Diagnostic Value of Mean Platelet Volume, Neutrophil-to-Lymphocyte Ratio, and Platelet to Lymphocyte Ratio for Late-Onset Neonatal Sepsis

Abstract

Background: Neonatal sepsis (NS) is the most common cause of neonatal mortality, currently confirmed with blood culture as the diagnostic gold standard. However, being time-consuming, false-negative results, being affected by even a single dose of antibiotics, and expensiveness are negative aspects. Therefore, we aimed to investigate the diagnostic value of complete blood count (CBC) parameters: mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), and platelet to lymphocyte ratio (PLR) which have been suggested in previous studies. **Methods:** A total of 100 term and preterm neonates (age $\geq$ 32 weeks) hospitalized in Alzahra and Shahid Beheshti hospitals in Isfahan, Iran, were studied. Fifty neonates with late neonatal sepsis were placed in the case group, and 50 neonates with other diagnoses were placed in the control group. Neonatal blood samples were sent to the laboratory, and MPV, NLR, and PLR were measured. **Results:** The mean (standard deviation) of MPV was 7.20 (4.39) in the case group and 9.55 (0.87) in the control group, and there was a significant difference between them (P value = 0.001). At the cutoff point of 8.25 in MPV, the area under the curve (AUC) was 0.594 with a sensitivity of 100% and specificity of 30%. The mean (standard deviation) of NLR was 1.79 (1.21) in the case group and 2.28 (1.25) in the control group, and there was no significant difference between them (P value = 0.692). The mean (standard deviation) of PLR was 62.58 (34.57) in the case group and 65.11 (28.55) in the control group, and there was no significant difference between them (P value = 0.836). **Conclusions:** MPV, unlike NLR and PLR, can be used as a sensitive and cost-effective primary screening index in late NS at the cutoff point of 8.25 due. However, low specificity suggests a poor diagnostic value.

Keywords: *Lymphocyte, neonatal sepsis, neutrophil, platelet*

**Behzad Barekatain[1],
Elahe Mardani[1],
Alireza Sadeghnia[1],
Zahra Heidari[2]**

[1]Department of Pediatrics, Division of Neonatology, Child Growth and Development Research Center, Isfahan, Iran, [2]Department of Epidemiology and Biostatistics, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction

Neonatal sepsis (NS) is an important cause of mortality and morbidity among newborns (age less than 28 days), presenting with systemic symptoms of infection confirmed by isolation of a bacterial pathogen from the blood.[1] NS is divided into two categories of early and late sepsis based on the onset of symptoms. Early-onset NS occurs during the first 7 days from birth (according to some experts, during the first 72 hours) in contrast with late-onset sepsis that occurs after 7th day (or 72 hours).[2,3] The prevalence of neonatal sepsis is estimated to be 1–5 cases per 1,000 births, depending on the study population and the case definition.[4] Group B Streptococcus (GBS) and *Escherichia coli* (E-coli) have been identified as the most common etiologic agents in both types of NS.[4] Late NS (in this study: after 7 days from birth) can be transmitted in two ways: vertically (from the mother to the fetus) or horizontally (via contact with health care professionals or environmental factors).[5] Considering the symptoms of sepsis are nonspecific and can be minor—including temperature instability, irritability, lethargy, respiratory symptoms (tachypnea, grunting, hypoxia), poor feeding, tachycardia, poor perfusion, and hypotension—it is important to identify infants with risk factors and investigate laboratory tests for suspicious cases.[5,6] A complete diagnostic evaluation includes blood culture, spinal fluid culture, complete blood count (CBC), chest X-ray, tracheal secretion culture (if intubated), C-reactive protein (CRP), a urine culture, and culture of any other suspicious source (purulent secretions of eyes or pustules for instance), among which the gold standard is a positive blood culture with a bacterial pathogen. In different medical settings, 1–2 blood cultures are sent before the onset of

Address for correspondence:
Dr. Behzad Barekatain, Department of Pediatrics, Division of Neonatology, Child Growth and Development Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: b_barekatain@med.mui.ac.ir

experimental antibiotics, which become positive within 24–36 hours in most NS cases, with 90% sensitivity.[5,7]

According to the literature, experimental antibiotics cannot currently be initiated based on CBC results and CBC is mostly used to determine less probable NS cases at the moment.[5,8-10] However, a number of CBC parameters have recently been proposed to predict NS, including decreased white blood cells (WBC), decreased absolute neutrophil count (ANC), increased ratio of immature neutrophils to total (I: T Ratio), mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR).[8-25] Nevertheless, further studies are required to clarify the diagnostic value of CBC in NS as a simple, cost-effective diagnostic method particularly in developing countries. This study aims to investigate MPV, NLR, and PLR in the diagnosis of NS.

Methods

This is a case–control, descriptive–analytical research study conducted at Alzahra and Ayatollah Beheshti hospitals of Isfahan University of Medical Sciences, Isfahan, Iran. Study Review Board of the university approved the written protocol, and informed consent was obtained from all the parents before the study (code: IR.MUI.REC.1398.009).

Subjects

Study population consisted of hospitalized neonates (age ≥32 gestational week), between September 2020 and March 2022. Fifty newborns with late-onset neonatal sepsis as the case group and 50 neonates with same matched demographic data (weight and height at birth, gender, maternal pregnancy complications, type of delivery, APGAR score) hospitalized for reasons other than sepsis in the control group. Sepsis was diagnosed based on positive blood culture or clinical sepsis criteria after 7 days from birth. Exclusion criteria were parental dissatisfaction to continue the research, history of asphyxia or IUGR in the neonate and history of preeclampsia, eclampsia, or thrombocytopenia (due to lupus, ITP, etc.) in the mother.

Sampling

Blood samples were sent and tested within 60 minutes to prevent platelet swelling and false rise of MPV. MPV, NLR, and PLR were measured and analyzed.

Laboratory investigations

A CBC was performed on all specimens using the Sysmex KX-21N to determine total and differential white blood cell (WBC) count, platelet count, and mean platelet volume (MPV).

Statistical analysis

Data were analyzed using SSPS software, version 22.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation and qualitative data as frequencies and percentages. An independent samples *t*-test was used to compare the two means. Receiver operating characteristic (ROC) curve analysis was used to determine the overall predictive ability of the parameters and find the best detection threshold value as well as sensitivity and specificity. Sensitivity is defined as the probability that a test result will be positive in the presence of disease. Specificity is defined as the probability that a test result will be negative in the absence of disease [Figure 1].

Results

The mean (standard deviation) of MPV was 7.2 (4.40) in the case group and 9.56 (0.87) in the control group, and there was a significant difference between the two groups (*P* value = 0.001). The mean (standard deviation) of NLR was 1.8 (1.2) in the case group and 2.3 (1.25) in the control group, and there was no significant difference between them (*P* value = 0.692). The mean (standard deviation) of PLR was 62.6 (34.6) in the case group and 65.1 (25.5) in the control group, and no significant difference was found (*P* value = 0.836) [Table 1]. The area under the ROC curve (AUC) for MPV, NLR, and PLR indices was 0.594, 0.632, and 0.534, respectively, all of which was smaller than 0.7 and none of them had a high AUC [Table 2]. In the table of MPV ROC curve coordinates, the greatest Youden index (sensitivity + specificity) was 8.25 with 100% sensitivity and 30% specificity.

Discussion

Neonatal sepsis is a principal cause of mortality and morbidity in newborns. The possibility of serious complications is so important that necessitates health care professionals to consider a low threshold for the investigation of probable NS cases. The diagnostic gold standard currently is blood culture with the sensitivity of 90% for a single culture and in most cases, results are positive within 24–36 hours.[5,7,26]

Currently, CBC is not considered to be determining the onset of experimental antibiotics and is mostly interpreted in combination with other workups to rule out NS.[5,8-10]

Table 1: Comparison of different indicators between case and control groups

Group	Mean	Standard deviation	*P*
MPV			
control	9.556	0.8702	0.001
Case	7.204	4.3988	
NLR			
control	2.284	1.2520	0.692
Case	1.792	1.2127	
PLR			
control	65.114	28.5531	0.836
Case	62.587	34.5753	

Table 2: ROC curve analysis results

Index	AUC	Standard deviation	Confidence interval		Sensitivity	Specificity	Cut-off point
			Upper limit	Lower limit			
MPV	0.594	0.058	0.707	0.480	1	0.28	8.15
					1	0.3	8.25
NLR	0.632	0.056	0.742	0.523	0.68	0.58	1.635
					0.72	0.56	1.535
PLR	0.534	0.058	0.649	0.420	0.98	0.122	23.85
					0.48	0.633	68.7
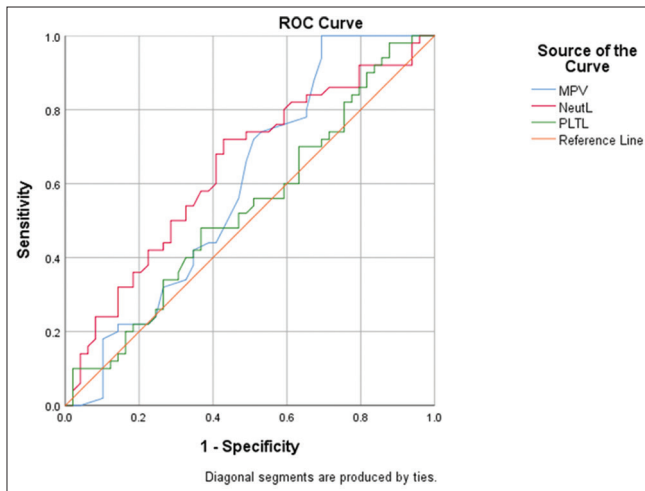
Figure 1: ROC curve and AUC for three indicators

However, a number of CBC parameters have recently been suggested to predict NS, and their sensitivity and diagnostic value have been studied, including decreased white blood cells (WBC), decreased absolute neutrophil count (ANC), increased ratio of immature to total neutrophils (I: T ratio), mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR)[8-25] A number of these studies are specifically in the field of early sepsis.[19,25] For example, Karabulut and colleagues have introduced NLR and MPV and calculated a cutoff point of 9.3 with 84% sensitivity and 32% specificity for MPV.[24] A number of studies have established the diagnostic value and cost-effectiveness of NLR specially in developing countries.[15-17] Fewer articles have examined PLR.[23] Another group of articles have investigated MPV which was significantly higher in the sepsis group than the control group. In a systematic review and meta-analysis by Wang *et al*.,[18] MPV is introduced as an indicator of sepsis. In the review study by Milas *et al*.,[21] a cutoff point of 9.28 with 67% sensitivity and 73% specificity is introduced for MPV. Hanaganahalli and colleagues suggested MPV as a simple and economical index.[20] In the study of Yao *et al*.,[22] a cutoff point of 11.4, sensitivity of 40%, and a specificity of 88% have been measured for MPV.

Conclusion

According to this study, no significant difference was detected in NLR and PLR between case and control groups.

On the other hand, regarding 100% sensitivity, MPV can be considered as a simple and cost-effective primary screening indicator for NS at the cutoff point of 8.25. However, due to 30% specificity and variability in the calculated cutoff point, sensitivity and specificity in different studies, which may be the consequence of limitations including sample sizes, more investigation is required to determine a single and integrated cutoff point for MPV, and it is considered to be a poor diagnostic indicator.

Ethical approval

The study protocol was approved by the ethical committee of Isfahan University of Medical Sciences (code: IR.MUI. REC.1398.009).

Conflicts of interest

There are no conflicts of interest.

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