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Original Article

Platelet Parameters and Red Cell Distribution Width as Diagnostic Markers for Early Diagnosis of Neonatal Sepsis. A Prospective Comparative study

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Abstract

Background: Early identification of neonatal sepsis improves the outcomes. Therefore, identifying new diagnostic tests for newborn sepsis is crucial.

Aim: This study aimed to determine total platelet count (TPC), mean platelet volume (MPV), MPV/TPC ratio, platelet distribution width (PDW), and red cell distribution width (RDW) in neonates with sepsis and to evaluate their potential as early diagnostic indicators of newborn sepsis at Minia University Children's Hospital.

Methods: This one-year prospective comparative study was conducted in the neonatal intensive care unit (NICU). The study included 100 neonates, aged 28–38 weeks gestational age and within the first 28 days of life. Participants were divided into two groups: Group I (septic group), comprising 50 neonates exhibiting signs and symptoms suggestive of sepsis or with risk factors for sepsis; and Group II (control group), comprising 50 clinically stable neonates without risk factors for sepsis. All neonates underwent sepsis screening and clinical assessment.

Results: Significant variations were observed in the mean TPC, MPV, MPV/TPC ratio, PDW, and RDW between the septic and non-septic groups. The sensitivity and specificity values were as follows: TPC (cut-off <208.5×10³/µL), 84% and 88%; MPV (cut-off <9.95 fL), 80% and 88%; MPV/TPC (cut-off <0.065), 82% and 88%; PDW (cut-off <208.5), 84% and 88%; and RDW (cut-off <14.25%), 84% and 82%, respectively. All the parameters have a significant p-value <0.001.

Conclusions: Platelet parameters (TPC, MPV, and MPV/TPC ratio, PDW) and RDW a potential role in the early detection of sepsis in newborns.

Keywords: Sepsis, Gestational age, Platelet parameters, Neonatal intensive care unit (NICU)

Introduction

Neonatal sepsis is the second leading cause of neonatal deaths.[1] It is classified into two main types—early-onset sepsis and late-onset sepsis—based on the causative organisms, transmission mechanism, and time of infection.[2]

Neonatal sepsis is a clinical syndrome that triggers a systemic inflammatory response and multi-organ dysfunction. Therefore, early diagnosis is crucial to prevent adverse outcomes such as visual or hearing impairments and cerebral palsy. [3]

Hematological indicators, inflammatory biomarkers, molecular approaches, and microbiological cultures are examples of modern diagnostic tools. Among hematological indices, platelet parameters; total platelet count (TPC), mean platelet volume (MPV), MPV/TPC ratio, and platelet distribution width have been identified as a major contributor to thrombosis and inflammation. [4,5]

Also red cell distribution width (RDW) is a simple tool for early diagnosis and prognosis of neonatal sepsis. [5-7]

Patients and methods

The study included 100 neonates, categorized into two groups: Group I (Septic Group): 50 neonates exhibiting clinical signs and symptoms suggestive of sepsis. Group II (Control Group): 50 neonates without risk factors for sepsis and clinically free of signs and symptoms indicative of sepsis.

Ethical considerations

The study was approved by the ethics committee of the Faculty of Medicine, Minia University (Approval No. 1083/2024).

Participant anonymity and confidentiality were maintained,

and deceptive practices were avoided. Caregivers were informed of their right to withdraw from the research. Written informed consent was obtained from the caregivers.

Inclusion criteria

Preterm and term neonates with signs and symptoms suggestive of sepsis or with risk factors for sepsis. Gestational age between 28 and 38 weeks, and age from day one to 28 days of life.

Exclusion criteria

Other causes of thrombocytopenia like intrauterine growth restriction (IUGR) neonates, maternal conditions (DM, HTN, cardiac and respiratory disorders), hypoxic–ischemic encephalopathy, (TORCH) infection, neonates with syndromic babies, chromosomal aneuploidy, hydrops fetalis, hemolytic anemia, and necessity for exchange transfusion, neonatal polycythemia or previous transfusion of platelets.

All patients were subjected to

History taking: Prenatal history: Maternal medical conditions as DM, HTN, PROM more than 18 hours, chorioamniitis which includes maternal fever >100.4 °F with ≥ 2 with:(Maternal leukocytosis, foul smelling vaginal discharge, uterine tenderness, fetal tachycardia, (GBS) colonization or previous history of GBS disease). Natal history: Type of delivery, obstructed labor and asphyxiated insult. Post-natal history: Feeding intolerance, lethargy, hypothermia, hypotension, respiratory distress, cyanosis, convulsion, and skin mottling.

Clinical examination: Cardiopulmonary mainly in the form of respiratory distress, persistent pulmonary hypertension of the newborn (PPHN) which can be diagnosed clinically by difference in oxygen saturation between pre-ductal and post-ductal

saturation, delayed capillary refill time and hypotension, irritability, lethargy or temperature instability. Disseminated intravascular coagulation (DIC), gastrointestinal symptoms including poor feeding, vomiting, and ileus. Signs of meningitis.

Investigations: Complete blood picture (CBC) with special emphasis on; Total platelet count (TPC), Mean Platelet Volume (MPV), MPV/TPC ratio, Platelet distribution width (PDW) and Red cell distribution width (RDW), Blood culture, Cerebro-spinal fluid (CSF), Urine and other body site cultures as aspiration of septic arthritis, C-reactive protein (CRP), Arterial blood gases (ABG) or capillary blood sample, Serum lactate and ESR, Serum electrolytes, renal function tests, indirect and direct bilirubin.

Statistical Analysis

All data were collected, tabulated, and statistically analyzed using SPSS 26 for windows (SPSS Inc., Chicago, IL, USA).

Quantitative data were expressed as mean ± SD (Standard deviation), median and range for parametric and non-parametric data.

Independent T test and Mann Whitney test were used to calculate difference between quantitative variables in two groups for parametric and non-parametric variables respectively.

Univariate and multivariate regression analysis was done for determination of risk factors.

All statistical comparisons were two tailed with significance Level of P-value ≤ 0.05 indicates significant, p <0.001 indicates highly significant difference while, P> 0.05 indicates non-significant

Results

Table (1): Demographic data among cases and control

Item	Septic cases (n=50)	Control (n=50)	P value
Gestational age			
Mean ±SD	33±2.6	37.6±0.48	<0.001*
Range	27-38	37-38	
Gender			
Males	29 (58%)	23 (46%)	0.23
Females	21 (42%)	27 (54%)	
Post natal days			
Mean ±SD	3.38±4.2	4.28±3.8	0.26
Median (Range)	1 (1-19)	4 (1-15)	
Birth weight			
Mean ±SD	1.171±0.49	3.18±0.36	<0.001*
Range	0.95-2.8	2.7-4.2	
Mode of delivery			
• **NVD**	14 (28%)	6 (12%)	
• **CS**	36 (72%)	44 (88%)	0.07

_* significant at p value <0.05

Table (2): Clinical data (history) among cases and control

Item	Complain	Septic cases (n=50)	Control (n=50)	P value
Prenatal	**PROM**	47 (94%)	0 (0%)	<0.001*
	Chorioamnitis	9 (18%)	0 (0%)	0.003*
	Maternal fever	33 (66%)	0 (0%)	<0.001*
	UTI	48 (96%)	0 (0%)	<0.001*
	Maternal GBS	2 (4%)	0 (0%)	0.49
	DM	25 (50%)	0 (0%)	<0.001*
	Preeclampsia	32 (64%)	3 (10%)	<0.001*
	Recurrent abortion	1 (2%)	0 (0%)	0.99
Natal	**Asphyxiated insult**	11 (22%)	0 (0%)	0.001*
Postnatal	**Feeding intolerance**	38 (76%)	0 (0%)	<0.001*
	Lethargy	38 (76%)	0 (0%)	<0.001*
	Temperature instability			
	• Fever	8 (16%)	0 (0%)	<0.001*
	• Hypothermia	42 (84%)	0 (0%)	

	Cyanosis	19 (38%)	0 (0%)	<0.001*
	Convulsion	5 (10%)	0 (0%)	0.05*
	Respiratory distress	33 (66%)	15 (30%)	0.001*

_* significant at p value <0.05

Table (3): Comparison of CBC parameters between cases and control

Item	**Septic cases (n=50)**	**Control (n=50)**	**P value**
Platelet			
Mean ±SD	119.7±115	281.2±82.2	<0.001*
Median (Range)	13-480	253 (123-438)	
MPV			
Mean ±SD	11.5±2.09	8.67±1.16	<0.001*
Range	8.5-18.7	7.2-11.4	
MPV/ TPC			
Mean ±SD	0.17±0.14	0.04±0.05	<0.001*
Median (Range)	0.01-0.70	0.02-0.19	
PDW			
Mean ±SD	14.39±3.3	12.7±4.2	0.03*
Range	10.2-21	8.5-24.4	
RDW-CV			
Mean ±SD	16.27±2.8	13.02±1.3	<0.001*
Range	12.6-29	11.3-15.9	
RDW.SD			
Mean ±SD	51.7±7.1	43.5±4	<0.001*
Range	34.1-68	39.4-53.7	

_* significant at p value <0.05

Table (4): ROC curve analysis for platelet and other CBC parameters for prediction of sepsis

Item	**RDW-CV**	**RDW-SD**	**Platelet**	**MPV**	**MPV/TBC**	**PDW**
AUC	0.90	0.86	0.86	0.92	0.80	0.69
95% CI	0.85-0.96	0.78-0.94	0.78-0.95	0.87-0.97	0.71-0.90	0.59-0.80
P value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
Cut off value	>14.25	>44.75	<208.5	>9.95	>0.065	>12.5
Sensitivity	84%	84%	84%	80%	82%	68%
Specificity	82%	82%	88%	88%	88%	79%
PPV	82,4%	82,4%	87.5%	87%	87.2%	69.4%
NPV	83.7%	83.7%	84.6%	81.5%	83%	68.6%
Total accuracy	83%	83%	86%	84%	85%	69%

Discussion

Our study revealed higher incidence of sepsis among preterm and lower birth weight infants. This finding is consistent with Jatsho, et al., (2020) [8], and Stoll et al., (2020) [9], who found that preterm neonates and low birth weight neonates were associated with late onset sepsis. Flannery et al., (2021) [10] reported 10-fold higher rate of sepsis among preterm infants with low birth weight. Also, Das, et al., (2024) [11], reported high incidence of sepsis in preterm neonates with low birth weight<2kgs.

Our study revealed a high incidence of sepsis among patients with a history of PROM, chorioamnionitis, maternal fever, UTI, DM and preeclampsia. This was in line with Hincu, et al., (2020) [12] and Reddy, et al., (2023) [13] who reported high incidence of sepsis in patients with the previous parameters. On the other hand, maternal GBS status was insignificant in our studies. This might be due to universal screening and management of maternal GBS disease, also may be due to the small sample size of the study that need to be studied in many neonates.

The previous findings were consistent with Omer, et al., (2021) [14], who reported that the most encountered clinical conditions were respiratory distress, lethargy, feeding problems, hyper/hypothermia, and seizures. In addition, a study by Jajoo, et al., (2019) [15] showed that hypothermia and respiratory distress were the common clinical presentations.

Patel, et al., (2023) [16], reported that thrombocytopenia was the most sensitive marker for culture-positive sepsis. In the current analysis the mean platelet count was significantly lower among cases while the mean MPV, MPV/TPC, PDW, RDW were significantly higher among cases than control. In harmony with our results, Arshad, et al., (2024) [17], mentioned that the mean platelet count was significantly lower while MPV and PDW were significantly elevated. Das, et al., (2024) [11] and Goyal, et al., (2024) [18] reported high incidence of thrombocytopenia among septic neonates.

On contrary of the previous results, Mittal, et al, (2018) [19] reported that a greater number of neonates with culture positive sepsis had thrombocytopenia and a high

MPV and PDW. However, these differences were not statistically significant for sepsis

Our study revealed that MPV was significantly higher among cases than control. This finding is consistent with Agnello, et al., (2021) [20] who proved that a rise in MPV occurred in response to systemic infection. Majumdar, et al., (2021) [21] reported increased MPV in septic cases. Recently, Guney, et al, (2023) [22] showed that MPV could play a role in the early detection of sepsis. Moreover, in three different studies, Wang, et al., (2020) [23], Shaaban, et al., (2020) [24] and Shalaby, et al., (2018) [25], MVP was higher in septic cases compared to control.

Despite the previous results, Sagheb, et al, (2022) [26] reported that the sensitivity and specificity of MPV were inadequate to be used as diagnostic tests. Moreover, our findings were relatively consistent with those of previous studies and indicated that platelet counts were consistent among preterm neonates, but MPV was slightly increased in neonates with a lower GA. (Hsieh, et al., 2023) [27]. Also, Mishra, et al., (2021) [36] found that MPV was higher in the (PROM) group as compared to the control group. Along with MPV, our study revealed MPV/TPC was significantly higher among septic cases. This is consistent with Panda, et al., (2021) [28] who determined that the MPV/TPC ratio performed better diagnostically than both MPV and TPC alone. Our study demonstrated that the mean PDW was higher among cases than control. This was in line with Patel, et al., (2023) [16] who reported increase PDW in septic cases. Majumdar, et al., (2021) [21] found that PDW were increased in septic conditions. Also, Wu J, et al., (2019) [29] revealed that a rise in PDW was related to increased platelet destruction and production during sepsis

On the contrary side, Meena, et al., (2017) [30] and Mittal, et al., (2018) [19] reported no significant correlation between a high PDW and culture positive sepsis.

Additionally, Cai, et al., (2021) [31] revealed that the RDW was high among septic cases, suggesting that high RDW was a risk factor for sepsis death. Furthermore, Hu, et al. (2020) [32] speculated that RDW could be used as a

prognostic index in septic patients. Also Suzan, et al., (2019) [33] reported that RDW had prognostic value in sepsis.

Our study revealed sensitivity and specificity for MPV/TPC 82% and 88% respectively and for PDW, the sensitivity and specificity were 68% and 79% respectively. This was constant with the result of Panda et al., (2022) [28].

This study reported that platelet parameters have a high sensitivity and specificity for prediction of sepsis for RDW-CV, the sensitivity and specificity were 84% and 82% respectively. This was in line with Bulut et al., (2021) [34].

For platelet count, the sensitivity was 84% while the specificity was 88% while for MPV, the sensitivity and specificity were 80% and 88% respectively. This result confirmed by Hayato Go et al., (2020) [35] who reported that MPV predicts prognosis in neonates with a sensitivity of 72.4% and a specificity of 58.6%.

Conclusions

Platelet parameters (TPC, MPV, and MPV/TPC ratio, PDW) and RDW can aid in the early detection of sepsis in newborns

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Author's contributions

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Conflict of interest

We declared no conflict of interest concerning the study.

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