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Role of Initial Procalcitonin in Predicting Mortality in Sepsis

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Abstract

Context: There exists a deficiency in literature regarding the importance of procalcitonin in predicting mortality in sepsis patients. *Aim:* To determine the role of initial procalcitonin in predicting 7-day mortality in sepsis patients. *Materials and methods:* A prospective observational study was conducted on 200 sepsis patients admitted to the Emergency Department of a Medical College Hospital at Kochi. Blood culture samples and serum procalcitonin samples were withdrawn immediately and sent to lab. Mortality data of those patients were charted at the end of 7 days. Procalcitonin values were compared in both survivors and non survivors using paired Student *t*-test. $p < 0.05$ was accepted as statistically significant. *Results:* Out of the 200 patients, 131 were males and 69 were females. 17% expired and 83% survived at the end of 7 days of hospital stay. Mean procalcitonin value in survivors and non survivors were 16.41 ng/ml and 23.09 ng/ml respectively, which showed statistical significance [*p*-value = 0.026]. *Conclusion:* Initial procalcitonin plays an important role in predicting 7-day mortality in sepsis patients.

Keywords: Sepsis; Procalcitonin; Mortality.

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Introduction

Background/Rationale

Currently, sepsis and septic shock with subsequent multiorgan failure are the leading causes of death in adult intensive care units (ICUs). Epidemiological studies shows increased incidence of sepsis for last 20 years even after improvement in sepsis therapy.[1] Early identification of patients with sepsis helps to initiate appropriate therapeutic intervention and reduces sepsis related mortality and morbidity.

PCT is a recently re-discovered biomarker that is helpful for early detection of sepsis as well as to monitor the antimicrobial treatment regimen. PCT is located on the CALC-1 gene on chromosome 11. Bacterial lipopolysaccharides and sepsis related cytokines causes increased expression of CALC-1 gene and increased production of PCT. This indicates that PCT level is useful for the diagnosis of systemic bacterial infections.[2] PCT level reflects the severity of the disease with higher levels associated with more severe disease and declining levels with resolution of illness. Normal reference value is < or = 0.15 ng/mL. PCT level between 0.15 and 2.0 ng/mL do not exclude an infection, because localized infections (without systemic signs) may be associated with such low levels. Levels > 2.0 ng/mL are highly suggestive of systemic bacterial infection/sepsis or severe localized bacterial infection.

Objectives

The primary objective of the study is to determine the role of initial procalcitonin in predicting 7-day mortality in sepsis patients with and without blood positivity.

Materials and Methods

Study design: Prospective observational study

***Setting*:** Study conducted in Emergency Medicine Department in A tertiary care Medical College Hospital, Kochi from June 2018 to May 2019 with annual patient load around 50000.

Participants: The study was conducted on 200 patients [age group between 18 and 60 yrs.] with suspected sepsis [patients with q-SOFA criteria more than or equal to 2]. Those patients with autoimmune infection, chronic kidney disease and malignancy were excluded from our study.

Variables: Qualitative variables: 7-day mortality denoted as survivors and nonsurvivors, Quantitative variables: Serum procalcitonin levels.

Data Sources/Measurements

Blood culture sample as well as blood samples for procalcitonin drawn simultaneously and sent to lab. Procalcitonin was measured using ROCHE COBAS 8000 using electrochemiluminence technique. Mortality at the end of 7 days were recorded. Initial procalcitonin value in both survivors and nonsurvivors were compared and statistically analyzed.

Bias: We excluded patients who died for reasons other than sepsis to reduce bias while analysis.

Study size: Based on previous study by Jain S et al. minimum sample size was determined as 200 with a power of 80% and 95% confidence interval.

Statistical analysis: Statistical analysis was performed using IBM SPSS version 20.0 software. Categorical variables were expressed using frequency and percentage. Numerical variables were presented using mean and standard deviation. Chi-square test was used to study the statistical significance of the association of procalcitonin between survivors and nonsurvivors groups. A *p*-value of <0.05 was considered to be statistically significant.

Results

Participants: Study conducted on total of 200 patients with q-SOFA more than or equal to 2.

Descriptive data: Out of the 200 patients, 65.5% (131) were males and 34.5% (69) were females and 14% belongs to age between 18 and 40 years of age and remaining 86% belongs to age group between 41 and 60 years of age. The minimum age was 19. and maximum age was 60. Out of 200 patients 17% (34) expired and remaining 83% (166) survived at end of 7 days of hospital stay.

Outcome data: Mean procalcitonin value in survivors and non survivors were 16.41 ng/ml and 23.09 ng/ml respectively, which showed statistical significance [*p*-value = 0.026] (Table 1).

Table 1: Mean procalcitonin value in survivors and non survivors

Groups	n	Mean procalcitonin value	Standard deviation	*p*-value
Survivors	166 (83%)	16.41	28.37	0.026
nonsurvivors	34 (17%)	23.09	30.52	

Discussion

Majority of patients (86%) were in the 41–60 age group.. There was a male predominance (65.5%) in the study group. The elderly peoples are more prone to sepsis due to underlying comorbidities, reduced immunity, repeated and prolonged hospitalization and aging. A few studies conducted in specific patient population shown that sepsis and septic shock and mortality are common in elderly patients as compared to their younger population.[3] Female gender has been demonstrated to be protective under sepsis conditions because of protective effects of female sex hormones. Male sex hormones-androgens have been shown to be suppressive effect on cell-mediated immune responses.

Mean procalcitonin value in survivors and non survivors were 16.41 ng/ml and 23.09 ng/ml respectively, which showed statistical significance [*p* value = 0.026]. Our findings suggest that high

PCT values associated with high mortality rate when compared to patients with lower values. According to Jensen et al. high PCT levels is an independent predictor of mortality.[4] On the other hand, Ruiz-Alvarez et al. observed that PCT did not predict mortality whereas CRP did.[5] Pettila et al. find that there was statistically significant difference in the PCT values measured on first and second days in patients who survived than patients who did not survive.[6] According to Krüger S et al. PCT was shown to be a biomarker of poor outcome in community acquired pneumonia.[7,8] Serum PCT levels could predict death and septic shock in ventilator-associated pneumonia as per Hillas et al. studies.[9] Garnacho-Montero et al. observed that elevated PCT strongly associated with mortality in septic patients supports our study.[10]

The high PCT levels were associated with increased inotropic drug usage and mechanical ventilation in adults, and PCT was considered as an important prognostic marker in intensive care unit.[11] Bloos et al. conducted a multicenter adult study observed that PCT was associated with severity of pneumonia and MV support.[12] In a prospective international multicenter study by Rau et al. conducted in 82 surgical patients with secondary peritonitis, procalcitonin level early in the course of illness predicted the presence of septic multiorgan failure and persistent sepsis, but was poorly correlated with death. Rau et al. conducted study in 54 septic patients from a medical ICU in New Delhi, India, find out a procalcitonin level ≥ 7 ng/ml at admission predicted 28 days mortality with a hazard ratio of 2.6.[13] A systemic review and meta-analysis study by Jain et al. showed that PCT levels were significantly different between surviving and non-surviving sepsis patients.[14]

Our study has some limitations. Few patients were managed in local hospital and subsequently brought to our hospital hence the time of the first procalcitonin estimation is not necessarily the 1st day of sepsis. In our study, we evaluated prognostic power of procalcitonin in predicting mortality. We found that initial serum PCT levels were high in nonsurvivors as compared to survivors.

Therefore we conclude that initial serum procalcitonin value plays an important role in predicting 7-day mortality in sepsis patients.

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Research Ouality and Ethics Statement

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting and reproducibility guidelines set forth by the Equator Network. The authors also attest that this clinical investigation was determined to require the institutional review board/ethics committee review, and the corresponding protocol/ approval number is IRB-AIMS-2019-313 We also certify that we have not plagiarized the contents in the submission and have done a plagiarism check.

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