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The role of hematological parameters in estimating nosocomial sepsis

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ABSTRACT

Background: Sepsis is a systemic inflammatory condition with high mortality rate. It is important to estimate nosocomial sepsis in order to manage the patients earlier. The aim of this study was to investigate the role of hematological parameters in estimating nosocomial sepsis.

Material and Methods: A retrospective examination was conducted on 121 nosocomial sepsis patients between 01 January 2014 and 30 June 2017. Neutrophil to lymphocyte ratio (NLR) and C-reactive protein (CRP) of the patients at the onset of sepsis were compared with baseline values.

Results: The mean CRP level of the cohort at admission was 55±5.4 mg/dL and 139.2±6.2 mg/dL at the onset of sepsis ($p<0.001$). The mean NLR at admission was 10.64±10.6 and 13.69±14.5 at the onset of sepsis ($p=0.037$). In contrast, the differences in white blood cell, and mean platelet volume values at admission and sepsis onset were not statistically significant ($p>0.05$). Significant correlation was found between CRP and NLR values at both admission ($r=0.365$, $p<0.001$) and at the onset of sepsis ($r=0.261$, $p=0.004$).

Conclusion: We concluded that the NLR is a useful marker in estimating nosocomial sepsis especially when considered together with CRP.

Keywords: nosocomial sepsis, systemic inflammation, inflammatory marker, C-reactive protein, neutrophil to lymphocyte ratio

INTRODUCTION

Sepsis is a systemic inflammatory condition triggered by microbial components. Nosocomial sepsis is classically defined as one which develops in a patient after 48–72 hours of hospital admission and is a significant cause of mortality in critically ill patients (1,2). Blood culture is the standard diagnostic method for sepsis. However, it usually takes 2–5 days to identify the bacterial or fungal growth in blood culture. In addition, the diagnostic sensitivity of a blood culture decreases if antibiotic treatment is initiated before setting up the culture or if the pathogens are slow growing (3). Therefore, other tests such as complete blood counts, biochemical assays, and C-reactive protein (CRP) levels are often conducted simultaneously with blood culture if sepsis is suspected.

Hematological parameters are simple parameters that can be easily calculated from a patient's hemogram. Previous studies showed an association between sepsis and hematological parameters such as neutrophil to lymphocyte ratio (NLR), mean platelet volume (MPV), red cell distribution width (RDW) and platelet distribution width (PDW) (4-7). Among these parameters, NLR was previously found to be useful in discriminating patients with blood stream infection (BSI) from patients without BSI (8). Another study found that it is a superior parameter compared to CRP, white blood cell (WBC) counts and neutrophil counts in predicting bacteremia (9).

Considering the fact that sepsis is a systemic inflammatory condition, we hypothesized that hematological parameters could be altered in nosocomial sepsis, and therefore may be helpful in estimating the onset of nosocomial sepsis. The objective of this study was to determine whether these parameters at the onset of sepsis differed significantly from the baseline levels in nosocomial sepsis patients.

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Table 1: *Characteristics of nosocomial sepsis patients*

Number of patients, n (%)	121 (100)
Age (mean ±SD)	69.8 ±16.2
Gender, n (%)	
Female	47 (38.8)
Male	74 (61.2)
Admission unit	
Intensive care unit	87 (71.9)
Surgical wards	19 (15.7)
Medical wards	15 (12.4)
Sepsis source	
Central venous catheter-related bloodstream infection	36 (29.8)
Bloodstream infection proved in laboratory	85 (70.2)
Risk Factors	
Mechanical ventilation	88 (72.7)
Hemodialysis	39 (32.2)
Hemodynamic instability	72 (59.5)

n- number; SD- standard deviation

METHODS

Patients and Study Design

A retrospective examination was conducted on 121 patients diagnosed with nosocomial sepsis between 01 January 2014 and 30 June 2017 in Bolu Abant Izzet Baysal University Medical Faculty. Sepsis was defined as the presence of two or more qSOFA criteria (10), and positive blood culture results. Nosocomial sepsis was defined as one which develops in a patient after 48–72 hours of hospital admission. Only the first episode of sepsis in any patient was considered for the study so as to prevent confounding effects of other hemogram parameters. Patients with hematological diseases such as hematological malignancies, metastatic bone marrow infiltration by malignancy, immune thrombocytopenic purpura, reactive thrombocytosis or acute bleeding were excluded from the study. The baseline hemogram, NLR, and CRP levels of each patient were obtained at least 72 hours before the onset of sepsis. The same parameters were also obtained at the time of collecting blood for culture. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. Ethical consent was obtained from Bolu Abant Izzet Baysal University ethical committee (Decision number: 2017/154).

Isolation and Identification of the Microorganism from Blood Cultures

Blood cultures were performed in the BACTEC 9240 blood culture system (Becton Dickinson, USA).

Statistical Analysis

SPSS software (SPSS version 15 for Windows; IBM, Chicago, Illinois) was used for statistical analysis. Homogenously distributed variables were expressed as a mean±standard deviation and compared with ANOVA test. Non-homogenously distributed variables were expressed as median (min-max) and compared with Kruskal–Wallis test. Paired samples test was used to determine the difference in the same variable at two different time points. Correlation analysis was conducted using Pearson's correlation. A p value of less than 0.05 was considered statistically significant.

RESULTS

A total of 121 inpatients, 74 male and 47 female, were enrolled in this study. Demographical characteristics of the study cohort are shown in **Table 1**.

The mean CRP level of the cohort at admission was 55±5.4 mg/dL and 139.2±6.2 mg/dL at the onset of sepsis ($p<0.001$). The mean NLR at admission was 10.64±10.6 and 13.69±14.5 at the onset of sepsis ($p=0.037$). As seen in **Table 2**, NLR changes are due mainly to lymphocyte decrease. The mean hemoglobin at admission was 11.8±2.2 gr/dL and 9.8 ±1.5 gr/dL at the onset of sepsis ($p<0.001$). The mean RDW at admission was 16.9%±3.4 and 17.6%±2.7 at the onset of sepsis ($p=0.002$). There were no statistically significant differences in white blood cell, neutrophil and mean platelet volume levels between admission and sepsis ($p>0.05$). Hematological parameters of the study cohort at admission and sepsis are shown in **Table 2**.

Table 2: *Hematological parameters of the study cohort at admission and sepsis (n=121)*

	Baseline parameter	Sepsis parameter	p
	Mean ±SD		
White Blood Cell (kU/l)	11.6 ±6.4	12.06 ±7.7	0.609
Lymphocyte (kU/l)	1.39 ±0.93	1.04 ±0.63	**0.001**
Neutrophil (kU/l)	9.4 ±6.1	10.2 ±7.7	0.277
Hemoglobin (gr/dL)	11.8 ±2.2	9.8 ±1.5	**<0.001**
Red cell distribution Width (%)	16.9 ±3.4	17.6 ±2.7	**0.002**
Mean platelet volume (fL)	8.56 ±1.7	8.8 ±1.9	0.127
C-reactive protein (mg/dL)	55±59.6	139.2±68.9	**<0.001**
Neutrophil to lymphocyte ratio	10.6±10.6	13.6±14.5	**0.037**

SD- standard deviation

Correlation between CRP and NLR values at admission and sepsis were also evaluated, and significant correlation was seen at both admission (r=0.365, p<0.001) and at the onset of sepsis (r=0.261, p=0.004).

DISCUSSION

Sepsis is a systemic inflammatory reaction caused by certain microbial components. Excessive systemic inflammation as a consequence of impaired immune response has been shown to be related to worse outcome in sepsis patients (11,12). So, early diagnosis of sepsis is a very important for patient prognosis and survival.

During a systemic inflammatory response, significant changes are seen in WBC counts that present as neutrophilia and/or relative lymphocytopenia (13). The NLR is a common inflammatory marker that can be easily calculated from complete blood cell counts. As a marker of systemic inflammation, NLR is associated with critical infections such as bacteremia and sepsis (4,5,8,14-20).

Although several studies investigated the role of NLR in sepsis prognosis (5,17-23), few have investigated its role in diagnosing sepsis in adult patients (6,8,18,24). Our study showed that elevation in NLR may be beneficial in estimating nosocomial sepsis in inpatients. Another important finding of this study is the correlation between NLR elevation and CRP elevation at the time of nosocomial sepsis. Elevation in RDW levels at the time of sepsis has also been observed, but this elevation was related with concomitant decrease in hemoglobin levels.

Loonen et al. (8) studied the diagnostic roles of CRP, NLR, procalcitonin, and soluble urokinase plasminogen activator receptor in 140 patients with various bloodstream infections, and concluded NLR to be a cheap, rapid and practical biomarker in differentiating BSI from non-BSI patients. Consistent with this study, we were also able to present NLR as a practical biomarker in estimating blood culture positivity.

Lowsby et al. (4) investigated the role of NLR in 1954 sepsis suspected patients admitted to the emergency department and found that NLR alone was insufficient in predicting bacteremia since the blood cultures were positive in only 270 patients (13.8%). In contrast, we found NLR useful in estimating sepsis, especially in combination with CRP. This may be due to the fact that we evaluated NLR in the same patients at two different time points. The WBC counts in their study were not different among the bacteremic and non-bacteremic patients, which corresponds to our finding that WBC counts did not change at the onset of sepsis compared to baseline values.

Naess et al. (24) also investigated the diagnostic role of NLR in bacterial infections and reported that patients with septicemia had significantly higher NLR compared to patients with other bacterial infections, therefore concluding that NLR can be useful in discriminating between the septicemic and non-septicemic patients. In agreement to this, we also found that NLR increased at the onset of nosocomial sepsis.

Zhang et al. (6) studied the diagnostic value of various hemogram parameters in sepsis and found NLR to be superior in predicting sepsis compared to CRP. They also reported that the predictive value of the combination of RDW, PDW, and NLR was almost equivalent to that of procalcitonin. In our study, we found elevated RDW and decreased hemoglobin levels in nosocomial sepsis, indicating that the two may be correlated. In addition, we found that NLR elevation correlated with CRP elevation in nosocomial sepsis.

There were some limitations in the present study, mainly the retrospective design and the small number of patients. Secondly, concurrent inflammatory conditions such as tumors or collagen vascular diseases were not evaluated. Thirdly, confounding effects of simultaneously used drugs which might affect hemogram results such as corticosteroids were not considered. Fourthly, single measurements of laboratory parameters do not reflect their dynamics. Fifthly, long duration of subjects' enrollment requires correction for seasonal variability of hemogram indexes, and finally, the long-term follow-up data of the patients were missing.

In conclusion, NLR is a simple and practical biomarker which can rapidly be obtained from hemogram. Since, NLR was found to be increased concomitantly with CRP in nosocomial sepsis patients, it can be a useful early indicator of blood culture growth especially for hospitals with limited laboratory facilities. Early detection of nosocomial sepsis will be helpful for optimal management of hospitalized patients.

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