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RESEARCH ARTICLE

Comparison of the Neutrophil Lymphocyte Ratio in the Inflammatory Response with Immigrant and Non-immigrant Critical Patients

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ABSTRACT

Objective: Global mobility has heightened the necessity to addressing racial diversity in healthcare. Recognizing variations that influence diagnosis and treatment can enhance patient outcomes. We aimed to assess if the Neutrophil Lymphocyte Ratio (NLR) reflects inflammation differently in Arab-origin immigrant patients admitted to the Anaesthesia Intensive Care Unit (ICU) compared to non-immigrants.

Materials and Methods: This retrospective, single-center study examined ICU records from January 2011 to January 2014. Patients were categorized as Turkish or Arab immigrants. Exclusions comprised patients under 18, those deceased within 24 hours of admission, malignancy cases, systemic steroid users, and those with immunosuppressive histories. A total of 100 patients over 18 were analyzed.

Results: Of the 100 patients (63 men, 33 women), 49 were immigrants and 51 non-immigrants. No significant differences were found in CRP, neutrophil-lymphocyte count, or NLR upon admission. However, CRP and neutrophil counts differed significantly on culture-positive days ($p<0.005$). NLR did not significantly vary between the groups on culture-positive days.

Conclusion: No substantial association was observed between NLR levels in critically ill Arab-origin immigrants versus non-immigrants in the ICU. Larger studies and detailed genetic analyses are warranted to inform critical patient care.

Keywords: Inflammation, genetic, neutrophil-lymphocyte ratio

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INTRODUCTION

Changing political balances around the world, business, tourism, increased communication and travel opportunities have led to an increase in individual and mass human mobility. Especially, the rising wave of migrations toward Europe presents many questions and problems for health. [1] Although interaction between health systems is fast and advanced, the ethnic or environmental factors of country-changing people through migration may differ in their diagnosis and treatment processes.

The inflammatory response has been shown to vary between races in previous studies.[2,3] Ratiani et al.[4] emphasized in their analysis of sepsis that differences in mortality and morbidity may depend on racial and ethnic characteristics.

In the intensive care units, various laboratory parameters and indexes are used to determine prognosis and in the follow-up. [5–7] In the last two decades, the Neutrophil Lymphocyte Ratio (NLR) has been a frequently researched parameter in the detection of inflammation. In intensive care practice, the ratio of these two subgroups to each other is used as an inflamma-

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tion indicator, as the physiological response to the stress of the circulating lucidities causes an increase in the number of neutrophils and a decrease in the number of lymphocytes.[8–10]

It is a known fact that the immune response and inflammation are controlled by genes. Human leukocyte antigen (HLA) genes are one of the most polymorphic genes, and their lymphocyte functions show polymorphism genetically. [11] While there are studies that show that genetic control of T lymphocyte functions is different in different groups, NLR is likely to be affected by genetic diversity.

In this study, we aimed to compare the NLR in the evaluation of inflammatory responses in two groups of patients with different ethnicities.

MATERIALS and METHODS

Our study is a single-center, observational, retrospective cohort study. This study was approved by the local ethics committee and was conducted in accordance with the Helsinki Declaration. Institutional ethics board approval has been obtained (08.03.2017/448). The records of patients who were in intensive care unit between January 2011 and January 2014 were analyzed. A total of 100 patients were included in the study. Patients under the age of 18, those who died within the first 24 hours, malignity patients, those who use systemic steroids, and immunosuppressive cases were excluded.

Primarily, patients were divided into two groups as Turkish (Group 1) and immigrants (Group 2). The age, gender, diagnosis, comorbidity, application features, complete blood count and CRP values of Turkish patients with bacteremia, and Arab migrants who have had to migrate to Türkiye due to war and have bacteremia were recorded. The results of the patients' tracheal, urine, blood and other material samples and the antibiotherapy reports were analyzed. The antibiotics that the patients used after the antibiogrammes were also recorded.

Statistical Analysis

SPSS 20 (SPSS Inc., Chicago, IL, USA) package program was used for statistical analysis. Descriptive statistics were given as numbers and percentage for categorical variables; and as mean, standard deviation, median for numerical variables. The comparison of numerical variables in the two independent groups was made by the Student t Test when the normal distribution condition was met, and the Mann Whitney U test was performed when the normal distribution condition was not met. In independent groups, the ratio was compared with Chi Square Analysis. The level of statistical significance was accepted as $p<0.05$.

RESULTS

The average age of non-migrant patients (n=51) was 56.9±16.8 (20–93). 60.8% (n=31) of patients were men and 39.2% (n=20) were women. In 100% of patients (n=51), there was a comorbidity. The average age of migrant patients (n=49) was identified as 54.7±17.6 (19–83). 65.3% of migrant patients (n=32) were men and 34.7% (n=17) were women. In 97.9% of migrant patients (n=48), there was a comorbidity (Table 1).

In the analyzed blood, sputum and urine cultures of the migrant patients, the most common (42.8%) (n=21) positivity was seen in the sputum culture. The most identified microorganism was Acinetobacter Baumanii while Pseudomonas Aeroginosa, Klebsiella Pneumonia and Methicillin Resistance Staf Aerius were also isolated.

As antibiotherapy, it was often found that Meropenem and Moxyfloxacin were used, however, Ampicillin-Sulbactam, Ceftriaxone, Piperacillin Tazobactam, Colistin, Teicoplan and Tigecycline were seen to be used as well.

In the blood, sputum and urine cultures of non-migrant patients, the most commonly identified microorganism 56.9% (n=29) was Acinetobacter Baumanii, while Psodomonas Aeroginosa, Klebsiella Pnomonia and MRSA were also isolated.

In the antibiotherapies, Meropenem and Ampiciline Sulbactam were seen often, while moxyfloxin, cheftriakson, piperasiline tazobactam, colistin, teicoplanin and tigesicillin were also seen to be used.

Table 1. Characteristics of the study group

	Group 1 (%)	Group 2 (%)	p
Age (mean±SD)	56.9±16.8	54.7±17.6	>0.05
Gender			>0.05
Male	31	32	
Female	20	17	
HT	59.2	64.7	>0.05
DM	55.1	51	>0.05
CAD	22.4	24.4	>0.05
COPD	20.4	18.4	>0.05
CRF	10.2	9.8	>0.05
CVA	10.2	12.2	>0.05
CHF	10.2	9.8	>0.05

Data are presented as percentage, mean standard deviation or median (interquartile range). SD: Standard deviation; HT: Hypertension; DM: Diabetes mellitus; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; CRF: Chronic renal failure; CVA: Cerebra vascular accident; CHF: Congestive heart failure

Table 2. Differences between the two groups on the hospitalization and the culture positive day of inflammatory markers

	Immigrant	Non-immigrant	p
	Mean±SD	Mean±SD	
Initial			
CRP	97±84.9	76.1±68.7	0.190
Neutrophil	11.1±6.2	12±16.2	0.206
Lymphocyte	1.4±1.1	1.38±1.54	0.370
NLR	12.2±10.9	13.9±27.7	0.975
Culture positive day			
CRP	135.8±69	193.5±60	**<0.001**
Neutrophil	12.1±8	9.6±5.3	**0.047**
Lymphocyte	1.34±0.9	1.07±0.65	0.312
NLR	11.9±10	12.5±14.7	0.632

SD: Standard deviation; NLR: Neutrophil lymphocyte ratio; CRP: C-reactive protein

While there was no statistically significant difference between the CRP, the number of neutrophils-lymphocytes and the NLR values on the day of hospitalization of migrant and non-migrant patients, there was a significant difference in the number of CRP and neutrophils on the culture-positive day ($p<0.05$). It was seen that there was no statistically significant difference between the two groups on the culture-positive day of infectious inflammation in NLR (Table 2).

DISCUSSION

In our study, while NLR values of critical patients admitted to the ICU were found to be high in accordance with reproduction, no statistical significance was determined between NLR values of migrant and non-migrant patients. Our results suggest that neutrophil activation has not changed in critical patients due to genetic differences. Although many diseases have been mentioned in the literature that NLR has a significant role in inflammation, this study is one of the few studies that investigates whether genetic differences affect neutrophil activation.

Although CRP, WBC, neutrophil and procalcitonin levels are often used as an infection marker, NLR has recently been used as biomarker in many diseases.[12,13] When de Jager et al.[14] compared 48 patients with bacterial disease community-acquired with the healthy group, they determined that NLR is a good indicator of detecting bacteria. They also argued that lymphocytopenia is an important indicator of community-acquired pneumonia bacteria. In a broader study conducted by the same group, they evaluated 395 patients, again with community-acquired pneumonia, and compared their neutrophil numbers, leukocytes and CRP levels with NLR. In their study, they found that NLR is more sensitive in determining community-acquired pneumonia from neutrophils, leukocytes and CRP levels. NLR was found to be higher in patients with a higher CURB-65 ratio. NLR of patients who have positive blood cultures, who have been in the hospital for a long time and who have died has been detected as higher.[15] In our study, NLR was found to be high in patients with positive blood cultures.

NLR also increases in all cases of infection and inflammation. From appendicitis to coronary artery bypass surgery, it increases in many cases.[16–20] In our study, NLR was found to be high because both infection and inflammation are present in critical patients hospitalized in the intensive care unit.

NLR can also be used as an early infection indicator in emergency services. In the study of Lowsby et al.,[21] according to the NLR ratios of 270 patients who had positive blood cultures from 1954 patients who applied to the hospital, they determined that it is beneficial for patient management, mortality and morbidity determination. They also argued that NLR is superior to the number of leukocytes and CRP.

In light of all these studies, as we have determined in our study, NLR is expected to increase in critical patients who are hospitalized in intensive care units and have positive blood cultures. The difference of our study from other studies was to investigate whether the genetic structure

had an impact on NLR. The study of Rimando et al.[22] in this matter supports the results of our study. In this study, the effect of NLR was evaluated in determining the mortality of 236 black and 225 white patients with breast cancer; however, it was found that the genetic difference was not related to NLR.

Misumida et al.[23] compared African-Americans with white-race patients who applied with non-ST elevated myocardial infarction and reported that the NLR value in Afro-Americans was significantly lower. In our study, the Arab immigrants who had to migrate to Türkiye for the cause of the war and have bacteria and Turkish patients with bacteria were compared and no difference was found between them. The main reason for this may be that the two groups are genetically different but white.

The Benign Ethnic Neutropenia is the low number of asymptomatic neutrophils seen in different ethnic groups. The frequency is 4.5% in African-Americans, while it is 0.8% in the white race.[24] The low number of neutrophils in isolation also causes NLR to be low. In a similar way, we think that large-volume studies should be performed on different ethnicity patients to detect new cut-off values, given that different rates may arise in different races.

Limitations

Firstly, our number of patients is limited, due to the low patient capacity of our intensive care unit and our study is not multi-centered. In our study, it is also another limitation that only the NLR levels of patients were analyzed and they have not been associated with mortality or prognosis. The fact that the genetic characteristics of the patients were not investigated since our study is retrospective, is another lack. While no relationship between NLR and ethnic origin was found due to these limitations, we believe that there may be significant differences in the NLR response to inflammation in the prospective studies with larger patient groups.

CONCLUSION

In our study, no statistical significance was found in the NLR values among critical patients admitted to the intensive care unit due to genetic differences. While NLR is noted to play a significant role in inflammation in many diseases in the literature, this study is one of the few investigating whether genetic differences affect neutrophil activation. As a result, while our study contributes to the increasing literature on NLR dynamics in critical patients, it also highlights the complexities inherent in elucidating the interplay between genetic factors and inflammatory biomarkers.

Disclosures

Ethics Committee Approval: The Haseki Training and Research Hospital Clinical Research Ethics Committee granted the decree that no ethics committee approval needed for this retrospective study (No: 448, Date: 08/03/2017).

Authorship Contributions: Concept: M.K.; Design: İ.A.; Supervision: M.T.; Materials: M.Ş.; Data Collection or Processing: M.K., İ.A.; Analysis or Interpretation: M.Ş.; Literature Search: M.K., İ.A., M.T.; Writing: M.K., A.Y.; Critical review: S.Y., H.N.E.

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Informed Consent: Written informed consent was obtained from all patients.

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