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Accuracy of Day 1 Procalcitonin and C-Reactive Protein Levels for Predicting Mortality in Burn Patients

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ABSTRACT

Objective: Although serum procalcitonin (PCT) and C-reactive protein (CRP) are currently used to predict infection, sepsis, and death in intensive care units, their application in burn mortality has received little attention. Thus, it is essential to do study on how day-one PCT and CRP patterns affect burn mortality. **Study design:** Cross-sectional study. **Settings:** Department of Plastic Surgery, Nishtar Medical University, Multan. **Duration of study:** January 2024 to May 2024. **Methodology:** Total 111 patients, both male and female, aged 18 to 60, within 48 hours of a thermal burn injury, with 20–60% of their total burn surface area free of inhalational injuries were included. Based on their medical history and medical records, patients with concomitant chronic diseases were not included. Venous blood samples were obtained aseptically on the first day of hospitalization and sent for CRP analysis; a cutoff of 71 mg/dl was used to predict mortality. PCT determination (PCT cutoff of 1770 ng/ml was used to predict mortality) and a level > 71 predicted mortality and <71 predicted survival. < 1770 predicted survival and >1770 projected mortality. The ultimate outcome (survivor or non-survivor) was recorded. **Results:** Day 1 CRP levels provide a 93.62% sensitivity, 93.75% specificity, 91.67% PPV, 95.24% NPV, and 93.69% diagnostic accuracy for predicting burn patient mortality. 90.99% diagnostic accuracy, 91.49% sensitivity, 90.62% specificity, 87.76% PPV, 93.55% NPV, and day 1 procalcitonin levels for burn patient mortality prediction. **Conclusion:** A poor prognosis is linked to increasing trends in serum PCT and CRP levels in patients with burn injuries.

INTRODUCTION

Burns are a major global public health concern because of the high morbidity and death rates they produce.[1] There are several grading systems used for prediction, including the Baux score, APACHE-II, Roi index, and body shape index (ABSI).[2] Age, total burn surface area (TBSA), and inhalational injury are the most common techniques used to assess burn prognosis; as a result, they are not enough to forecast changes in a patient's prognosis while they are in the hospital.[3] To enhance prognosis, it is critical to identify parameters that can predict mortality on the first day and during the hospital stay so that the appropriate remedial actions can be taken.

Although serum procalcitonin (PCT) and C-reactive protein (CRP) are currently used to predict infection, sepsis, and death in intensive care units, their application in burn mortality has received little attention. Consequently, studies on how day-one PCT and CRP trends affect burn mortality are required. Steroid and nonsteroid anti-inflammatory drugs (NSAIDs), immunodeficiency conditions, and neutropenia do not affect PCT, a reliable measure of burn inflammation.[5,6] CRP functions as a proinflammatory interleukin (IL-6) surrogate and is an acute-phase reactant.[7,8]

The purpose of this study is to assess how well day 1 procalcitonin and CRP levels predict burn patients' deaths. These will be used as prognostic indicators for burn patients who present to our local setting if they prove to be trustworthy. The evaluation of burn patients' mortality risk will aid in the creation of a management strategy that will lower the risk of death and enhance prognosis.

METHODOLOGY

Following institutional ethical review committee approval, this descriptive, cross-sectional study involved 111 patients, both male and female, aged 18 to 60, who were admitted to the Department of Plastic Surgery at Nishtar Medical University in Multan within 48 hours of a thermal burn injury, with 20–60% of their total burn surface area free of inhalational injuries. One sample sensitivity and specificity formula is used to determine the sample size. where the pct's sensitivity is 93.3%, its specificity is 72.2%, its mortality prevalence is 29.4%, its confidence level is 95%, and its absolute precision is 10%.[9] A non-random

consecutive sampling method was used to choose the nine patients. Based on their medical history and medical records, patients with concomitant chronic diseases (diabetes, heart disease, hypertension, or chronic lung disease, including asthma and COPD) were not included.

Records were kept of the patient's age, gender, burn length, degree of burn (first, second, or third, as shown in Annexure 2), and total body surface area affected. Venous blood samples were obtained aseptically on the first day of hospitalization and sent for CRP analysis; a cutoff of 71 mg/dl was used to predict mortality. PCT determination (PCT cutoff of 1770 ng/ml was used to predict mortality) and a level > 71 predicted mortality and < 71 predicted survival. < 1770 predicted survival and >1770 projected mortality. All patients received standard care for burn injuries in compliance with institutional policies, and patients were monitored throughout their stay in the burn unit. The ultimate outcome (survivor or non-survivor) was recorded. The proforma (attached) had all of the data.

Data analysis was conducted using SPSS version 23. The mean and standard deviation for age, burn duration, total body surface area affected, and CRP and PCT values on day one were displayed. Frequencies and percentages were displayed for gender, burn severity, and ultimate disposition. To ascertain the diagnostic accuracy of CRP and PCT in predicting mortality, a 2x2 contingency table was created using final disposition as the gold standard. Age, gender, burn length, burn severity, and total body surface area involved were used to stratify the data. Once more, the post-stratification diagnostic accuracy was computed.

RESULTS

The study's participants ranged in age from 18 to 60, with a mean age of 39.76 ± 7.12 years. Table I shows that 59 (53.15%) of the patients were in the 18–40 age range. The male to female ratio of these 111 individuals was 1.7:1, with 41 (36.94%) being male and 70 (63.06%) being female. The average burn time was 27.04 ± 3.38 hours. The average total surface area of the body included was 35.39 ± 879%. The distribution of patients with various variables is shown in Table 1.

We noticed that PCT and CRP's trend difference on day 1, in non-survivor (2462.53 ± 1234.51 and 89.34 ± 8.69) and survivor groups (1459.36 ± 11.31.38 and 61.52 ± 15.89) were extremely significant (p-value < 0.0001).

Of those with a CRP level more than 71, six patients (False Positive) had survived, whereas forty-three patients (True Positive) had not. Table 2 shows that 60 were True Negative and 3 were False Negative (p=0.0001). Day 1 CRP levels provide a 93.62% sensitivity, 93.75% specificity, 91.67% PPV, 95.24% NPV, and 93.69% diagnostic accuracy for predicting burn patient mortality.

Of those with procalcitonin levels more than 1770, four patients (False Positive) had survived, whereas forty-four patients (True Positive) had not. Table 3 shows that 3 were False Negative (p=0.0001) and 58% were True Negative. 90.99% diagnostic accuracy, 91.49% sensitivity, 90.62% specificity, 87.76% PPV, 93.55% NPV, and day 1 procalcitonin levels for burn patient mortality prediction. The diagnosis accuracy of day 1 procalcitonin and CRP levels stratified by age, gender, burn length, burn severity, and total body surface area involved is shown in Tables 4 and 5.

Table 1

Distribution of Patients with Variables (n=111)

Variables		Frequency	%age
Age (years)	18-40	59	53.15
	41-60	52	46.85
Gender	Male	41	36.94
	Female	70	63.06
Duration (hours)	≤24	67	60.36
	>24	44	39.64
Total body surface area involved	20-40%	71	63.96
	41-60%	40	36.04
Degree of burns	1	27	24.32
	2	49	44.14
	3	35	31.53

Table 2

Diagnostic Accuracy of Day 1 CRP Levels for Predicting Mortality in Burn Patients.

	Mortality	No mortality	P-value
CRP level > 71	44 (True positive)	04 (False Positive)	0.0001
CRP level ≤ 71	03 (False negative)	60 (True Negative)	

Sensitivity: 93.62%, Specificity: 93.75%, Positive Predictive Value (PPV): 91.67%, Negative Predictive Value (NPV): 95.24%
Diagnostic Accuracy: 93.69%

Table 3

Diagnostic Accuracy of Day 1 Procalcitonin Levels for Predicting Mortality in Burn Patients.

	Mortality	No mortality	P-value
Procalcitonin levels >1770	43 (True positive)	06 (False Positive)	0.0001
Procalcitonin levels ≤1770	04 (False negative)	58 (True Negative)	

Sensitivity: 91.49%, Specificity: 90.62%, Positive Predictive Value (PPV): 87.76%, Negative Predictive Value (NPV): 93.55%
Diagnostic Accuracy: 90.99%

Table 4

Stratification of Diagnostic Accuracy of Day 1 CRP Level with Respect to Age, Gender, Duration of Burn, Degree of Burn and Total Body Surface Area Involved.

		Sensitivity	Specificity	PPV	NPV	DA	
Age (years)	18-40	98.57%	82.05%	90.79%	96.97%	92.66%	0.001
	41-60	91.26%	75.0%	92.41%	72.0%	87.50%	0.001
Gender	Male	90.91%	92.0%	96.77%	79.31%	91.21%	0.001
	Female	97.62%	71.05%	88.17%	93.10%	89.34%	0.001
Duration (hours)	≤24	94.35%	74.42%	91.41%	82.05%	10.64%	0.001
	>24	96.15%	90.0%	92.59%	94.74%	93.48%	0.001
TBSA (%)	20-40%	92.91%	88.10%	92.19%	89.16%	90.99%	0.001
	41-60%	97.56%	76.47%	90.91%	92.86%	91.38%	0.001
Degree of burns	1	92.78%	90.48%	93.75%	89.06%	91.88%	0.001
	2	95.77%	78.95%	89.47%	90.91%	89.91%	0.001
	3	93.20%	88.68%	94.12%	87.04%	91.67%	0.001

Table 5

Stratification of Diagnostic Accuracy of Day 1 Procalcitonin Levels with Respect to Age, Gender, Duration of Burn, Degree of Burn and Total Body Surface Area Involved.

		Sensitivity	Specificity	PPV	NPV	DA	
Age (years)	18-40	95.0%	82.86%	92.68%	87.68%	91.30%	0.001
	41-60	88.75%	70.83%	91.03%	65.38%	84.62%	0.001
Gender	Male	87.88%	92.0%	96.67%	74.19%	89.01%	0.001
	Female	94.05%	60.53%	84.04%	82.14%	83.61%	0.001
BMI (kg/m^2)	≤30	91.13%	72.09%	90.40%	73.81%	86.23%	0.001
	>30	92.31%	75.0%	82.76%	88.24%	84.78%	0.001
Duration (hours)	≤24	96.55%	81.48%	84.85%	95.65%	89.29%	0.001
	>24	88.89%	85.71%	92.31%	80.0%	87.80%	0.001
TBSA (%)	20-40%	91.43%	85.71%	88.89%	88.89%	88.89%	0.001
	41-60%	95.24%	76.92%	86.96%	90.91%	88.24%	0.001
Degree of burns	1	96.67%	90.0%	93.55%	94.74%	94.0%	0.001
	2	88.46%	76.19%	82.14%	84.21%	82.98%	0.001
	3	95.24%	71.43%	76.92%	93.75%	83.33%	0.001

DISCUSSION

According to earlier research, non-survivors had much greater PCT and CRP levels than survivors. The risk of death was 3.163 times higher for burn patients with serum PCT ≥ 2 ng/mL than for those with < 2 ng/mL.[10] The highest PCT level was connected with TBSA, while the beginning PCT levels (upon admission) were not correlated with TBSA. The degree of burns and the TBSA involvement were directly correlated with the CRP level.[11] At admission, CRP levels were normal; they peaked 48 hours later and began to decline by the sixth day after the burn. When infections were present, the reaction to CRP production was stronger and lasted longer.[12] Children's scald burns can be effectively managed with the use of sequential CRP estimation.[12]

On day 1, we found that the trend differences in PCT and CRP were extremely significant (p-value < 0.0001) for the non-survivor group (2462.53 ± 1234.51 and 89.34 ± 8.69) and the survivor group (1459.36 ± 11.31.38 and 61.52 ± 15.89). Day 1 CRP levels provide a 93.62% sensitivity, 93.75% specificity, 91.67% PPV, 95.24% NPV, and 93.69% diagnostic accuracy for predicting burn patient mortality. 90.99% diagnostic accuracy, 91.49% sensitivity, 90.62% specificity, 87.76% PPV, 93.55% NPV, and day 1 procalcitonin levels for burn patient mortality prediction. 51 burn patients, ages 18 to 60, were included in a study by Sinha A et al. The death rate was 15/51, or 29.4%. The authors found that the trend difference in PCT and CRP on day 1 was extremely significant (p-value < 0.0001) for both the survivor group (1376.58 ± 1015.12 and 56.92 ± 24.38) and the non-survivor group (2637.87 ± 1505.45 and 91.33 ± 7.09). In terms of mortality prediction, Day 1 PCT at the cutoff of > 1772 showed a sensitivity of 93.33% and a specificity of 72.22%. In a similar vein, the day 1 CRP at the cutoff of >71 exhibited a 100% sensitivity and a 72.22% specificity for mortality prediction.[9] Oncul U et al. comprised seventy-two burn patients. 40.0% of patients had SIRS, and 15.2% of patients had a diagnosis of sepsis. Sepsis patients were identified by their CRP and PCT levels, although PCT showed a greater positive predictive value (50.0% vs. 45.0%). The ideal CRP and PCT cutoff levels for differentiating sepsis were 0.95 ng/mL and 66.75 mg/L, respectively.[13]

Furthermore, compared to the survivor group, the non-survivor burn patients had considerably higher CRP and PCT, according to our meta-analysis of 11 CRP and 11 PCT investigations. It's critical to comprehend the CRP and PCT levels at which the inflammatory process becomes prominent for both groups because this will help determine when therapies should begin. Although PCT and CRP are still the most commonly utilized biomarkers in sepsis patients, the degree of change and associated mortality time course are still unclear.[14]

For the most part, CRP levels obtained from burn patients remain high throughout their hospital stay, and variations in CRP are unreliable.[15] Yigit and Yigit discovered that septic burns were not directly linked to higher CRP. They discovered no connection between CRP levels and the clinical condition of the patient.[15] According to their research, CRP is a valuable biomarker for inflammation, although it is still unclear how well it predicts the course of sepsis.[15] Tan and colleagues' meta-analysis revealed that PCT had a much higher diagnostic specificity and accuracy for sepsis than CRP.[16] According to our findings, CRP is best at estimating mortality but is not always able to identify relevant factors.

The primary source of PCT, a precursor protein for calcitonin, is thyroid C-cells. Because the protein is not normally released into the bloodstream, serum PCT is undetectable in those without systemic inflammation.[17] Sepsis caused by bacterial infections can be identified in the bloodstream because PCT production is triggered in almost all organs. In these situations, the production of PCT is stimulated by bacterial toxins, such as endotoxin, and cytokines, such as tumor necrosis factor-alpha, interleukin (IL)-1beta, and IL-6.[18] Since cytokines produced during viral infections inhibit the generation of TNF-alpha, the majority of viral infections do not promote PCT synthesis. Furthermore, PCT has a short induction period following bacterial stimulation, a long half-life, and a wide biological range. As a result, PCT is a useful instrument that offers quick and easily accessible data and has outstanding discriminatory qualities for differentiating between bacterial and viral inflammations.[19] Because burned patients are more susceptible to infections, especially nosocomial ones, it is crucial to monitor their PCT levels. A useful indicator for bacterial infections in this patient population, elevated PCT levels show a systemic reaction to bacterial invasion. Immune response dysregulation in sepsis may cause a substantial increase in PCT levels, and a persistent increase may indicate a more severe and protracted

inflammatory condition. The overall prognosis of burn patients may be significantly impacted by this persistent increase in PCT levels.[20]

The importance of high PCT levels in the identification of burn sepsis in the context of infection—the most frequent complication and cause of death among burn patients—has been confirmed by numerous studies.[21] The risk of death was 21.3 times higher for patients with PCT levels above three ng/mL than for those with levels below three ng/mL, and the diagnostic value of PCT was highest for levels over three ng/mL, according to Piroglu and colleagues. 22. The variables that are most closely linked to increased PCT in the early stages of severe burn patients include the degree of inhalation, burn index, and APACHE-II score. As previously stated, Xu and associates verified these associations and assessed the usefulness of PCT in the early phases of the illness. According to their findings, a major risk factor for sepsis within 60 days after severe burns was an early-phase PCT higher than 4.275 ng/mL.[23] When an infection is suspected, PCT levels can assist clinicians in distinguishing between sepsis and systemic inflammation. Additionally, PCT, blood cultures, and clinical evaluation can be used to track the response to treatment. Yigit and Yigit discovered that as patients' clinical condition improved, their PCT levels went back to their initial levels.[24] In patients who went on to develop burn sepsis, PCT levels continued to be consistently increased. Therefore, PCT is not as strongly associated with inflammation as CRP, and its kinetics aid physicians in differentiating between septic episodes and a systemic inflammatory state in burn patients. Following burn injuries or surgical procedures, even slight increases in PCT are predicted and will quickly go away provided there is no infection.[25]

Our investigation was subject to several limitations. Since it was a single-center study, the findings require additional evaluation and are not widely relevant. Second, our study design's power and significance may be impacted by confounding variables. The rationale was that these measures are not unique to burn injuries and are mostly used to predict pediatric outcomes generally. Lastly, we only saw the cross-sectional values of the research measures (PCT and CRP) on alternate days during the first week following burn injury, even though they are continuous variables.

CONCLUSION

In patients with burn injuries, rising trends of serum PCT and CRP values are associated with poor prognosis. Any value of serum Procalcitonin levels >1770 pg/mL and serum CRP >71 mg/L during hospitalization indicates poor prognosis, and the likelihood of death increasing by 4.5 and 23.6 times, respectively. The trend of change in serum values of PCT and CRP can be used for prognostication of mortality and patient's response to treatment.

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