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Procalcitonin Level Evaluation for Prediction of Sepsis-Associated Mortality Rate in a Subset of Karachi Population

Iffat Ara Aziz[1], Fizza Tariq[2], Faiza Agha[3], Nasir Jamil[4], Misbah Riaz[5], Syed Zaryab Ahmed[6] and Tauseef Ali Memon[7*]

[1]Department of Biochemistry, Baqai Medical University, Karachi, Pakistan
[2]Department of Physiology, Baqai Medical University, Karachi, Pakistan
[3]Department of Biochemistry, Liaquat National Hospital, Karachi, Pakistan
[4]Department of Physiology, Liaquat College of Medical and Dentistry, Karachi, Pakistan
[5]Department of Biochemistry, Bahria University Health Sciences Campus, Karachi, Pakistan
[6]Department of Biochemistry, Ziauddin Medical College, Ziauddin University, Karachi, Pakistan
[7]Department of Emergency Medicine, Ziauddin University, Karachi, Pakistan

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***Corresponding Author:**
Tauseef Ali Memon
Department of Emergency Medicine, Ziauddin University, Karachi, Pakistan
memontauseefali@gmail.com

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ABSTRACT

Procalcitonin (PCT) has been recognized as a crucial biomarker in the diagnosis and prognosis of sepsis, as it reflects the body's response to infection. **Objective:** To identify the association of procalcitonin level for the prediction of sepsis-associated mortality rate in a subset of the Karachi population. **Methods:** It was an analytical cross-sectional study conducted at Ziauddin Medical College with approval of the ERC. The sample size was n=130. The set inclusion criteria were patients in whom sepsis was suspected, who given consent to participate in the study, and were within the range of 18-60 years. The exclusion criteria were patients from other hospitals, patients with malignancies and known ischemic heart diseases, patients with thyroid disorders, patients who had leukopenia, and patients who did not give consent to participate in the study. The data were collected through a pre-developed questionnaire, which included questions regarding demographics, presenting complaint, PCT levels at the time of admission, and outcome as positive (recovered) or negative (died). The minimum PCT levels considered as negative were 0.1 – 0.25ng/mL, if the outcome seemed to be positive. **Results:** Most of the patients with sepsis had 4-6 ng/mL of PCT levels. The increased mortality was found to be significantly associated with high levels of PCT, specifically in patients having PCT 6-8 ng/mL and greater than 8 ng/mL. **Conclusions:** High PCT levels can predict the outcome of sepsis; PCT levels more than 6 were associated with a high mortality rate in a subset of the Karachi population.

INTRODUCTION

Sepsis is a life-threatening medical disorder caused by the body's immune system responding to an infection in an excessive and dysregulated manner, resulting in extensive inflammation that destroys its own tissues and organs [1]. Normally, the immune system fights infections to defend the body. Still, in sepsis, this reaction becomes uncontrolled, resulting in organ failure and, in severe cases, shock or death if not diagnosed and treated very quickly. This inflammatory reaction can induce irregular blood flow, such as the creation of blood clots inside arteries, which deprive organs of oxygen and nutrients, exacerbating the damage [2]. Sepsis can be caused by a variety of factors that include bacterial infections, but fungi, viruses, and parasites can also cause it. Sepsis can quickly progress to severe sepsis, which causes significant organ dysfunction in the kidneys, lungs, liver, or heart, and septic shock, which

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is defined by dangerously low blood pressure that does not respond adequately to fluid resuscitation and necessitates vasopressor support. This development dramatically raises the chance of mortality [3]. Sepsis is a prominent cause of morbidity and mortality and a significant health burden globally. It is thought to be responsible for over 11 million fatalities a year, or 20% of all deaths globally [4]. It has been documented that in underdeveloped nations, sepsis-related mortality is disproportionately prevalent, particularly among infants and young children; the burden is considerably greater [5]. Furthermore, antimicrobial resistance makes treatment more difficult and raises the death rate from sepsis, causing hospital-acquired illnesses. Improving results requires early diagnosis, suitable antibiotic treatment, fluid resuscitation, and supportive care [6]. However, diagnosing sepsis and its consequences in the early stages of its development is difficult, but researchers are working on different markers that can highlight the complications of sepsis and predict mortality in severe cases [7]. Procalcitonin (PCT) has been recognized as a crucial biomarker in the diagnosis, treatment, and prognosis of sepsis, as it reflects the body's response to infection [8]. Unlike traditional indicators such as C-reactive protein or white blood cell counts, PCT rises swiftly and specifically in bacterial sepsis, making it useful for early diagnosis and distinction from non-infectious systemic inflammation. It is a precursor of the hormone calcitonin, which is typically undetectable in healthy people [9, 10]. However, during bacterial infections, its blood levels rise significantly because proinflammatory cytokines and bacterial endotoxins drive increased production in different tissues [11]. Because PCT levels tend to decrease with successful treatment, this feature helps clinicians not only detect sepsis early but also track the efficacy of antimicrobial therapy [12]. In terms of predicting sepsis-related mortality, increased procalcitonin levels are highly correlated with the severity of illness and bad outcomes [13]. According to studies, greater PCT concentrations at the time of ICU admission are related to increased organ failure, as indicated by scores such as the Sequential Organ Failure Assessment (SOFA), as well as higher short-term death rates [14]. A procalcitonin level equal to or greater than roughly 7 ng/mL upon admission has been associated with a considerably higher risk of 28-day death [15]. Considering its effectiveness in the prognosis of sepsis, identifying its association and levels that may predict highly susceptible individuals. The PCT analysis in individuals who may develop organ failure or sepsis-associated complications, such as death, will help inform health professionals about the expected outcome and may facilitate the improvised management to improve the outcome.

Although procalcitonin (PCT) is widely recognized as a useful biomarker for early diagnosis and monitoring of sepsis, its role in accurately predicting sepsis-associated mortality remains variably reported across different populations. Local data correlating PCT levels with mortality outcomes are limited. Therefore, this study aims to evaluate the association between procalcitonin levels and sepsis-related mortality in a subset of the Karachi population to aid early risk stratification and clinical decision-making.

METHODS

It was an analytical cross-sectional study conducted at the Department of Emergency of Ziauddin Medical College with approval of the ERC (Ref code: 2610920TAEM). The sample size n=130 was calculated through the open epi calculator, keeping the proportion of the population at 50% and the prevalence of 37% at 95% confidence intervals and 5% margin of error. The sample was segregated by a non-probability consecutive sampling technique according to the inclusion criteria from July 2022 to December 2024. The set inclusion criteria were patients in whom sepsis was suspected, who given consent to participate in the study, and were within the range of 18-60 years. The exclusion criteria were patients from other hospitals, patients with malignancies and known ischemic heart diseases, patients with thyroid disorders, patients who had leukopenia, and patients who did not give consent to participate in the study. The data was collected through a predeveloped questionnaire which included questions regarding demography, presenting complaint. PCT levels at the time of admission were measured. Outcome was considered positive if the patient recovered or negative if the patient died. The questionnaire was self-developed and validated by a pilot trial on 20 patients; the Cronbach's alpha score was checked, which was 0.8. After validating the questionnaire, the data were collected. At the time of admission, patients with a history of high-grade fever, chills, productive cough, suspected cellulitis, and purulent swelling were considered as potential candidates for the study. For diagnostic reason PCT levels were performed by sending a blood sample in a sterile vacutainer tube to the associated lab. Briefly, PCT levels were measured using an automated quantitative immunoassay technique. The sample was loaded into the automated analyser, and the automated analyser performed PCT analysis as per the lab manual protocol of the sandwich ELISA technique and generated the results as per the detection range of the Kit. The results were received from the lab, and patients with minimum PCT levels of 0.1–0.25ng/mL were excluded from the study. Patients with PCT levels more than 0.25ng/mL were considered septic [16]. The included patients who were diagnosed with sepsis and survived were marked as a

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positive outcome, and those who died during the hospital stay were recorded as a negative outcome. The number of survivors and deaths was associated with the already acquired PCT levels (recorded at the time of admission). Data were analysed by using SPSS version 27.0. PCT levels were categorized into 5 different categories: 0.25-2 ng/mL, 2-4 ng/mL, 4-6, 6-8, and >8. Mean ± SD were calculated for quantitative data, and frequency and percentages were calculated for qualitative data. To generate the association at the marked PCT level, associated mortality was checked as yes or no. Chi- square analyses were performed to generate the association and to identify the significance.

RESULTS

The mean age of study participants was 52.16 ± 6.31; among them, 77 (54.6%) were male and (45.4%) were female. Out of 130 (100%), 71 (54.6%) participants were diabetic, and 63 (48.4%) had a history of hypertension. The study shows the gender wise distribution of associated comorbidities. Most of the patients with sepsis had 4-6 ng/mL of PCT levels (Figure 1).

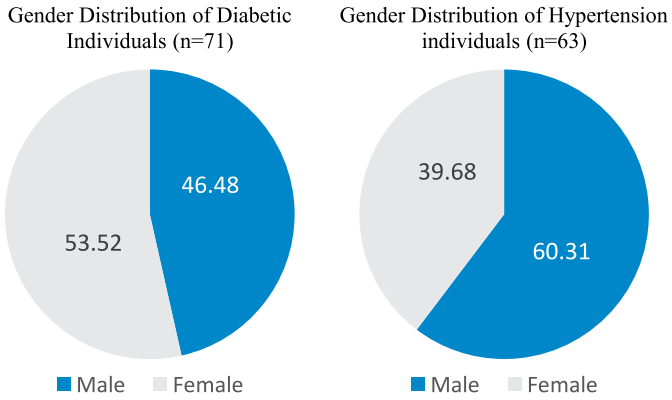

Figure 1: Presence of Comorbidities in the Participants of the Study (Male and Female)

The procalcitonin levels (ng/mL) among admitted participants at the time of hospital admission are illustrated (Figure 2).

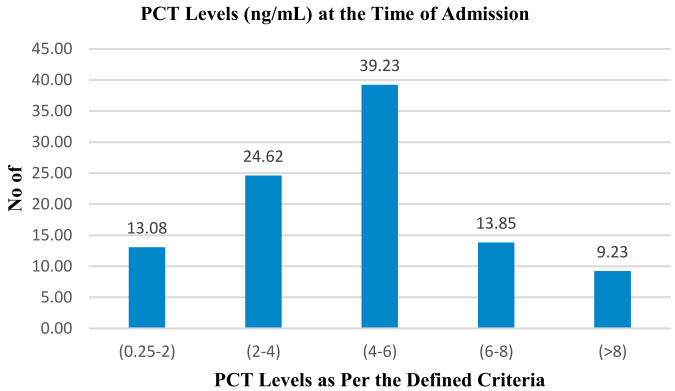

Figure 2: PCT Levels (ng/mL) in the Admitted Participants at the Time of Admission

The increased mortality was found to be significantly associated with high levels of PCT, specifically in patients having PCT 6-8 ng/mL and greater than 8 ng/mL. The mortality among the patients occurred on different days; however, the mean day of mortality was 11.1 ± 2.3 after admission (Table 1).

Table 1: Association of PCT Levels with the Outcome in Diagnosed Patients of Sepsis

PCT Level (ng /mL) (n=130)	Mortality Rate Recorded at Different PCT levels F (%)		p-value
	Yes	No	
(0.25-2) n= 17	0	17 (100%)	–
(2-4) n= 32	3 (9.38%)	29 (90.62%)	0.241
(4-6) n= 51	11 (21.57%)	40 (78.3%)	0.111
(6-8) n= 18	9 (50.00%)	9 (50.00%)	0.012*
(>8) n= 12	8 (66.67%)	4 (0.33%)	0.001*

*Significant p-value (p<0.05)

DISCUSSION

Procalcitonin (PCT) levels have emerged as a crucial biomarker in the setting of sepsis, with a substantial correlation with both sepsis severity and mortality rate, highlighting their relevance in clinical practice [16]. Elevated PCT levels correspond with the severity of systemic inflammation and bacterial infection that characterize sepsis, and multiple studies have shown that greater PCT concentrations are associated with an increased risk of death [17]. The dynamics of PCT, particularly its rise and fall over time, are also key prognostic indicators: a significant drop in PCT within 72 hours of initial evaluation predicts improved survival, whereas persistently high or growing levels indicate treatment failure and increased mortality risk [12]. Beyond prognosis, assessing PCT levels aids in antibiotic therapy by enabling early detection of bacterial sepsis and tracking therapeutic response, reducing wasteful antibiotic use and associated consequences [18]. Given these convincing findings, routine PCT assessment in all patients with suspected sepsis is critical for enabling rapid risk classification, optimizing clinical choices, tailoring antibiotic stewardship, and, ultimately, improving patient outcomes [19]. Therefore, the study was conducted to identify the association of PCT with mortality rate and to document the critical range of PCT in a subset of the Karachi Population. This study examined the correlation between procalcitonin (PCT) levels and sepsis in a sample of 77 men (54.6%) and 59 females (45.4%). The average age was 52.16 ± 6.31 years. In this middle-aged group, measuring PCT gave critical information into the inflammatory state and severity of sepsis, with substantial relationships with clinical outcomes that were independent of patient variables such as age and gender [20]. The balanced gender distribution enabled testing of

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both males and females, demonstrating that PCT elevation as a sepsis marker is constant, independent of gender [21]. The study's findings demonstrate that PCT is a valid indication of sepsis in a typical adult population in their fifth decade of life, which is a frequent age range for septic patients in clinical settings. This shows that frequent PCT assessment might improve early diagnosis and risk classification in sepsis care, allowing for timely and focused therapeutic interventions [22]. In this study, the majority of patients with sepsis had procalcitonin (PCT) levels ranging from 4 to 6 ng/mL at the time of hospital admission, as shown in figure 1, which depicts the distribution of PCT concentrations among admitted participants. This range of PCT increase confirms the biomarker's known significance in reflecting the bacterial load and systemic inflammatory response associated with sepsis [23]. Importantly, our findings demonstrated that greater PCT levels were substantially linked with increased mortality, particularly in individuals with levels between 6 and 8 ng/mL and above 8 ng/mL. This conclusion is consistent with a growing body of recent literature over the last five years, which has repeatedly shown that increased PCT levels are predictive of poor outcomes in septic patients. For example, multiple studies have found that PCT concentrations more than 6 ng/mL serve as a threshold beyond which the risk of death significantly increases, indicating not only the severity of the infection but also the level of organ failure and the body's immunological dysregulation [24]. Clinical scientists conducted a study in early 2020 that found that patients with PCT levels more than 7 ng/mL had significantly higher 28-day death rates, supporting our discovery of increased fatality at PCT values of 6-8 ng/mL and above [25]. Similar findings were observed in a multicentre cohort analysis, where PCT levels more than 8 ng/mL were substantially predictive of ICU mortality, highlighting the biomarker's potential in risk stratification and early clinical decision making [26]. The pathophysiological reason for this connection is PCT production, which occurs largely by parenchymal cells in response to pro-inflammatory cytokines generated during severe bacterial infections [11]. Elevated PCT levels suggest excessive systemic inflammation and the possibility of progressing to septic shock, both of which increase the risk of death. Aside from the threshold effect, temporal dynamics of PCT, such as consistently high or rising levels throughout hospitalization, have been associated with a worse outcome, stressing the necessity of both initial measurement and serial monitoring [1]. Our findings add to the body of data that individuals with PCT levels of 6-8 ng/mL or above are at high risk and should be monitored closely, treated aggressively, and given cautious organ support. Furthermore, compared to patients with PCT levels in the moderate range of 4-6 ng/mL, those with higher values had more frequent acute organ failure, longer ICU admissions, and a greater requirement for vasopressor medication, indicating more severe sepsis courses, as documented in previous research. While some research shows that PCT cut-offs vary among situations and groups, the convergence of numerous independent studies on the mortality hazards associated with PCT levels more than 6 ng/mL supports the biomarker's therapeutic usefulness [27]. In conclusion, our analysis confirms that most septic patients had moderately elevated PCT levels (4-6 ng/mL) at admission, but considerably higher PCT concentrations, particularly between 6 and 8 ng/mL and beyond, are predictive of poor survival. This pattern represents an established and current awareness that PCT is not just a diagnostic tool, but also a potent predictive biomarker.

This was a single-center study with a relatively small sample size, which may limit the generalizability of the findings. Additionally, PCT levels were measured only at admission, and serial measurements were not evaluated to assess dynamic prognostic changes. Future multicenter studies with larger samples and serial PCT monitoring are recommended to validate optimal cutoff values and improve prognostic accuracy in sepsis.

CONCLUSIONS

High PCT levels can predict the outcome of sepsis; PCT levels more than 6 were associated with a high mortality rate in a subset of the Karachi population.

Authors' Contribution

Conceptualization: IAA
Methodology: IAA, FT, TAM
Formal analysis: IAA, FT, NJ, MR, SZA, TAM
Writing and drafting: FA, NJ, MR, SZA, TAM
Review and editing: IAA, FT, TAM, NJ, MR, SZA, FA

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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