Original Article

The Use of Platelet Count and Indices as Prognostic Factors for Mortality in Children with Sepsis

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Abstract

Background: Sepsis is still one of the leading causes of mortality and morbidity in children worldwide. Consumptive coagulopathy and suppression of thrombopoiesis in the bone marrow resulting from immune dysregulation are pathological mechanisms that cause thrombocytopenia in sepsis. Platelet count (PLT) and indices, such as mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) are markers of platelet activation and are strongly influenced by platelet morphology and proliferation kinetics. We aimed to study the use of platelet count and indices as predictors of mortality in children with sepsis.

Methods: This is a cross-sectional study of 45 children diagnosed with sepsis on admission at Haji Adam Malik Hospital, Medan, North Sumatra, Indonesia, between October and November 2022. Blood samples were drawn upon admission, and platelet count and indices were then determined for all children. Subjects were followed up till discharge from hospital or death. Receiver Operating Characteristic (ROC) curve analysis of platelet parameters was done to determine the area under the curve (AUC), optimal cut-off value, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) in predicting mortality in children with sepsis. Using the cut-off values from ROC curve analysis, the odds ratio with 95% confidence interval was calculated using multiple logistic regression analyses. A P value less than 0.05 was considered statistically significant.

Results: MPV, PDW, and PDW/PLT were significantly higher in non-survivors than survivors (P=0.04, P=0.02, and P=0.04, respectively). ROC curve analysis showed that PDW had the largest AUC (0.708 [95% CI=0.549–0.866]) with a cut-off value of 14.1%, sensitivity of 63.6%, and specificity of 82.6%. PDW was also the only parameter that significantly affected the outcome of children with sepsis. PDW≥14.1% at admission increases the risk of mortality by 5.7 times.

Conclusion: Admission PDW is a fast and specific tool to predict the outcome of children with sepsis.

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Keywords ● Sepsis ● Platelet count ● Mean platelet volume ● Mortality

What's Known

- Previous studies have shown that platelet count and indices can be used to predict mortality in patients with sepsis.

What's New

- Not only platelet count and indices but also platelet indices ratio, specifically platelet distribution width to platelet count ratio (PDW/PLT), was found to be a useful parameter in predicting mortality in children with sepsis.
- Platelet distribution width (PDW)≥14.1% at admission increases the risk of sepsis mortality by 5.7 times.

Introduction

Sepsis is still one of the leading causes of mortality and morbidity in children worldwide.[1] Globally, the estimated burden of pediatric

sepsis is 1.2 million cases per year, with mortality rates of 1-5% for sepsis and 9-20% for severe sepsis.[2] Most children who died from sepsis had refractory shock and/or multiple organ failure, which occurred within the first 48-72 hours of diagnosis. Early identification, resuscitation, and appropriate management are important to optimize outcomes in children with sepsis.[3]

It is still difficult to diagnose sepsis in children due to its variety of clinical symptoms in the early phase of infection; also microbiological culture results can take up to 48-72 hours, and frequent false negative results are seen.[1] Further in resource-limited settings, there is limited availability of diagnostic tools for inflammatory responses (*i.e.,* C-reactive protein, procalcitonin) to guide sepsis diagnosis.[4] The absence of a standardized definition of sepsis is also a major obstacle to the epidemiology of pediatric sepsis. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) in 2016 defined sepsis as a life-threatening organ dysfunction caused by a dysregulated host response to infection.[5]

Platelets are known to be involved in the inflammatory process, microbial host defense, wound healing, angiogenesis, and remodeling, in addition to their role in hemostasis and thrombosis.[6] Thrombocytopenia is often found in sepsis patients admitted to the intensive care unit (ICU) and can be used to predict mortality.[1, 7] Several mechanisms are responsible for thrombocytopenia in sepsis patients, including consumptive coagulopathy in disseminated intravascular coagulation (DIC), where platelets are overactivated due to extensive vascular inflammation, leading to the formation of microthrombi in the systemic circulation. This leads to the consumption of platelets and coagulation factors, which in turn increases the risk of bleeding. In addition, the bone marrow, which acts as a site for thrombopoiesis, is also depressed due to dysregulation of the immune response in sepsis patients. Approximately 40% of patients with severe sepsis have platelet count <80,000/mm^3.[8] Platelet indices, such as mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT), are markers of platelet activation and are strongly influenced by platelet morphology and proliferation kinetics.[1]

In recent years, several studies have shown that platelet count and indices can be used to predict mortality in patients with sepsis.[1, 6, 9-12] Platelet count and indices are parts of complete blood count readily available in most health facilities in rural areas and does not require high costs. Clinicians can make good use of them, especially in developing countries where the incidence of sepsis in children is still high.[13] The objective of this study was to determine the use of admission platelet count and indices as predictors of outcomes in children with sepsis.

Patients and Methods

This cross-sectional study was conducted on children aged 0-18 years old who were admitted to Haji Adam Malik Hospital, Medan, Indonesia, with sepsis as a diagnosis during the period from October to November 2022. The sample size was calculated using a mortality rate of 27.8% obtained from a previous study,[1] resulting in a total sample size of 45 subjects. All patients who were diagnosed with sepsis based on the PELOD-2 score were included in this study.[14] Patients with hematologic abnormalities, including hematological malignancies, autoimmune diseases, primary immunodeficiency diseases, such as Wiskott-Aldrich syndrome, cancer, and/or receiving cancer treatment, such as chemotherapy and radiotherapy, and splenomegaly were excluded. Patients whose parents refused to participate in the study were excluded. Ethical approval was obtained from the Medical Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara/ Haji Adam Malik Hospital, Medan (Reference No. 1101/KEPK/USU/2022). Informed consent was taken from the guardians of all participants.

Blood samples were drawn in a BD Vacutainer K2 EDTA tube (Becton Dickinson, USA) upon admission to the hospital. Platelet count and indices, as part of complete blood count (CBC), were then determined for all children using a fully automated hematology analyzer Sysmex XN-1000 (XN-Series Corporation, Kobe, Japan). Patients were then followed up till discharge from hospital or death.

Statistical Analysis

Data were analyzed using SPSS software (Statistical Package for Social Sciences, Chicago, IL, USA) version 20.0. The normality of the distribution of the data was tested using the Kolmogorov-Smirnov test. Bivariate analysis was done with chi Square, Independent *t* test, and Mann-Whitney tests. Receiver Operating Characteristic (ROC) curve analysis of platelet parameters was done to determine the area under the curve (AUC), optimal cut-off value, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) in predicting mortality in children with sepsis. Using the cut-off values from ROC curves analyses, the odds ratio with 95% confidence interval was calculated using multiple logistic

regression analyses. A P value less than 0.05 was considered statistically significant.

Results

A total of 45 children who met the study criteria were included in this study. Of the 45 children, 25 (55.6%) were female. The majority of the subjects (35.6%) were in the age group of 1 month to <1 year old with a median of age was 1.5 years old. The median length of stay of the subjects in this study was 13 days. The mortality rate was 48.9%, and there were no differences in the mortality rates between gender, age group, and length of stay (table 1).

Platelet count, indices, and ratios of platelet indices of the subjects are presented in table 2. PLT and PCT were observed to be lower in non-survivors than survivors, but the differences were not statistically significant. MPV and PDW were significantly lower in survivors than non-survivors (P=0.04 and P=0.02, respectively). PDW/PLT was the only ratio of all platelet indices with a significant difference in both groups (P=0.04).

ROC curve analysis of MPV, PDW, and PDW/PLT to predict mortality in children with sepsis, showed that PDW was the parameter with the largest AUC=0.708 with sensitivity of 63.6% and specificity of 82.6%, at cut-off≥14.1% (figure 1).

Table 1: Demographic characteristics of subjects according to their outcome

Characteristics		All subjects (n=45)	Non-survivors (n=22)	Survivors (n=23)	P value
Sex	Male	20 (44.4%)	10 (50.0%)	10 (50.0%)	0.89[a]
	Female	25 (55.6%)	12 (48.0%)	13 (52.0%)	
Age	<28 days	6 (13.3%)	3 (50.0%)	3 (50.0%)	0.82[a]
	1 month≤1 year	16 (35.6%)	9 (56.0%)	7 (44.0%)	
	1≤5 years	8 (17.8%)	4 (50.0%)	4 (50.0%)	
	5≤12 years	8 (17.8%)	4 (50.0%)	4 (50.0%)	
	12≤18 years	7 (15.6%)	2 (29.0%)	5 (71.0%)	
	Median (IQR)	1.5 (0.0-17.1)	1.2 (0.0-17.0)	4 (0.0-17.1)	
Length of stay (days)		13.0 (0.0-54.0)	11.5 (2.0-54.0)	17 (0.0-54.0)	0.16[b]

[a]Chi Square test; [b]Mann Whitney U test; IQR: Interquartile range; P<0.05 was considered statistically significant.

Table 2: Platelet count, indices, and ratios of platelet indices of the subjects based on the outcome

Variables	Non-survivors (n=22)	Survivors (n=23)	P value
PLT, ×10³/μL	102.9±73.8	149.8±98.5	0.10[a]
MPV, fL	11.5±1.3	10.7±1.3	0.04[a]
PDW, %	15.5±4.6	12.5±3.3	0.02[b]
PCT, %	0.1±0.1	0.2±0.1	0.11[a]
MPV/PLT	0.1 (0.0-1.0)	0.07 (0.03-0.91)	0.07[b]
MPV/PCT	79.9 (40.7-373.3)	66.9 (21.8-1000.0)	0.13[b]
PDW/PLT	0.3 (0.0-1.2)	0.1 (0.0-1.0)	0.04[b]
PDW/PCT	97.9 (38.6-453.3)	81.4 (23.7-1130.0)	0.09[b]

[a]Independent *t* test; [b]Mann Whitney U test; PLT: Platelet count; MPV: Mean platelet volume; PDW: Platelet distribution width; PCT: Plateletcrit; P<0.05 was considered statistically significant.

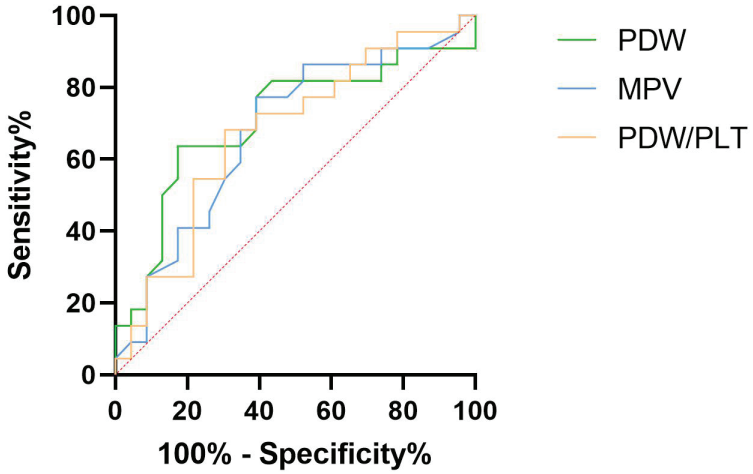

Figure 1: The receiver operating characteristic (ROC) curves for MPV, PDW, and PDW/PLT as predictors of mortality in children with sepsis are shown. MPV and PDW/PLT showed higher sensitivity than PDW, but PDW was the most specific parameter in predicting mortality in children with sepsis, as indicated by the largest area under the curve (AUC).

Table 3: Predictive values of MPV, PDW, and PDW/PLT for mortality

Variables	Cut-off[a]	AUC (95%CI AUC)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
MPV, fL	≥11.2	0.677 (0.517–0.837)	68.2	65.2	65.2	68.2	66.7
PDW, %	≥14.1	0.708 (0.549–0.866)	63.6	82.6	77.8	70.4	73.3
PDW/PLT	≥0.1	0.674 (0.514–0.834)	68.2	69.6	68.2	69.6	68.9

[a]Receiver operating characteristic (ROC) curve analysis. MPV: Mean platelet volume; PDW: Platelet distribution width; PLT: Platelet count; AUC: Area under the curve; PPV: Positive predictive value; NPV: Negative predictive value

Table 4: Multiple logistic regression analysis of factors affecting the outcome of children with sepsis

Variable	OR[a]	95% CI for OR		P value
		Lower	Upper	
MPV	2.0	0.4	8.9	0.35
PDW	5.7	1.3	29.9	0.03
PDW/PLT	1.3	0.3	5.8	0.74

Multiple logistic regression analysis. MPV: Mean platelet volume; PDW: Platelet distribution width; PLT: Platelet count; OR: Odds ratio; PPV: Positive predictive value; NPV: Negative predictive value; P<0.05 was considered statistically significant.

PDW was found to be the most specific parameter in predicting death in children with sepsis. MPV had the same sensitivity as PDW/PLT (sensitivity=68.2%). Predictive values of MPV, PDW, and PDW/PLT for mortality are shown in table 3.

Multiple logistic regression analysis showed that PDW was the only independent variable significantly affecting the outcome of children with sepsis with an odds ratio of 5.7 (95% CI=1.3-29.9) with P value of 0.03 (table 4).

Discussion

Our results demonstrated that elevated PDW was a significant predictor of mortality in children with sepsis. Early prediction of mortality would help clinicians take measures needed to alleviate morbidity and decrease mortality in children with sepsis. Readily available, cheaper, and reliable parameters are most needed to help with the management of children with sepsis.

In this study, the mortality rate of sepsis in children was found to be 48.9%. In Indonesia, the mortality rate of sepsis in children varies across different regions, ranging from 23.9% to 65% between 2011 and 2020. The sepsis mortality rate in children was reported as 52% in Yogyakarta (2014), 45% in Medan (2017), and 35.6% in Manado (2020).[15] At Cipto Mangunkusumo Hospital in Jakarta, the sepsis mortality rate in children was recorded as 54% in 2009, 23.9% in 2011, and 65% in 2020.[15] The higher mortality rate in our study might be due to Haji Adam Malik Hospital being a tertiary hospital, therefore patients were admitted in more severe and advanced conditions leading to poorer outcomes.

Females were also found to be slightly more likely to be diagnosed with sepsis, but mortality was higher in males, although this was not statistically significant. This finding was similar to a previous study that also found the incidence of sepsis in children to be higher in females (54.3% vs 45.7%).[16] Majority of the subjects were in the age group of under 1 year old, reflecting the vulnerability of children in this age group to life-threatening illness due to immaturity of the immune system and higher risk of developing respiratory tract infections. The length of stay was observed to be shorter among children with poor outcomes than those who survived (11.5 days vs. 17 days), similar to the previous study.[17] The shorter length of stay in the children who died might be due to delay in receiving medical treatment and the severity of the disease.

Analysis of platelet indices showed that the non-survivors had higher MPV than those who survived, similar to previous studies.[18, 19] Higher MPV indicates increased platelet turnover by bone marrow in response to stress, and younger and larger platelets are more functionally active.[19] PDW also increased significantly in the non-survivors compared to survivors, which was in line with the study done previously.[20, 21] PDW increases when the number and size of platelet pseudopodia increase. Platelet activation causes morphological changes in platelets, such as a change in shape to spherical and the formation of pseudopodia. Increased number and size of pseudopodia will cause the platelet size to vary, thus affecting PDW. As for PLT and PCT, children who died had lower PLT and PCT than those who survived, but the difference was

not statistically significant. This was similar to a previous study that found no differences in PLT levels on admission between the two groups.[22] Another study also found that PLT and PCT did not vary significantly between survivors and non-survivors on admission but showed predictable time trends. PLT did decrease over time in non-survivors, and both PLT and PCT improved over time among survivors.[19] Therefore, serial measurements of platelet count and indices might be needed to address the changes occurring in these parameters during the clinical course of sepsis.

PDW/PLT was the only ratio of platelet indices that was significantly increased in the non-survivors compared to survivors. This finding is consistent with other studies which also found that PDW/PLT at the time of admission could be used as a predictor of mortality.[23, 24] A study used PDW/PLT>0.07 at the time of admission as an independent predictor of mortality with a sensitivity of 77.1% and specificity of 77.5%.[24] An increase in PDW and a decrease in PLT in sepsis patients will lead to an increase in PDW/PLT. Other platelet indices including MPV/PLT, MPV/PCT, and PDW/PCT were higher in non-survivors than survivors, but the differences were not statistically significant.

MPV and PDW/PLT were the most sensitive parameters in terms of predicting mortality. While PDW was not only the most specific parameter, it was also the only independent variable that significantly affected the outcome of children with sepsis. This finding was in line with previous studies that also concluded PDW was a significant predictor of mortality in children with sepsis.[20, 25] The limitation of our study is that the measurement of platelet count and indices in this study was only done once, (upon admission), which might have not allowed us to observe the changes of these parameters during the clinical course of sepsis.

Conclusion

Admission PDW is a fast and specific tool that can be used as a predictor for outcome in children with sepsis at health facilities with limited diagnostic tools. PDW can be used to guide aggressive management to improve outcomes of children with sepsis. Further studies with serial measurements of platelet count and indices and in combination with other known sepsis biomarkers such as CRP, PCT, IL-6, and presepsin are needed, as the combination of these biomarkers and their serial measurements may be strategical to enhance diagnostic accuracy.

Authors' Contribution

M: conceptualization and methodology, collection and analysis of the data, drafting and revising the manuscript; JS: monitoring the project and revising the manuscript; INDL: monitoring the project and revising the manuscript. All authors contributed in writing the manuscript. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Conflict of Interest: None declared.

References

1 Sriram SM, Aroor S, Kini PG, Kanaparthi S, Chakravarthy K. Platelet indices in children with sepsis and their relation to the outcome. Sri Lanka Journal of Child Health. 2018;47:301-5. doi: 10.4038/sljch.v47i4.8589.

2 Massaud-Ribeiro L, Silami P, Lima-Setta F, Prata-Barbosa A. Pediatric Sepsis Research: Where Are We and Where Are We Going? Front Pediatr. 2022;10:829119. doi: 10.3389/fped.2022.829119. PubMed PMID: 35223703; PubMed Central PMCID: PMCPMC8873512.

3 Weiss SL, Peters MJ, Alhazzani W, Agus MSD, Flori HR, Inwald DP, et al. Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children. Pediatr Crit Care Med. 2020;21:e52-e106. doi: 10.1097/PCC.0000000000002198. PubMed PMID: 32032273.

4 Southeast Asia Infectious Disease Clinical Research N. Causes and outcomes of sepsis in southeast Asia: a multinational multicentre cross-sectional study. Lancet Glob Health. 2017;5:e157-e67. doi: 10.1016/S2214-109X(17)30007-4. PubMed PMID: 28104185; PubMed Central PMCID: PMCPMC5332551.

5 Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus

Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:801-10. doi: 10.1001/jama.2016.0287. PubMed PMID: 26903338; PubMed Central PMCID: PMCPMC4968574.

6 Sayed SZ, Mahmoud MM, Moness HM, Mousa SO. Admission platelet count and indices as predictors of outcome in children with severe Sepsis: a prospective hospital-based study. BMC Pediatr. 2020;20:387. doi: 10.1186/s12887-020-02278-4. PubMed PMID: 32814554; PubMed Central PMCID: PMCPMC7437045.

7 Ree IMC, Fustolo-Gunnink SF, Bekker V, Fijnvandraat KJ, Steggerda SJ, Lopriore E. Thrombocytopenia in neonatal sepsis: Incidence, severity and risk factors. PLoS One. 2017;12:e0185581. doi: 10.1371/journal.pone.0185581. PubMed PMID: 28977011; PubMed Central PMCID: PMCPMC5627935.

8 Choi SJ, Ha E-J, Jhang WK, Park SJ. Platelet indices as predictive markers of prognosis in pediatric septic shock patients. Iranian Journal of Pediatrics. 2017;27. doi: 10.5812/ijp.7212.

9 Catal F, Tayman C, Tonbul A, Akca H, Kara S, Tatli MM, et al. Mean platelet volume (MPV) may simply predict the severity of sepsis in preterm infants. Clin Lab. 2014;60:1193-200. doi: 10.7754/clin.lab.2013.130501. PubMed PMID: 25134389.

10 1 Iskandar A, de Rosari MA, Yuliarto S. Nilai Diagnosis dan Prognosis Jumlah dan Indeks Trombosit, Mean Platelet Volume (MPV) dan Plateletcrit (PCT) pada Penderita Sepsis Neonatorum. Majalah Kesehatan FKUB. 2018;5:33-41. doi: 10.21776/ub.majalahkesehatan.005.01.5.

11 Karyana IPSR, Mahartini NN, Kardana IM. Rasio Mean Platelet Volume (MPV) terhadap hitung trombosit dan Interleukin-6 (IL-6) sebagai prediktor awal kematian pada sepsis neonatal di RSUP Sanglah, Bali, Indonesia. Intisari Sains Medis. 2020;11:839-44. doi: 10.15562/ism.v11i2.755.

12 Sekhar SR, Naidu P, Kumar EG, Shamili M, Rao ES. Prognostic Role of Platelet Indices in Sepsis Patients. Saudi Journal of Pathology and Microbiology. 2019;4:898-901. doi: 10.36348/sjpm.2019.v04i12.005.

13 Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395:200-11. doi: 10.1016/S0140-6736(19)32989-7. PubMed PMID: 31954465; PubMed Central PMCID: PMCPMC6970225.

14 Leteurtre S, Duhamel A, Salleron J, Grandbastien B, Lacroix J, Leclerc F, et al. PELOD-2: an update of the PEdiatric logistic organ dysfunction score. Crit Care Med. 2013;41:1761-73. doi: 10.1097/CCM.0b013e31828a2bbd. PubMed PMID: 23685639.

15 Ministry of Health [Internet]. Minister of Health of the Republic of Indonesia Decree Number HK.01.07/MENKES/4722/2021 on the National Guidelines for Medical Services in the Management of Sepsis in Children. Jakarta: Ministry of Health; 2021. Available from: https://yankes.kemkes.go.id/unduhan/fileunduhan_1681539780_895283.pdf

16 Isguder R, Ceylan G, Agin H, Nacaroglu HT, Korkmaz HA, Devrim I, et al. Increased mean platelet volume in children with sepsis as a predictor of mortality. Turk J Pediatr. 2016;58:503-11. doi: 10.24953/turkjped.2016.05.007. PubMed PMID: 28621091.

17 Kaur G, Vinayak N, Mittal K, Kaushik JS, Aamir M. Clinical outcome and predictors of mortality in children with sepsis, severe sepsis, and septic shock from Rohtak, Haryana: A prospective observational study. Indian J Crit Care Med. 2014;18:437-41. doi: 10.4103/0972-5229.136072. PubMed PMID: 25097356; PubMed Central PMCID: PMCPMC4118509.

18 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. doi: 10.1371/journal.pone.0103761. PubMed PMID: 25118886; PubMed Central PMCID: PMCPMC4131909.

19 Mangalesh S, Dudani S, Malik A. Platelet Indices and Their Kinetics Predict Mortality in Patients of Sepsis. Indian J Hematol Blood Transfus. 2021;37:600-8. doi: 10.1007/s12288-021-01411-2. PubMed PMID: 33776267; PubMed Central PMCID: PMCPMC7988247.

20 Guclu E, Durmaz Y, Karabay O. Effect of severe sepsis on platelet count and their indices. Afr Health Sci. 2013;13:333-8. doi: 10.4314/ahs.v13i2.19. PubMed PMID: 24235932; PubMed Central PMCID: PMCPMC3824485.

21 Yanni GN, Saragih RAC. Platelet profile as prognostic factor in critically ill children. Open Access Macedonian Journal of Medical Sciences. 2020;8:966-8. doi: 10.3889/oamjms.2020.4448.

22 Oh GH, Chung SP, Park YS, Hong JH, Lee HS, Chung HS, et al. Mean Platelet Volume to Platelet Count Ratio as a Promising Predictor of Early Mortality in Severe Sepsis.

Shock. 2017;47:323-30. doi: 10.1097/SHK.0000000000000718. PubMed PMID: 27504801.

23 Celegen M, Kesici S, Yavuz S, Celegen K, Bayrakci B. Are platelet indices promising ratios for predicting pediatric septic shock prognosis? Bratisl Lek Listy. 2022;123:444-8. doi: 10.4149/BLL_2022_069. PubMed PMID: 35576547.

24 Purbiya P, Golwala ZM, Manchanda A, Sreenivas V, Puliyel JM. Platelet Distribution Width to Platelet Count Ratio as an Index of Severity of Illness. Indian J Pediatr. 2018;85:10-4. doi: 10.1007/s12098-017-2432-z. PubMed PMID: 28842812.

25 Mousa SO, Moustafa AN, Aly HM. Prognostic value of red cell distribution width, platelet parameters, and the hematological scoring system in neonatal sepsis. The Egyptian Journal of Haematology. 2019;44:183-9. doi: 10.4103/ejh.ejh_12_19.