

# Association Between Neutrophil-to-Lymphocyte Ratio and Mortality in Neurological Intensive Care Unit Patients

Muhammed Nur Ogun<sup>1</sup> and Elif Yaksi<sup>2</sup>

*Department of Neurology<sup>1</sup>/Physical Therapy and Rehabilitation<sup>2</sup>, Faculty of Medicine, Abant Izzet Baysal University, Bolu, Turkey*

## ABSTRACT

**Objective:** To investigate the effect of neutrophil-lymphocyte ratio (NLR) on survival and mortality in patients who were interned in the Neurology Intensive Care Unit (NICU).

**Study Design:** A cohort study.

**Place and Duration of Study:** Tertiary referral hospital in Bolu, Turkey, between February 2016 and November 2017.

**Methodology:** Demographic data, hemogram and other laboratory parameters of the patients who were treated in NICU were retrospectively recorded. The patients who had a history of hematologic disease and/or premorbid use of corticosteroids were excluded from the study. Patients were divided into two groups: surviving and dead patients. Mann-Whitney U-test, Independent sample t-test or Chi-square test was used to compare the data between the groups, including demographic parameters, NLR and other blood parameters.

**Results:** A total of 120 patients were studied. There was no significant difference in age, gender, hemoglobin (Hb), platelet (PLT), and erythrocyte distribution width (RDW) between the two groups. On the other hand, The NLR values [(3.9 (0.9-48) vs. 11.9 (0.9-69, p <0.001)], C-reactive protein [CRP=(25.6 mg/dL (0.1-250) vs. 57.7 mg/dL (1.2-337, p <0.002)] and white blood cell [WBC=(8.9  $\mu$ mm<sup>3</sup> (3-59.8) vs. 12.4  $\mu$ mm<sup>3</sup> (5-41.3, p <0.002)] were significantly higher in dead patients compared to survived patients.

**Conclusion:** Elevated NLR ratio in NICU patients may be considered as a poor prognostic factor. Clinicians should be more cautious in the follow-up of these patients.

**Key Words:** Mortality, Neuro-ICU, Neutrophil to lymphocyte ratio.

**How to cite this article:** Ogun MN, Yaksi E. Association between neutrophil-to-lymphocyte ratio and mortality in neurological intensive care unit patients. *J Coll Physicians Surg Pak* 2019; **29(10)**:919-22.

## INTRODUCTION

Intensive care units (ICUs) are specially designed units where life-threatening organ deficiencies seen during the course of acute and chronic diseases are treated and monitored. Health personnel working in intensive care units consist of specially trained individuals. All-cause mortality rates are higher in ICUs than other services.<sup>1</sup> Neurological intensive care units (NICUs) are designed to provide special care for patients with acute neurological and neurosurgical illnesses such as intracranial pressure elevation, subarachnoid hemorrhage and status epilepticus.<sup>2</sup> Patients in the ICU have higher morbidity and mortality risks due to underlying disease, acute lung injury, and critical illness syndromes such as sepsis.<sup>3</sup> It is very important to determine the prognosis of these patients.

In recent years, some laboratory parameters are thought to be used as a reliable and cost-effective method of

showing inflammation and survival. Neutrophil-to-lymphocyte ratio (NLR), calculated by dividing the absolute lymphocyte count by absolute neutrophil count, is an easily applicable biomarker to assess inflammatory status.<sup>4,5</sup> The normal values of NLR vary between 0.78 and 3.53, depending on age and race.<sup>6,7</sup> According to recent studies, NLR serves as a stronger inflammatory marker than neutrophils or lymphocyte itself.<sup>8</sup> It has been shown that the NLR is an important predictor of poor clinical outcome in various diseases, such as cardiovascular disease, cancer, infectious disease and ischemic stroke.<sup>9-12</sup> The white blood cell (WBC) count is a clinical biomarker of systemic inflammation and a powerful prognosticator of mortality. Acutely, the WBC is increased by infection and other stressors and chronically by toxic or irritative exposures. As WBC count is a nonspecific marker, it can be used to predict risk for several diseases.<sup>13</sup> Elevation in WBC count is shown to be associated with all-cause of mortality as well as cerebrovascular diseases, cardiovascular diseases, and cancer.<sup>14-16</sup> In clinical practice, count of WBC is the most commonly used marker for systemic inflammation. However, it is considered that C-reactive protein (CRP) is the most valuable diagnostic marker predicting mortality. In several studies, an increased

*Correspondence to:* Dr. Muhammed Nur Ogun, Department of Neurology, Faculty of Medicine, Abant Izzet Baysal University, Golkok Campus, 14280, Bolu, Turkey  
E-mail: dr.mogun@gmail.com

*Received: December 17, 2018; Revised: June 04, 2019;*

*Approved: June 27, 2019*

CRP level found to be associated with higher vascular and nonvascular mortality risk in elderly patients.<sup>16,17</sup>

In this study, the aim was to evaluate the admission NLR and hemogram parameters of NICU patients, and determine the difference between survived and dead patients in terms of those parameters.

## METHODOLOGY

This cohort study includes 120 patients who were treated in NICU, between February 2016 and November 2017. Based on the data of a previous study,<sup>17</sup> a total of 110 patients were required to achieve  $\alpha <0.05$ , and  $1-\beta=0.80$ . All patients admitted to the NICU were included in the study except those who had a history of hematologic disease and/or premorbid use of corticosteroids which would affect the distribution of WBC.

After approval from the local editorial board of Bolu Abant İzzet Baysal University, demographic data, hemogram and other laboratory parameters of the patients were retrospectively recorded. Patients were divided into two groups: surviving patients and dead patients. Age, gender, number of comorbid diseases (hypertension, diabetes, congestive heart failure, cancer, ischemic or hemorrhagic stroke, coronary artery disease, and chronic renal failure), length of stay in NICU (days) and initial laboratory data on admission were recorded. Laboratory and hemogram parameters included WBC, hemoglobin (Hb), hematocrit (Htc), red cell distribution width (RDW), platelet (Plt), mean platelet volume (MPV), CRP and plasma glucose levels. For all statistical analysis, statistical software package 15.0 for Windows (SPSS) was used. The homogeneous distribution was expressed as mean and standard deviation (SD) and the independent sample t-test was used to compare parameters between the groups. The group with no homogeneous distribution was noted as median (maximum- minimum) and the Mann-Whitney U-test was used for comparison. To compare categorical variables, Chi-square test was used. A p-value of lower than 0.05 was considered as statistically significant. Power analysis was performed using the statistical software G\*Power.

## RESULTS

One hundred, and twenty patients were included in the current study. Twenty-eight of these patients died and 92 of them survived during follow-up in the NICU. Mean ages of the survived and dead patients were 74.5 (1-96) and 74.5 (61-90) years, respectively. Of the 92 survived patients, 45 were males. Fourteen of 28 patients who died during the follow-up were males. There was no any significant difference between the dead and survived groups terms of gender ( $p = 0.920$ ) and existing of comorbid disease ( $p = 0.951$ , Table I). The length of hospital stay was 4 (1-85) in the survived group and 7 (1-57) days in the dead group. The difference between the two groups in terms of hospital stay (days) was

**Table I:** General characteristics of the groups.

	Dead (n:28)	Survived (n:92)	p-value
Gender n (%)			
Male	14 (50)	45 (49)	0.920
Female	14 (50)	47 (51)	
Comorbidities n (%)			
Present	9 (33)	63 (68)	0.951
Absent	19 (67)	29 (32)	
Median (minimum-maximum)			
Age, years	74.5 (61-90)	74.5 (19-96)	0.260

**Table II:** Comparison of admission laboratory data between the groups.

	Dead (n:28)	Survived (n:92)	p-value
	Median (minimum- maximum)	Median (minimum- maximum)	
Duration of ICU, days	7 (1-57)	4 (1-85)	0.001
PLT, $\mu$ /mm <sup>3</sup>	197 (103-445)	229 (46.9-572)	0.170
Plasma glucose, mg/dL	146 (65-401)	113 (39-394)	0.001
C-reactive protein, mg/dL	57.7 (1.2-337)	25.6 (0.1-250)	0.002
NLR	11.9 (0.9-69)	3.9 (0.9-48)	<0.001
WBC, $\mu$ /mm <sup>3</sup>	12.4 (5-41.3)	8.9 (3-59.8)	0.002
RDW, %	17 (14.5-22.1)	16.5 (12.4-26.5)	0.195
MPV, fL	8.4 (1.7)	8.5 (1.5)	0.533
	Mean (SD)	Mean (SD)	
Hb, g/dL	11.9 (2.4)	12.4 (2.3)	0.401
Htc, %	36.4 (7.4)	37.6 (6.8)	0.442

Abbreviations: Hb: hemoglobin; Htc: hematocrit; ICU: intensive care unit; MPV: mean platelet volume; PLT: platelet count; RDW: red cell distribution width; NLR: Neutrophil to Lymphocyte Ratio; SD: standard deviation; WBC: white blood cell count. Note: A bold value signifies  $p < 0.05$ .

significant ( $p = 0.001$ ). No significant difference was found between the two groups in hemoglobin, hematocrit, red cell distribution width, platelet count, and mean platelet volume ( $p > 0.05$ ). The NLR was found to be 3.9 (0.9-48) in the survived group and 11.9 (0.9-69) in the dead group; and the difference between the two groups was significant ( $p < 0.001$ ). The WBC values were found to be 8.9  $\mu$ /mm<sup>3</sup> (3-59.8) in the survived group and 12.4  $\mu$ /mm<sup>3</sup> (5-41.3) in the dead group, and the difference between the two groups was significant ( $p = 0.002$ ). C-reactive protein values were found to be lower in the survived group, 25.6 mg/dL (0.1-250), than in the dead group, 57.7 mg/dL (1.2-337), and the difference was also significant ( $p = 0.002$ ). Plasma glucose levels were found lower in the survived group 113 mg/dL (39-394) than in the dead group 146 mg/dL (65-401) and this difference was significant ( $p = 0.001$ , Table II). There was no significant difference regarding the NLR values between the patients who had comorbid disease and those who had no comorbid disease [(4.4 (0.9-32.3) and 4.8 (0.9-69.1) respectively,  $p=0.475$ )]

## DISCUSSION

The results of this study showed that a high NLR value was associated with mortality and could be considered a predictor of survival in neurological ICU patients. Additionally, CRP, plasma glucose levels, WBC count and prolonged ICU stay were found to be associated with mortality.

Prolonged ICU stay after transcatheter aortic valve replacement has been found to be associated with worse short- and long-term outcomes and increased mortality in a report by Hiquchi *et al.* Patients with prolonged ICU stay had worse long-term survival and a predictor of mortality.<sup>18</sup> In another study, prolonged ICU stay was found to be associated with a worse clinical course and decreased overall survival.<sup>19</sup> Consistent with the literature, we found the median value of ICU stay significantly higher in dead patients compared to survived patients.

A limited number of studies have evaluated NLR in neurological diseases. In several studies, it has been shown that elevated NLR is a significant predictor of poor outcomes in patients with ischemic stroke.<sup>20</sup> Tao *et al.* reported that higher NLR were independently associated with mortality and worse outcome. Elevated NLR were independently related to poor 90-day outcome after intracerebral hemorrhage (ICH). It was suggested that NLR may be a novel inflammatory biomarker following ICH.<sup>21</sup> In another study, it was found that non-surviving patients with ICH had significantly higher NLR values than survived patients. Mortality was found to be significantly higher in patients with NLR values of 7.35 and above. Additionally, it was stated that NLR could be used as a predictor of 30-day outcome.<sup>7</sup> Similar to these reports, we found a significant association between higher NLR and increased mortality rate.

The WBC is a widely accepted predictor of prognosis and mortality of disease due to the fact that it indicates the host's response level to stressors and ensures an indicator for acute and also chronic inflammatory processes. Jee *et al.* reported that WBC and CRP levels are independent predictors of mortality in the older ages.<sup>13</sup> In several studies, it has been shown that an increased CRP level in elderly patients predicts increased mortality risk.<sup>15</sup> Consistent with literature, the present study confirmed these reports by demonstrating higher CRP and WBC levels in dead patients compared to survived patients.

Krinsley *et al.* reported that tight glycemic control was associated with decreased mortality in a heterogeneous critically ill adult patient population.<sup>22</sup> In our study, we also found significantly higher plasma glucose levels in unsurviving group.

Relatively small sample size and retrospective design are the limitations of this study. These limitations may cause difficulty for interpretation of the results. However, to authors' knowledge, it is the first study that investigated the relation between mortality and hemogram parameters in neurological ICU patients.

## CONCLUSION

In NICU patients, the NLR counted from the CBC parameters obtained at the time of hospital admission may

be a predictor of mortality. We consider that randomised controlled studies should be carried out in NICU patients in order to investigate the mortality prediction strength of NLR due to the fact that hemogram analysis is a routinely used and inexpensive test.

## ETHICAL APPROVAL:

Ethical aproval from the Local Ethical Committee of Bolu Abant Izzet Baysal University was obtained before the study commenced.

## PATIENTS' CONSENT:

All patients were informed about the study and a written informed consent was obtained from each patient.

## CONFLICT OF INTEREST:

Authors declared no conflict of interest.

## AUTHORS' CONTRIBUTION:

MNO, EY: The design and conduct of the study.

## REFERENCES

1. Unal AU, Kostek O, Takir M, Caklili O, Uzunlulu M, Oguz A. Prognosis of patients in a medical intensive care unit. *North Clin Istanbul* 2015; **2**:189.
2. Gold C, Mayer S, Lennihan L, Claassen J, Willey J. Unplanned transfers from hospital wards to the neurological intensive care unit. *Neurocrit Care* 2015; **23**:159-65.
3. Kim MM, Barnato AE, Angus DC, Fleisher LF, Kahn JM. The effect of multidisciplinary care teams on intensive care unit mortality. *Arch Intern Med* 2010; **170**:369-76.
4. Moreau N, Wittebole X, Fleury Y, Forget P, Laterre PF, Diego CZ. Neutrophil-to-lymphocyte ratio predicts death in acute-on-chronic liver failure patients admitted to the intensive care unit: A retrospective cohort study. *Shock* 2018; **49**:385-92.
5. Wang F, Hu S, Ding Y, Ju X, Wang L, Lu Q, *et al.* Neutrophil-to-lymphocyte ratio and 30-day mortality in patients with acute intracerebral hemorrhage. *J Stroke Cerebrovasc Dis* 2016; **25**: 182-7.
6. Forget P, Khalifa C, Defour J-P, Latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? *BMC Res Notes* 2017; **10**:12.
7. Azab B, Camacho-Rivera M, Taioli E. Average values and racial differences of neutrophil lymphocyte ratio among a nationally representative sample of United States subjects. *PLoS One* 2014; **9**:e112361.
8. Sun Y, You S, Zhong C, Huang Z, Hu L, Zhang X, *et al.* Neutrophil to lymphocyte ratio and the hematoma volume and stroke severity in acute intracerebral hemorrhage patients. *The American journal of emergency medicine*. 2017; **35**:429-33.
9. Bhat T, Teli S, Rijal J, Bhat H, Raza M, Khoueiry G, *et al.* Neutrophil to lymphocyte ratio and cardiovascular diseases: A review. *Expert Rev Cardiovasc Ther* 2013; **11**:55-9.
10. Mei Z, Shi L, Wang B, Yang J, Xiao Z, Du P, *et al.* Prognostic role of pretreatment blood neutrophil-to-lymphocyte ratio in advanced cancer survivors: A systematic review and meta-analysis of 66 cohort studies. *Cancer Treat Rev* 2017; **58**:1-13.

11. Chandrashekara S, Renuka P, Anupama K, Renuka K. Characterization of neutrophil-to-lymphocyte ratio as a measure of inflammation in rheumatoid arthritis. *Int J Rheum Dis* 2017; **20**: 1457-67.
12. Suh B, Shin DW, Kwon H-M, Yun JM, Yang H-K, Ahn E, et al. Elevated neutrophil to lymphocyte ratio and ischemic stroke risk in generally healthy adults. *PLoS One* 2017; **12**: e0183706.
13. Jee SH, Park JY, Kim H-S, Lee TY, Samet JM. White blood cell count and risk for all-cause, cardiovascular, and cancer mortality in a cohort of Koreans. *Am J Epidemiol* 2005; **162**: 1062-9.
14. Ruggiero C, Metter EJ, Cherubini A, Maggio M, Sen R, Najjar SS, et al. White blood cell count and mortality in the Baltimore longitudinal study of aging. *J Am Coll Cardiol* 2007; **49**:1841-50.
15. Willems JM, Trompet S, Blauw GJ, Westendorp RG, de Craen AJ. White blood cell count and C-reactive protein are independent predictors of mortality in the oldest old. *Biomed Sci Med Sci* 2010; **65**:764-8.
16. Brown DW, Giles WH, Croft JB. White blood cell count: An independent predictor of coronary heart disease mortality among a national cohort. *J Clin Epidemiol* 2001; **54**:316-22.
17. Karagoz I, Aktas G, Yoldas H, Yildiz I, Ogun MN, Bilgi M, et al. Association between hemogram parameters and survival of critically ill patients. *J Intensive Care Med* 2019; **34**: 511-3.
18. Higuchi R, Takayama M, Hagiya K, Saji M, Mahara K, Takamisawa I, et al. Prolonged intensive care unit stay following transcatheter aortic valve replacement. *J Intensive Care Med* 2017; 0885066617732290.
19. Joskowiak D, Kappert U, Matschke K, Tugtekin S. Prolonged intensive care unit stay of patients after cardiac surgery: Initial clinical results and follow-up. *Thorac Cardiovasc Surg* 2013; **61**:701-7.
20. Giede-Jeppe A, Bobinger T, Gerner ST, Sembill JA, Sprügel MI, Beuscher VD, et al. Neutrophil-to-lymphocyte ratio is an independent predictor for in-hospital mortality in spontaneous intracerebral hemorrhage. *Cerebrovasc Dis* 2017; **44**:26-34.
21. Tao C, Hu X, Wang J, Ma J, Li H, You C. Admission neutrophil count and neutrophil to lymphocyte ratio predict 90-day outcome in intracerebral hemorrhage. *Biomark Med* 2017; **11**: 33-42.
22. Krinsley JS, editor. Effect of an intensive glucose management protocol on the mortality of critically ill adult patients. Mayo Clin Proc 2004; Elsevier.

.....★.....