VIA MEDICA

ORIGINAL ARTICLE

Disaster and Emergency Medicine Journal
2022, Vol. 7, No. 2, 100–106
DOI: 10.5603/DEMJ.a2022.0020

ISSN 2451–4691, e-ISSN 2543–5957

NEW HEMATOLOGICAL PARAMETERS AS EARLY DIAGNOSIS AND PROGNOSTIC MARKERS IN CRITICALLY PATIENTS

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Abstract

INTRODUCTION: Nucleated red blood cells and immature granulocytes are not normally detected in the blood of healthy adults. We aimed to investigate the effect of nucleated red blood cells and immature granulocytes on mortality in order to identify critically ill patients who were admitted to the emergency department, at high risk of death, and who was not traumatic.

MATERIAL AND METHODS: This study was performed retrospectively in the emergency department of a tertiary education and research hospital between January 2021 and June 2021. All patients who died out of trauma and patients who were discharged from the emergency department on the same day were included. Nucleated red blood cells and immature granulocytes parameters were compared between the two groups. The primary outcome was all-cause death in the emergency department.

RESULTS: Of the 188 patients included in the study, 129 (68.6%) were male. Nucleated red blood cells (1.88 ± 6.9/μL; 0.02 ± 0.08), % immature granulocytes (2.91 ± 3.04/μL; 0.58 ± 1.63) and immature red blood cells in deceased patients' granulocyte count (0.38 ± 0.46/μL; 0.04 ± 0.04) was significantly more significant than the control group ($p < 0.001$). When the area under the curve was examined, the highest value was found in nucleated red blood cells (Area under the curve = 0.920, $p < 0.001$). In multivariate regression analysis, high nucleated red blood cells, immature granulocyte count, and white blood cell levels were associated with all-cause mortality in the emergency department.

CONCLUSIONS: High nucleated red blood cells and immature granulocyte levels may be associated with increased mortality during admission to the emergency department.

KEY WORDS: critically patients; death; emergency department; immature granulocyte; nucleated red blood cells

Disaster Emerg Med J 2022; 7(2): 100–106

INTRODUCTION

Nucleated red blood cells (NRBC) are immature erythrocyte cells that are the progenitor cells of the erythropoietic series. They disappear within a few weeks after birth in healthy newborns and are not found in peripheral blood in a healthy adult [1]. NRBC appears in circulation in a variety of situations. These are conditions such as inflammation-causing he-

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Received: 18.04.2022 Accepted: 23.05.2022 Early publication date: 23.06.2022

matopoietic stress, massive bleeding, hematological cancer, extramedullary hematopoiesis, or severe hypoxia [2, 3]. The increase in erythropoietin and high proinflammatory cytokine (IL-3 and IL-6) levels after local and systemic disorders are associated with the formation of NRBC in the blood [4]. Although a precise mechanism for the transfer of NRBCs from the bone marrow to the circulation is still unclear, it has been emphasized that their detection in peripheral blood may be associated with increased mortality and poor prognosis [5]. It has also been shown that NRBCs can occur up to three weeks before death [2, 5, 6]. Recently, studies performed on ARDS, sepsis, internal medicine, surgery, and coronary intensive care patients have shown that NRBCs have a high prognosis in terms of mortality [3, 5–8].

Immature granulocytes (IG) are neutrophils that come from progenitor cells in the bone marrow during maturation and are not normally seen in healthy people [9]. IGs are a new marker of inflammation and are released into the systemic circulation in cases such as bacterial infections, acute inflammatory diseases, cancer, tissue necrosis, acute transplant rejection, surgical and orthopedic traumas, myeloproliferative diseases, steroid use, and the last trimester of pregnancy [10]. It has been emphasized that the emergence of IG is an effective marker in predicting the severity of the disease in the early period [11].

It can be measured easily and quickly from a complete blood count on both NRBC and IG automated analyzers. Non-traumatic critical patients in the emergency department (ED) are an important group that has not been adequately studied in the scientific literature. These hematological markers may be useful in identifying patients who present to the ED and have a high risk of mortality. To the best of our knowledge, there are no studies investigating the relationship between NRBC and IG and mortality in ED patients. We thought that both NRBC and IG levels would increase in patients who presented to the ED and died within the first 24 hours. The aim of this study was to investigate the effects of NRBC and IG on mortality in order to better identify critically ill patients presenting to the ED, at high risk of death, and non-traumatic.

MATERIAL AND METHODS

This study was designed as a single-center, retrospective cross-sectional study, and ethics committee approval was obtained from Medipol University. The study was carried out in a tertiary education and research hospital with a capacity of 700 beds, with an annual average of 150,000 patients. Patients aged 18 years and older and who died within the first 24 hours, admitted to the ED between January 2021 and June 2021 were screened. Patients under the age of 18, pregnant women, trauma patients, patients without laboratory data, cancer patients, immunosuppressive patients, patients with hematological and immunological diseases, and patients receiving chemotherapy and steroids were excluded from the study. It was divided into two as the dead group and the control group. The control group consisted of patients who did not have any serious disease, did not meet the exclusion criteria, and were discharged from the ED. In addition, patients in the control group were included in the same number, same day, and age group as the dead group. For this purpose in the study form, parameters were recorded using the hospital information management system database, age, gender, white blood cell (WBC), hemoglobin (Hb), red cell distribution width (RDW), NRBC, immature granulocyte count (IGS) and percentage (IG%) at the time of admission to the ED. These parameters were measured with an autoanalyzer after blood was drawn into the EDTA tube, and normal reference values were leukocytes (4500–11.000/mm^3), Hb (12.6 17.4 g/dL), RDW (11.6–14.8%), NRBC (0), IGS (0), and IG % (0). All parameters were statistically compared between the dead and control groups.

Statistical method

Statistical analysis of the data was done in IBM SPSS Statics Version 26 program. Pearson Chi-Square and Fisher's Exact test were used to comparing categorical data between groups, and Mann Whitney U statistical analyzes were used for comparisons between the two groups since continuous data were not normally distributed. The relationship between laboratory values and mortality was evaluated by logistic regression analysis and their predictive power of mortality was evaluated using ROC analysis. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 188 patients, including 94 dead and 94 control patients, who met the inclusion criteria in this study, were included in the study. 129 (68.6%) of the patients were male and 59 (31.4%) were fe-

Table 1. Demographic and laboratory findings distribution of patients

	Control	Ex	Total	p
	Mean ± SD	Mean ± SD	Mean ± SD	
Age [years]	68.95 ± 9.97	70.35 ± 12.83	69.65 ± 11.4	0,099
WBC [/mm$_3$]	8.83 ± 2.8	13.57 ± 6.13	11.2 ± 5.31	**< 0.001**
Hemoglobin [g/dL]	12.24 ± 2.2	11.36 ± 2.75	11.8 ± 2.52	**0.026**
RDW	15.04 ± 2.55	16.37 ± 3.23	15.71 ± 2.97	**0.007**
NRBC	0.02 ± 0.08	1.88 ± 6.9	0.95 ± 4.96	**< 0.001**
IG%	0.58 ± 1.63	2.91 ± 3.04	1.74 ± 2.7	**< 0.001**
IGS	0.04 ± 0.04	0.38 ± 0.46	0.21 ± 0.36	**< 0.001**
Sex	n (%)	n (%)	n (%)	
Male	65 (69.1)	64 (68.1)	129 (68.6)	**0.875**
Female	29 (30.9)	30 (31.9)	59 (31.4)	
Causes of death	**n (%)**			
Cardiovascular	31 (33%)			
Pulmonary	21 (22.3%)			
Infective	20 (21.3%)			
Neurological	10 (10.6%)			
Gastrointestinal	6 (6.4%)			
Other	6 (6.4%)			
Total	94 (100%)			

Pearson Chi Square, Fisher's Exact test Mann Whitney U analysis

IG% — percentage of immature granulocytes; IGS — immature granulocyte count; NRBC — nuclear red blood cell; RDW — red blood cell distribution width; WBC — white blood cell

male, and the mean age was 69.65 ± 11.4 years. It was NRBC value 1.88 ± 6.9/μL, 0.02 ± 0.08, %IG 2.91 ± 3.04/μL, 0.58 ± 1.63 and IGS 0.38 ± 0.46/μL, 0.04 ± 0.04 in the dead group and control group, respectively. There was a statistically significant difference between the two groups in terms of all parameters. ($p < 0.001$) (Tab. 1). When the distribution of causes of death in the ED was examined, the first three cases were due to cardiovascular (33%), pulmonary (22.3%), and infective (21.3%) pathologies. (Tab. 1).

According to the results of the analysis made for the estimation of all-cause deaths in the ED; The sensitivity of NRBC is 87.23 specificity is 93.62%, positive predictive value was 93.2% and negative predictive value was 88% ($p < 0.0001$). The sensitivity of IG % is 75.27%, specificity is 92.55%, positive predictive value was 90.9% and negative predictive value was 79.1% ($p < 0.0001$), Sensitivity for IGS is 86.17%, specificity is 81.91%, positive predictive value was 82.7% and negative predictive value was 85.6% ($p < 0.0001$). The specificity and sensitivity of Hb and RDW values were lower. When the area under the curve (AUC) values were examined, the highest value was found in NRBC (AUC = 0.920, $p < 0.001$). AUC values for IGS, IG %, WBC, RDW, and Hb respectively were 0.900, 0.895, 0.790, 0.613, and 0.594, (Tab, 2, Fig. 1).

Univariate logistic regression analysis was performed to determine the factors affecting deaths. In univariate analysis, WBC, Hb, RDW, NRBC, IG %, and IGS were found to be statistically significant with mortality. According to the results of multivariate regression analysis, it was determined that high NRBC, IGS, and WBC levels were associated with increased mortality. It causes 69.59 times more deaths for every 1 unit increase in NRBC values ($p = 0.000$). It causes 5.43 times more deaths for every 1 unit increase in IGS values ($p = 0.019$). Likewise, as WBC values increase, 1.25 times more deaths occur ($p = 0.011$) (Tab. 3).

DISCUSSION

In this study, we found that NRBC, IG %, and IGS were useful in identifying non-traumatic critical

Table 2. Performance characteristics of laboratory parameters in determining mortality

	Cut-off	AUC	p	Sensitivity	Specificity	+PV	–PV
		(95% CI)		(95% CI)	(95% CI)	(95% CI)	(95% CI)
WBC	> 9.6	0.790	< 0.0001	79.79	69.15	72.1	77.4
		(0.725-0.846)		(70.2–87.4)	(58.8–78.3)	(62.5–80.5)	(67.0–85.8)
Hemoglobin	≤ 8.8	0.594	0.023	22.34	95.74	84	55.2
		(0.520–0.665)		(14.4–32.1)	(89.5–98.8)	(63.9–95.5)	(47.2–63.0)
RDW	> 16.5	0.613	0.005	41.49	75.53	62,9	56.3
		(0.540–0.683)		(31.4–52.1)	(65.6–83.8)	(49.7–74.8)	(47.2–65.2)
NRBC	> 0	0.920	< 0.0001	87.23	93.62	93.2	88
		(0.871–0.954)		(78.8–93.2)	(86.6–97.6)	(85.7–97.5)	(80.0–93.6)
IG%	> 0.8	0.895	< 0.0001	75.27	92.55	90.9	79.1
		(0.842–0.935)		(65.2–83.6)	(85.3–97.0)	(82.2–96.3)	(70.3–86.3)
IGS	> 0.06	0.900	< 0.0001	86.17	81.91	82.7	85.6
		(0.848–0.939)		(77.5–92.4)	(72.6–89.1)	(73.7–89.6)	(76.6–92.1)

IG% — immature granulocyte percentage; IGS — immature granulocyte count; NRBC — nuclear red blood cell; RDW — red blood cell distribution width; WBC — white blood cell

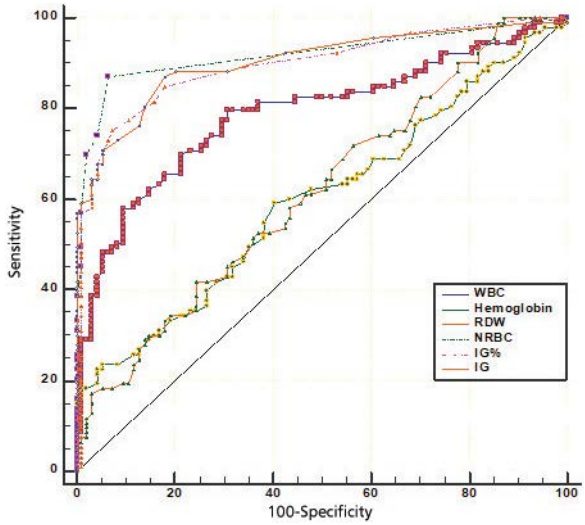

FIGURE 1. ROC curve drawn for the diagnostic power of laboratory parameters in determining mortality

patients in the emergency department. We also showed that the presence and levels of NRBC, IG %, and IGS in peripheral blood are independent variables of all-cause mortality in patients admitted to the ED. These results can help emergency physicians identify critically ill patients so that earlier action can be taken for the patient.

In our results, we found that NRBC, IG %, IGS, WBC, Hb, and RDW values were higher in patients who died compared to the control group. In addition, the sensitivity and specificity rates of NRBC, IG %, and IGS values were found to be quite high in identifying critically ill patients. NRBC had the highest overall sensitivity and specificity in distinguishing patients who died.

Immature blood cells are not normally found in the systemic circulation in healthy adults. Hematological and oncological diseases, as well as inflammatory and hypoxemic processes, are the main stimuli for the further production of blood elements by the bone marrow. The presence of these immature young cells in the peripheral circulation is directly related to the intensity of systemic inflammation and hypoxemia and consequently is associated with a worse prognosis [8, 12] Stachon et al in their study on 4173 patients, showed that NRBC was seen with the highest incidence in the intensive care unit (ICU), the mortality rate was 21.1% in patients with NRBC positive and it was associated with in-hospital mortality. They also noted that NRBCs have high prognostic power for in-hospital mortality and may serve as an early indicator of patients at increased risk. [13]. In the observational study of Menk et al in 404 patients with severe acute respiratory distress syndrome (ARDS); They showed that NRBC was associated with longer intensive care unit stay and higher mortality rates, and NRBCs were more than 3-fold higher risk of mortality if > 220/μL. [3]. Stachon et al. [2] revealed a significant relationship between NRBC and increased mortality in a prospective study of 284 surgical intensive care patients. Stachon et al. [7] in their study on intensive care patients; the mortality rate was determined as 44.0% in NRBC-positive

Table 3. Results of multivariate logistic regression analysis for the effect of laboratory values on survival

	B	Wald	p	OR (95% CI)
WBC	0.220	6.411	0.011	1.25 (1.051–1.478)
Hemoglobin	–0.104	0.498	0.480	0.9 (0.675–1.203)
RDW	–0.062	0.231	0.631	0.94 (0.73–1.21)
NRBC	4.243	41.374	0.000	69.59 (19.104–253.529)
IG%	0.082	0.449	0.503	1.09 (0.854–1.379)
IGS	1.691	5.478	0.019	5.43 (1.317–22.37)
Constant	–3.030	0.838	0.360	

IG% — percentage of immature granulocytes; IGS — immature granulocyte count; NRBC — nuclear red blood cell; RDW — red blood cell distribution width; WBC — white blood cell

patients, and NRBCs in blood showed 83.3% sensitivity and 78.9% specificity regarding intensive care mortality. They also reported that it can serve as a daily indicator of patients at high risk of mortality [7]. Stachom et al in their prospective study; They looked at the NRBC value in the daily follow-up of 383 intensive care patients, and the mortality of NRBC-positive patients was 50.7%, and 78.6% of patients with NRBCs greater than 200/microliter [5]. In the study of Stachom et al on 421 intensive care patients; they showed that ICU mortality is higher in NRBC positive patients [14]. In a retrospective study by Narcı et al; NRBC has been shown to be associated with increased mortality [15]. In our study, the NRBC cut-off value was > 0/μL, indicating that it is not normally found in peripheral blood. This result was compatible with the literature [15]. At this cut-off value, NRBC was more associated with mortality than other markers. Similar to the studies above, we found that NRBC was associated with mortality and had high sensitivity and specificity in our study.

Although the mechanism of NRBC production in critically ill is unclear, the presence of NRBCs in critically ill patients is associated with increased mortality. It has been reported in many publications that this may be due to severe hypoxemia and systemic inflammation [2–8]. In our study, cardiovascular, pulmonary, and infective pathologies were the leading causes of death in emergency room patients, which supports this.

IGS and IG % are new markers of inflammation that are poorly known by most clinicians [16]. Detection of IG in peripheral blood, which is not normally seen in healthy people, is an indicator of bone marrow activation and serious infection [11, 16]. Thanks to technological advances in automatic hematological analyzers, IG can be measured easily and quickly with a routine complete blood count [9]. Recent studies have shown that IG increases earlier in inflammatory conditions than traditional markers such as WBC, CRP, and Neutrophil-lymphocyte ratio and is a more effective marker in predicting the severity of infection [16, 17]. Ayres et al. [18] reported in their study that IG % is an adequate marker for the diagnosis of sepsis. Tan et al in a retrospective study of 1973 patients, found it to be a potential indicator for SIRS. [19]. Huang et al. [20] friends reported that IG % is a new biomarker in determining the incidence and severity of ARDS in their multicenter prospective study. In another study, Ansari-Lari et al found a significantly higher IG% in infected patients than in uninfected patients, with a specificity of greater than 90%, as an indicator of IG > 3% sepsis [9]. Bedel et al. [21] found that IG% and IGS were more effective than traditional inflammatory markers in determining the severity of acute pancreatitis in their study on acute pancreatitis patients. Sauneuf et al. reported that the immature/total granulocyte ratio is an indicator of poor prognosis in out-of-hospital cardiac arrest cases in their prospective cohort study [23]. Our results showed that IG % and IGS were associated with increased mortality and poor prognosis, similar to the studies above.

According to the results of multivariate regression analysis, it was determined that high NRBC, IGS, and WBC levels were associated with increased mortality. In their study, Narcı et al reported the probability of an increase in the mortality rate of NRBC as 1.02 [15]. In the study performed by Kuert et al in surgical intensive care patients, the mortality rate was found to be 41.8% in patients with NRBC positivity, and lower arterial oxygen partial tension levels were observed. In addition, the probability ratio of increased mortality in NRBC-positive patients was found to be 5.79. In our study, we found that every 1 unit increase in NRBC values causes a 69.59 fold increase in mortality.

However, this study had several limitations. First of all, the data were collected retrospectively, the study is a single-center study, and therefore the results may not be generalizable to all critically ill patients. Secondly, the study population was relatively small, and multicenter, larger, prospective studies will be required. Thirdly, the mechanisms of NRBC, IG%, and IGS are unclear. Many clinical conditions that may affect them need to be considered.

CONCLUSIONS

Peripheral blood NRBC, IG count, and percentage may be an early predictor of mortality in patients admitted to the emergency department. In addition, these markers can be used in the follow-up of suspected critical patients in emergency departments. Further research may be needed to elucidate possible mechanisms.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

The author(s) declare(s) that there is no conflict of interest.

Ethical approval

The study was approved by the ethical review board. (Istanbul Medipol University- non-interventional clinical trials ethics committee, number: E-10840098-772.02-3146 and date:07/01/2021)

Written or verbal informed consent was not obtained from the patients because it was a retrospective study.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in *a priori* approval by the institution's human research committee.

REFERENCES

1. May JE, Marques MB, Reddy VVB, et al. Three neglected numbers in the CBC: The RDW, MPV, and NRBC count. Cleve Clin J Med. 2019; 86(3): 167–172, doi: 10.3949/ccjm.86a.18072, indexed in Pubmed: 30849034.
2. Stachon A, Holland-Letz T, Kempf R, et al. Poor prognosis indicated by nucleated red blood cells in peripheral blood is not associated with organ failure of the liver or kidney. Clin Chem Lab Med. 2006; 44(8): 955–961, doi: 10.1515/CCLM.2006.183.
3. Menk M, Giebelhäuser L, Vorderwülbecke G, et al. Nucleated red blood cells as predictors of mortality in patients with acute respiratory distress syndrome (ARDS): an observational study. Ann Intensive Care. 2018; 8(1): 42, doi: 10.1186/s13613-018-0387-5, indexed in Pubmed: 29589209.
4. Stachon A, Bolulu O, Holland-Letz T, et al. Association between nucleated red blood cells in blood and the levels of erythropoietin, interleukin 3, interleukin 6, and interleukin 12p70. Shock. 2005; 24(1): 34–39, doi: 10.1097/01.shk.0000164693.11649.91, indexed in Pubmed: 15988318.
5. Stachon A, Segbers E, Holland-Letz T, et al. Nucleated red blood cells in the blood of medical intensive care patients indicate increased mortality risk: a prospective cohort study. Crit Care. 2007; 11(3): R62, doi: 10.1186/cc5932, indexed in Pubmed: 17550592.
6. Desai S, Jones SL, Turner KL, et al. Nucleated red blood cells are associated with a higher mortality rate in patients with surgical sepsis. Surg Infect (Larchmt). 2012; 13(6): 360–365, doi: 10.1089/sur.2011.089, indexed in Pubmed: 23237100.
7. Stachon A, Kempf R, Holland-Letz T, et al. Daily monitoring of nucleated red blood cells in the blood of surgical intensive care patients. Clin Chim Acta. 2006; 266(1-2): 329–335, doi: 10.1016/j.cca.2005.11.022, indexed in Pubmed: 16388791.
8. Monteiro Júnior JG, Torres Dd, da Silva MC, et al. Nucleated red blood cells as predictors of all-cause mortality in cardiac intensive care unit patients: a prospective cohort study. PLoS One. 2015; 10(12): e0144259, doi: 10.1371/journal.pone.0144259, indexed in Pubmed: 26713613.
9. Ansari-Lari MA, Kickler TS, Borowitz MJ. Immature granulocyte measurement using the Sysmex XE-2100. Relationship to infection and sepsis. Am J Clin Pathol. 2003; 120(5): 795–799, doi: 10.1309/LT30-BV9U-JJV9-CFHQ, indexed in Pubmed: 14608908.
10. Monteiro Júnior JG, de Oliveira Cipriano Torres D, Filho DC. Hematological parameters as prognostic biomarkers in patients with cardiovascular diseases. Curr Cardiol Rev. 2019; 15(4): 274–282, doi: 10.2174/1573403X15666190225123544, indexed in Pubmed: 30799790.
11. Senthilnayagam B, Kumar T, Sukumaran J, et al. Automated measurement of immature granulocytes: performance characteristics and utility in routine clinical practice. Patholog Res Int. 2012; 2012: 483670, doi: 10.1155/2012/483670, indexed in Pubmed: 22448336.
12. Verbrugge SE, Huisman A. Verification and standardization of blood cell counters for routine clinical laboratory tests. Clin Lab Med. 2015; 35(1): 183–196, doi: 10.1016/j.cll.2014.10.008, indexed in Pubmed: 25676379.
13. Stachon A, Sondermann N, Imohl M, et al. Nucleated red blood cells indicate high risk of in-hospital mortality. J Lab Clin Med. 2002; 140(6): 407–412, doi: 10.1067/mlc.2002.129337, indexed in Pubmed: 12486408.
14. Stachon A, Holland-Letz T, Krieg M. High in-hospital mortality of intensive care patients with nucleated red blood cells in blood. Clin Chem Lab Med. 2004; 42(8): 933–938, doi: 10.1515/CCLM.2004.151, indexed in Pubmed: 15387445.

15. Narcı H, Oktay MM, Ayrık C, et al. Nucleated red blood cells as predictor of all-cause mortality in emergency department. Am J Emerg Med. 2021; 46: 335–338, doi: 10.1016/j.ajem.2020.10.002.
16. Park JH, Byeon HJu, Lee KH, et al. Delta neutrophil index (DNI) as a novel diagnostic and prognostic marker of infection: a systematic review and meta-analysis. Inflamm Res. 2017; 66(10): 863–870, doi: 10.1007/s00011-017-1066-y, indexed in Pubmed: 28646289.
17. Ünal Y. A new and early marker in the diagnosis of acute complicated appendicitis: immature granulocytes. Ulus Travma Acil Cerrahi Derg. 2018; 24(5): 434–439, doi: 10.5505/tjtes.2018.91661, indexed in Pubmed: 30394497.
18. Ayres LS, Sgnaolin V, Munhoz TP. Immature granulocytes index as early marker of sepsis. Int J Lab Hematol. 2019; 41(3): 392–396, doi: 10.1111/ijlh.12990, indexed in Pubmed: 30806482.
19. Tan C, Huang Y, Zhang L, et al. [Predictive value of immature granulocytes for persistent systemic inflammatory response syndrome in patients with acute pancreatitis: analysis of 1 973 cases]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2018; 30(12): 1123–1127, doi: 10.3760/cma.j.issn.2095-4352.2018.012.004, indexed in Pubmed: 30592943.
20. Huang Y, Xiao J, Cai T, et al. Immature granulocytes: A novel biomarker of acute respiratory distress syndrome in patients with acute pancreatitis. J Crit Care. 2019; 50: 303–308, doi: 10.1016/j.jcrc.2018.12.002, indexed in Pubmed: 30558840.
21. Bedel C, Korkut M, Selvi F. New markers in predicting the severity of acute pancreatitis in the emergency department: Immature granulocyte count and percentage. J Postgrad Med. 2021; 67(1): 7–11, doi: 10.4103/jpgm.JPGM_784_20, indexed in Pubmed: 33533745.
22. Sauneuf B, Bouffard C, Cornet E, et al. Immature/total granulocyte ratio: a promising tool to assess the severity and the outcome of post-cardiac arrest syndrome. Resuscitation. 2014; 85(8): 1115–1119, doi: 10.1016/j.resuscitation.2014.04.017, indexed in Pubmed: 24795281.
23. Kuert S, Holland-Letz T, Friese J, et al. Association of nucleated red blood cells in blood and arterial oxygen partial tension. Clin Chem Lab Med. 2011; 49(2): 257–263, doi: 10.1515/CCLM.2011.041, indexed in Pubmed: 21118046.