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CLINICAL STUDY

Association between hemogram-derived indices and culture-positive infections in intensive care population

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ABSTRACT

AIM: To investigate the relationship between hemogram parameters and bacterial growth in cultures of blood, urine or sputum in intensive care unit patients.

METHODS: This retrospective, observational, cross-sectional study was conducted in a tertiary referral hospital between March 2015 and December 2017. Baseline demographic and clinical characteristics, hemogram parameters and other laboratory test results of patients admitted to intensive care unit were recorded. Patients were divided into two groups as patients who were infected, and those who did not have any infectious agents grown in the culture dish, and then the groups were compared with each other.

RESULTS: There were no significant differences between the groups in terms of baseline demographic and clinical characteristics. When the groups were compared in terms of hemogram parameters, the neutrophil-to-lymphocyte ratio ($p < 0.001$), platelet-to-lymphocyte ratio ($p = 0.013$), plateletcrit ($p = 0.028$) and mean platelet volume ($p < 0.001$) were significantly higher in infected patients than in non-infected patients.

CONCLUSION: We suggest that neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, plateletcrit, and mean platelet volume could be used as infection markers in the intensive care unit population *(Tab. 1, Ref. 25)*. Text in PDF *www.elis.sk.*

KEY WORDS: hemogram parameters, hospital infection, intensive care unit.

Introduction

Hospital infections globally continue to be the cause of significant mortality and morbidity. Although the capacity of intensive care unit (ICU) accounts for 5–10 % of hospital capacity, ICU infections account for 20–25 % of all hospital infections (1).

Factors causing the susceptibility of infection in ICU patients include underlying comorbid diseases, immunosuppression, malnutrition, intravascular catheter, endotracheal tube, urinary catheter, and application of surgical drainage catheters (2). Since almost 53.6 % of nosocomial infections seen in patients admitted to ICU are mortal, there is a need for prophylaxis and early detection of these infections to be better understood (3).

There are some tests that can estimate the risk of morbidity and mortality in ICUs and predict the prognosis (4). Early diagnosis of systemic inflammatory response at the entrance to ICU is very important in detecting organ failure and subsequent death. There are studies using some hematologic parameters that are affordable and easy to use for achieving early detection of this response (5).

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C-reactive protein (CRP), an acute-phase reactant, is present only in small amounts in the serum of healthy individuals (< 1 mg/dL) and does not show any diurnal variation (6). As with other positive acute-phase reactants, levels of CRP increase in many cases such as acute infections, rheumatologic diseases, inflammatory conditions, malignancies, tissue damage and acute myocardial infarction (7). Recent studies have been focused on using novel and affordable hemogram indices such as inflammatory markers and prognostic predictors as compared with CRP. Platelet count (PLT), mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW) are some of these hemogram indices (8).

In a recent study, red cell distribution width (RDW), another hemoglobin parameter, has been associated with thyroid cancer and thyroiditis (9). Another study suggested that hemogram-derived indices such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were associated with the prognosis in cancer patients (10).

In this present study, we aimed to investigate the relationship between the changes in hemogram parameters and bacterial growth in cultures of blood, urine or sputum in ICU patients.

Materials and methods

The study protocol was approved by the institutional ethics committee, and the study was conducted in accordance with the principles of Declaration of Helsinki. All relevant guidelines and regulations were completely complied with.

Between March 2015 and December 2017, a total of 153 patients who were admitted to the ICU of a tertiary referral hospital were enrolled to this study. Of them, 73 were non-infected while 80 were infected patients. After receiving the approval from the institutional ethics committee, the data of patients were recorded from the institution's computerized database and analyzed retrospectively. According to the *in vitro* culture test results, the patients were divided into two groups, while the first group contained patients who were infected, and the second group was composed of patients who did not have any infectious agents grown in the culture dish. This study had no exclusion criteria.

Laboratory parameters including age, gender, duration of ICU treatment and white blood cell counts, neutrophil count, lymphocyte count, hemoglobin, hematocrit, platelet counts, urea creatinine, aspartate transaminase (AST), alanine transaminase (ALT) and CRP were recorded. In addition, the genus and species information of microorganisms bred in the cultures of infected patients were also recorded. In the analyses, the initial hemogram values that were obtained at the admission to ICU were used. NLR was calculated by dividing the number of neutrophils by the number of lymphocytes. PLR was calculated by dividing the number of platelets by the number of lymphocytes.

The primary endpoint of our study was the NLR value in ICU patients with or without culture positive infections. Sample size estimation was inspired from the study performed by Liao et al (11). In order to detect a 95 % change in NLR value (3.57 ± 3.41 control values in study by Liao et al (11). with an α error of 0.05 and a power of 95 %), we calculated that the sample should have at least 57 patients per group. While estimating an approximate 95 % increase rate, we included 80 patients in the infected group and 73 patients in the non-infected group. The sample size estimation was performed using G Power3 Calculator.

Statistical analyses were performed using SPSS software (SPSS 15.0 for Windows, IBM Co, Chicago, IL, SA). Continuous variables were expressed as median (interquartile range). Categorical variables were expressed in frequency and percent value. The Kolmogorov–Smirnov test was used to evaluate the distribution of variables between the two groups. Mann-Whitney U test was used for non-homogeneous variables. Chi-square test was used for categorical variables. Pearson correlation was used to evaluate the correlation between variables. A p value of less than 0.05 was considered significant.

Results

A total of 153 patients were included in the study, of whom73 (47.7 %) were non-infected and 80 (52.3 %) were infected. The median age of non-infected subjects was 74 (34) years and the median age of the infected individuals was 73 (20) years. The age difference between the two groups was not statistically significant (p = 0.49). There was also no statistically significant gender difference between the two groups (p = 0.19). There were 46 (63 %) males and 27 (37 %) females in the non-infected group and 42 (52.5 %) males and 38 (47.5 %) females in the infected group. The median duration of treatment at ICU was 7 (15) days for non-infected patients and 52 (66) days for infected subjects. The difference was statistically significant (p < 0.001).

Tab. 1. General characteristics and laboratory data of the groups.

Feature/Variable		Non-enfected group	Enfected group	p value
Gender(n)	Male	46 (63%)	42 (52.5%)	0.190
	Female	27 (37%)	38 (47.5%)	
Median (IQR)				
Age, years		74 (34)	73 (20)	0.490
WBC count, u/mm^3		7.9 (4.3)	11.2 (7.2)	**0.005**
Hb, g/dL		11 (3)	9.9 (3)	**<0.001**
Htc, %		35 (10)	30 (9)	**<0.001**
CRP, mg/dl		25 (77)	96 (155)	**<0.001**
Median (IQR)				
ICU stay, days		7 (15)	52 (66)	**<0.001**
RDW, %		17 (3.9)	17 (2.7)	0.594
MPV, fL		7.17 (1.85)	8.69(2.55)	**<0.001**
MCV, fL		89 (7)	88 (8)	0.516
PCT		0.15 (0.1)	0.18 (0.1)	**0.028**
NLR		3.62 (4.9)	7.79 (8.4)	**<0.001**
PLR		0.13 (0.1)	0.2 (0.1)	**0.013**

CRP – C-reactive protein; ICU – intensive care unit; IQR – interquartile range; Hb – hemoglobin; Htc – hematocrit; NLR – neutrophil to lymphocyte ratio; PLR – platelet to lymphocyte ratio; PCT – Plateletcrit; MCV:mean corpusculer volume; MPV:mean platelet volume; RDW – red cell distribution width SD – standard deviation;WBC – white blood cell.
→The quantitative values are presented as number (%) or median (interquartile range).

The median CRP levels of non-infected and infected patients were 25 (77) and 96 (155), respectively (p < 0.001). Urea, creatinine, AST, ALT, calcium (Ca), MCV, RDW, PLT and PDW levels were not significantly different in non-infected subjects compared to the infected patients (their p values were 0.130 for urea, 0.104 for creatinine, 0.114 for AST, 0.470 for ALT, 0.974 for Ca, 0.516 for MCV, 0.594 for RDW, 0.865 for PLT and 0.124 for PDW).

The median MPV values of the non-infected and infected patients were 7.17 fL (1.85) and 8.69 fL (2.55), respectively (p < 0.001). PCT of non-infected and infected subjects were 0.15 (0.1) and 0.18 (0.1), respectively. PCT values were also significantly different between the groups (p = 0.028).

The median NLR values of the non-infected and infected patients were 3.62 (4.9) and 7.79 (8.4), respectively (p < 0.001). The median PLR values of the non-infected and infected patients were 0.13 (0.1) and 0.20 (0.1), respectively (p = 0.013).

In Pearson's correlation test, NLR was correlated with CRP levels (r =.32; p < 0.001). Likewise, MPV was correlated with CRP (r =.38; p < 0.001).

According to the results obtained from the current study, 65 (81.25 %) of the microbial growth in cultures were gram (–) bacteria, 10 (12.50 %) were gram (+) bacteria and 5 (6.25 %) were *Candida albicans*. General characteristics and laboratory data of the study cohort are shown in Table 1.

Discussion

The most important finding of present study is that simple hemogram indices, PCT, MPV, PLR and NLR, are as useful

as CRP levels in selecting infected patients among the ICU population.

The frequent use of invasive diagnostic and treatment procedures at intensive care units, and long hospitalization lead to a high incidence of infections in patients (12, 13). Previously published studies suggest that most of the infections observed in the ICU are gram (–) bacteria (14). Our results are likewise correlated with the findings published in the literature. *Acinetobacter baumannii*, *Staphylococcus aureus* and *Escherichia coli* were identified as the most frequently isolated pathogens in the study by Dikici et al (15). In this present study, the most frequently isolated agents were determined as *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia*e.

It is known that infections in ICU increase mortality and morbidity as well as the duration and cost of the treatment. Recent studies have been focused on certain parameters that predict mortality and morbidity. The main finding in our study is that equally as well as CRP values, the values of NLR, PLR, MPV and PCT obtained from hemogram can be important prognostic markers.

In the inflammatory response, some changes take place in the nearby leukocytes. The nephrotic syndrome is associated with lymphopenia. Zahorec for the first time suggested that NLR may be a marker of the inflammatory response (16). Neutrophilia and lymphopenia were found in trauma and systemic inflammatory response syndrome. In another study, it has been suggested that NLR may be more valuable than other markers in anticipating bacteremia under emergency conditions. NLR has been also shown to be present as a marker in inflammatory diseases (17). In our study, we have reached the conclusion that NLR can be used as an indicator of inflammation by reasoning that NLR was higher in the infected group compared to the non-infected group.

Inflammatory reactions have been shown to increase the platelet count by stimulating megakaryopoiesis (18). Many diseases may cause a deterioration in the volume and function of platelets. The thrombocyte volume is assessed on the basis of mean platelet volume (MPV) (18). Many diseases, including even acute exacerbation of chronic obstructive pulmonary disease, have been investigated for MPV (19). In a recent study by Velioglu et al (20), the authors found a significant association between MPV and peripheral arterial disease. In our study, the MPV value of the infected group was significantly higher compared to the non-infected group. Therefore, we have reached the conclusion that MPV can be used as a marker for inflammatory response.

According to one study, PLR is one of the best markers of inflammatory events. In the present study, we reached the conclusion that NLR and PLR could be used as mortality markers (21). In a recent study, PLR has been shown to be an important prognostic factor in some types of cancer (22). In accordance with the literature, the result of our study suggests that PLR can be used as a prognostic factor in infected patients in the ICU.

In a previous study, it was emphasized that CRP is a reliable prognostic marker in patients in ICU (23). In accord with previous studies, the results obtained from our study also suggest that CRP may be evaluated as a prognostic factor in ICU patients.

One of the platelet indices obtained in the whole blood count is plateletcrit (PCT). It has been suggested that severe inflammation and increased cardiovascular risk are important predictors of the prognosis. In some studies, PCT has been shown to be of value in terms of prognosis in slow coronary flow phenomenon (24), ST segment elevation myocardial infarction (MI) and non-ST segment elevation MI (25). We also found that PCT is high in patients who are infected. This finding suggests that PCT is an important prognostic factor to be evaluated in ICU patients.

The main limitations of present study are its single-centered nature and retrospective design. The third main limitation could lie in the small size of study cohort.

In conclusion, we suggest that similar to CRP values, the values of NLR, PLR, MPV and PCT could be used as infection markers in ICU population.

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