Research Article
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Can blood groups, neutrophil-lymphocyte ratio and mean platelet volume predict mortality in critically ill patients developing acute kidney injury?

Abstract

Introduction and Aim: Acute kidney injury (AKI) in the recent years, is one of the main causes of morbidity and mortality in critically ill patients. Neutrophil lymphocyte ratio (NLR) is a novel and practical indicator of inflammation, and its effectiveness has been demonstrated in many diseases.

Material and Method: We retrospectively reviewed the medical records of totally 300 patients diagnosed with AKI, admitted to our intensive care unit between January 2010 and December 2017. As laboratory parameters, blood urea nitrogen (BUN) and creatinine levels, and glomerular filtration rate (GFR) as calculated according to MDRD formula were assessed both on the first day (BUN1, Cre1, GFR1) and last day (BUN2, Cre2, GFR2) of admission. C-reactive protein (CRP) level, white blood cell (WBC) count, neutrophil, lymphocyte and platelet values, mean platelet volume (MPV) and neutrophil lymphocyte ratio (NLR) were recorded.

Results: There was no association of blood groups with mortality or with other laboratory parameters (respectively p=0.986, p=0.456, p=0.872 all values not significance p>0,05). There was no statistically significant relationship of MPV value with mortality (p=0,314). Statistically, NLR showed very strong association with both mortality and AKI development (respectively p<0.0001, p<0.0001). There was also very strong association between mortality and other laboratory parameters (BUN1, BUN2, GFR1, GFR2, WBC, Platelet, NLR; all p<0.0001).

Conclusion: MPV and blood groups are not predictors of mortality in critically ill patients. The change in NLR can be an important follow-up parameter to predict survival of critically ill patients. As NLR increases, so does the rate of intensive care mortality and AKI risk.

Keywords: acute kidney injury, neutrophil-lymphocyte ratio, mean platelet volume, blood group, mortality

Volume 8 Issue 1 - 2017

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Received: May 08, 2017 | **Published:** May 17, 2017

Introduction and aim

Acute renal failure (ARF) is described as deterioration of renal functions where elimination of nitrogen waste products (urea) is restrained and body's fluid-electrolyte balance is impaired as a result of sudden decrease in glomerular filtration rate within hours to days. Since there is no complete biochemical definition of ARF, more than 35 definitions have been proposed so far. ARF is a conventional term that is frequently used for patients admitted to intensive care unit due to acute dialysis requirement. However, evidence shows that even a minimal decline in renal function has profound effect on mortality and morbidity.[1,2] For this reason, the term ARF has been replaced by the term "acute kidney injury" (AKI) that was proposed by Acute Kidney Injury Network.[3] Despite all the advanced life-support systems and treatment options, AKI is still an important cause of mortality and morbidity for patients monitored in intensive care units (ICU). Epidemiological data regarding AKI varies greatly in the literature. While its prevalence varies between 1-31%, associated mortality rates are between 28-82%.[4,5] The reason for this wide range is the difference between the criteria used to diagnose AKI. The most frequent cause of AKI in patients admitted to ICU is sepsis and septic shock. AKI occurs in various degrees and is generally progressive, and it is often described as a syndrome due to these properties. Although it is potentially reversible, AKI is an important cause of chronic renal failure. AKI frequently accompanies other severe diseases, and causes significant increases in mortality and morbidity rates. The prevalence of AKI among patients monitored in ICU is 1-25%, and 5% of these patients require dialysis.[6-8]

Systemic inflammatory response is associated with changes in white blood cell count in the peripheral blood, especially neutrophilia that is seen concurrent with relative lymphocytopenia.[9] Neutrophil lymphocyte ratio (NLR) is a practical, repeatable and inexpensive marker that can be used in assessment of systemic inflammation.[10] Mean platelet volume (MPV) is an indicator of platelet function and activation.[11] While children and young adults have higher MPV values, MPV does not vary between the sexes.[12] Increased MPV is an indicator of megakaryocytic enlargement occurring as a response to thrombopoietic stress. Large platelets can be defined as stress-platelets. MPV is increased when there is increased destruction of peripheral platelets, and is decreased when there is impairment of platelet production.[13] Since larger platelets are more reactive, MPV is regarded as an indicator of increased cardiovascular disease risk in the general population. Several studies have shown MPV as an indicator for atherosclerotic diseases.[14] In addition to atherosclerosis, platelet volume is also increased in the presence of atherosclerotic risk factors including hypertension, hyperlipidemia, diabetes mellitus, end-stage renal disease and obesity.[14-16]

Blood groups were discovered in the 19th century, and they are kind of cellular identity that is determined by the antigenic structure present on the surface of red blood cells. The blood group system discovered by Landsteiner is the general blood group system that is known as the ABO blood groups. Another commonly used blood grouping system is known as the Rh system, and depends on the presence or absence of this antigenic structure. ABO and Rh blood group system is currently most commonly used grouping system used

today. Nevertheless, many blood group systems have been developed in addition to the ABO and Rh system, and many studies have been conducted on this subject. Numerous studies from different fields have examined the importance of blood group systems in tissue and organ transplantations and the genetic basis of blood groups.[17] Regarding the diseases associated with mortality, early detection and diagnosis have utmost significance in terms of treatment success. Diseases that are considered as causes of mortality in especially the developed countries include cancers and cardiovascular diseases, which are thought to have a genetic background. The treatment of these diseases is quite cumbersome and expensive. Despite all the troubles and long treatment processes, it is not possible to completely cure these diseases. Nonetheless, as stated before, early diagnosis is very important regarding the course and treatment of these diseases. Considering all these reasons, it is important to investigate the relationship between some common diseases and the blood groups as they are very easily detectable genetical properties that are free from the influence of environmental factors.[17,18]

In this retrospective study, we aimed to investigate the relationship between mortality and blood groups, neutrophil lymphocyte ratio (NLR) and mean platelet volume (MPV) in critically ill patients developed AKI, additionally to determine whether NLR and MPV have predictive value regarding AKI development.

Material and methods

Following approval from Ordu University Clinical Studies Ethics Committee (Issue Nr:2016-14), medical records of 300 patients admitted to General Intensive Care Unit of Ordu University Training and Research Hospital and diagnosed with AKI were reviewed. Demographical properties (age, weight, height, sex) of all patients were recorded. Diagnosis at admission, accompanying comorbidities, whether mechanical ventilation was applied, whether the case was discharged or deceased, were noted for every case.As laboratory parameters, blood urea nitrogen (BUN) and creatinine levels, and glomerular filtration rate (GFR) as calculated according to MDRD formula were assessed both on the first day (BUN1, Cre1, GFR1) and last day (BUN2, Cre2, GFR2) of admission. C-Reactive Protein (CRP) level, white blood cell (WBC) count, neutrophil, lymphocyte and platelet values, mean platelet volume (MPV) and neutrophil lymphocyte ratio (NLR) were recorded. NLR values were categorized into three groups according to the percentage frequency among cases. Values between 0-40 were grouped as NLR 1, values between 41-60 were grouped as NLR 2, and values above 60 were grouped as NLR 3. Additionally blood groups (A, B, O, AB) and Rh factors (Rh^+, Rh^-) were noted for every case.

Statistical analysis

Normality assessment was made with Kolmogorov-Smirnov test, and homogeneity check of group variances was made with Levene test. Means of two independent groups were compared with t-test, whereas comparison of the means of three or more groups were made with one-way analysis of variance. Identification of the different groups was made with Tukey multiple comparison test with 5% significance level. Results of Tukey test were expressed in letters along with the descriptive statistics results. Calculations and interpretations were made at 5% significance level. All calculations were performed using SPSS v24 (IBM Inc., Chicago, IL, USA) statistics package software.

Results

Frequency distribution of patients according to examined parameters are presented in Table 1. One-way analysis of variance was performed in order to determine whether the studied parameters showed any difference according to blood groups. The results are presented in Table 2. As it is shown in Table 2, variance analysis for BUN 1 indicates there is no statistically significant difference between the blood groups ($p>0.05$). Similarly, there is no significant difference between the blood groups regarding other variables ($p>0.05$). Therefore, studied parameters did not show any difference according to the blood groups. It is concluded that blood groups are not predictors for AKI development. Studies with larger sample size are required to determine the effect of blood groups on AKI development. Student t-test was performed in order to determine whether the studied parameters showed any change according to sex, and the results are presented in Table 3.

Table 1 Frequency table based on patients' demographic variables and examined parameters

Variables		Frequency	%
ABO Groups	0	56	18.4
	A	187	61.5
	B	36	11.8
	AB	21	6.9
RH	Negative	89	29.3
	Positive	211	69.4
Sex	Male	144	48
	Female	156	52
Renal failure	AKI	135	44.4
	Non-AKI	165	54.3
Mechanical ventilation	MV applied	142	47.3
	MV not applied	158	52.7
Discharge state	Exitus	146	48.7
	Discharged	154	51.3
Diagnosis	CVA	42	13.8
	Pneumonia	36	11.8
	Intoxication	26	8.6
	CHF	36	11.8
	Trauma	11	3.6
	COPD	29	9.5
	DM	30	9.9
	Malignancy	33	10.9
	Pulmonary edema	17	5.6
	GIS hemorrhage	14	4.6
	CAD	26	8.6
Age		Mean±Std.Dev.: 67.727±15.954	

CVA: Cerebrovascular Accident; DM: Diabetes Mellitus; CAD: Coroner Artery Disease; CHF: Congestive Heart Failure; COPD: Chronic Obstructive Pulmonary Disease

Citation: Canakci E, Karatas A, Kaya Y. Can blood groups, neutrophil-lymphocyte ratio and mean platelet volume predict mortality in critically ill patients developing acute kidney injury? *J Anesth Crit Care Open Access.* 2017;8(1):188–194. DOI: 10.15406/jaccoa.2017.08.00290

Table 2 Descriptive statistics and ANOVA results for the variables according to ABO groups

Variables	0 (n=56)		A (n=187)		B (n=36)		AB (n=21)		P-Value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
BUN1	42,786	23,593	43,255	25,753	44,000	28,354	45,095	29,665	0,986 NS
BUN 2	35,460	16,559	32,683	16,536	36,611	16,517	35,343	17,371	0,456 NS
Cre1	1,970	1,482	4,681	35,507	1,804	1,672	5,971	15,043	0,872 NS
Cre2	1,743	1,450	2,232	6,349	1,647	1,206	2,091	1,548	0,882 NS
GFR1	56,804	43,414	56,182	41,350	62,767	46,365	56,000	49,159	0,866 NS
GFR2	52,321	39,154	58,286	39,289	59,972	39,874	46,238	39,374	0,437 NS
CRP	7,518	5,916	7,397	5,990	8,161	6,437	7,760	6,715	0,917 NS
WBC	13,597	13,059	15,294	14,072	11,418	7,600	13,051	9,316	0,361 NS
Neutrofil	30,199	31,079	32,891	32,065	31,542	31,700	37,919	35,507	0,815 NS
Lymphosit	6,048	7,058	8,672	29,429	7,894	9,088	5,269	5,929	0,851 NS
Platelet	2,69,923	1,38,961	2,90,344	1,45,426	2,69,469	1,45,743	2,73,048	1,34,710	0,712 NS
MPV	8,131	1,924	12,197	49,404	8,252	2,813	9,034	2,723	0,875 NS
NLR	28,916	30,184	30,966	59,948	25,609	29,886	29,443	34,622	0,949 NS

SD: Standard deviation; $_{NS}$: Statistically not significant (p>0,05).

Table 3 Descriptive statistics and Student's t-test results for the variables according to Sex

Variables	Male (n=144)		Female (n=156)		t-Value	P-Value
	Mean	SD	Mean	SD		
BUN 1	41,063	25,221	45,530	26,318	-1,499	0,135 NS
BUN 2	31,752	15,887	35,805	17,025	-2,127	0,034*
Cre 1	2,227	5,926	5,483	38,854	-0,995	0,321 NS
Cre 2	2,107	6,851	2,018	2,561	0,153	0,879 NS
GFR 1	62,097	42,498	52,440	42,606	1,964	0,051 NS
GFR 2	64,050	41,178	49,591	36,295	3,232	0,001**
CRP	7,086	6,211	7,953	5,900	-1,239	0,216 NS
WBC	12,949	12,966	15,653	12,932	-1,807	0,072 NS
Neutrofil	30,700	31,495	34,313	32,419	-0,978	0,329 NS
Lymphosit	8,989	22,213	6,801	25,010	0,799	0,425 NS
Platelet	2,78,489	1,39,449	2,86,811	1,46,891	-0,502	0,616 NS
MPV	13,154	56,217	8,518	3,702	1,028	0,305 NS
NLR	23,110	28,944	36,040	64,378	-2,212	0,028*

SD: Standard deviation; ^{NS}: Statistically not significant (p>0,05); *: Statistically significant (p<0,05); **: Statistically significant (p<0,01).

As it is shown in Table 3, mean BUN 1 level was slightly higher in females than in males; however, the difference was not statistically significant according to t-test (p>0.05). Mean BUN 2 level was significantly higher in females compared to males (p<0.05). Similarly, NLR was significantly higher in females compared to males (p<0.05). Similarly, other variables did not show significant difference between the blood groups (p>0.05). Therefore, blood group is not important factor for the variables examined in this study. Mean GFR 2 level was statistically higher in males compared to females (p<0.01). Other variables did not show statistically significant difference between the sexes (p>0.05). This can be explained by the relationship of creatinine level with the muscle mass in the body, and additionally because there was not so much difference between the initial and last creatinine measurement values as it is present in BUN level. In addition, although the GFR shows greater change during the initial stages of the renal function loss, the expected change in creatinine levels is smaller.

In order to determine whether other parameters showed any change according to presence of AKI, Student t-test was applied, and the results are presented in Table 4. As shown in Table 4, mean levels of Cre1, Cre2, lymphocyte and MPV did not change depending on the presence of AKI (p>0.05). Student t-test results showed that mean levels of BUN1, BUN2, CRP, WBC, Neutrophil and NLR were significantly higher among patients with AKI, compared to the non-AKI group (p<0.001/p<0.05). In contrast, mean levels of GFR1, GFR2 and platelet were significantly higher in the non-AKI group compared to the AKI group (p<0.001). These statistical results are in perfect agreement with our clinical observations. We observed increased mortality risk in patiens with AKI. This can be explained by the relationship between creatinine level and body muscle mass, and because there was not so much difference between initial and last creatinine measurement values as compared to BUN levels. In addition, although the GFR shows greater change during the initial stages of the renal function loss, the expected change in creatinine levels is smaller. Furthermore, creatinine levels may be misleading in patients with sepsis. In order to determine whether the studied parameters showed any change according to discharge situation, Student t-test was applied, and the results are presented in Table 5. As shown in Table 5, mean levels of Cre1, Cre2, CRP, neutrophil, lymphocyte and MPV did not show change depending on the discharge states of patients (p>0.05). Student t-test results indicate that mean levels of BUN 1, BUN2, WBC and NLR were significantly higher among the deceased patients compared to the discharged patients (p<0.001/p<0.01). This statistical result is in perfect agreement with our clinical observations. Indeed, elevated levels of BUN 1, BUN 2, WBC and NLR values are commonly observed in patients who end up with mortality. Because, bacteremia can develop in many critically ill patients; and renal perfusion can deteriorate due to hypotension, BUN levels can increase. Furthermore, bacteremia causes neutrophilia and increased white blood cell count. This supports our hypothesis which states that increased NLR can predict mortality. By contrast, mean levels of GFR1, GFR2 and platelet were significantly higher in discharged patients compared to the deceased patients (p<0.001). Higher mean levels of GFR 1 and GFR 2 in discharged patients, and the statistically significant difference also supports our hypothesis that states NLR is a predictor of AKI. Platelet counts were higher in discharged patients, and lower in deceased patients, and the difference was statistically significant. This may be because thrombocytopenia is more frequent in critically ill patients, and especially in mortal cases. Thrombocytopenia with accompanying sepsis and thrombocytopenia

due to polypharmacy, or thrombocytopenia due to heparin is frequently encountered in critically ill patients. This may be the reason why mean platelet count was significantly lower in deceased patients, and why mean platelet count was higher among discharged patients since the aforementioned clinical situations are rare in discharged patients.

In order to determine whether the studied parameters showed change according to NLR groups, one-way analysis of variance was applied, and results are presented in Table 6. NLR values were categorized. Values between 0-40 were grouped as NLR1, values between 41-60 were grouped as NLR2, and values above 60 were grouped as NLR3. As it is seen from Table 6, results of variance analysis indicate that the difference between NLR groups were statistically significant for lymphocyte and MPV variables (p>0.05). Other variables did not show significant difference between the NLR groups (p<0.01/p<0.001). In order to determine the different groups, Tukey test was applied, and the results are expressed with letters along with the means. The fact that the studied parameters showed statistically significant difference between the NLR groups proves that NLR is a predictor of AKI and mortality in critically ill patients. The fact that GFR, BUN and Cre results became significant as NLR increased emphasizes the predictive strength of NLR in AKI patients. Mortality rate is increased as the NLR is increased. Our results prove that MPV is not a predictor of mortality in critically ill patients.

Table 4 Descriptive statistics and Student's t-test results for the variables according to AKI Groups

Variables	AKI (n=142)		Non AKI (n=158)		t-Value	P-Value
	Mean	SD	Mean	SD		
BUN 1	59,901	26,899	28,542	12,426	13,175	0,000***
BUN 2	40,878	18,250	27,551	11,838	7,576	0,000***
Cre1	6,520	40,655	1,583	5,612	1,511	0,132 NS
Cre2	2,331	1,759	1,817	6,806	0,874	0,383 NS
GFR 1	30,645	29,579	80,829	38,681	-12,516	0,000***
GFR 2	35,720	28,385	75,236	38,434	-10,036	0,000***
CRP	8,303	5,462	6,848	6,485	2,090	0,038*
WBC	17,234	14,640	11,768	10,724	3,713	0,000***
Neutrophil	36,565	33,702	28,996	29,999	2,058	0,040*
Lymphosit	5,399	21,558	10,055	25,329	-1,705	0,089
Platelet	2,42,249	1,26,987	3,19,276	1,47,441	-4,822	0,000***
MPV	8,344	2,418	12,899	53,733	-1,009	0,314 NS
NLR	43,366	45,632	17,672	52,439	4,504	0,000***

SD: Standard deviation; NS: Statistically not significant (p>0,05); *: Statistically significant (p<0,05); ***: Statistically significant (p<0,001).

Table 5 Descriptive statistics and Student's t-test results for variables according to Discharge situation

Variables	Ex (n=146)		Discharge (n=154)		t-Value	P-Value
	Mean	SD	Mean	SD		
BUN 1	58,932	27,227	28,647	12,417	12,501	0,000***
BUN 2	40,909	18,130	27,176	11,561	7,864	0,000***
Cre1	6,381	40,098	1,587	5,685	1,468	0,143 NS
Cre2	2,346	1,759	1,791	6,887	0,945	0,345 NS
GFR1	31,641	30,498	81,188	38,583	-12,296	0,000***
GFR2	35,460	28,701	76,508	37,624	-10,583	0,000***
CRP	8,065	5,499	7,036	6,520	1,474	0,142 NS
WBC	16,995	14,510	11,852	10,847	3,489	0,001**
Neutrofil	36,261	33,723	29,088	29,921	1,951	0,052 NS
Lenfosit	5,446	21,286	10,131	25,633	-1,717	0,087 NS
Platelet	2,42,269	1,26,500	3,21,258	1,47,806	-4,961	0,000***
MPV	8,357	2,391	13,005	54,426	-1,031	0,303 NS
NLR	42,926	45,428	17,422	52,811	4,473	0,000***

SD: Standard deviation; NS: Statistically not significant (p>0,05); *: Statistically significant (p<0,05); ***: Statistically significant (p<0,001).

Table 6 Descriptive statistics and ANOVA results for the variables according to NLR groups

Variables	NLR 1 (n=223) Low (0-40)		NLR 2 (n=33) Moderate (41-60)		NLR 3 (n=44) High (61 above)		P-Value
	Mean	SD	Mean	SD	Mean	SD	
BUN 1	38,106B	23,957	59,909A	19,338	57,750A	28,988	0,000***
BUN 2	31,388B	15,389	32,955B	16,294	47,064A	16,786	0,000***
Cre1	1,987B	4,875	18,897 A	84,046	2,484B	1,980	0,000***
Cre2	1,538B	2,148	2,641AB	2,433	4,275A	12,033	0,000***
GFR1	67,422A	43,596	16,685B	12,292	34,932B	21,869	0,005**
GFR2	64,665A	41,094	41,642B	22,852	26,477B	14,373	0,004**
CRP	7,081B	6,241	12,242A	4,747	6,318B	4,197	0,000***
WBC	11,359C	8,008	27,575A	14,234	19,624B	21,995	0,000***
Neutrofil	24,939B	26,770	54,773A	35,353	54,653A	36,067	0,000***
Lymphocyt	7,956	21,680	10,552	43,852	5,293	5,816	0,625 NS
Platelet	301,747A	1,39,976	242,201AB	1,04,820	217,336B	1,60,387	0,000***
MPV	11,641A	45,193	8,54B5	2,686	7,840B	5,536	0,793 NS
NLR	10,247C	10,243	58,825B	6,811	107,362A	93,033	0,000***

SD: Standard deviation; NS: Statistically not significant (p>0,05);

*: Statistically significant (p<0,05); ***: Statistically significant (p<0,001).

Means that do not share a letter are significantly different (P<0,05)

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Discussion

Acute kidney injury (AKI) is a clinical syndrome in which there is often reversible reduction of GFR accompanied by accumulation of nitrogen metabolites such as urea and creatinine, fluid and electrolyte imbalances, and disorders of acid base metabolism. It is gaining increasing importance due to the high prevalence in critically ill patients and its close association with mortality.[19] Many different factors may play role in the etiology of AKI. One of the leading cause of AKI observed in critically ill patients is sepsis. In one study by Palmar et al.,[20] the prevalence of AKI was reported as 19% in sepsis, 23% in severe sepsis, and 51% in septic shock.[20] In another epidemiological study involving patients diagnosed with AKI, Wang et al. found that more than 50% of the patients had accompanying sepsis or septic shock. In our study, 60% of the patients with AKI had septic shock.[21] High NLR, CRP and WBC levels in our cases suggest presence of bacteremia and sepsis in majority of our cases. According to our clinical observations, most of the cases diagnosed with AKI have accompanying bacteremia or sepsis. Our results are in agreement with the literature data. Presence of AKI significantly increases the risk of mortality in intensive care, and mortality rate is increased up to 90% in case renal replacement therapy is required.[22] In one study including 211 patients with sepsis, Peng et al. found significantly increased 28-day mortality rate in the AKI group.[23] In the present study, the comparison of patients with and without AKI showed higher mortality rate in patients with AKI. This result is consistent with the literature data. Studies that examined AKI development during ICU stay have found that RIFLE and AKIN had significant effects on in-hospital survival; and no difference was found between the two classifications with regard to their ability to predict survival,[24] Park et al.,[25] evaluated AKI development in ICU patients based on RIFLE classification alone, and they found significant effect of RIFLE on hospital survival.[25] In the present study, we also used RIFLE classification for diagnosing AKI.

Whether there is an association between blood groups and various diseases, or in other words, whether some blood groups are associated with higher risk for some diseases has been investigated by many researchers.[26,27] In literature, its associations with some infectious diseases, some cancer types and especially cardiovascular diseases have been investigated. Kaya et al. found lower risk of coronary artery disease in individuals with blood group O, whereas this risk was found to be higher with A, B and AB blood groups.[27] In the present study, we did not find association of blood groups with mortality or AKI. Additionally, the present study is to first study to examine the relationship of blood groups with mortality and AKI. Considering that the present study included a sample size of 300 patients and data collected over 7years, it is obvious that studies with even larger sample size, and longer study period are needed to demonstrate any possible association with blood groups.

In our review of literature, we encountered many studies examining whether NLR is a predictor of various diseases. A great number of these studies are related with the association with coronary artery disease. One study from Michigan University, USA, evaluated NLR values measured at the time of admission and all-cause mortality at 6th month in 2833 patients diagnosed with acute coronary syndrome (ACS) (564 ACS with ST-segment elevation, 2269 ACS with unstable angina pectoris/ non-ST-segment elevation); and similar to our results, NLR was found as an effective predictor of mortality. That study had the largest sample size in related literature.[28] One study that evaluated NLR values measured at the time of presentation and in-hospital and all-cause 30th day mortality found that NLR was an effective parameter in only Type 2 diabetes.[29] Studies investigating the association with mortality evaluated in-hospital, post-discharge, 30th day and 6th month mortality rates.[28,29] The study by Azab et al. from Staten University (Staten Island, New York, USA) had the longest follow-up period.[30] This study evaluated NLR values at presentation and mean NLR values (average NLR value calculated from 3 different differential white blood cell count on different days) in 619 ACS patients with unstable angina pectoris/ non-ST segment elevation, and 4th year mortality rates from USA Social Security Mortality Index records.[28,29] Our study had a retrospective design, and a comparison regarding follow-up time cannot be made. However, our results in terms of the association between NLR and mortality are in agreement with the literature data.

There are few studies that examined the relationship between AKI and NLR. Considering this fact, our study is among the first few studies related with AKI and NLR. Besides this good situation, but unfortunately there are some limitations of our study. It is primarily a retrospective file review, so we can not predict the degree of correlation with clinical outcomes. We could grade kidney injury according to the RIFLE or KDIGO guide. We still believe that the results are in accordance with the literature. In one study involving patients diagnosed with AKI and severe sepsis, Yılmaz et al.,[31] reported that NLR is a predictor with higher sensitivity and specificity compared to CRP or WBC.[31] Their study was a 3-year retrospective study including 118 critically ill patients, whereas our study is 7-year retrospective study including 300 patients. In comparison to the study by Yılmaz et al., larger sample size and longer study period bestow more strength to the present study. Analyzed laboratory parameters, demographic variables and accompanying comorbidities show great similarity between the studies. On the other hand, one superior side of the study by Yılmaz et al. is that they included APACHE II and SOFA scores of the patients in the analysis. Since the ICU in our hospital is categorized as grade II ICU, we could not obtain APACHE II and SOFA scores of all our patients, therefore these scores were not included in analysis. Because Yılmaz et al. used these intensive care scoring systems, their study is superior in this regard.[31] In one study involving hemodialysis patients, Neuen et al.,[31] stated that NLR was a simple and inexpensive predictor of mortality. They followed up 170 hemodialysis patients for 3 weeks, and they found NLR could predict all-cause mortality, and particularly mortality due to cardiovascular reasons. Additionally, they found positive correlation between increased CRP and increased NLR levels.[32] The study results of Neuen et al.,[32] are in complete agreement with our results. In our study, we also found significant results for CRP, platelet, WBC and neutrophil values in addition to NLR when cases with AKI were compared to the non-AKI group.[32] In their letter to editor, Balta et al. criticized some aspects of the study by Yılmaz et al. Balta et al. stated that NLR could not be a predictor in cases with AKI, because NLR can be affected by many factors including the methods used for phlebotomy, and NLR could be lower in patients receiving statin treatment and antihypertensive treatment (valsartan, nebivolol, amlodipin), and they stated that the results reported by Yılmaz et al.,[31] were not reliable, and that these results should be supported with other serum inflammation markers.[33] In our opinion, the critical reviews put forward by Balta et al. are not justifiable. Yılmaz et al. could achieve a homogenous sample, and included critically ill patients with concurrent severe sepsis and AKI. These cases with severe sepsis do not receive antihypertensive medications, instead, they are hypotensive patients that require positive inotropic support. Moreover, the authors even detected the origin of infection in cases diagnosed with severe sepsis. Additionally, Yılmaz et al.,[31] categorized NLR values, and NLR values were found in a close range. For this reason, we think the criticisms by Balta et al. have no ground. Our study is the third study to evaluate the association between NLR

and AKI, coming after the studies by Yılmaz et al.,[31] and Neuen et al.,[32] and our results are in complete agreement with their results.

Güldiken et al.,[34] compared MPV values and other peripheral blood cell counts in cases with acute ischemic stroke, and they reported that although MPV did not show significant change in acute ischemic stroke, increased leukocyte and neutrophil counts were good indicators of major vessel disease subtype and stroke severity. In our study, we did not find association between MPV values and AKI or mortality,[34] In one study, Karagöz et al.,[35] categorized critically ill patients in two groups as deceased and discharged patients, and they examined the associations of hemogram parameters and especially MPV with mortality. They found strong association between increased MPV values and mortality.[35] Their results are not in agreement with our results. In our study, when we compared discharged and deceased cases, we found statistically significant results for platelet, NLR, GFR and BUN levels, whereas we did not find significant association between MPV and mortality. The study by Karagöz et al.,[34] is a retrospective study including critically ill patients, and they did not conduct their study on a specific disease group. The reason why we had different results may be related to the fact that we included cases with a specific disease. In one study, Farah and Samra[36] compared NLR and MPV values between cases diagnosed with ischemic stroke and 30 healthy volunteers, and they found higher NLR values in cases with ischemic stroke compared to healthy volunteers, whereas they did not find difference in MPV values. Farah and Samra[36] proposed that NLR was a good predictor for stroke and prognosis of stroke, while MPV was not.[36] Their results are in complete agreement with our results. We also found that while NLR was a good predictor for mortality, MPV did not have a predicting value. In their study, Liu et al. investigated the association between MPV and mortality in cases with acute myocardial infarction. In that retrospective study including 567 cases, they concluded that MPV was a predictor for mortality. Their results are in contrast with our results. This may be because they had a larger sample size and included a different patient group.[37] In another study, Yilmaz G et al.,[38] compared NLR and MPV values and their relationship with proteinuria level between cases with chronic renal failure (CRF) and healthy volunteers. While there was statistically strong correlation between NLR level and proteinuria level in cases with CRF, there was no correlation between MPV and proteinuria levels.[38] These results are in agreement with our results. Our results are consistent with literature data. There are few studies examining the association between MPV and intensive care mortality, therefore our study is among the first studies on this subject.

Conclusion

In conclusion, considering the literature knowledge and our study results, it can be stated that MPV and blood groups are not predictors for AKI or mortality in critically ill patients, whereas NLR appears to be a strong predictor of AKI and mortality in critically ill patients. It should be emphasized that the NLR ratio should be calculated for each hospitalized ICU patient and if the ratio is high, it is likely that kidney injury may develop and measures should be taken accordingly. We believe that NLR ratio should be included in follow-up and treatment of intensive care patients.

Acknowledgements

We wish to thank Assist. Prof. Dr. YelizKasko Arıcı (Ph.D) for helping us with the statistical analyses of the present study.

Conflicts of interest

Author declares there are no conflicts of interest.

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Citation: Canakci E, Karatas A, Kaya Y. Can blood groups, neutrophil-lymphocyte ratio and mean platelet volume predict mortality in critically ill patients developing acute kidney injury? *J Anesth Crit Care Open Access*. 2017;8(1):188–194. DOI: 10.15406/jaccoa.2017.08.00290