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Research Article

Value of Red Cell Distribution Width (RDW) in Predicting Neonatal Outcome in Neonatal Sepsis

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Abstract

Background: In the world, Neonatal Sepsis firmly to their morbidity and mortality; it constitutes a significant public health challenge. Infections were the most common causes of neonatal deaths, followed by prematurity, intrapartum complications, and asphyxia. The diagnosis is based on anamnestic, clinical and laboratory findings. Although the defined diagnosis is based on the isolation of the causative organism by culture on a fluid sample (blood, cerebrospinal fluid, urine, etc.), low sensitivity of the culture leads to the use of inflammatory markers such as C-reactive protein, procalcitonin and interleukins. Many studies worldwide have commenced to evaluate a new nontraditional value of red cell distribution width as a diagnostic and prognostic biomarker in neonatal sepsis.

Objective: To assess the value of Red Cell Distribution Width (RDW) in predicting neonatal outcome in neonatal sepsis.

Method: In a retrospective, observational study, we enrolled 100 term neonates who were diagnosed with neonatal sepsis who were admitted at a Soba University hospital during the period January 2021- January 2022.

Results: Of 100 neonates, 57% were males and 43% were females. Increased RDW was seen in 86.8% of neonates who had systemic involvement during illness, 100% of deceased patients had high RDW at their deaths, and 90% of survived neonates had normal RDW (p=0.000). The association between the RDW value and the duration of admission was found to be of statistical significance, as the p-value was 0.012.

Conclusion: RDW can be used for evaluating neonates with suspected sepsis, especially in low-resource countries. Increased RDW can be a prognostic marker in neonates with sepsis.

Keywords: Neonate; Sepsis; RDW

Introduction

Sepsis is defined as a life-threatening condition due to regular host response to infection [1]. Sepsis is responsible for approximately 45% of emergency visits by neonates and is a leading cause of neonatal mortality and morbidity, accounting for 14% of deaths in that age group [2,3].

Neonatal sepsis is an infection involving the bloodstream in infants under 28 days old. In developing countries, neonatal sepsis is the leading cause of morbidity and mortality [4,5]. Neonatal sepsis is classified into two groups based on the age of presentation to the emergency department: Early-Onset Sepsis (EOS) and Late-Onset Sepsis (LOS). EOS is sepsis in neonates at or before 72 hours of life (some experts use seven days), and LOS is sepsis occurring at or after 72 hours of life [6].

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Early-Onset Sepsis (EOS) is due to the transmission of pathogens from the mother to the newborn or the fetus. These pathogens can ascend the vagina, the cervix, and the uterus and can also infect the amniotic fluid. Neonates can also get an infection in utero or during their passing through the vaginal canal during delivery. Typical bacterial pathogens for EOS include Group B streptococcus (GBS), *Escherichia coli*, coagulase-negative *Staphylococcus*, Haemophilus influenza, and Listeria monocytogenes. Neonatal sepsis risk is increased by many maternal factors, including chorioamnionitis, GBS colonization, and delivery before 37 weeks, and prolonged rupture of membranes more significant than 18 hours [7].

The early neonatal sepsis symptoms and signs are usually mild and nonspecific but can rapidly progress to shock, Disseminated Intravascular Coagulation (DIC), and death. Therefore, finding a tool for early detection of infants who are more likely to have a worse clinical outcome is essential to offer closer monitoring and more aggressive treatment [8].

Early diagnosis and initiation of antimicrobial therapy are essential to mitigate the high case fatality and to avert morbidity associated with late-onset neonatal sepsis. In recent years, biochemical markers have been influential in research areas on neonatal infections. Inflammatory cascades respond to an infection and comprise many elevated markers frequently used for diagnosing and monitoring sepsis [8].

Many molecules have been studied as potentially useful prognostic

markers in neonatal sepsis. These include C-Reactive Protein (CRP) and CD64 [9] procalcitonin and preseason, [10] and soluble E-selectin [11], IL-6, IL-8 [12].

The Cell Distribution Width (RDW) is a marker studied in neonatal sepsis [13]. The RDW measures the variability of red blood cells in size (anisocytosis) and is routinely evaluated as a part of the complete blood count. The RDW may be elevated in conditions of ineffective production or increased destruction of red blood cells, which commonly occur in inflammatory or infectious situations [14].

Red cell distribution width has been classically used as a screening index for iron deficiency anaemia. However, there is now strong evidence that this simple marker can have a role in detecting adverse outcomes in sepsis as well as in diverse clinical situations [13], including coronary artery disease, [15] heart failure, [16] acute pancreatitis, [17] malignancy, [18] infective endocarditic, peritoneal dialysis, [19] and in critically ill children in general [20].

The path physiology of the elevation of RDW in these patients has yet to be well known. Still, it has been reported that elevated RDW is associated with elevation of other acute inflammatory markers such as C-Reactive Protein (CRP), erythrocyte sedimentation rate, interleukin-6 and tumour necrosis factor-alpha. Proinflammatory cytokines of sepsis have been shown to suppress the maturation of Red Blood Cells (RBC) and decrease the half-life of RBCs, resulting in the elevation of RDW values. Most previous studies investigating the predictive value of RDW were conducted on adult patients, and similar studies in neonatal sepsis are rare and minor [8].

The predictive effect of RDW as an early marker for neonatal sepsis outcomes is interesting. It is routinely found in automated Complete Blood Count (CBC) analyses in hospitalized patients and is thus available at no additional cost for clinicians [8].

Objectives

To study the Prognostic value of red Cell Distribution Width (RDW) in predicting neonatal outcomes in patients admitted at Soba University Hospital 2021-2022.

Methodology

Study design

This is a descriptive observational cross-sectional hospital-based study.

Study area and study settings

This research was conducted in Soba Teaching Hospital, located in Khartoum state. This hospital is considered an important referral hospital in Sudan, where education opportunities are provided for medical students, house officers, and registrars. This hospital also provides care for delivering mothers who are referred from all over the surrounding residential and rural areas.

Study duration

The study was carried out during the period from January 2021 to January 2022.

Study population

Any term neonate diagnosed diagnosis as a definite or probable sepsis was included in the study. A diagnosis of definite sepsis is made when a pathogenic agent is isolated from the blood or cerebrospinal fluid in the presence of clinical signs suggestive of sepsis. Probable sepsis is diagnosed when positive cultures are lacking in the presence of signs suggestive of sepsis and two positive screening parameters (abnormal CRP, erythrocyte sedimentation rate, platelet count, total leucocytic count, absolute neutrophilic count, or immature/total neutrophils ratio >0.2). When signs of sepsis exist but both sepsis screening parameters and cultures are negative, this is deemed as no sepsis.

Inclusion criteria

Any term neonate with a diagnosis of definite or probable sepsis will include in the study.

Exclusion criteria

1. Gestational age less than 37 weeks.
2. Perinatal asphyxia.
3. Neonates with more than 1 episode of sepsis; only the first one was included.
4. Neonates with Dysmorphic features suggestive of chromosomal abnormalities.
5. Neonates under a course of antibiotics before appropriate blood sampling.

Sample size

All neonates fulfilling our criteria of inclusion during the study period were included.

Results

The total study population was 100 neonates (57%) were male neonates. Regarding the mode of delivery, 67 neonates (67%) were delivered through cesarean section, 28% underwent expected vaginal delivery, and 5% with assisted instrumental vaginal delivery. Neonates who delivered between 37-40 weeks gestational age represented 84%, whereas 16% were delivered beyond 40 weeks gestation (Table 1).

The risk factors for neonatal sepsis were found as follows: 20% of neonates had prolonged rupture of membrane (more than 18 hours), maternal urinary tract infection in 15% of neonates, low birth Weight 8% of neonates, complicated delivery in (7%), fetal tachycardia in (5%), multiple births in (4%), maternal fever in (3%) and chorioamnionitis repressing 1% (Table 2).

Positive blood culture for sepsis was found in 59 neonates (59%), while in the rest, 41 neonates (41%) were diagnosed as not culture-based neonatal sepsis (Figure 1).

Regarding the symptoms and signs of neonatal sepsis, 45% showed tachypnea, 43% were found to have poor feeding, 31% had a change in body temperature, 27% had jaundice, 9% had pallor, and 3% manifested with bleeding disorders.

Regarding parameters of sepsis other than blood culture, it was found that symptoms and signs of sepsis were present in 95%, 90% had abnormal CRP,75% had RDW value above 18 % on admission, 66% showed abnormal total leucocyte count and 55% had abnormal platelet count (Table 3).

Regarding the outcome of neonates admitted, our data showed that discharged in good condition represented 74%, 20% passed away (died), and 6% were discharged against medical advice (DAMA) (Table 4).

The association between duration of admission and RDW value was significant statistically, with a p-value of 0.012 (Table 5). The

Table 1: Personal information of the study population.

Variable	N	%
Age at delivery in gestation:		
37-40 weeks	84	84
More than 40 weeks	16	16
Gender:		
Male	57	57
Female	43	43
Mode of delivery:		
Vaginal	28	28
Cesarean section	67	67
Instrumental delivery	5	5
Total	100	100

Table 2: frequencies of risk factors for Neonatal sepsis among the study population (N=100).

Variable	N	%
Risk factor of sepsis detected		
1-Chorioamnionitis:		
Yes	1	1
No	99	99
2-Prolonged rupture of membrane more than 18 hours:		
Yes	20	20
No	80	80
6-Complicated delivery:		
Yes	7	7
No	93	93
7-Low birth weight:		
Yes	8	8
No	92	92
8-Maternal urinary tract infection:		
Yes	15	15
No	85	85
9-Multiple births:		
Yes	4	4
No	96	96
10-Maternal fever:		
Yes	3	3
No	97	97
11-Fetal tachycardia:		
Yes	5	5
No	95	95

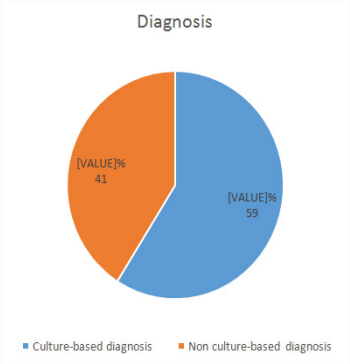

Figure 1: Distribution of diagnosis of neonatal sepsis based on blood culture.

association between RDW value and survival rate in neonates with sepsis was significant as the p-value was 0.000 (Table 6).

Discussion

Diagnosis of neonatal sepsis is a significant problem and is challenging because neonates have an unspecific clinical presentation [21]. Most of our neonates in the study were delivered via caesarean section. A study by Ilham et al. [22] had similar results.

Table 3: The frequencies of parameters of neonatal sepsis among the study population (N=100).

Variable	N		%	
1-Diagnosis: symptoms and signs of sepsis:				
Yes	95		95	
No	5		5	
2-Abnormal CRP:				
Yes	90		90	
No	10		10	
3-Abnormal platelet count:				
Yes	55		55	
No	45		45	
4-Abnormal total leucocytes count:				
Yes	66		66	
No	34		34	
5-RDW value on admission:				
13-18.1	25		25	
18.1-20	43	75	43	75
20.1-22	11		11	
22.1-24	12		12	
More than 24	9		9	

Table 4: Distribution of outcomes among the study participants (N=100).

Variable	N	%
Discharge o	74	74
Discharged with sequalae	0	0
Referred	0	0
DAMA	6	6
Death	20	20

Males were predominant in our study, similar to Golhar et al. [23] and Bella et al. [24]. Usually, the diagnosis of NS is based on blood culture, as in Turkey [25] and Khartoum hospital in Sudan [25]. In our study, the diagnosis is based on blood culture and patient clinical progression in correlation to blood laboratory results, as we had limited resources to perform blood cultures on all patients.

The most frequent symptoms and signs of neonatal sepsis in this study were respiratory distress; the common causes of admission in the Ilham et al. [22] group were respiratory distress, jaundice and lethargy respectively. This study found that most sepsis patients had abnormal CRP and RDW values. In Egypt, a case-control study and other cross sectional studies showed that RDW had significant value in diagnosing neonatal sepsis [26]. Hodeib et al. in their study, neonatal sepsis was associated with abnormal CRP, RDW and Platelets [27].

Most of our study population during admission showed high abnormal RDW values. Martin et al. [28,29] reported elevated RDW in neonates with sepsis during their study. In Sudan [31], a survey at Omdurman Teaching Hospital showed that RDW is significantly higher in septic neonates than in healthy ones.

Kader et al. [30] reported that the incidence of RDW increases in neonatal sepsis and is related to the increasing severity of the sepsis in neonates.

Most of our study population showed abnormal platelets. In their study, HJ, Park JT et al. concluded that platelet abnormalities are associated with neonatal sepsis [31].

Our findings were also similar to those of MS Ahmed et al. [32], WU et al. [33], and Arif et al. [34], who found a significant association between platelet abnormalities and neonatal sepsis.

Limitations

There are several limitations to our study:

Table 5: Association between RDW on admission and duration of NICU admission (N=100).

RDW first read	Duration of NICU admission										Pearson Chi-Square P-value
	1-5 days N=20		6-10 days N=26		11-15 days N=25		16-20 days N=16		>20 days N=13		
	N	%	N	%	N	%	N	%	N	%	
13-18	10	50%	5	19.20%	7	28%	2	12.50%	1	7.70%	
18.1-20	8	40%	13	61.50%	11	44%	3	18.70%	8	61.50%	
20.1-22	0	0%	3	11.50%	5	20%	3	18.70%	0	0%	0.012
22.1-24	1	5%	2	7.30%	1	4%	6	37.60%	2	15.40%	
More than 24	1	5%	3	11.50%	1	4%	2	12.50%	2	15.40%	

Table 6: Association between RDW value and Outcome (N=100).

RDW value	Outcome		Pearson Chi-Square P-value
	Death N = 20	Survival N = 80	
13 -18	0(0%)	72(90%)	
18.1 -20	8 (40%)	(10%)8	
20.1 -22	7 (35%)	(0%)0	0
22.1-24	(15%)3	(0%)0	
More than 24	(10%)2	(0%)0	

1. Small sample size.
2. The study was limited to a single hospital.

Conclusion

The study concluded that 75% of the patients had high RDW values. Over half of the study population had systemic involvement and demonstrated high RDW values. Those with hospital stays of more than five days exhibited high RDW values. All of the deceased patients had high RDW, while most of the survived neonates returned within the average ratio.

References

1. Inger 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(8):801-10.
2. Abiodun MT, Oluwafemi RO. Spectrum and outcome of neonatal emergencies seen in a free health-care program in South-Western Nigeria. Niger J Clin Pract. 2017;20(3):283-9.
3. Omoigberale AI, Sadoh WE, Nwaneri DU. A 4 year review of neonatal outcome at the University of Benin Teaching Hospital, Benin City. Niger J Clin Pract. 2010;13(3):321-5.
4. Tran HT, Doyle LW, Lee KJ, Graham SM. A systematic review of the burden of neonatal mortality and morbidity in the ASEAN Region. WHO South East Asia J Public Health. 2012;1(3):239-48.
5. Seale AC, Blencowe H, Manu AA, Nair H, Bahl R, Qazi SA, et al. Estimates of possible severe bacterial infection in neonates in sub-Saharan Africa, south Asia, and Latin America for 2012: a systematic review and meta-analysis. Lancet Infect Dis. 2014;14(8):731-41.
6. Wynn JL. Defining neonatal sepsis. Curr Opin Pediatr. 2016;28(2):135-40.
7. Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset neonatal sepsis. Clin Microbiol Rev. 2014;27(1):21-47.
8. El Shimi MS, Abou Shady NM, Hamed GM, Shedeed NS. Significance of neutrophilic CD64 as an early marker for detection of neonatal sepsis and prediction of disease outcome. J Matern Fetal Neonatal Med. 2017;30(14):1709-14.
9. Liu B, Chen YX, Yin Q, Zhao YZ, Li CS. Diagnostic value and prognostic evaluation of Presepsin for sepsis in an emergency department. Crit Care. 2013;17(5):R244.
10. Zaki Mel-S, el-Sayed H. Evaluation of microbiologic and hematologic parameters and E-selectin as early predictors for outcome of neonatal sepsis. Arch Pathol Lab Med. 2009;133(8):1291-6.
11. Boskabadi H, Maamouri G, TavakolAfshari J, Mafinejad S, Hosseini G, Mostafavi-Toroghi H, et al. Evaluation of serum interleukins-6, 8 and 10 levels as diagnostic markers of neonatal infection and possibility of mortality. Iran J Basic Med Sci. 2013;16(12):1232-7.
12. Sadaka F, O'Brien J, Prakash S. Red cell distribution width and outcome in patients with septic shock. J Intensive Care Med. 2013;28(5):307-13.
13. Jo YH, Kim K, Lee JH, Kang C, Kim T, Park HM, et al. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. Am J Emerg Med. 2013;31(3):545-8.
14. Açıkgöz SK, Açar B, Aydın S, Açıkgöz E, Er O, Şensoy B, et al. Red Cell Distribution Width Can Predict the Significance of Angiographically Intermediate Coronary Lesions. Med Princ Pract. 2016;25(1):31-5.
15. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJ, Pfeffer MA, et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. J Am Coll Cardiol. 2007;50(1):40-7.
16. Li Y, Zhao Y, Feng L, Guo R. Comparison of the prognostic values of inflammation markers in patients with acute pancreatitis: a retrospective cohort study. BMJ Open. 2017;7(3):e013206.
17. Zhou S, Fang F, Chen H, Zhang W, Chen Y, Shi Y, et al. Prognostic significance of the red blood cell distribution width in diffuse large B-cell lymphoma patients. Oncotarget. 2017;8(25):40724-31.
18. Hsieh YP, Tsai SM, Chang CC, Kor CT, Lin CC. Association between red cell distribution width and mortality in patients undergoing continuous ambulatory peritoneal dialysis. Sci Rep. 2017;7:45632.
19. Ramby AL, Goodman DM, Wald EL, Weiss SL. Red Blood Cell Distribution Width as a Pragmatic Marker for Outcome in Pediatric Critical Illness. PLoS One. 2015;10(6):e0129258.
20. Kim CH, Park JT, Kim EJ, Hyun Han JH, Han JS, Choi JY, et al. An increase in red blood cell distribution width from baseline predicts mortality in patients with severe sepsis or septic shock. Crit Care. 2013;17:R282.
21. Hassan H, Gohil J, Desai R, Mehta R, Chaudhary V. Correlation of Blood Culture Results with the Sepsis Score and Sepsis Screen in the Diagnosis of Early-Onset Neonatal Septicemia. J Clin Neonatol. 2016;5(3):193-8.
22. Omer IM, Mohammed BAA. A study of red cell distribution width and neonatal sepsis at Soba University Hospital, Khartoum, Sudan. Sudan J Paediatr. 2021;21(1):42-7.
23. Golhar S, Madhura A, Chauhan U, Nayak A. Utility of red cell distribution width (RDW) in diagnosis and prognosis of early-onset neonatal sepsis in term neonates. Sci Med J. 2021;3(3):257-64.
24. Stevanny B, Akbari A, Mariana. Red Cell Distribution Width Value Supports the Diagnosis of Neonatal Sepsis in 34-42 Week Gestational Age Neonates. J Nepal Paediatr Soc. 2021;41(2):233-8.
25. Bulut O, Akcakaya A, Bulut N, Ovali F. Elevated Red Cell Distribution Width as a Useful Marker in Neonatal Sepsis. J Pediatr Hematol Oncol. 2021;43(5):180-5.
26. Gupita AS. Uji Hemoglobin dan Indeks Eritrosit Dalam Diagnostikdan Prognostik Pada Sepsis Neonatorum. 2017.
27. Hodeib M, Morgan D, Hedaya A, Waked N. A study of elevated red cell distribution width (RDW) in early-onset neonatal sepsis. Egyptian Pediatric Association Gazette. 2022;70:21
28. Martin SL, Desai S, Nanavati R, Colah RB, Ghosh K, Mukherjee MB. Red cell distribution width and its association with mortality in neonatal sepsis. J Matern Fetal

Neonatal Med. 2019;32(12):1925-30.

29. Albara Ahmed et al. Saudi J Biomed Res. 2020;5(7):175-179.

30. Kader A, Islam MS, Ferdoushi S, Chowdhury AA, Mortaz RE, Sultana T, et al. Evaluation of red cell width in critically ill patients admitted in intensive care unit. Dinajpur Med Col J. 2015;8(1):67-73.

31. Kim CH, Kim SJ, Lee MJ, Kwon YE, Kim YL, Park KS, et al. An increase in mean platelet volume from baseline is associated with mortality in patients with severe sepsis or septic shock. PloS One. 2015;10(3):e0119437.

32. Wu Q, Ren J, Wu X, Wang G, Gu G, Liu S, et al. Recombinant human thrombopoietin improves platelet counts and reduces platelet transfusion possibility among patients with severe sepsis and thrombocytopenia: a prospective study. J Crit Care. 2014;29(3):362-6.

33. Arif SH, Ahmad I, Ali SM, Khan HM. Thrombocytopenia and bacterial sepsis in neonates. Indian J Hematol Blood Transfus. 2012;28(3):147-51.

34. de Stoppelaar SF, van 't Veer C, Claushuis TAM, Albersen BJA, Roelofs JJTH, van der Poll T. Thrombocytopenia impairs host defense in gram-negative pneumonia–derived sepsis in mice. Blood. 2014;124(25):3781-90.