European Review for Medical and Pharmacological Sciences 2022; 26: 3200-3205

Evaluation of the relationships between procalcitonin and neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in patients with pneumonia

E. ÇIL[1], G. KARADENIZ[2], S. YENIGÜN[1], G. ÇORAPLI[1]

[1]Department of Chest Diseases, Adıyaman University Training and Research Hospital, Adiyaman, Turkey
[2]Department of Chest Diseases, University of Health Sciences Dr Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital, Izmir, Turkey

Abstract. – OBJECTIVE: The aim of this study is to examine whether there is a relationship between procalcitonin and neutrophil/lymphocyte ratio or platelet/lymphocyte ratio in patients with pneumonia.

PATIENTS AND METHODS: The data of 54 patients hospitalized in the respiratory unit of the Adıyaman University Faculty of Medicine Hospital (Adıyaman, Turkey) with the diagnosis of pneumonia between January 2018 and July 2019 were reviewed retrospectively. The patients' complete blood count, procalcitonin, erythrocyte sedimentation rate, and C-reactive protein data were obtained. Diagnosis was made by chest X-ray and, for some patients, by thorax computed tomography together with appropriate clinical findings. Patients with a history of tumors, trauma, burns, surgery, kidney failure, inflammatory diseases or non-pulmonary infections were excluded from the study.

RESULTS: The mean age of the patients was 59.04±20.00 years in the group with normal procalcitonin and 66.04±18.28 years in the group with elevated procalcitonin (*p*: 0.186). The female/male sex ratio of the patients was 15/13 in the group with normal procalcitonin and 8/18 in the group with elevated procalcitonin (*p*: 0.090). Neutrophil/lymphocyte ratio was 3.97 (1.20-10.77) in the group with normal procalcitonin and 7.21 (0.60-29.50) in the group with elevated procalcitonin (p: 0.012). Platelet/lymphocyte ratio was 155.54±68.89 in the group with normal procalcitonin and 157.48±81.38 in the group with elevated procalcitonin (*p*: 0.925). In ROC analysis performed to predict elevated levels of procalcitonin, cut-off values were 16.4 $\times 10^3/mm^3$ for white blood cells (*p*: 0.003), 11.7 $\times 10^3/mm^3$ for neutrophils (*p*: 0.001), 5.47 for neutrophil/lymphocyte ratio (*p*: 0.005), and 7.4 mg/dL for C-reactive protein (*p*: 0.005).

CONCLUSIONS: In our study, white blood cell, neutrophil, neutrophil/lymphocyte ratio, and C-reactive protein values were found to be significantly higher in patients with elevated procalcitonin. The neutrophil/lymphocyte ratio was also significantly correlated with white blood cell count and platelet/lymphocyte ratio.

Key Words:
Pneumonia, Neutrophil/lymphocyte ratio, Procalcitonin.

Introduction

Pneumonia is the inflammation and infection of the lung parenchyma tissue, generally caused by microorganisms such as bacteria, viruses, and fungi. Parenchymal inflammation caused by non-infectious agents (e.g., acid-alkaline substance inhalation or radiation) is called pneumonitis[1]. Although C-reactive protein (CRP) levels increase with inflammation, CRP cannot be used to differentiate between bacterial and non-bacterial inflammation[2]. On the other hand, the elevated procalcitonin levels induced by bacterial infections indicate the general immunological activity of the organism. Viral infections do not cause increases in procalcitonin[3]. Studies have shown that procalcitonin and the neutrophil/lymphocyte ratio (NLR) have equivalent diagnostic accuracy in bacterial infections[4]. The aim of our study is to examine whether there is any relationship between procalcitonin and the neutrophil/lymphocyte ratio (NLR) or platelet/lymphocyte ratio (PLR) in patients with pneumonia.

Corresponding Author: Ercan Çil, MD; e-mail: cil.ercan@hotmail.com

Patients and Methods

The outpatient clinic data of a total of 54 patients hospitalized in the respiratory unit of the Adıyaman University Faculty of Medicine Hospital (Adıyaman, Turkey) with the diagnosis of community-acquired pneumonia between January 2018 and July 2019 were reviewed retrospectively. The patients' complete blood count, procalcitonin, erythrocyte sedimentation rate, and CRP data were obtained. The diagnosis of pneumonia was made according to appropriate clinical findings such as fever, cough, and sputum, as well as increased density such as parenchymal infiltration and consolidation in chest X-rays and thorax computed tomography in some cases. Patients with a history of tumors, trauma, burns, surgery, kidney failure, inflammatory diseases, immunosuppressive conditions, and extrapulmonary infections were excluded from the study. Patients were divided into two groups as those with normal procalcitonin levels (≤0.12 ng/mL) and those with elevated procalcitonin levels (>0.12 ng/mL).

Complete blood count results were studied with a 24-parameter CELL-DYN Ruby device (Abbott, Wiesbaden, Germany) and procalcitonin with an AQT90 Flex device (Radiometer, Bronshoj, Denmark).

Statistical Analysis

All data were analyzed using IBM SPSS Statistics 23.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean±standard deviation (minimum-maximum) and numbers (percentages). Chi-square tests were used to compare categorical data. Independent Student's *t*-tests were employed to compare normally distributed continuous data and the data were expressed as mean±standard deviation. Mann-Whitney U tests were used to compare data that did not show normal distribution, which were expressed as median (minimum-maximum). Pearson correlation tests were used to determine correlations between procalcitonin and other laboratory parameters. Analysis of the area under receiver operating characteristic curves (AU-ROC) was performed to calculate the cut-off values for the parameters of NLR, white blood cell (WBC) count, and CRP in the diagnosis of bacterial pneumonia. Values of $p<0.05$ were considered statistically significant.

Results

The mean age of the patients was 59.04±20.00 years in the group with normal procalcitonin and 66.04±18.28 years in the group with elevated procalcitonin (*p*: 0.186). The sex distribution of the patients (female/male) was 15/13 in the group with normal procalcitonin and 8/18 in the group with elevated procalcitonin (*p*: 0.090). Demographic data and blood parameters of the groups are shown in Table I. WBC, neutrophil, NLR, and CRP values were found to be significantly higher in the group with elevated procalcitonin. The WBC value was 11.90 (5.00-16.40) × 10^3/mm^3 in the group with normal procalcitonin and 15.40 (4.20-26.00) × 10^3/mm^3 in the group with elevated

Table I. Demographic data and blood parameters in patients with pneumonia with normal and elevated procalcitonin levels.

	Patients with nomal procalcitonin (procalcitonin ≤ 0.12 ng/mL) n: 28	Patients with elevated procalcitonin (procalcitonin> 0.12 ng/mL) n: 26	*p*-value
Age[a]	59.04 ± 20.00	66.04 ± 18.28	0.186
Sex (female/male)[b]	15/13	8/18	0.090
White blood cells[c] × 10^3/mm^3	11.90 (5.00-16.40)	15.40 (4.20-26.00)	0.008*
Neutrophils[c] × 10^3/mm^3	8.20 (2.90-14.00)	11.75 (2.80-22.70)	0.005*
Lymphocytes[a] × 10^3/mm^3	2.13 ± 0.82	2.23±1.90	0.784
Platelets[a] × 10^3/mm^3	291.41 ± 86.74	254.16 ± 87.17	0.122
Neutrophil/lymphocyte ratio[c]	3.97 (1.20-10.77)	7.21 (0.60-29.50)	0.012*
Platelet/lymphocyte ratio[a]	155.54 ± 68.89	157.48 ± 81.38	0.925
Sedimentation rate[a] (mm/h)	38.62 ± 21.84	39.00 ± 23.53	0.952
C-reactive protein[c] (mg/dL)	7.70 (1.20-43.00)	12.25 (1.90-35.80)	0.014*

[a]Independent Student *t*-test (mean ± SD); [b]Chi-square test (numbers); [c]Mann-Whitney U test [median (minimum-maximum)], *$p < 0.05$.

Table II. AU-ROC analysis results for the prediction of bacterial pneumonia.

	Cut-off value	AUC	95% CI	*p*
White blood cells (× 10^3/mm^3)	16.4	0.709	0.569-0.824	0.003*
Neutrophils (× 10^3/mm^3)	11.7	0.723	0.585-0.836	0.001*
Neutrophil/lymphocyte ratio	5.47	0.700	0.560-0.817	0.005*
C-reactive protein (mg/dL)	7.4	0.694	0.554-0.812	0.007*

*$p < 0.05$.

procalcitonin (*p*: 0.008). The neutrophil count was 8.20 (2.90-4.00) × 10^3/mm^3 in the group with normal procalcitonin and 11.75 (2.80-22.70) × 10^3 /mm^3 in the group with elevated procalcitonin (*p*: 0.005). The NLR was 3.97 (1.20-10.77) in the group with normal procalcitonin and 7.21 (0.60-29.50) in the group with elevated procalcitonin (*p*: 0.012). CRP values were 7.70 (1.20-43.00) mg/dL in the group with normal procalcitonin and 12.25 (1.90-35.80) mg/dL in the group with elevated procalcitonin (*p*: 0.014) (Table I).

In the AU-ROC analysis conducted to predict elevated procalcitonin, the WBC cut-off value was found as 16.4 (×10^3/mm^3) (AUC: 0.709, 95% CI: 0.569-0.824; *p*: 0.003), the neutrophil cut-off value was 11.7 (×10^3/mm^3) (AUC: 0.723, 95% CI: 0.585-0.836; *p*: 0.001), the NLR cut-off value was 5.47 (AUC: 0.700, 95% CI: 0.560-0.817; *p*: 0.005), and the CRP cut-off value was 7.4 mg/dL (AUC: 0.694, 95% CI: 0.554-0.812; *p*: 0.005) (Table II; Figure 1).

In correlation analysis, significant correlations were found between NLR and WBC and between NLR and PLR (r: 0.442, *p*: 0.001 and r: 0.495, *p*: 0.000, respectively). However, no significant correlation was observed between procalcitonin and WBC, CRP, NLR, and PLR (Table III).

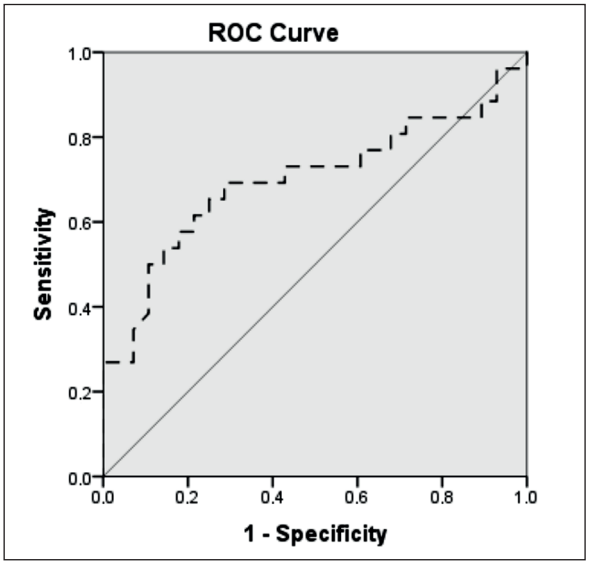

Figure 1. ROC curve for neutrophil/lymphocyte ratio in the prediction of bacterial pneumonia.

Discussion

WBC, neutrophil, NLR, and CRP values were found to be significantly higher in patients with elevated procalcitonin in our study, but PLR

Table III. Correlation table of white blood cell (WBC), C-reactive protein (CRP), neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and procalcitonin levels.

	WBC	CRP	NLR	PLR	Procalcitonin
WBC		r: 0.188 *p*: 0.173	r: 0.442 ***p*: 0.001**	r: -0.086 *p*: 0.537	r: 0.055 *p*: 0.693
CRP	r: 0.188 *p*: 0.173		r: 0.162 *p*: 0.243	r: 0.116 *p*: 0.403	r: 0.219 *p*: 0.112
NLR	r: 0.442 ***p*: 0.001**	r: 0.162 *p*: 0.243		r: 0.495 ***p*: 0.000**	r: 0.138 *p*: 0.318
PLR	r: -0.086 *p*: 0.537	r: 0.116 p: 0.403	r: 0.495 ***p*: 0.000**		r: -0.006 *p*: 0.968
Procalcitonin	r: 0.055 *p*: 0.693	r: 0.219 p: 0.112	r: 0.138 *p*: 0.318	r: -0.006 *p*: 0.968	

*$p < 0.05$.

was not found to differ significantly. NLR was significantly correlated with WBC and PLR. In ROC analysis performed to predict elevated levels of procalcitonin, cut-off values were 16.4 for WBC, 11.7 for neutrophils, 5.47 for NLR, and 7.4 for CRP. Procalcitonin, CRP, NLR, PLR, and WBC levels are important prognostic markers in pneumonia[5-12].

In our study, a significant relationship was found between elevated procalcitonin levels and NLR and CRP. In the mortality study conducted by Beyaz et al[13], a significant positive correlation was found between procalcitonin and NLR and CRP in patients with pneumonia. However, no significant correlation was found between procalcitonin and CRP and NLR in our study.

In the study conducted by Huang et al[14], 80 individuals with pneumonia and 49 healthy individuals were included. In their study, similar to ours, no significant correlation was found between procalcitonin and PLR. While no significant correlation was found between procalcitonin and NLR in our study, a significant relationship was found between procalcitonin and NLR in theirs.

In the study conducted by Yang et al[15] involving patients with community-acquired pneumonia, NLR showed a positive correlation with CRP and procalcitonin. In that study, no significant difference was found in the ROC analysis of the AUC values for WBC, CRP, NLR, and PLR levels ($p>0.05$).

In another study, values of CRP, NLR, and PLR were found to be higher among pneumonia patients compared to a control group. Considering the cut-off values, the following results were obtained: CRP, 20.25 mg/L; NLR, 2.54; PLR, 105.17 ($p<0.05$). According to ROC analysis, AUC values were 0.69 for CRP, 0.68 for NLR, and 0.63 PLR, and no significant difference was found between the two variables ($p>0.05$)[16]. In our study, the NLR cut-off value was determined as 5.47 with an AUC of 0.700 and the CRP cut-off was 7.4 with an AUC of 0.694 for predicting elevated levels of procalcitonin in pneumonia patients ($p<0.05$).

In the study conducted by Zheng et al[17], the highest AUC value was obtained for CRP when CRP, NLR, and WBC values were compared in ROC analysis. In our study, on the other hand, the highest AUC value was obtained for neutrophil count.

Lee et al[18] found a significant correlation between procalcitonin and CRP and NLR in their study involving 154 patients. In our study, a significant relationship was found between elevated procalcitonin levels and NLR and CRP. In the study of Lee et al[18], a positive correlation was found between procalcitonin and CRP, but no correlation was found between procalcitonin and NLR. In our study, however, no significant correlation was found between procalcitonin and CRP, NLR, and PLR.

In the prospective study conducted by Sosrohandoyo et al[19] that included 48 patients with sepsis, no correlation was found between procalcitonin and NLR and PLR. In our study, similarly, no correlation was found between procalcitonin and NLR and PLR. In certain other studies[20,21] conducted with sepsis patients, as in our study, no significant correlation was found between procalcitonin and NLR. In the study conducted Nurdani et al[22], contrary to our findings, a strong correlation was reported between procalcitonin and NLR in sepsis patients. In a study conducted by Arif et al[23] that included 65 patients, it was shown that procalcitonin was superior to NLR in distinguishing between patients with sepsis and severe sepsis. In the same study, a significant correlation was found between procalcitonin and NLR. In another study of sepsis conducted by Rehman et al[24], a significant correlation was found between NLR and procalcitonin, unlike our study. In a study conducted by Dursun et al[25] with pediatric patients with a diagnosis of sepsis, a positive correlation was found between procalcitonin and CRP and NLR, unlike in our study. In another study conducted by Cengiz et al[26] in a pediatric intensive care unit, a positive correlation was found between NLR and CRP and procalcitonin. In our study, however, no correlation was found between procalcitonin and NLR.

In our study, a significant relationship was found between elevated levels of procalcitonin and WBC, NLR, and CRP levels. However, no significant finding was found for the correlation of procalcitonin. Findings related to correlation are different in the literature, and it was thought that the reason for this might be the lack of differentiation between viral and bacterial infections because NLR increases due to lymphopenia in cases of viral infections while procalcitonin does not increase. Therefore, there may not be a correlation between procalcitonin and NLR. Further studies are needed to compare procalcitonin with NLR and PLR while separating cases of viral and bacterial infections.

The limitations of our study are that it was retrospective, the number of patients was small, the diagnosis of pneumonia was performed according to clinical and radiological findings, and

sputum culture results were not available for every patient. In our study, there were no patients who passed away in the ward; thus, no mortality comparisons could be made.

Conclusions

Complete blood count parameters such as WBC count, neutrophil count, and NLR are easier and cheaper to obtain than procalcitonin levels. However, complete blood count parameters may be affected by countless different biological processes and events. Therefore, it may be necessary to evaluate procalcitonin and complete blood count parameters together in some cases.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Funding

None.

Authors' Contribution

Data collection: EÇ, GK and SY. Data analysis: EÇ, GK and GÇ. Writting the manuscript: EÇ, GK, SY and GÇ. Reviewed and edited of the manuscript: All authors.

Ethics Approval and Consent to Participate

The study was in accordance with Declaration of Helsinki and was approved by the Adıyaman University Faculty of Medicine Ethical Committee.

ORCID ID

Ercan Çil: 0000-0002-8981-4232.

References

1) Özhan MH. Pömoni: Giriş ve Sınıflama. Tüsad 2016: 7-9.
2) Ertuğrul Ö, Ertuğrul MB. Prokalsitonin ve infeksiyon. Klimik Dergisi 2005; 18: 59-62.
3) Ortatatlı M, Özgüven V, Şengül A. Sepsis ve ağır infeksiyonların tanı ve takibinde yeni bir marker: Prokalsitonin. Flora 2009; 4: 151-155.
4) Ljungström L, Pernestig AK, Jacobsson G, Andersson R, Usener B, Tilevik D. Diagnostic accuracy of procalcitonin, neutrophil-lymphocyte count ratio, C-reactive protein, and lactate in patients with suspected bacterial sepsis. PLoS One 2017; 12: e0181704.
5) Schuetz P, Albrich W, Mueller B. Procalcitonin fo rdiagnosis of infection and guide to antibiotic decisions: past, present, andfuture. BMC Med 2011; 9: 107.
6) Sager R, Wirz Y, Amin D, Amin A, Hausfater P, Huber A, Haubitz S, Kutz A, Mueller B, Schuetz P. Are admission procalcitonin levels universal mortality predictors across different medical emergency patient populations? Results from the multi-national, prospective, observational TRIAGE study. Clin Chem Lab Med 2017; 55: 1873-1880.
7) Berg P, Lindhardt BØ. The role of procalcitonin in adult patients with community-acquired pneumonia—A systematic review. DanMedJ 2012; 59: A4357.
8) Chalmers JD, Singanayagam A, Hill AT. C-reactive protein is an independent predictor of severity in community acquired pneumonia. Am J Med 2008; 121: 219-225.
9) Smith RP, Lipworth BJ. C-reactive protein in simple community-acquired pneumonia. Chest 1995; 107: 1028-1031.
10) Kim H, Kim Y, Kim KH, Yeo CD, Kim JW, Lee HK. Use of delta neutrophilindex for differentiating low-grade community-acquired pneumonia from upper respiratory infection. Ann Lab Med 2015; 35: 647-650.
11) Lee JH, Song S, 2, Yoon SY, Lim CS, Song JW, Kim HS. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio as diagnostic markers for pneumonia severity. Br J Biomed Sci 2016; 73: 140-142.
12) Ebell MH, Bentivegna M, Cai X, Hulme C, Keaney M. Accuracy of Biomarkers for the Diagnosis of Adult Community-acquired Pneumonia: A Meta-analysis. Acad Emerg Med 2020; 27: 195-206.
13) Beyaz A, Atilla N, Arpağ H, Bozkuş F, Kahraman H, Uğuz F. The effect of C-reactive protein, procalcytonine, neutrophil/lymphocytelevels on mortality and duration of hospital stay in pneumonia. Anatolian Curr Med J 2021; 3; 15-19.
14) Huang Y, Liu A, Liang L, Jiang J, Luo H, Deng W, Lin G, Wu M, Li T, JiangY. Diagnostic value of blood parameters for community-acquired pneumonia. Int Immunopharmacol 2018; 64: 10-15.
15) Yang T, Wan C, Wang H, Qin J, Chen L, ShenY, Wen F. The prognostic and risk-stratified value of neutrophil–lymphocyte coun tratio in Chinese patients with community-acquired pneumonia. Eur J Inflamm 2017; 15: 22-27.
16) Kartal O, Kartal AT. Value of neutrophil to lymphocyte and platelet to lymphocyte ratios in pneumonia. Bratisl Lek Listy 2017; 118: 513-516.
17) Zheng N, Zhu D, Han Y. Procalcitonin and C-reactive protein perform beter than the neutrophil/lymphocyte count ratio in evaluating hospital acquired pneumonia. BMC Pul Med 2020; 20: 166.

18) Lee JH, Yoon SY, Kim HS, Lim CS. Characteristics of the mean platele volume, neutrophiltolymphocyte ratio, and C-reactive protein compared to the procalcitonin level in pneumonia patients. Platelets 2015; 26: 278-280.

19) Sosrohandoyo SU, Abadi S, Katu S, Halim R, Bakri S, Kasim H, Benyamin AF, Seweng A. Neutrophil-to-Lymphocyte Ratio, Monocyte-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and, Mean Platelet Volume-to-Platelet Count Ratio with Procalcitonin in Sepsis Patients. Annals of R.S.C.B. ISSN: 1583-6258.2021; 25: 6708-6713.

20) Jonathan J, Pradian E, Zulfariansyah A. Correlation between neutrophil lymphocyte count ratio and procalcitonin in sepsis and septic shock. Majalah Kedokteran Bandung 2019; 51: 165-171.

21) Djordjevic D, Rondovic G, Surbatovic M, Stanojevic I, Udovicic I, Andjelic T, Zeba S, Milosavljevic S, Stankovic N, Abazovic D, Jevdjic J, Vojvodic D. Neutrophil-to-Lymphocyte Ratio, Monocyte-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and, Mean Platelet Volume-to-Platelet Count Ratio as Biomarkers in Critically Ill and Injured Patients: Which Ratio to Choose to Predict Outcome and Nature of Bacteremia? Mediators Inflamm 2018; 2018: 3758068.

22) Nurdani A, Hadi U, Arfijanto MV, Rusli M, Bramantono, Miftahussurur M. Neutrophil-lymphocyte ratio and procalcitonin levels in sepsis patient. The New Armenian Medical Journal 2019; 13: 48-54.

23) Arif SK, Rukka ABS, Wahyuni S.Comparison of neutrophils-lymphocytes ratio and procalcitonin parameters in sepsis patient treated in intensive care unit Dr. Wahidin Hospital, Makassar, Indonesia. J Med Sci 2017; 17: 17-21.

24) Rehman FU, Khan A, Aziz A, Iqbal M, Mahmood S, Ali N. Neutrophils to Lymphocyte Ratio: Earliest and Efficacious Markers of Sepsis. Cureus 2020; 12: e10851.

25) Dursun A, Ozsoylu S, Akyildiz BN. Neutrophil-to-lymphocyte ratio and mean platelet volume can be useful markers to predict sepsis in children. Pak J Med Sci 2018; 34: 918-922.

26) Cengiz H, Yılmaz K, Pirinççioğlu AG, Kan A. Evaluation of Biomarkers in Patients with Sepsis Diagnosis in Pediatric Intensive Care Unit. The Ulutas Medical Journal 2021; 7: 77-85.