 mg/l ($p>0.05$). According to the clinical presentation of the patients, only 18 (24.7%) had no symptoms of SIRS. The remaining individuals (75.3%) manifested with a variety of systemic inflammatory reactions (Table 2).

The study patients' mean serum PCT and CRP concentrations differed significantly across clinically diagnosed groups. In numerous comparison tests (Games-Howell test), serum PCT and CRP revealed substantial increases in mean values, as did the severity of clinical presentations in the study individuals. The mean PCT levels in cases with sepsis, severe sepsis and septic shock were considerably greater than those with SIRS and no SIRS ($P < 0.01$). CRP concentrations were similar among the groups described; however, the level of significance was statistically higher (0.001) for severe sepsis compared to SIRS and no SIRS. There was no significant difference in mean serum PCT and CRP values between cases with and without SIRS, or between the severe sepsis group and patients with sepsis and septic shock ($p>0.05$).

The patients with PCT level > 10 ng/ml revealed mortality rate of 16.6%; the remainder of the patients showed adequate evolution with a tendency of getting better. The average hospital stay was 8.2 days. As shown in Table 3, the sensitivity of CRP was the highest of all. However, PCT shows the highest level of accuracy (75.34%) with greater specificity, positive and

negative predictive values, positive likelihood ratio as well as the smaller negative likelihood ratio. Microbiological culture results reveal 53.42% accuracy with higher specificity (50%) than CRP (Table 3).

DISCUSSION

PCT was first described as a marker of the extent and course of systemic inflammatory response to bacterial and fungal infections in 1993 by Assicot[13]. Since then, Procalcitonin (PCT) has been intensively investigated as a marker for systemic inflammation, infection and sepsis in adults and children in ICU settings, both alone and in conjunction with other markers such as CRP. The majority of investigations have used an immunoluminometric assay known as the LUMI test, which is made by Brahms. In recent years, immune fluorescent tests have been given prominence.

In this study, Cultures were positive in 53.4% of microbiological culture specimens (n = 39), with E. coli the most common (35.8%), followed by Klebsiella, Pseudomonas and Acinetobacter. This was consistent with the reports of Karlsson *et al*.[14] though the rate of positive culture was less than ours. Karlsson *et al*.[14] There were also reports of significantly greater PCT levels in positive culture cases than in negative ones. In our study, both PCT and CRP levels were greater in instances with positive cultures, however this was not statistically significant ($p>0.05$). Another Korean study found that positive cultures were associated with higher CRP levels ($p<0.001$) compared to PCT levels ($p<0.05$)[15].

The present investigation examined plasma levels of PCT and CRP in individuals with and without infection at various stages of SIRS. Patients with moderate to severe sepsis had significantly greater PCT concentrations than those with no/local infections ($p<0.01$).

Both serum PCT and CRP exhibited significant increases in mean values, as did the severity of clinical manifestations in the research individuals. When comparing the severity of systemic inflammation and sepsis, mean PCT and CRP values were significantly greater in sepsis, severe sepsis and septic shock cases than in SIRS and no SIRS. Although the mortality rate was modest (16.6%), it was limited to individuals with a PCT level of more than 10 ng/ml[16].

Regarding the diagnostic performance of PCT, many worldwide literatures determined PCT to be a valuable marker in the identification of a septic process with a sensitivity of 78% and a specificity of 94% when comparing these values to CRP[17]. These research used a more exact methodology to get the intended results and the sample size was significantly larger, resulting in a higher statistical significance. In this investigation, PCT demonstrated the best level of accuracy (75.34%) with larger specificity (72.2%), positive and negative predictive values, positive likelihood ratio and a smaller negative likelihood ratio. However, CRP had a higher sensitivity in the diagnosis of sepsis (85.45%) than PCT (76.36%). By convention, PLR > 10.0 and NLR < 0.1 indicate significant changes in past disease risk. Procalcitonin exhibited a greater PLR and lower NLR than CRP and complement proteins.

Few investigations have found that PCT had inferior diagnostic performance than CRP in discriminating between sepsis and SIRS.In contrast, the majority of research have shown that procalcitonin was a better marker to evaluate the severity, prognosis, or future course of the sepsis[18]. This study was similar to the others, with a few minor restrictions. First, serial PCT monitoring every day was avoided, which may have improved its performance as a sepsis follow-up tool. Second, antimicrobial medication may have an effect on PCT values that cannot be explained by our research methodology.

CONCLUSIONS

Rapid detection of infection has a significant impact on the clinical course, management and outcome of critically ill ICU patients. In this investigation, both PCT and CRP demonstrated limited diagnostic usefulness in critical patients in terms of detecting viral sources. However, procalcitonin outperforms C-reactive protein as a measure of clinical severity. Procalcitonin should be incorporated in sepsis diagnostic criteria, as well as clinical practice in our country's intensive care units.

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