Original Article

An Investigation of the Effects of the Mean Platelet Volume, Platelet Distribution Width, Platelet/Lymphocyte Ratio, and Platelet Counts on Mortality in Patents with Sepsis who applied to the Emergency Department

M Orak, Y Karakoç, M Üstündag, Y Yildirim[1], MK Çelen[2], C Güloglu

Departments of Emergency, [1]Internal Medicine and [2]Infection Diseases, University of Dicle, Diyarbakır, Turkey

Abstract

Aim: The aim of this study is to examine the role of the mean platelet volume (MPV), platelet distribution width (PDW), platelet/lymphocyte ratio (PLR), and platelet values for predicting mortality in patients with sepsis. **Materials and Methods:** This is a retrospective study, involving patients 18 years and above who were diagnosed with sepsis. Blood samples were analyzed for platelets characteristics (counts, MPV, PDW, and PLR). The patients were separated into two groups namely the survivors and deceased. The two groups' MPV, PDW, PLR, and platelet counts which were considered to have an effect on mortality, were compared. **Results:** Three hundred and thirty patients who were diagnosed with sepsis in our emergency department and complying with the study participation criteria were studied retrospectively. Comparison of the MPV, PDW, PLR, and platelet counts of the deceased and survivors showed that the MPV, PDW, and PLR were higher in the deceased while the platelet counts were higher in the survivors. **Conclusion:** The low number of platelets in patients with sepsis at the moment of application and the high PDW and PLR values are valuable for predicting a high mortality.

Keywords: *Mean platelet volume, mortality, platelet distribution width, platelet/lymphocyte ratio, sepsis*

Date of Acceptance:
26-Oct-2017

Introduction

Sepsis is associated with morbidity and mortality and could be caused by community and hospital-acquired infections. Despite the supportive treatments and effective antibiotics, it leads to 30%–70% mortality in affected patients.[1] Sepsis is a significant cause of morbidity and mortality in the elderly and in patients whose immune system is repressed and in critically ill patients.[2] The delays in diagnosis also play a role in the escalation of mortality and morbidity. Therefore, recent sepsis guides emphasize the early diagnosis considerably. In this context, studies concentrate on the indicators for early diagnosis intensively.[3]

Nowadays, reports are submitted on sepsis pathogenesis and new molecular goals, novel diagnosis and follow-up parameters are designated however despite these innovations, the anticipated decline in the disease mortality has not been attained. One of the reasons for this is the inadequacy of effective, easily reproducible, and inexpensive follow-up parameters. The mean platelet volume (MPV) and platelet distribution width (PDW) are whole blood parameters studied in almost all laboratories routinely.[4] The MPV and PDW applications are the indicators for predicting clotting activation.[5] The MPV can reflect endothelial damages as well as platelet activation and is an easily accessible hematologic parameter.[6] Platelet/lymphocyte ratio (PLR) analysis is

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_44_17

Address for correspondence: Dr. M Üstündag, Department of Emergency Medicine, University of Dicle, 21280 Diyarbakır, Turkey.
E-mail: ustundag@dicle.edu.tr

How to cite this article: Orak M, Karakoç Y, Üstündag M, Yildirim Y, Çelen MK, Güloglu C. An investigation of the effects of the mean platelet volume, platelet distribution width, platelet/lymphocyte ratio, and platelet counts on mortality in patents with sepsis who applied to the emergency department. Niger J Clin Pract 2018;21:667-71.

Table 1: The distribution of gender, age, comorbid illness and hospitalization period of our patients

	Survivors *n*=111 (%33.6)	Deceased *n*=219 (%66.4)	Total *n*=330 (%100)	*P*
Gender				
Male	60(%54.1)	124(%56.6)	184(%55.8)	0.725
Female	51(%45.9)	95(%43.4)	146(%44.2)	
Age	52.94±20.05	67.78±17.04	62.79±19.39	<0.001
Comorbid Illness				
Diabetes Mellitus	32(%28.8)	95(%43.4)	127(%38.5)	0.012
Hypertension	8(%7.2)	44(%20.1)	52(%15.8)	0.002
Chronic Renal Failure	12(%10.8)	36(%16.4)	48(%14.5)	0.189
Chronic Liver Disease	1(%0.9)	8(%3.7)	9(%2.7)	0.282
Chronic Obstructive	0(%0)	7(%3.2)	7(%2.1)	0.100
Pulmonary Disease				
Malignancy	7(%6.3)	34(%15.5)	41(%12.4)	0.021
Other*	13(%11.7)	36(%16.4)	49(%14.8)	0.326
Absent	57(%51.4)	51(%23.3)	108(%32.7)	<0.001
Hospitalization Period	12.69±6.26	10.44±10.18	11.20±9.11	0.014

*Ischemic heart disease, Cerebrovascular disease, Tuberculosis, Alzheimer's disease, Congestive heart failure, Metabolic syndrome, Rheumatoid arthritis

Table 2: The distribution of whole blood parameters of our patients

Whole Blood Parameters	Survivors *n*=111 (%33.6)	Deceased *n*=219 (%66.4)	*P*
White Blood Cell (K/uL; mean±SD)	17.20±6.87	18.21±10.60	0.300
MPW (fL; mean±SD)	8.19±1.66	8.75±1.82	0.006
PDW [10(GSD);Mean±SD]	18.00±1.14	19.20±2.13	<0.001
Platelet (K/uL; Mean±SD)	268.07±132.10	227.59±127.81	0.008
PLR (Mean±SD)	240.97±171.54	364.05±452.56	<0.001
Hemoglobin (g/dl; mean±SD)	11.99±2.57	11.31±2.33	0.019
Hematocrit (%; mean±SD)	36.39±6.99	34.74±7.69	0.051
Neutrophil ($10e^3$/uL; Mean±SD)	16.91±24.23	15.33±7.80	0.503
Lymphocyte ($10e^3$/uL; Mean±SD)	1.44±1.24	1.29±1.39	0.308

used as a novel, an inexpensive and simple indicator of inflammation, and platelet activity searched in hemogram studies.[7] Previous studies reported that the changes in platelet functions and sizes were related to systemic inflammation and it was considered that PDW can be valuable in predicting some disease outcomes.[8,9] In this study, we aimed to examine the function of the MPV, PDW, PLR, and platelet values for predicting mortality in patients with sepsis.

Materials and Methods

This study was approved by Dicle University Faculty of Medicine Ethics Committee for a retrospective analysis of the medical information of patients presenting to Dicle University Faculty of Medicine Emergency Department with sepsis between January 2012 and May 2015. It included patients older than 18 years who admitted to our emergency department with various symptoms and were diagnosed with sepsis and who also had complete blood count results.

Criteria for exclusion from the study:

- Being younger than 18-year-old
- Having idiopathic thrombocytopenic purpura or thrombotic thrombocytopenic purpura or essential thrombocytosis
- Having a history of medication use leading to the disorders of platelet structure and function
- Missing medical information in hospital's automation system.

The age, gender, comorbid illness, whole blood count parameters, culture results, clinic, hospitalization period, and results of the patients were reviewed. The patients were separated into two groups, namely the survivors and deceased. The two groups' MPV, PDW, PLR, and platelet counts, which were considered to have an effect on mortality, were compared.

Statistical analyses

The univariate analyses of the categorical variables were performed by using Ki-square test (χ^2) and the univariate analyses of the continuous variables were carried out with the Student's *t*-test. The average values were estimated as a mean ± standard deviation. Values of $P < 0.05$ were considered as statistically significant.

Table 3: The distribution of our patients with other sepsis focuses

Sepsis Focus	Survivors *n*=111 (%33.6)	Deceased *n*=219 (%66.4)	*P*
Skin	31(%27.9)	13(%5.9)	<0.001
Lungs	8(%7.2)	71(%32.4)	<0.001
Gastrointestinal System	4(%3.6)	17(%7.8)	0.161
Genitourinary System	52(%46.8)	126(%57.5)	0.079
Other	16(%14.4)	37(%16.9)	0.636
Absent	13(%11.7)	30(%13.7)	0.730

Table 4: The distribution of the microorganisms reproduced in the cultures of the patients

Cultured microorganism	Survivors *n*=111 (%33.6)	Deceased *n*=219 (%66.4)	*P*
E. coli	42(%37.8)	104(%47.5)	0.102
Acinetobacter	3(%2.7)	32(%14.6)	0.001
Streptococcus	0(%0)	1(%0.5)	1.000
Staphylococcus	29(%26.1)	43(%19.6)	0.204
Candida	5(%4.5)	6(%2.7)	0.517
Pseudomonas	2(%1.8)	7(%3.2)	0.723
Other*	20(%18.0)	38(%17.4)	0.879

*Klebsiella, Proteus, Enterococcus, Bacteroides, Salmonella, Brucella

Results

Three hundred and thirty patients who were diagnosed with sepsis in our emergency department and complying with the study participation criteria were studied retrospectively. There were 111 (33.6%) survivors and 219 (66.4%) deceased patients. Nearly 44.2% (n = 146) of the patients were female and 55.8% (n = 184) were male. The average age was 62.79 ± 19.39. About 43.4% (n = 95) of the deceased patients were female and 56.6% (n = 124) of the patients were male and their average age was 67.78 ± 17.04. There was no statistically significant difference in terms of gender between the survivors and deceased, and the age average of the deceased was significantly higher than that of the survivors (P = 0.725 and P < 0.001, respectively,). The cases of diabetes mellitus, hypertension, and malignancy in terms of comorbidity were found statistically significant in favor of mortality (P was 0.012, 0.002, and 0.021, respectively). In contrast, the absence of comorbid conditions was found to be statistically significant in favor of surviving (P < 0.001). The hospitalization periods of the patients who were diagnosed with sepsis and deceased were found shorter statistically significantly in comparison to the survivors (P = 0.014). The distribution of gender, age, comorbid illness, and hospitalization period of our patients is shown in Table 1.

Comparison of the MPV, PDW, PLR, and platelet values of the deceased and survivors exhibited that the MPV, PDW, and PLR values of the deceased patients were high and their platelet counts were lower than the survivors. The difference was statistically significant in favor of mortality (P = 0.006, P < 0.001, P < 0.001, and P = 0.008, respectively). The distribution of whole blood parameters of our patients is shown in Table 2.

Considering the site of sepsis focuses of our patients, the mortality rate of the patients with septic focus in the lungs was higher, and the mortality rate of our patients with skin-focused sepsis was low statistically significantly (P < 0.001). The distribution of our patients with other sepsis foci) is shown in Table 3.

Considering the microorganisms in the patients' cultures, the most frequently detected microorganism was *Escherichia coli* however the mortality rate of the patients whose cultures grew Acinetobacter was higher and statistically significantly (P = 0.001). The distribution of the microorganisms in the cultures which produced blood sample of the patients is shown in Table 4.

Discussion

Sepsis is defined as a systemic inflammatory response of the host to infection. It is a significant cause of morbidity and mortality, especially in the elderly and in patients whose immune system is repressed and in critically ill patients. It is one of the causes of death most frequently seen in intensive care units in addition to coronary intensive care units. In sepsis, an inexpensive and easily obtained biomarker is needed with a high sensitivity and specificity.[10]

The hemodilution, increase in the rate of platelet consumption and platelet destruction caused by the immune system lead to thrombocytopenia in critically ill patients.[11] Production climbs at the beginning of septicemia due to platelet destruction, and larger and younger platelets are secreted to the peripheral blood. However, bone marrow is repressed subsequently, and thrombocytopenia is seen.[12,13] Bone marrow biopsy was performed in 59 patients with sepsis who were hospitalized in the intensive care unit, and by comparing these patients with the control group, macrophage colony-stimulating factor values were found to be high, and it was considered that thrombocytopenia occurred in patients with sepsis was related with this outcome.[14] Guida *et al*. have reported that the platelet level of the patients with neonatal sepsis was low.[15] In the study of Vanderschueren *et al*., 329 patients with sepsis hospitalized in the intensive care unit were studied and the relationship between thrombocytopenia and mortality was assessed and it was found that the patients had higher mortality rate whose platelet number was 150,000 and under, and had more than 50% reduction in

their platelet number during follow-ups. It was reported that the platelet number was an independent factor for the assessment of mortality of patients with sepsis and comparing this factor with the other factors exhibited that it was more statistically significant.[16] In this study, it was designated that the low platelet number was related to mortality similar to the literature.

The MPV is an average size of platelets. Elevated MPV may indicate endothelial damages as well as platelet activation and is an easily accessible hematological parameter.[6] In the clinical study of Nelson and Kehl, it was uncovered that the thrombocyte consumption and MPV values escalated in acute infections.[17] Becchi *et al*. showed in their study that the MPV could be used as an indicator of platelet behavior and malfunction in indirect platelet production and activation during sepsis response. The MPV escalation was found crucial for predicting prognosis in early stage sepsis. Moreover, the MPV values at the moment of application were higher in the deceased patients in comparison to the survivors.[18] The studies conducted on patients with neonatal sepsis reported that the MPV values were high.[15,19] In the study of Daniel conducted on 191 patients with sepsis, the increase in the MPV values was found significant in terms of prognosis and mortality.[20] In this study, the high MPV values were found significant in favor of mortality similar to the other studies.

The PDW is a marker indicating the changes indirectly measurable platelet size and the platelet activation.[21] Zhang *et al*. have reported that the MPV and PDW values were valuable for predicting mortality in patients hospitalized in intensive care units.[8] Patrick and Lazarchick found in their study that the PDW levels were dramatically high in patients with late-starting neonatal sepsis.[19] Gao *et al*. have reported that the platelet count decreased and the PDW amounts increased in patients with sepsis, due to this lead to increased mortality rate.[22] In the study of Njoroge *et al*. conducted on 125 cases for the use of hematological parameters for sepsis follow-ups and uncovered that the MPV and PDW escalation was a messenger for mortality.[23] In this study, the augmented PDW values were found significant in terms of mortality in parallel to the literature.

The PLR is designated by proportioning the platelet number and lymphocyte number. An escalated platelet number indicates excessive platelet activity caused by destructive pro-inflammatory and pro-thrombotic responses. On the contrary, lymphocytes contribute less for repressing this aggravated inflammatory process and controlling this process.[24] Therefore, for inflammatory and pro-thrombotic cases, the PLR is found high as a ratio of these two hematological indices, and it is more simple, convenient and superior in comparison to the thrombocyte or lymphocyte numbers that are used alone.[25] The PLR integrates the platelet and hematological indices as a novel indicator of inflammation in various pathological conditions and emerges as a simple and applicable prognosis marker.[24,25] Recent studies reported that the PLR was a better indicator for inflammation in comparison to the WBC number[24,26,27]. Balta and Ozturk have reported that the PLR could be used in cardiovascular cases as an inflammatory marker in the clinic.[28] It was reported that the PLR could be used as a valuable predictor for predicting poor clinic results in thrombotic cases and cancer patients.[24,25,29-31] Ozcan Cetin *et al*. conducted a study on patients with acute pulmonary emboli and reported that the PLR was valuable for predicting both hospital mortality and long-term morbidity.[25] Yaprak *et al*. reported in their study conducted on hemodialysis patients that the PLR value was an independent variable for predicting mortality in all cases.[32] In our literature search, we did not find any research investigating the PLR value for predicting mortality in patients with sepsis. In this context, our study will be the first in the literature. We found in our study that the PLR values were higher in the patient ending with death. Therefore, we think that the PLR can be used as a marker for predicting mortality in patients with sepsis.

Conclusion

The low number of platelets in patients with sepsis at the moment of application and the high PDW and PLR values are valuable for predicting a high mortality.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Heyland DK, Hopman W, Coo H, Tranmer J, McColl MA. Long-term health-related quality of life in survivors of sepsis. Short form 36: A valid and reliable measure of health-related quality of life. Crit Care Med 2000;28:3599-605.
2. Centers for Disease Control (CDC). Increase in national hospital discharge survey rates for septicemia – United States, 1979-1987. MMWR Morb Mortal Wkly Rep 1990;39:31-4.
3. Funk DJ, Parrillo JE, Kumar A. Sepsis and septic shock: A history. Crit Care Clin 2009;25:83-101, viii.
4. Kamisli O, Kamisli S, Kablan Y, Gonullu S, Ozcan C. The prognostic value of an increased mean platelet volume and platelet distribution width in the early phase of cerebral venous sinus thrombosis. Clin Appl Thromb Hemost 2013;19:29-32.
5. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I, *et al.* Platelet distribution width: A simple, practical and specific marker of activation of coagulation. Hippokratia 2010;14:28-32.

6. Eberhardt A, Lessig F, Schreiter K, Kellner N, Fuchs M, Sablotzki A, *et al*. Mean Platelet Volume(MPW) is an outcome marker in sepsis patients. 15th International Congress on Infectious Diseases (ICID) Abstracts. Int J Infect Dis 2012; Suppl 1:e218. [DOI: https://doi.org/10.1016/j.ijid.2012.05.813].
7. Ferroni P, Riondino S, Formica V, Vittore C, Livia T, Francesca LF, *et al*. Venous thromboembolism risk prediction in ambulatory cancer patients: Clinical signifi cance of plate/lymphocyte ratio and platelet/ lymphocyte ratio. Int J Cancer 2015;136:1234-40.
8. Zhang Z, Xu X, Ni H, Deng H. Platelet indices are novel predictors of hospital mortality in İntensive Care Unit patients. J Crit Care 2014;29:885.e1-6.
9. Öztürk ZA, Dag MS, Kuyumcu ME, Cam H, Yesil Y, Yilmaz N, *et al.* Could platelet indices be new biomarkers for inflammatory bowel diseases? Eur Rev Med Pharmacol Sci 2013;17:334-41.
10. Balk RA. Severe sepsis and septic shock. Definitions, epidemiology, and clinical manifestations. Crit Care Clin 2000;16:179-92.
11. Greinacher A, Selleng K. Thrombocytopenia in the İntensive Care Unit patient. Hematology Am Soc Hematol Educ Program 2010;2010:135-43.
12. Van der Lelie J, Von dem Borne AK. Increased mean platelet volume in septicaemia. J Clin Pathol 1983;36:693-6.
13. Guclu E, Durmaz Y, Karabay O. Effect of severe sepsis on platelet count and their indices. Afr Health Sci 2013;13:333-8.
14. François B, Trimoreau F, Vignon P, Fixe P, Praloran V, Gastinne H, *et al.* Thrombocytopenia in the sepsis syndrome: Role of hemophagocytosis and macrophage colony-stimulating factor. Am J Med 1997;103:114-20.
15. Guida JD, Kunig AM, Leef KH, McKenzie SE, Paul DA. Platelet count and sepsis in very low birth weight neonates: Is there an organism-specific response? Pediatrics 2003;111:1411-5.
16. Vanderschueren S, De Weerdt A, Malbrain M, Vankersschaever D, Frans E, Wilmer A, *et al.* Thrombocytopenia and prognosis in İntensive Care. Crit Care Med 2000;28:1871-6.
17. Nelson RB 3rd, Kehl D. Electronically determined platelet indices in thrombocytopenic patients. Cancer 1981;48:954-6.
18. Becchi C, Al Malyan M, Fabbri LP, Marsili M, Boddi V, Boncinelli S, *et al.* Mean platelet volume trend in sepsis: Is it a useful parameter? Minerva Anestesiol 2006;72:749-56.
19. Patrick CH, Lazarchick J. The effect of bacteremia on automated platelet measurements in neonates. Am J Clin Pathol 1990;93:391-4.
20. Daniel M. Keller Platelet Size Predicts Mortality in Patients With Sepsis. Available from: http://www.medscape.com/viewarticle/767116. [Last accessed on 2012 Jun 15].
21. Herve P, Humbert M, Sitbon O, Parent F, Nunes H, Legal C, *et al.* Pathobiology of pulmonary hypertension. The role of platelets and thrombosis. Clin Chest Med 2001;22:451-8.
22. Gao Y, Li Y, Yu X, Guo S, Ji X, Sun T, *et al.* The impact of various platelet indices as prognostic markers of septic shock. PLoS One 2014;9:e103761.
23 Njoroge SW, Thompson M, Colon-Franco SM,Litt S, Anderson DA, Rice TW *et al*. Clinical Utility of Hematological Parameters to Predict Sepsis Prior to Clinical Presentation in Medical Intensive Care Unit Patients. Clinical Chemistry 2014;60 Suppl;83.
24. Balta S, Demırkol S, Kucuk U. The platelet lymphocyte ratio may be useful inflammatory indicator in clinical practice. Hemodial Int 2013;17:668-9.
25. Ozcan Cetin EH, Cetin MS, Canpolat U, Akdi A, Aras D, Temizhan A, *et al.* Platelet-to-lymphocyte ratio as a novel marker of in-hospital and long-term adverse outcomes among patients with acute pulmonary embolism: A single center large-scale study. Thromb Res 2017;150:33-40.
26. Fox EA, Kahn SR. The relationship between inflammation and venous thrombosis. A systematic review of clinical studies. Thromb Haemost 2005;94:362-5.
27. Temiz A, Gazi E, Güngör Ö, Barutçu A, Altun B, Bekler A, *et al.* Platelet/lymphocyte ratio and risk of in-hospital mortality in patients with ST-elevated myocardial infarction. Med Sci Monit 2014;20:660-5.
28. Balta S, Ozturk C. The platelet-lymphocyte ratio: A simple, inexpensive and rapid prognostic marker for cardiovascular events. Platelets 2015;26:680-1.
29. Baranyai Z, Krzystanek M, Jósa V, Dede K, Agoston E, Szász AM, *et al.* The comparison of thrombocytosis and platelet-lymphocyte ratio as potential prognostic markers in colorectal cancer. Thromb Haemost 2014;111:483-90.
30. Yang W, Liu Y. Platelet-lymphocyte ratio is a predictor of venous thromboembolism in cancer patients. Thromb Res 2015;136:212-5.
31. Ferroni P, Riondino S, Formica V, Cereda V, Tosetto L, La Farina F, *et al.* Venous thromboembolism risk prediction in ambulatory cancer patients: Clinical significance of neutrophil/lymphocyte ratio and platelet/lymphocyte ratio. Int J Cancer 2015;136:1234-40.
32. Yaprak M, Turan MN, Dayanan R, Akın S, Değirmen E, Yıldırım M, *et al.* Platelet-to-lymphocyte ratio predicts mortality better than neutrophil-to-lymphocyte ratio in hemodialysis patients. Int Urol Nephrol 2016;48:1343-8.