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ORIGINAL ARTICLE

Diagnostic role of high Sensitive-CRP and procalcitonin in hospitalized patients.

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ABSTRACT... Objective: To assess the effectiveness of high sensitive CRP and Procalcitonin in admitted patients of Farooq Hospital Lahore, Pakistan. **Study Design:** Prospective study. **Setting:** Farooq Hospital Westwood, Lahore. **Period:** November 2023 to January 2024. **Methods:** The admitted patients of intensive care units, medical and cardiac care units, with acute kidney infection, chronic kidney disease, diabetes mellitus, hypertension, coronary artery bypass grafting, gastroenteritis, chronic obstructive pulmonary disease, liver disease, hepatitis, and bacterial infections were included. Serum albumin, high-sensitive C-reactive protein (hs-CRP), and procalcitonin were analyzed by automated analyzers. Data was analyzed by using SPSS (v.25.0). **Results:** Among 73 patients, 83.56% were critical and 16.44% stable. It was found that the critical patients were in the range of 61 to 90 years of age. The hs-CRP and procalcitonin levels were non-significantly correlated with age group. The hs-CRP exhibited higher sensitivity than procalcitonin in critical patients (AUC: 0.872 vs. 0.725). Likewise, serum albumin had a significant association with patients having critical conditions (AUC: 0.685). Moreover, it was found that hs-CRP and procalcitonin have a significant association with the period of patient stay in the hospital. **Conclusion:** The present study concluded that in critically ill patients having high levels of procalcitonin and hs-CRP had longer hospital stay and both biomarkers are equally important in the treatment of critically ill admitted patients.

Key words: Procalcitonin, High Sensitive-C-reactive Protein, Hospital stay.

INTRODUCTION

In modern medicine, the quest for accurate and efficient biomarkers to aid in the diagnosis, prognosis, and management of patients, especially those in critical conditions, is an ongoing pursuit.[1] Among the plethora of biomarkers available, hs-C reactive protein (hs-CRP) and procalcitonin (PCT) have emerged as prominent players in the field, each offering unique insights into the inflammatory and infectious processes within the human body.[2] hs-CRP, a classic acute-phase reactant, has been extensively studied and utilized in clinical settings for decades. It is primarily synthesized by hepatocytes in response to pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-alpha in reaction to tissue injury, infection, or inflammation.[3] The production of hs-CRP occurs rapidly, with levels peaking within 48 hours of the inflammatory stimulus. Its serum concentration reflects the severity and extent of the inflammatory process, making it a valuable tool in the assessment of various conditions ranging from bacterial infections to autoimmune diseases.[4]

PCT on the other hand has drawn a lot of interest as a bacterial infection biomarker, especially in critically ill patients. Unlike CRP, PCT is the precursor of calcitonin, a hormone involved in calcium homeostasis. PCT is produced in the thyroid gland under normal conditions, and promptly cleaves into calcitonin.[5] However in case of severe bacterial infections, extra-thyroidal organs such liver, intestines, and lungs secrete PCT in response to bacterial endotoxins and inflammatory mediators like TNF-α and IL-1β.[6] This increase in PCT levels makes it valuable indicator for bacterial infections, helping physicians to differentiate between bacterial and non-bacterial causes of systemic inflammation.[7]

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The comparison of high-sensitivity CRP (hs-CRP) and PCT[8] in both critical and stable patients is of paramount importance in clinical practice.[9] While both biomarkers reflect underlying inflammatory processes, their distinct kinetics, mechanisms of production, and clinical implications necessitate a nuanced understanding of their roles in various clinical scenarios.[10] Beyond its diagnostic utility, hs-CRP and PCT hold prognostic significance in predicting the clinical course, severity, and outcomes of critical illness. Elevated levels of both biomarkers have been associated with increased disease severity, organ dysfunction, and mortality in various clinical settings.[11] The objective of the present study was to assess the effectiveness of these two biomarkers in admitted patients of Farooq Hospital Lahore, Pakistan.

METHODS

This prospective study was carried out at Farooq Hospital Westwood in Lahore between November 2023 and January 2024. The Institutional Review Board of Akhtar Saeed Medical & Dental College in Lahore gave its approval (ASMD/FH/Cu/0041/2023). The study comprised patients who were admitted in medical units, intensive care unit (ICU), and cardiac care unit (CCU) and had one or more of the following conditions: gastroenteritis, chronic obstructive pulmonary disease, liver disease, hepatitis, diabetes mellitus, hypertension, acute kidney infection, or chronic kidney disease accompanied by hypertension. Patients with short stay in emergency, incomplete medical records, lack of informed consent, stay less than twelve hours at hospital and gynae patients were excluded. The questionnaire was designed as a data collection tool to collect information from the patients.

About 03 to 05 ml of venous blood was taken and added to the clotted vacutainer and sent to the chemical Pathology Laboratory. Plasma was separated by centrifugation, at a speed of three thousand revolutions per minute for ten minutes. The serum albumin was analyzed on an automated chemistry analyzer (SELECTRA-PRO M) by colorimetric method. The hs-CRP (Kit Lot#: 045230211), and PCT (Kit Lot#: 068230421) were analyzed by the chemiluminescence immunoassay automated analyzer(MAGLUMI-X3). Both internal and external quality controls were also run. Statistical Package for Social Sciences, version 25.0 (SPSS 25.0), was used to analyze the data. Standard deviation and mean were used to describe the quantitative data, and percentages and frequency were used to represent the qualitative variables. The areas under each corresponding curve and the receiver operating curve (ROC) were computed. To determine the relationship between the research variables, bivariate correlation analysis and the chi-square test were used.

RESULTS

Of the 73 patients, 42 (57.53%) were males and 31 (42.47%) were females. The ages of all participants were between 13 to 90 years. The mean age (+ standard deviation) of patients was 60.77 ± 19.089 years. The patients were categorized into three age groups. All the patients were admitted to different units of Farooq Hospital. The hospital stay of patients was categorized as one to five days and more than five days (Table-I).

Characteristics	Frequency (%)
Mean age (Years)	60.77 ± 19.089
Age groups	
(Years)	8 (11.00%)
31-60 (Years)	23 (31.50%)
61- 90 (Years)	42 (57.50%)
Gender	
Male	42 (57.53%)
Female	31 (42.47%)
Admission units	
Intensive care unit	35 (57.37%)
Cardiac care unit	26 (42.62%)
Medical unit	12 (16.44%)
Patient condition	
Critical	61 (83.56%)
Stable	12 (16.44%)
Hospital Stay	
1-5 (Days)	44 (60.27%)
More than 5 (Days)	29 (39.72%)

Table-I. Demographic and clinical characteristics of study patients

All the patients were divided into groups: critical (n=61, 83.56%) and stable (n=12, 16.44%). Critical patients were admitted to ICU (n=35, 57.37%) and CCU (n=26, 42.62%), and all stable

patients were admitted to medical units (Figure-1). The bivariate correlation analysis was performed to find the association between patient condition (critical and stable) with respective to age and gender groups (Table-II). According to the gender distribution, more male patients (43.83%) were found in critical condition and admitted in ICU and CCU units. Moreover, the 60-90 years of age group suffered from critical conditions among other age groups. There was no statistically significant association found between patient condition with gender (p= 0.680) and age group (p= 0.178). The chi-square test was also performed to find the association of hs-CRP (p= 0.031), and PCT (p= 0.004) values of patients with hospital stay. The p-value of <0.05 was considered statistically significant.

Character-istics	Critical	Stable	Bivariate Analysis (P-Value)
Age groups			
13-30	6 (8.2%)	2 (2.73%)	0.178
31-60	17 (23.28%)	6 (8.2%)	
61-90	38 (52.05%)	4 (5.47%)	
Gender			
Female	29 (39.72%)	2 (2.7%)	0.68
Male	32 (43.83%)	10 (13.69%)	

Table-II. Frequency and association of critical and stable patients with study variables
A p-value of <0.05 is considered statistically significant

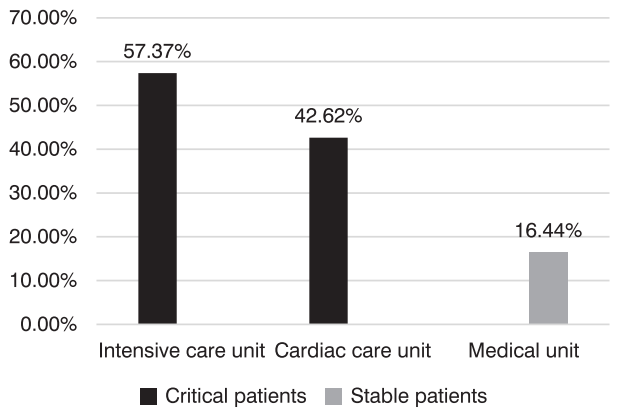

Figure-1. Frequency of critical and stable patients admitted in different units of the hospital

To evaluate the sensitivity of hs-CRP in comparison with PCT, ROC curves were calculated [Figure-2(a)]. The ROC analysis showed that hs-CRP was more sensitive in critical patients with the area under curve (AUC) 0.872 (95% confidence interval: 0.734-1.000; p=0.000) in contrast to PCT with AUC of 0.725 (95% CI: 0.588-0.862; p=0.018). An additional parameter showed a significant association with critical conditions, and that was serum albumin. The ROC curve was also analyzed for the serum albumin in critical and stable patients. The AUC in the case of serum albumin was 0.685 (95% CI: 0.519-0.852; p=0.044) [Figure-2(b)].

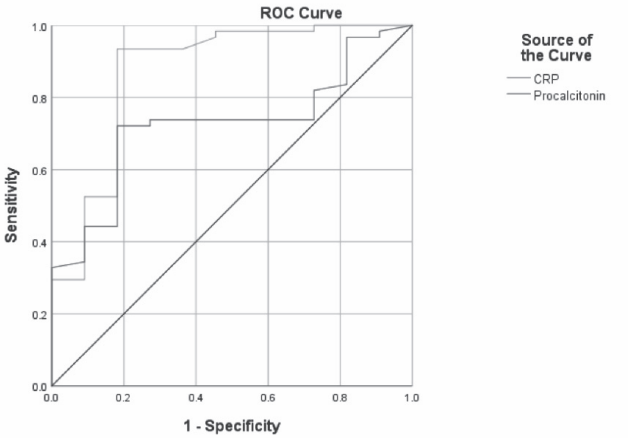

Figure-2(a). Comparison of hs-CRP and PCT estimated by receiver operating curve analysis

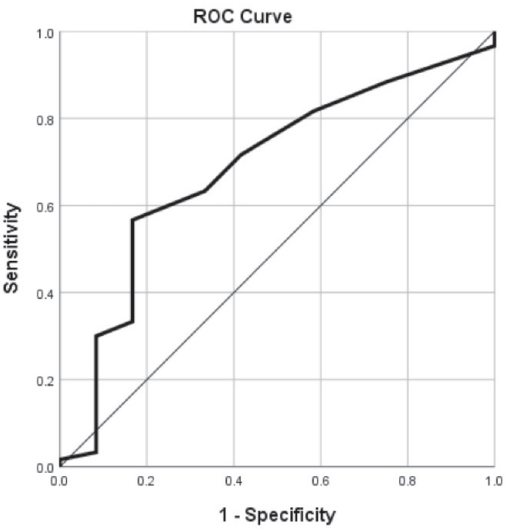

Figure-2(b). Sensitivity of serum albumin estimated by receiver operating curve analysis

DISCUSSION

The purpose of the current prospective study was to examine the clinical utility of serum albumin, PCT, and hs-CRP in the diagnosis and prognosis of patients who are stable and critically ill.[12] This

study enrolled 73 patients of different age groups, dividing them into critical and stable categories based on their clinical condition. A key finding was the predominance of critical patients (52.05%) among the older age groups, particularly those aged 61-90 years. As the patient's age advances, the risk of inflammation will increase dramatically. It is important to understand the morbidity, mortality biomarkers (hs-CRP, PCT, and serum albumin), and risk factors associated with inflammation for its prevention, early diagnosis, and management.[13]

In comparison to other relevant studies, the findings of our investigation align with previous research regarding the association between biomarker levels and patient outcomes in sepsis. Notably, the study conducted in 2023[14] reported similar trends in biomarker positivity rates among septic patients, with CRP being positive in 98 cases, followed by PCT in 75 cases. The sensitivity, specificity, and AUC for hs-CRP reported by Juneja et al were 98.6%, 3.3%, and 0.816. For procalcitonin (>0.5 ng/ml) it was 87.1%, 53.3%, and 0.776, and for procalcitonin (>1 ng/ml) 70%, 70%, and 0.816, respectively of these biomarkers for diagnosing sepsis were consistent with our findings, highlighting the clinical relevance of hs-CRP and PCT in identifying septic patients. Furthermore, another study[15] provided additional insights into the prognostic value of serum biomarkers, demonstrating their ability to predict mortality in septic patients within a specified timeframe. The high sensitivity of PCT (94.64%), and hs-CRP (83.93%) in predicting mortality aligns with our observations regarding findings underscore the importance of biomarker assessment in risk stratification and prognostication for septic patients.

Moreover, the study conducted in 2022[16] examined the levels of inflammatory indicators, including hs-CRP and PCT, in patients with bloodstream infection and sepsis. This study demonstrated the potential use of hs-CRP and PCT as markers of illness severity by finding substantial variations in biomarker levels between critically ill and non-critically ill individuals, which is consistent with our findings. The area under the curve was calculated and it was 0.83 in the case of PCT with a p-value 0.000, similarly p-value for hs-CRP was also 0.000. The study conducted by (Suhua et al)[15] reported the AUC was 0.88 for serum PCT and 0.76 for hs-CRP and it further supports the findings of the current study. Additionally, the correlation between biomarker levels and disease severity scores, such as APACHE II, further supports the prognostic value of these biomarkers in predicting patient outcomes.

Overall, the findings from the present study corroborate existing literature regarding the clinical utility of biomarkers in sepsis diagnosis and prognosis. Despite variations in study populations and methodologies, consistent trends emerge regarding the association between biomarker levels and patient outcomes, highlighting the importance of biomarker assessment in sepsis management. The present study was single-centered-hospital-based and conducted on a small cohort of patients for three months. Subsequently, researchers need to concentrate on verifying these results in more extensive populations and investigating novel biomarkers to enhance the identification and treatment of sepsis.

CONCLUSION

The present study concluded that both hs-CRP and PCT biomarkers have equal significance in the management of critically ill admitted patients. However, the PCT is more expensive and not performed by every Pathology laboratory as a routine inflammatory biomarker. So, the clinician can just refer to the hs-CRP as compared to both to reduce the unnecessary financial burden on the patient and their family. This study also concluded that the values of hs-CRP and PCT biomarkers can predict the duration of patients' stay at the Hospital. The patients with higher hs-CRP and PCT values were found to have more stay in the hospital.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Asim Mumtaz	Principal investigator and writer.	
3	Muhammad Touqeer Hanif	Results analysis and writing and review.	
4	Zaniab Akram	Correction in investigation and writing.	
5	Atika Masood	Critical analysis of results and writing.	
6	Atiqa Arshad	End critical corrections and analysis and formatting.	
7	Zainab Yousaf	Data collection & selection according to inclusion and exclusion criteria.