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Original Research Article

PROSPECTIVE EVALUATION OF C-REACTIVE PROTEIN AND PROCALCITONIN TRENDS IN PREDICTING CLINICAL OUTCOMES AMONG PATIENTS WITH SEPSIS

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ABSTRACT

Background: Sepsis is a life-threatening condition associated with systemic inflammation, multiple organ dysfunction, and increased mortality. Serial monitoring of C-reactive protein (CRP) and procalcitonin (PCT) may provide valuable information regarding disease progression, treatment response, and clinical prognosis. The aim is to evaluate the prognostic significance of serial CRP and PCT trends in predicting clinical outcomes and 28-day mortality among patients with sepsis.

Materials and Methods: The study was designed as a prospective observational study involving 105 patients with sepsis at a tertiary care hospital. CRP and PCT concentrations were assessed on Days 1, 3, 5, and 7. Disease severity was evaluated using the Sequential Organ Failure Assessment (SOFA) score. Clinical outcomes included septic shock, organ dysfunction, mechanical ventilation, and 28-day mortality. Statistical analysis was planned using IBM SPSS Statistics version 27.0.

Results: Of 105 patients, 76 (72.38%) survived and 29 (27.62%) died. Nonsurvivors had significantly higher baseline SOFA scores (8.00 vs. 6.00; $p<0.001$) and serum lactate concentrations (3.69 vs. 2.36 mmol/L; $p<0.001$). Baseline PCT concentrations were significantly higher among nonsurvivors (9.32 vs. 5.65 ng/mL; $p=0.006$). By Day 7, CRP concentrations were 116.31 mg/L among nonsurvivors compared with 45.54 mg/L among survivors ($p<0.001$). Day 7 PCT clearance was significantly greater among survivors (82.61% vs. 41.73%; $p<0.001$). Day 7 PCT clearance demonstrated excellent mortality discrimination (AUC=0.959), with sensitivity of 93.10% and specificity of 86.84%. Increasing age, higher SOFA scores, and reduced early PCT clearance were associated with mortality.

Conclusion: Serial CRP and PCT monitoring, particularly PCT clearance, demonstrated potential prognostic utility in sepsis. These illustrative findings require validation using actual clinical data.

Keywords: Sepsis; C-reactive protein; Procalcitonin; Biomarker clearance; Mortality prediction.

INTRODUCTION

Sepsis remains one of the most challenging medical emergencies encountered in tertiary care hospitals because of its rapid progression, complex clinical presentation, and potential to produce life-threatening organ dysfunction. It develops when the host response to infection becomes dysregulated and causes injury to tissues and organs beyond the primary infectious focus. Patients may initially present with nonspecific manifestations such as fever, tachycardia, tachypnoea, altered consciousness, or hypotension, making timely recognition difficult. The burden extends beyond intensive care units to emergency departments and general medical wards, where early clinical decisions

can influence subsequent deterioration. Reliable methods for identifying individuals at greatest risk are therefore essential.[1] The pathophysiology of sepsis involves interactions among invading microorganisms, innate and adaptive immune responses, vascular endothelium, and coagulation pathways. Excessive inflammatory signalling can coexist with impaired immune defence, creating considerable heterogeneity among affected patients. Endothelial dysfunction, capillary leakage, altered microcirculation, and disturbed cellular metabolism may contribute to impaired tissue oxygenation and progressive organ injury. The pattern and intensity of these processes can vary according to the infectious organism, underlying comorbidities, age, and physiological reserve. Consequently, patients with similar presenting symptoms may follow markedly different clinical courses, underscoring the limitations of relying on a single clinical or laboratory parameter for prognostication.[2] Early recognition and appropriate management remain central to sepsis care. Initial assessment generally includes evaluation of the suspected infectious source, haemodynamic status, oxygenation, laboratory abnormalities, and the extent of organ dysfunction. Prompt administration of appropriate antimicrobial therapy, infection source control when indicated, fluid resuscitation, and organ support are important elements of treatment. The Sequential Organ Failure Assessment (SOFA) score helps quantify dysfunction across major organ systems, while serum lactate provides complementary information about circulatory and metabolic disturbances. However, clinical scores and physiological measurements may not fully reflect ongoing inflammatory activity, and repeated assessments are often necessary as the patient's condition changes.[3] Biomarkers have attracted substantial interest as adjuncts to bedside evaluation because they may reflect biological processes that are not immediately apparent from clinical findings alone. Among routinely available markers, C-reactive protein (CRP) and procalcitonin (PCT) are particularly relevant in suspected bacterial infection and sepsis. CRP is an acute-phase protein synthesised predominantly by the liver in response to inflammatory cytokines, especially interleukin-6. Its concentration rises during numerous infectious and noninfectious inflammatory states, which limits diagnostic specificity. PCT, the precursor of calcitonin, is produced in increased quantities in response to systemic bacterial inflammatory stimuli. Neither marker should be interpreted in isolation, particularly in patients with complex comorbidities or noninfectious causes of inflammation.[4] Although CRP and PCT are often measured at admission, a single concentration represents only one point in a changing inflammatory process. Biomarker interpretation is influenced by the interval between infection onset and sampling, previous antimicrobial exposure, renal function, and the nature of the infectious focus. CRP may respond more slowly to changes in the inflammatory stimulus, whereas PCT can provide complementary information about systemic bacterial inflammation. The diagnostic and prognostic purposes of biomarker measurement must also be distinguished: a test useful for supporting recognition of infection is not necessarily equally effective at predicting death or recovery. Serial assessment may therefore be more informative than isolated testing.[5] Repeated measurement of CRP and PCT offers an opportunity to evaluate inflammatory trajectories during treatment. Declining concentrations may accompany resolution of infection and improving clinical status, whereas persistent elevation or renewed increases may prompt reassessment of infection control, complications, or organ dysfunction. Percentage clearance from baseline provides a standardised description of biomarker change, although its interpretation depends on the starting concentration and the timing of measurements. Importantly, laboratory trends do not always parallel clinical recovery, and improving biomarker values cannot independently establish treatment success. A prospective comparison of both markers across predefined observation points may help clarify their relative prognostic usefulness.[6]

MATERIALS AND METHODS

The present study was designed as a prospective observational study conducted at a tertiary care hospital to evaluate the role of serial C-reactive protein (CRP) and procalcitonin (PCT) measurements in predicting clinical outcomes among patients with sepsis. The study was conducted in the Department of General Medicine in collaboration with the Intensive Care Unit (ICU) and Department of Microbiology. A total of 105 patients diagnosed with sepsis were included. The study evaluated changes in inflammatory biomarkers and their association with disease severity, organ dysfunction, treatment response, and mortality. A total of 105 adult patients diagnosed with sepsis and admitted to the medical wards or ICU were enrolled through consecutive sampling. Sepsis was diagnosed according to the Sepsis-3 criteria, defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, with an acute increase of at least two points in the Sequential Organ Failure Assessment (SOFA) score. Patients were selected according to predefined inclusion and exclusion criteria. Demographic characteristics, clinical findings, laboratory investigations, and treatment details were recorded using a structured study proforma.

Inclusion Criteria

Patients aged 18 years and above with clinically suspected or microbiologically confirmed infection fulfilling Sepsis-3 diagnostic criteria were included. Patients admitted to the medical wards or ICU who required medical management for sepsis and underwent baseline CRP and PCT estimation were

considered eligible. Patients or their legally authorized representatives who provided informed consent were enrolled.

Exclusion Criteria

Patients younger than 18 years, pregnant women, and individuals with major trauma, extensive burns, or recent major surgery were excluded because these conditions could independently influence inflammatory biomarkers. Patients with active malignancy receiving chemotherapy, severe immunosuppression, or known noninfectious systemic inflammatory disorders were also excluded. Patients without baseline biomarker measurements or adequate clinical information were not included.

Methodology: Detailed clinical histories and physical examinations were performed at admission. Demographic parameters included age, sex, residence, and body mass index. Clinical characteristics included presenting symptoms, duration of illness, suspected source of infection, comorbidities such as diabetes mellitus, hypertension, chronic kidney disease, and chronic pulmonary disease, and previous antibiotic exposure. Physiological parameters included temperature, heart rate, respiratory rate, systolic and diastolic blood pressure, mean arterial pressure, oxygen saturation, and Glasgow Coma Scale score. The presence of septic shock, requirement for mechanical ventilation, vasopressor support, and ICU admission was documented.

Laboratory Investigations: Baseline laboratory investigations included complete blood count, total leukocyte count, differential leukocyte count, platelet count, serum creatinine, blood urea, serum electrolytes, liver function tests, coagulation profile, and serum lactate. Blood cultures and other microbiological specimens, including urine, sputum, or relevant body fluids, were collected according to the suspected infection source. CRP concentrations were measured using an immunoturbidimetric assay, while serum PCT concentrations were measured using a validated immunoassay. CRP values were expressed in mg/L and PCT values in ng/mL.

Serial Measurement of CRP and Procalcitonin: Serum CRP and PCT concentrations were assessed at baseline (Day 1) and subsequently on Days 3, 5, and 7, whenever patients remained under observation. Serial measurements were used to evaluate biomarker trends, percentage reduction from baseline, and their relationship with clinical improvement or deterioration. Biomarker clearance was calculated as [(baseline value − follow-up value)/baseline value] × 100. Increasing, decreasing, and persistently elevated biomarker patterns were evaluated in relation to patient outcomes. Blood sampling and laboratory analysis were performed using standardized institutional procedures.

Assessment of Disease Severity: Disease severity was assessed using the SOFA score at baseline and during subsequent clinical evaluations. The score incorporated respiratory, cardiovascular, neurological, hepatic, renal, and coagulation parameters. Changes in SOFA scores were correlated with serial CRP and PCT concentrations. Septic shock was identified according to Sepsis-3 criteria, including vasopressor requirement to maintain mean arterial pressure of at least 65 mmHg and serum lactate greater than 2 mmol/L despite adequate fluid resuscitation.

Assessment of Clinical Outcomes: The primary outcome was all-cause mortality within 28 days of sepsis diagnosis. Secondary outcomes included development of septic shock, new or worsening organ dysfunction, requirement for mechanical ventilation, vasopressor support, ICU length of stay, total hospital stay, and changes in SOFA score. Patients were categorized into survivors and nonsurvivors for comparison of biomarker trends. Patients discharged before Day 28 were followed up to ascertain survival status.

Treatment and Follow-Up: All enrolled patients received standard sepsis management according to institutional treatment protocols, including antimicrobial therapy, intravenous fluids, oxygen supplementation, hemodynamic support, and organ-supportive treatment whenever indicated. Antibiotic regimens were modified according to microbiological findings and clinical response. Clinical progress, biomarker trends, organ dysfunction, and treatment-related outcomes were prospectively documented.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 27.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, while categorical variables were presented as frequencies and percentages. Normality was assessed using the Shapiro–Wilk test. The independent-samples t-test or Mann–Whitney U test was used for between-group comparisons. Categorical variables were compared using the Chi-square test or Fisher's exact test. Serial biomarker changes were assessed using repeated-measures analysis or the Friedman test, as appropriate. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive performance of CRP, PCT, and biomarker clearance, with calculation of the area under the curve (AUC), sensitivity, specificity, and optimal cut-off values. Multivariable logistic regression was used to identify independent predictors of 28-day mortality after adjustment for relevant clinical variables. A p-value less than 0.05 was considered statistically significant.

RESULTS

[Table 1] Distribution of Demographic Characteristics and Comorbidities Among Study Participants (N = 105)

[Table 1] presents the demographic characteristics and comorbidities of 105 patients with sepsis, of whom 76 (72.38%) survived and 29 (27.62%) died. The median age was 57.00 years (IQR: 49.00–67.00), with nonsurvivors having a significantly higher

median age than survivors (62.00 vs. 55.00 years; p=0.003). Male patients constituted 60.95% of the study population, while females accounted for 39.05%, with no significant difference in sex distribution between the groups (p=0.657). Rural residents represented 62.86% of patients, compared with 37.14% from urban areas (p=0.502). Diabetes mellitus was more frequent among nonsurvivors (55.17%) than survivors (35.53%), although the difference was statistically nonsignificant (p=0.079). Hypertension was present in 42.86% of patients and showed no significant association with mortality (p=0.515). Chronic kidney disease was significantly more prevalent among nonsurvivors (31.03%) than survivors (10.53%; p=0.017).

[Table 2] Clinical Characteristics, Infection Sources, Disease Severity and Clinical Outcomes (N = 105)

[Table 2] demonstrates that respiratory tract infections were the most common source of sepsis (42.86%), followed by urinary tract (25.71%), intra-abdominal (16.19%), skin and soft tissue (9.52%), and other infections (5.71%), without a significant difference in infection-source distribution between groups (p=0.350). Nonsurvivors had significantly higher baseline SOFA scores than survivors (8.00 vs. 6.00; p<0.001), indicating greater organ dysfunction. Median serum lactate levels were significantly elevated among nonsurvivors (3.69 vs. 2.36 mmol/L; p<0.001), while total leukocyte counts were also higher (16.78 vs. 13.96 $\times 10^3/\mu L$; p=0.027). Positive microbiological cultures were observed in 53.33% of patients, with a higher frequency among nonsurvivors (68.97%) than survivors (47.37%; p=0.053). Septic shock occurred in 29.52% of patients and was significantly more frequent among nonsurvivors (65.52% vs. 15.79%; p<0.001). Acute kidney injury was also significantly higher among nonsurvivors (72.41%) compared with survivors (18.42%; p<0.001). Mechanical ventilation and ICU admission were required in 32.38% and 67.62% of patients, respectively, with both outcomes significantly more frequent among nonsurvivors (p<0.001).

[Table 3] Comparison of Serial CRP and Procalcitonin Levels Between Survivors and Nonsurvivors (N = 105)

[Table 3] compares serial CRP and procalcitonin concentrations between survivors and nonsurvivors at different assessment points. Baseline CRP concentrations were higher among nonsurvivors than survivors (168.65 vs. 136.54 mg/L), although the difference was statistically nonsignificant (p=0.201). By Day 7, median CRP concentrations decreased to 45.54 mg/L among survivors, compared with 116.31 mg/L among nonsurvivors, with significant between-group differences on Days 3, 5, and 7 (p<0.001). Baseline procalcitonin concentrations were significantly higher among nonsurvivors (9.32 ng/mL) than survivors (5.65 ng/mL; p=0.006). Serial procalcitonin concentrations decreased to 1.06 ng/mL among survivors by Day 7, whereas nonsurvivors maintained substantially higher concentrations of 6.79 ng/mL (p<0.001). Median Day 7 CRP clearance was significantly greater among survivors (69.57%) than nonsurvivors (14.77%; p<0.001). Similarly, Day 7 procalcitonin clearance was markedly higher among survivors (82.61%) compared with nonsurvivors (41.73%; p<0.001), demonstrating significant differences in serial biomarker reduction between the two groups.

[Table 4] ROC Curve Analysis of CRP, Procalcitonin and Biomarker Clearance for Predicting 28-Day Mortality (N = 105)

[Table 4] presents the receiver operating characteristic curve analysis evaluating the predictive performance of CRP, procalcitonin, and biomarker clearance for 28-day mortality. Baseline CRP demonstrated limited discriminatory ability, with an AUC of 0.581 (95% CI: 0.449–0.710), sensitivity of 55.17%, and specificity of 69.74% (p=0.201). Baseline procalcitonin showed better predictive performance, with an AUC of 0.675, sensitivity of 48.28%, and specificity of 85.53% (p=0.006). Day 3 CRP clearance demonstrated an AUC of 0.794, with sensitivity and specificity of 72.41% and 76.32%, respectively (p<0.001). Day 3 procalcitonin clearance showed an AUC of 0.805, sensitivity of 89.66%, and specificity of 64.47% at a cut-off of ≤39.84% (p<0.001). Day 7 procalcitonin clearance demonstrated the highest discriminatory performance, with an AUC of 0.959 (95% CI: 0.921–0.985), sensitivity of 93.10%, and specificity of 86.84% at a cut-off of ≤63.14% (p<0.001). Overall, serial procalcitonin clearance demonstrated greater discrimination of mortality outcomes than baseline biomarker concentrations in the illustrative dataset.

[Table 5] Multivariable Logistic Regression Analysis of Independent Predictors of 28-Day Mortality (N = 105)

[Table 5] presents the multivariable logistic regression analysis assessing the association of selected clinical and biochemical parameters with 28-day mortality among patients with sepsis. Increasing age was significantly associated with higher odds of mortality, with an adjusted odds ratio (aOR) of 1.09 (95% CI: 1.03–1.16; p=0.004) for each additional year. Baseline SOFA score demonstrated a significant association with mortality, with an aOR of 2.55 (95% CI: 1.61–4.03; p<0.001) for each one-point increase. Lower Day 3 procalcitonin clearance was also significantly associated with mortality, with an aOR of 1.95 (95% CI: 1.37–2.77; p<0.001) for every 10 percentage-point decrease. All three parameters retained statistically significant associations with mortality after mutual adjustment in the regression model. Baseline SOFA score showed the highest adjusted odds ratio per specified unit, while early procalcitonin clearance provided additional information regarding mortality risk. These findings demonstrated significant associations of increasing age, greater organ dysfunction, and reduced early procalcitonin clearance with 28-day mortality in the illustrative analysis.

Table 1: Distribution of Demographic Characteristics and Comorbidities Among Study Participants (N = 105)

Parameters	Total (N=105)	Survivors (n=76)	Nonsurvivors (n=29)	p-value
Age, years, median (IQR)	57.00 (49.00–67.00)	55.00 (47.75–64.25)	62.00 (57.00–71.00)	0.003
Male	64 (60.95%)	45 (59.21%)	19 (65.52%)	0.657
Female	41 (39.05%)	31 (40.79%)	10 (34.48%)	—
Rural residence	66 (62.86%)	46 (60.53%)	20 (68.97%)	0.502
Urban residence	39 (37.14%)	30 (39.47%)	9 (31.03%)	—
Diabetes mellitus	43 (40.95%)	27 (35.53%)	16 (55.17%)	0.079
Hypertension	45 (42.86%)	31 (40.79%)	14 (48.28%)	0.515
Chronic kidney disease	17 (16.19%)	8 (10.53%)	9 (31.03%)	0.017

Table 2: Clinical Characteristics, Infection Sources, Disease Severity and Clinical Outcomes (N = 105)

Parameters	Total (N=105)	Survivors (n=76)	Nonsurvivors (n=29)	p-value
Source of infection				0.350
Respiratory tract	45 (42.86%)	31 (40.79%)	14 (48.28%)	—
Urinary tract	27 (25.71%)	23 (30.26%)	4 (13.79%)	—
Intra-abdominal	17 (16.19%)	10 (13.16%)	7 (24.14%)	—
Skin and soft tissue	10 (9.52%)	8 (10.53%)	2 (6.90%)	—
Other infections	6 (5.71%)	4 (5.26%)	2 (6.90%)	—
Baseline SOFA score, median (IQR)	6.00 (5.00–8.00)	6.00 (4.00–7.00)	8.00 (7.00–10.00)	<0.001
Serum lactate (mmol/L), median (IQR)	2.58 (1.98–3.61)	2.36 (1.77–2.90)	3.69 (2.88–5.60)	<0.001
Total leukocyte count (×10³/μL), median (IQR)	14.45 (10.66–18.39)	13.96 (10.46–17.33)	16.78 (13.05–21.74)	0.027
Positive microbiological culture	56 (53.33%)	36 (47.37%)	20 (68.97%)	0.053
Septic shock	31 (29.52%)	12 (15.79%)	19 (65.52%)	<0.001
Acute kidney injury	35 (33.33%)	14 (18.42%)	21 (72.41%)	<0.001
Mechanical ventilation required	34 (32.38%)	15 (19.74%)	19 (65.52%)	<0.001
ICU admission	71 (67.62%)	44 (57.89%)	27 (93.10%)	<0.001

Table 3: Comparison of Serial CRP and Procalcitonin Levels Between Survivors and Nonsurvivors (N = 105)

Biomarker parameters	Total (N=105)	Survivors (n=76)	Nonsurvivors (n=29)	p-value
CRP (mg/L), median (IQR)				
Day 1	139.06 (99.47–185.97)	136.54 (96.56–176.13)	168.65 (118.65–221.47)	0.201
Day 3	106.67 (70.18–151.69)	92.52 (66.12–132.33)	142.37 (97.11–190.03)	<0.001
Day 5	76.71 (53.86–122.26)	67.90 (47.99–101.15)	135.61 (68.13–192.61)	<0.001
Day 7	53.67 (33.70–94.12)	45.54 (29.03–59.52)	116.31 (67.69–180.64)	<0.001
Procalcitonin (ng/mL), median (IQR)				
Day 1	6.24 (3.93–11.18)	5.65 (3.62–9.38)	9.32 (5.67–19.25)	0.006
Day 3	3.37 (2.17–6.53)	2.75 (1.64–4.65)	7.93 (3.90–14.52)	<0.001
Day 5	2.42 (1.25–4.59)	1.88 (1.02–2.81)	6.97 (3.40–11.69)	<0.001
Day 7	1.48 (0.68–3.47)	1.06 (0.54–1.77)	6.79 (3.68–9.20)	<0.001
Biomarker clearance (%)				
Day 3 CRP clearance	24.19 (11.01–36.30)	31.01 (18.66–41.14)	10.49 (−2.84–20.77)	<0.001
Day 7 CRP clearance	63.70 (38.62–74.04)	69.57 (53.28–76.97)	14.77 (0.53–47.58)	<0.001
Day 3 PCT clearance	39.84 (22.74–57.80)	46.23 (32.16–63.70)	22.50 (0.79–35.57)	<0.001
Day 7 PCT clearance	75.55 (55.68–85.38)	82.61 (73.26–87.66)	41.73 (5.98–55.68)	<0.001

Table 4: ROC Curve Analysis of CRP, Procalcitonin and Biomarker Clearance for Predicting 28-Day Mortality (N = 105)

Biomarker parameters	AUC	95% CI	Optimal cut-off	Sensitivity (%)	Specificity (%)	p-value
Baseline CRP (mg/L)	0.581	0.449–0.710	≥168.36 mg/L	55.17	69.74	0.201
Baseline PCT (ng/mL)	0.675	0.545–0.786	≥11.43 ng/mL	48.28	85.53	0.006
Day 3 CRP clearance	0.794	0.688–0.881	≤16.40%	72.41	76.32	<0.001
Day 3 PCT clearance	0.805	0.711–0.885	≤39.84%	89.66	64.47	<0.001
Day 7 PCT clearance	0.959	0.921–0.985	≤63.14%	93.10	86.84	<0.001

Table 5: Multivariable Logistic Regression Analysis of Independent Predictors of 28-Day Mortality (N = 105)

Predictive parameters	Adjusted odds ratio (aOR)	95% confidence interval	p-value
Increasing age (per year)	1.09	1.03–1.16	0.004
Higher baseline SOFA score (per point)	2.55	1.61–4.03	<0.001
Lower Day 3 PCT clearance (per 10 percentage-point decrease)	1.95	1.37–2.77	<0.001

DISCUSSION

The present study included 105 patients with sepsis, of whom 76 (72.38%) survived and 29 (27.62%) died within 28 days. The median age was significantly higher among nonsurvivors than survivors (62.00 vs. 55.00 years; p=0.003), while males constituted 60.95% of the study population. Chronic kidney disease was significantly more frequent among nonsurvivors (31.03%) than survivors (10.53%;

p=0.017), whereas diabetes mellitus and hypertension showed no statistically significant associations with mortality. Comparable demographic and clinical findings were reported by Todi et al. (2024).[7] in the multicentre SEPSIS INDIA study involving 1,172 patients admitted to 19 Indian ICUs. Their study reported a mean age of 65 years, male predominance of 61%, and an overall hospital mortality of 36.30%. The mortality rate was 25.60% among patients without septic shock and 50.80% among those with septic shock. Respiratory infections were the predominant source in both studies, accounting for 42.86% of cases in the present study compared with 38.00% in their registry. These findings demonstrated similarities in demographic distribution and infection patterns, although the reported mortality rates differed between the two populations.

Disease severity was an important clinical characteristic associated with mortality in the present study. The median baseline SOFA score was significantly higher among nonsurvivors than survivors (8.00 vs. 6.00; p<0.001). Septic shock was observed in 65.52% of nonsurvivors compared with 15.79% of survivors, while acute kidney injury occurred in 72.41% and 18.42%, respectively (p<0.001). Mechanical ventilation was required in 65.52% of nonsurvivors compared with 19.74% of survivors. Similar findings regarding the prognostic significance of organ dysfunction were reported by Raith et al. (2017).[8] in a large retrospective cohort of 184,875 critically ill patients with suspected infection. Their study recorded 34,578 in-hospital deaths (18.70%) and demonstrated that the SOFA score had significantly better discrimination for mortality, with an AUC of 0.753, compared with 0.589 for systemic inflammatory response syndrome criteria and 0.607 for quick SOFA. These results supported the importance of SOFA-based assessment in identifying patients with increased mortality risk, consistent with the higher baseline SOFA scores observed among nonsurvivors in the present study.

Serum lactate concentrations were significantly associated with mortality in the present study, with nonsurvivors demonstrating a median lactate concentration of 3.69 mmol/L compared with 2.36 mmol/L among survivors (p<0.001). Higher total leukocyte counts were also observed among nonsurvivors (16.78 vs. 13.96 $\times 10^3/\mu L$; p=0.027). These findings were consistent with the observations of Shapiro et al. (2005).[9] who prospectively evaluated 1,278 patients admitted with suspected infection and reported an overall hospital mortality of 8.20%. Mortality increased progressively with increasing serum lactate concentrations, from 4.90% among patients with lactate concentrations of 0–2.5 mmol/L to 9.00% among those with concentrations of 2.5–4.0 mmol/L and 28.40% among those with concentrations of at least 4.0 mmol/L. Their study also demonstrated that a lactate concentration of at least 4.0 mmol/L had a specificity of 92.00% for predicting mortality. Although the study populations differed, both analyses demonstrated a strong relationship between elevated serum lactate concentrations and adverse clinical outcomes among patients with infection.

Serial CRP measurements demonstrated distinct trends between survivors and nonsurvivors in the present study. Baseline CRP concentrations were higher among nonsurvivors than survivors (168.65 vs. 136.54 mg/L), although the difference was statistically nonsignificant (p=0.201). However, by Day 7, CRP concentrations had decreased to 45.54 mg/L among survivors, compared with 116.31 mg/L among nonsurvivors (p<0.001). Median Day 7 CRP clearance was also significantly greater among survivors (69.57%) than nonsurvivors (14.77%; p<0.001). Similar observations were reported by Póvoa et al. (2011).[10] in a multicentre prospective observational study involving 891 patients with community-acquired sepsis. Their study reported hospital mortality of 38.00% and demonstrated that CRP concentrations were significantly lower among survivors from Day 3 onward (p<0.001). Mortality varied according to CRP response patterns, being 23.00% among fast responders, 30.00% among slow responders, and 41.00% among nonresponders (p=0.001). Their findings were consistent with the greater CRP reduction observed among survivors in the present study and supported the prognostic relevance of serial CRP monitoring rather than relying exclusively on baseline measurements.

Procalcitonin concentrations demonstrated significant differences between survivors and nonsurvivors throughout the observation period. Baseline PCT concentrations were significantly higher among nonsurvivors (9.32 ng/mL) compared with survivors (5.65 ng/mL; p=0.006). By Day 7, concentrations decreased to 1.06 ng/mL among survivors, whereas nonsurvivors maintained higher concentrations of 6.79 ng/mL (p<0.001). Median Day 3 PCT clearance was 46.23% among survivors compared with 22.50% among nonsurvivors (p<0.001). These observations were comparable with the findings of Karlsson et al. (2010).[11] who prospectively investigated 242 patients with severe sepsis and septic shock. Their study reported overall hospital mortality of 25.60%, with median baseline PCT concentrations of 5.00 ng/mL and concentrations of 1.30 ng/mL after 72 hours. Patients demonstrating greater than 50.00% PCT reduction within 72 hours experienced significantly lower mortality than those with less than 50.00% reduction (12.20% vs. 29.80%; p=0.007). Unlike the present study, their absolute PCT concentrations did not significantly distinguish survivors from nonsurvivors, highlighting the particular importance of changes in PCT concentrations over time.

The present study demonstrated that procalcitonin clearance was considerably greater among survivors, with median Day 7 clearance of 82.61% compared with 41.73% among nonsurvivors (p<0.001). Similar findings were documented by Schuetz et al. (2017).[12] in the multicentre Procalcitonin

Monitoring Sepsis (MOSES) study, which enrolled 858 patients with severe sepsis or septic shock. Among the 646 patients included in the principal Day 4 analysis, 28-day mortality was significantly higher in patients whose PCT concentrations failed to decrease by more than 80.00%, compared with patients achieving greater reductions (20.00% vs. 10.00%; p=0.001). Failure to achieve this reduction remained independently associated with mortality after adjustment for relevant clinical variables, with a hazard ratio of 1.97 (95% CI: 1.18–3.30). Although biomarker assessment intervals differed, both studies demonstrated that inadequate reduction in PCT concentrations was associated with increased mortality. These findings supported the clinical relevance of serial PCT trends for assessing patient response and identifying individuals with an increased risk of adverse outcomes.

Receiver operating characteristic curve analysis in the present study demonstrated that serial biomarker clearance provided greater discrimination of 28-day mortality than baseline biomarker concentrations. Baseline CRP demonstrated an AUC of 0.581, whereas baseline PCT showed an AUC of 0.675. Day 3 CRP and PCT clearance demonstrated higher AUC values of 0.794 and 0.805, respectively. Day 7 PCT clearance demonstrated the highest AUC of 0.959 (95% CI: 0.921–0.985), with sensitivity of 93.10% and specificity of 86.84% at a cut-off of ≤63.14%. Comparable findings were reported by Ryu et al. (2015).[13] who retrospectively evaluated 171 sepsis episodes among 157 critically ill patients. Their study demonstrated that PCT and CRP clearance were associated with treatment outcomes, with both biomarkers showing AUC values of 0.710 for predicting treatment success. For survival prediction, both PCT and CRP clearance demonstrated an AUC of 0.770, with 95% confidence intervals of 0.66–0.88 and 0.67–0.88, respectively. The higher Day 7 AUC observed in the present dataset requires cautious interpretation because differences in sampling times, patient selection, and lack of external validation can affect predictive performance.

Multivariable logistic regression analysis in the present study demonstrated that increasing age, higher baseline SOFA score, and reduced early PCT clearance were significantly associated with 28-day mortality. Each additional year of age was associated with an adjusted odds ratio of 1.09 (95% CI: 1.03–1.16; p=0.004), while each one-point increase in SOFA score was associated with an adjusted odds ratio of 2.55 (95% CI: 1.61–4.03; p<0.001). Furthermore, every 10 percentage-point decrease in Day 3 PCT clearance was associated with higher odds of mortality (aOR=1.95; 95% CI: 1.37–2.77; p<0.001). Similar findings were reported by Pieralli et al. (2015).[14] in a prospective observational study involving 144 patients with severe sepsis or septic shock, in which 30-day mortality was 28.50%. Their ROC analysis demonstrated that PCT reductions of less than 15.00% over 72 hours and less than 20.00% between 24 and 72 hours predicted mortality, with AUC values of 0.750 and 0.830, respectively. In their multivariable analysis, these inadequate PCT reductions remained independent predictors of mortality, with reported risk estimates of 3.90 (95% CI: 1.60–9.50) and 3.10 (95% CI: 1.20–7.90), respectively. These findings were consistent with the association between reduced early PCT clearance and mortality observed in the present study, although the models used different clearance definitions and effect measures.

CONCLUSION

The present study suggested that serial C-reactive protein (CRP) and procalcitonin (PCT) measurements may be useful in predicting clinical outcomes among patients with sepsis. Survivors demonstrated greater reductions in CRP and PCT concentrations, whereas persistently elevated biomarker levels were associated with increased mortality. Procalcitonin clearance, particularly on Day 7, demonstrated better prognostic discrimination than baseline biomarker concentrations. Increasing age, higher baseline SOFA scores, and reduced early PCT clearance were associated with greater mortality risk. These illustrative findings suggest that serial biomarker monitoring, combined with clinical assessment, may facilitate early risk stratification, but require validation using actual patient data.

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