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ORIGINAL ARTICLE

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Use of the systemic immune-inflammation index to predict the severity of pneumonia in the emergency department

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Medical Research Journal 2023; Volume 8, Number 3, 186–191
10.5603/mrj.96312

ISSN 2451-2591
e-ISSN 2451-4101

ABSTRACT

Introduction: This study aimed to investigate the use of the systemic immune-inflammation index obtained by hemogram parameters in determining the clinical severity of pneumonia.

Material and methods: This study was conducted retrospectively with a total of 6,802 patients diagnosed with viral and bacterial pneumonia from January 1, 2013, through January 1, 2023, at the emergency department of a tertiary hospital. The patients' age, gender, white blood cell, neutrophil, lymphocyte, and platelet counts, clinical outcomes (mortality and discharge), and mechanical ventilator requirements during treatment were obtained from the electronic patient files.

Results: The mean age of the patients was 62.3 ± 17.3 years, and 57.8% (n = 3,928) were male. The systemic immune-inflammation index was found to predict mortality in patients with a sensitivity of 77.9% and a specificity of 36.2% at a cut-off value of 114.72 [area under the curve (AUC): 0.654]. The receiver operating characteristic (ROC) curve analysis showed that the systemic immune-inflammation index was statistically significant in determining mortality among the patients ($p < 0.001$, 95% confidence interval: 0.639–0.669). The systemic immune-inflammation index was found to predict the mechanical ventilator requirement with a sensitivity of 70.0% and a specificity of 47.5% at a cut-off value of 137.88 (AUC: 0.629). According to the ROC curve analysis, the systemic immune-inflammation index was also statistically significant in determining the mechanical ventilator requirement among the patients ($p < 0.001$, 95% CI: 0.599–0.658).

Conclusions: The systemic immune-inflammation index was found to be valuable in determining clinical severity in patients with pneumonia.

Keywords: Pneumonia, systemic immune-inflammation index, SII, NLR, PLR, mortality

Med Res J 2023; 8 (3): 186–191

Introduction

Pneumonia is an inflammation of tissues in one or both lungs, usually caused by a bacterial agent. In the USA, more than 1 million people are admitted to hospitals annually due to pneumonia, and 50,000 of these cases result in mortality [1]. Although pneumonia is a treatable disease, it remains mortal; therefore, patients presenting to the emergency department with pneumonia are evaluated for disease severity and hospitalization indication. During this evaluation, scoring systems, such as the Pneumonia Severity Index (PSI), CURB-65, and CRB-65 are generally used [2]. However, the performance of these scoring systems may vary due to differences in the distribution of etiological agents, comorbidities, and the presence of social support [2].

Studies investigating the severity of pneumonia also assess various haematological or biochemical parameters in addition to scoring systems [3–4]. There are ongoing studies on the testing of certain biomarkers, such as C-reactive protein, procalcitonin, presepsin, adrenomedullin, and proenkephalin [5]. In a previous study addressing the advantages of different biomarkers, it was reported that procalcitonin had the highest accuracy for bacterial aetiologies and the presence of bacteraemia, lactate was a biomarker of hypoxia and tissue hypoperfusion, and proadrenomedullin was successful in predicting mortality when used together with prognostic exposures [6]. However, most of these biomarkers are not used during routine patient care in emergency departments. In addition, some require very expensive assays to obtain. Therefore,

their applicability in the emergency department does not seem feasible.

The systemic immune-inflammation index (SII) is obtained by multiplying the platelet count and the neutrophil-to-lymphocyte ratio (NLR) and is used to simultaneously evaluate the inflammatory and immune status of patients [7]. Previous studies have determined a relationship between SII and mortality or clinical severity in cases such as malignancies, coronary diseases, and heart failure [8–10]. Due to its very low cost and acquisition through a routine hemogram test, SII has been evaluated in different disease groups.

This study aimed to evaluate whether SII could be used in the evaluation of clinical severity in patients presenting to the emergency department with pneumonia. To this end, the relationship was investigated between SII and hospitalization requirements, mortality, and mechanical ventilator (MV) requirements in patients diagnosed with pneumonia at the emergency department.

Material and methods

Study design

This study was conducted retrospectively at the emergency department of a tertiary hospital and included patients diagnosed with viral and bacterial pneumonia (the International Classification of Diseases diagnosis codes: J10.0, J11.0, J12, J12.8, J12.9, J13, J14, J15.0, J15.3, J15.7, J15.8, J15.9, J16.0, and J18.1) from January 1, 2013, through January 1, 2023. The data were obtained by screening electronic patient files from the hospital information management system. Ethical approval for the study was obtained from the local ethics committee, and the study was conducted in accordance with the tenets of the Declaration of Helsinki.

Study population

Using the hospital management system, a total of 25,756 patients who presented to the emergency department and were diagnosed with pneumonia were identified for the study period, and those aged > 18 years whose data and patient files were available in the electronic system were included in the study. Patients with malignancies, immunodeficiency, known renal or hepatic dysfunction, inflammatory bowel disease or other inflammatory conditions, and pregnant women (considering that their systemic immune status might be affected by their current state) were excluded from the study. Pre-existing diseases (especially chronic renal failure, chronic liver failure, and inflammatory bowel disease) that would affect the systemic immune status of these patients were determined by screening the electronic patient files. Further excluded were patients diagnosed with COVID-19 based on a positive COVID-19 test. Lastly, of the patients who were planned to be included in the study, those with missing data and those who wanted to be discharged from the hospital during their clinical follow-up were also excluded. After applying all inclusion and exclusion criteria, a total of 6,802 patients were included in the sample. The details of patient selection are presented in Figure 1.

Data collection

Data on the patients' age, gender, white blood cell (WBC), neutrophil count, lymphocyte count, platelet count, clinical outcomes (mortality and discharge) and MV requirements and the use of MV during treatment were obtained from the electronic patient files.

The WBC, neutrophil, lymphocyte, and platelet counts obtained from the first hemogram test performed at the time of presentation to the emergency department or in the inpatient ward were used. The NLR and platelet-to-lymphocyte ratio (PLR) was calculated by dividing the absolute neutrophil and platelet counts by the absolute lymphocyte count, respectively. SII was calculated using the following formula: platelet count × neutrophil count/lymphocyte count [11].

Statistical analysis

In this study, statistical analyses were performed using the IBM SPSS package program v. 25.0. The Kolmogorov-Smirnov test was used to evaluate the normality of the data distribution. Categorical variables were given as frequency and percentage, and continuous variables as mean and standard deviation. Categorical variables were analysed using the chi-square test, while continuous variables were analysed using Student's t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. The area under the receiver operating characteristic (ROC) curves of SII for the prediction of hospitalization, MV, and mortality were calculated. The Youden J index was used to estimate the optimal cut-off points. Sensitivity and specificity were calculated at the 95% confidence interval (CI). For all analyses, $p < 0.05$ was considered statistically significant.

Results

Table 1 shows demographics (age and gender) and laboratory parameters. Accordingly, the mean age of the patients was 62.3 ± 17.3 years, and 57.8%

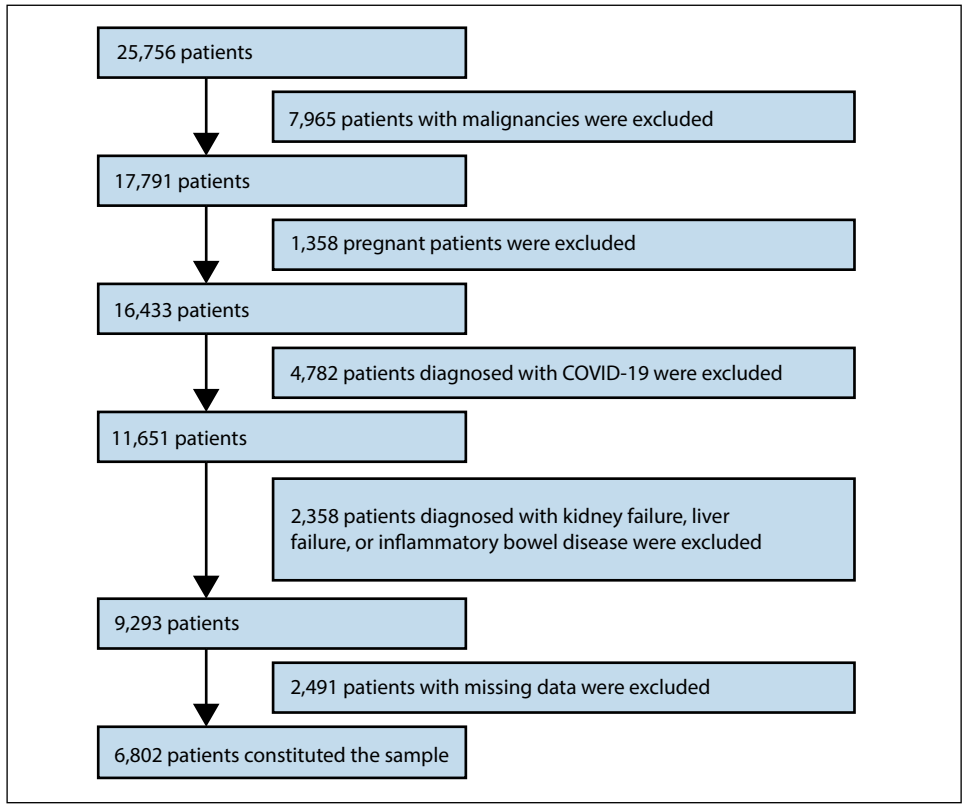

Figure 1. Flow chart of patient selection

Table 1. Demographic characteristics and laboratory parameters of the patients

Variable	Mean ± SD (min–max); n (%)
Age (years)	62.3 ± 17.3 (18–102)
Gender	
Female	2,873 (% 42.2)
Male	3,928 (% 57.8)
Neutrophil count ($\times 10^3$ μL)	7.16 ± 4.77 (0–67.08)
Platelet count ($\times 10^3$ μL)	274.40 ± 10,333 (1–1215)
Lymphocyte count ($\times 10^3$ μL)	2.22 ± 7.52 (0.03–407.23)
WBC (μL)	10.34 ± 9.49 (0.11–440.51)
NLR	5.81 ± 8.30 (0–181.07)
PLR	1,553.54 ± 2,411.56 (0–41,102.13)
Type of treatment	
Outpatient	4,686 (68.9%)
Inpatient	2,115 (31.1%)
MV requirement	
Patients requiring MV	540 (7.9%)
Patients not requiring MV	6,261 (92.1%)
Outcome	
Mortality	508 (7.5%)
Discharge	6,293 (92.5%)
SII	191.70 ± 164.68 (0.15–2.240)

SD — standard deviation; WBC — white blood cell; NLR — neutrophil-to-lymphocyte ratio; PLR — platelet-to-lymphocyte ratio; MV — mechanical ventilation; SII — systemic immune-inflammation index

(n = 3,928) were male. Of the patients, 7.9% (n = 540) required MV, and 7.5% (n = 508) died.

Table 2 shows the comparison of the demographic characteristics, laboratory values, and treatments of the patients according to mortality. Gender did not statistically significantly differ between the mortality and survivor groups ($p > 0.05$), but there were statistically significant differences in relation to the remaining parameters ($p < 0.001$).

SII was found to predict inpatient treatment with a sensitivity of 77.9% and a specificity of 36.2% at a cut-off value of 114.73 [area under the curve (AUC): 0.654]. The ROC curve analysis showed that SII was statistically significant in determining inpatient treatment ($p < 0.001$, 95% CI: 0.639–0.669) (Fig. 2).

SII was found to predict the MV requirement of the patients with a 70.0% sensitivity and 47.5% specificity at a cut-off value of 137.88 (AUC: 0.629). According to the ROC curve analysis, SII was statistically significant in determining the MV requirement ($p < 0.001$, 95% CI: 0.599–0.658) (Fig. 3).

It was determined that at a cut-off value of 137.99 (AUC: 0.626), SII had a sensitivity of 70.1% and a specificity of 47.4% in the prediction of mortality among the patients. The ROC curve analysis revealed that SII was statistically significant in determining mortality ($p < 0.001$, 95% CI: 0.596-0.657) (Fig. 4).

Table 2. Comparison of demographic characteristics, laboratory values, and treatments according to mortality

Variable	Survivor group (n = 6,293)	Mortality group (n = 508)	P-value
Age (years)	61.5 ± 17.1 (18–102)	72.5 ± 15.6 (20–101)	**< 0.001**
Gender			0.779
Female	3,638 (57.8%)	290 (57.1%)	
Male	2,655 (42.2%)	218 (42.9%)	
Neutrophil count (× 10^3 μL)	6.89 ± 4.37 (0–67.08)	10.45 ± 7.54 (0.01–48.32)	**< 0.001**
Platelet count (×10^3 μL)	277.74 ± 100.78 (1–1215)	233.15 ± 123.68 (4–792)	**< 0.001**
Lymphocyte count (×10^3 μL)	2.21 ± 5.88 (0.1–363.65)	2.35 ± 18.16 (0.03–407.23)	**< 0.001**
WBC (μL)	10.05 ± 7.71 (0.20–375.88)	13.85 ± 21.39 (0.11–440.51)	**< 0.001**
NLR	5.17 ± 7.13 (0–181.07)	13.75 ± 14.98 (0.02–102.29)	**< 0.001**
PLR	1,408.80 ± 2,085.18 (0–41,102.13)	3,346.48 ± 4,534.25 (0.27–34,951.44)	**< 0.001**
Type of treatment			**< 0.001**
Outpatient	4,686 (74.5%)	–	
Inpatient	1,607 (25.5%)	508 (100%)	
MV			**< 0.001**
Patients requiring MV	34 (0.5%)	506 (99.6%)	
Patients not requiring MV	6,259 (99.5%)	2 (0.4%)	
SII	183.51 ± 149.08 (0.18–2,240)	293.22 ± 277.06 (0.15–2,231.82)	**< 0.001**

WBC — white blood cell; NLR — neutrophil-to-lymphocyte ratio; PLR — platelet-to-lymphocyte ratio; MV — mechanical ventilation; SII — systemic immune-inflammation index

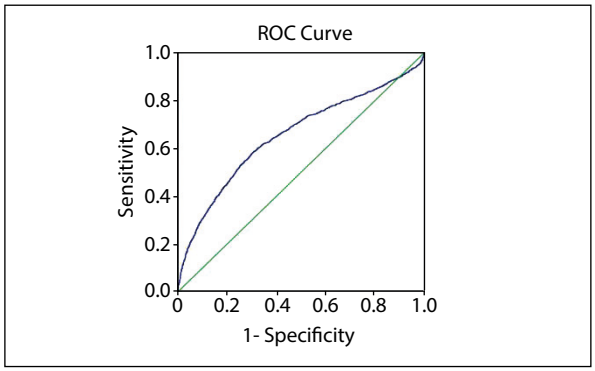

Figure 2. Receiver operating characteristic graph of the systemic immune-inflammation index in the prediction of patients' treatment types

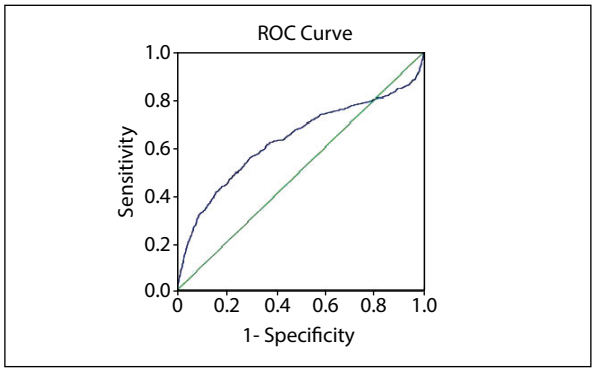

Figure 3. Receiver operating characteristic graph of the systemic immune-inflammation index in the prediction of patients' mechanical ventilation requirements

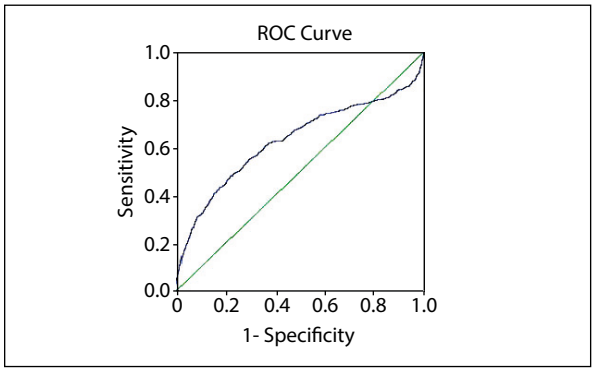

Figure 4. Receiver operating characteristic graph of the systemic immune-inflammation index in the prediction of mortality among the patients

Discussion

On completion of the study, it was determined that SII was successful in distinguishing patients who required hospitalized treatment among those presenting to the emergency department with pneumonia. In addition, it was observed that SII could assist in the prediction of mortality and the MV requirement among patients diagnosed with pneumonia.

A review of the literature shows that SII has been frequently used in the evaluation of inflammatory conditions and COVID-19 pneumonia. However, studies on pneumonia cases other than COVID-19 pneumonia are limited. In one of these studies, Wang et al. used SII to predict the development of stroke-associated

pneumonia (SAP) and determine clinical severity in patients with intracranial haemorrhage (ICH) [11]. The authors argued that SII could predict the development of SAP and show the severity of the disease in patients with ICH. However, an increased inflammatory response in cases of ICH may affect SII values; therefore, the presence of ICH in those patients may have been a factor that increased SII [11]. Similarly, in a study by Jiang et al., SII was found to be significant in predicting the development of postoperative pneumonia in patients with non-small cell lung cancer [12]. However, the presence of a history of malignancy among their patients may have affected the SII values. Examining long-term mortality in patients with ischaemic stroke who developed SAP, Xie et al. determined that SII values successfully predicted long-term mortality [13]. In the present study, patients with conditions that could affect SII values, such as a history of malignancy, were excluded from the study. In addition, pneumonia was the main reason for presentation to the emergency department among the patients selected for this study. Therefore, this study differs from previous studies in which cases of pneumonia that developed during another disease were examined (11–13). The study's patient selection was similar to that of Acar et al., who investigated the use of SII values in determining clinical severity and 28-day mortality in patients with community-acquired pneumonia [14]. Consistent with the study findings, the authors concluded that SII values were valuable in predicting mortality and clinical severity in patients with pneumonia [14].

NLR and PLR, which are among the inflammatory parameters used to evaluate patients with pneumonia presenting to the emergency department in terms of clinical severity, mortality, and hospitalization, have also been the subject of many studies [15, 16]. Altas et al. recommended the use of NLR and PLR together with clinical scores in determining clinical severity [15]. In a study by Enersen et al., NLR and PLR values were reported to be associated with 90-day mortality [16]. Although the evaluation of NLR and PLR was not the primary objective of the present study, when the effects of these parameters on clinical severity were evaluated, it was determined that they were both also associated with mortality and the use of MV during treatment.

One of the factors that determines both the development and clinical severity of pneumonia is advanced age. Age is considered an important part of clinical scoring systems, such as PSI and CURB-65, used to make the hospitalization decision in patients with pneumonia [17]. In the current study, the patient group with a mortal course of pneumonia was found to be older than the discharged patient group.

Conclusion

According to the results of this study, SII was valuable in determining the MV requirement and mortality among patients with pneumonia presenting to the emergency department. It is considered that SII values determined by a hemogram analysis, which is a low-cost and simple test, may be more feasible than expensive, time-consuming tests for the determination of patients at the emergency department.

Limitations

Our study has several limitations. Due to its retrospective nature, the data were obtained by screening electronic patient files; therefore, patients who did not have a COVID-19 test result in their electronic files but were infected with COVID-19 may have been overlooked. In addition, the data of patients who were referred to the emergency department of the hospital from another hospital and received pneumonia treatment were not included in the electronic files. These factors may have affected the present SII results.

Article information

Data availability statement: *All data is available.*

Ethics statement: *Ethical approval for the study was obtained from the local ethics committee.*

Funding: *None.*

Acknowledgements: *None.*

Conflict of interest: *None.*

Supplementary material: *None.*

References

1. Ayan E, Unver H. Diagnosis of Pneumonia from Chest X-Ray Images Using Deep Learning. 2019 Scientific Meeting on Electrical-Electronics & Biomedical Engineering and Computer Science (EBBT). 2019, doi: 10.1109/ebbt.2019.8741582.
2. Hincapié C, Ascuntar J, León A, et al. Community-acquired pneumonia: comparison of three mortality prediction scores in the emergency department. Colomb Med (Cali). 2021; 52(4): e2044287, doi: 10.25100/cm.v52i4.4287, indexed in Pubmed: 35499040.
3. Ko SH, Lee JS, Kim SK, et al. Serum cholesterol as a predictor of mortality among the elderly patients with pneumonia in the emergency department. Am J Emerg Med. 2021; 45: 404–409, doi: 10.1016/j.ajem.2020.09.012, indexed in Pubmed: 33039214.
4. Kim MW, Lim JY, Oh SH. Mortality prediction using serum biomarkers and various clinical risk scales in community-acquired pneumonia. Scand J Clin Lab Invest. 2017; 77(7): 486–492, doi: 10.1080/00365513.2017.1344298, indexed in Pubmed: 28678546.
5. Papasidero ID, Valli G, Marin D, et al. Utility of Measuring Circulating Bio-Adrenomedullin and Proenkephalin for 30-Day Mortality Risk Pre-

diction in Patients with COVID-19 and Non-COVID-19 Interstitial Pneumonia in the Emergency Department. Medicina (Kaunas). 2022; 58(12), doi: 10.3390/medicina58121852, indexed in Pubmed: 36557054.
6. Julián-Jiménez A, Castillo JG, Candel F. Usefulness and prognostic value of biomarkers in patients with community-acquired pneumonia in the emergency department. Medicina Clínica (English Edition). 2017; 148(11): 501–510, doi: 10.1016/j.medcle.2017.04.033.
7. Öcal L, Keskin M, Cerşit S, et al. Systemic immune-inflammation index predicts in-hospital and long-term outcomes in patients with ST-segment elevation myocardial infarction. Coron Artery Dis. 2022; 33(4): 251–260, doi: 10.1097/MCA.0000000000001117, indexed in Pubmed: 35044330.
8. Jomrich G, Paireder M, Kristo I, et al. High Systemic Immune-Inflammation Index is an Adverse Prognostic Factor for Patients With Gastroesophageal Adenocarcinoma. Ann Surg. 2021; 273(3): 532–541, doi: 10.1097/SLA.0000000000003370, indexed in Pubmed: 31425286.
9. Seo M, Yamada T, Morita T, et al. P589Prognostic value of systemic immune-inflammation index in patients with chronic heart failure. European Heart Journal. 2018; 39(suppl_1), doi: 10.1093/eurheartj/ehy564.p589.
10. Candemir M, Kiziltunç E, Nurkoç S, et al. Relationship Between Systemic Immune-Inflammation Index (SII) and the Severity of Stable Coronary Artery Disease. Angiology. 2021; 72(6): 575–581, doi: 10.1177/0003319720987743, indexed in Pubmed: 33685239.
11. Wang RH, Wen WX, Jiang ZP, et al. The clinical value of neutrophil--to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), platelet-to-lymphocyte ratio (PLR) and systemic inflammation response index (SIRI) for predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. Front Immunol. 2023; 14: 1115031, doi: 10.3389/fimmu.2023.1115031, indexed in Pubmed: 36860868.
12. Jiang R, Li P, Shen W, et al. The predictive value of the preoperative systemic immune-inflammation index in the occurrence of postoperative pneumonia in non-small cell lung cancer: A retrospective study based on 1486 cases. Thorac Cancer. 2023; 14(1): 30–35, doi: 10.1111/1759-7714.14691, indexed in Pubmed: 36495040.
13. Xie M, Yuan K, Zhu X, et al. Systemic Immune-Inflammation Index and Long-Term Mortality in Patients with Stroke-Associated Pneumonia. J Inflamm Res. 2023; 16: 1581–1593, doi: 10.2147/JIR.S399371, indexed in Pubmed: 37092129.
14. Acar E, Gokcen H, Demir A, et al. Comparison of inflammation markers with prediction scores in patients with community-acquired pneumonia. Bratisl Lek Listy. 2021; 122(6): 418–423, doi: 10.4149/BLL_2021_069, indexed in Pubmed: 34002616.
15. Altas OF, Kizilkaya M. The Effects of Neutrophil-Lymphocyte Ratio, Platelet-Lymphocyte Ratio and Prognostic Markers in Determining the Mortality in Patients Diagnosed With Pneumonia in Intensive Care. Medeni Med J. 2021; 36(2): 130–137, doi: 10.5222/MMJ.2021.64160, indexed in Pubmed: 34239765.
16. Enersen CC, Egelund GB, Petersen PT, et al. The ratio of neutrophil-to--lymphocyte and platelet-to-lymphocyte and association with mortality in community-acquired pneumonia: a derivation-validation cohort study. Infection. 2023 [Epub ahead of print], doi: 10.1007/s15010-023-01992-2, indexed in Pubmed: 36763284.
17. Martin-Loeches I, Torres A. New guidelines for severe community--acquired pneumonia. Curr Opin Pulm Med. 2021; 27(3): 210–215, doi: 10.1097/MCP.0000000000000760, indexed in Pubmed: 33405483.