Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Paediatrics

Association between Red Blood Cell Distribution Width (RDW) and Early-Onset Neonatal Sepsis

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DOI: https://doi.org/10.36347/sjams.2024.v12i11.008 | **Received:** 26.09.2024 | **Accepted:** 31.10.2024 | **Published:** 05.11.2024

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Abstract **Original Research Article**

Background: Neonatal sepsis contributes substantially to neonatal morbidity and mortality and is an ongoing major global public health challenge. The aim of this study was to find out the association between RDW and early onset Neonatal Sepsis. ***Methods:*** This case-control study was conducted at the Paediatrics inpatient department of Shaheed Suhrawardy Medical College Hospital, Dhaka, from May 2019 to November 2019. ***Results:*** In this study shows mean postnatal age was 1.86±0.730days and gestational age was 38.83±1.59 weeks in case group besides mean postnatal age was 1.88±0.738 days and gestational age was 39.06±1.78weeks in control group. Mean birth weight of case group was 3240±135.44gm and control group was 3346.66±139.57gm. The mean heamoglobin was 12.76±0.85, WBC was 20.12±1.27, RBC was 4.63±0.77, MCV was 85±0.97, platelet was 232±11.86, CRP was 21±0.77 and RDW Percentage was 21.83±2.39 in case group whereas mean heamoglobin was 12.86±0.83, WBC was 14.81±1.23, RBC was 4.85±0.71, MCV was 82.23±1.19, platelet was 280±14.26, CRP was 3.55±0.70 and RDW Percentage was 15.23±1.85 in control group. The ROC analysis of RDW% in the diagnosis of neonatal sepsis found an AUC of 0.967 (95%CI 0.867- 0.017) which is statistically significant ($p<0.001$). A cut-off value of ≥ 20.60 showed an 86.6% sensitivity and 95% specificity. ***Conclusion:*** RDW indices were higher in neonate present with early onset of neonatal sepsis. There is a strong correlation between RDW and CRP in the early onset of neonatal sepsis.

Keywords: Red Blood Cell Distribution Width (RDW), Early-Onset Neonatal Sepsis (EONS), Neonatal Sepsis, Newborn Infections, Paediatrics.

INTRODUCTION

Neonatal sepsis contributes substantially to neonatal morbidity and mortality and is an ongoing major global public health challenge [1]. According to the World Health Organization (WHO), four million newborn children die each year during the first four weeks of their lives [2]. Sepsis is one of the major causes of neonatal mortality and is probably responsible for 30-50% of the total neonatal deaths each year in developing countries [3].

Currently, neonatal mortality rate in Bangladesh is 28/1000 live births [4]. In a study assessing causes of neonatal deaths in rural Bangladesh it is shown that sepsis/ meningitis constituted 12% of direct causes of neonatal deaths [5]. In another study conducted in Dhaka slums showed sepsis as a direct cause of neonatal deaths in 20% cases [6]. In another study in Bangladesh, estimated causes of mortality around the year 2010 for 102,000 neonatal deaths showed that severe infections (sepsis, meningitis, pneumonia and tetanus) contributed 20% of neonatal deaths [7,8].

Neonatal sepsis has been classified as either early onset (The first 72 hours of life) or late onset sepsis (Occurring after 3 days of age) i.e. infections occurring before and after 72 hours of life [9]. As the signs and symptoms of sepsis are nonspecific, early diagnosis poses a challenge to the clinicians. Blood culture is traditionally used to detect sepsis, but it has limitations,

as it requires 2–5 days to identify organisms in the blood. Additionally, its sensitivity decreases significantly if antibiotics have already been started or when dealing with slow-growing or fastidious pathogens [10].

Therefore, additional tests like a complete blood count (CBC) are performed alongside blood cultures to help diagnose sepsis. However, despite the use of severity scores and biomarkers derived from CBC, predicting the outcomes of neonatal sepsis remains challenging. Conventional screening methods, such as total and differential leukocyte counts, band cells, neutrophil counts, and rapid immunological tests like C-reactive protein (CRP) assays, aid in diagnosing septicemia but are limited in their ability to predict the severity of the condition [11].

For this reason, neonatologists have explored various biochemical markers to achieve a quicker and more accurate diagnosis of sepsis [12]. In our study, we focused on red cell distribution width (RDW) as a potential early, cost-effective, and readily available biomarker for the diagnosis of neonatal sepsis.

A readily available biomarker, Red Cell Distribution Width (RDW), which is derived from CBC, provides a simple and pragmatic means to stratify patients by severity of illness to facilitate focused interventions without any additional costs. It will also mitigate the need for a novel laboratory assay [13].

RDW is a quantitative measure of the variation in the size of circulating erythrocytes. Conditions that affect red blood cell (RBC) production or destruction can cause increased variability in RBC size, resulting in elevated RDW. It represents the variation in red blood cell volume within a blood sample and is routinely included in standard complete blood count (CBC) tests as a numerical indicator of erythrocyte anisocytosis [14].

Objective

The objective of this study was to find out the association between RDW and early onset Neonatal Sepsis.

METHODOLOGY & MATERIALS

This case-control study was conducted at the Paediatrics inpatient department of Shaheed Suhrawardy Medical College Hospital, Dhaka, from May 2019 to November 2019. The study included 90 neonates (30 cases with early-onset neonatal sepsis [EONS] and 60 controls without sepsis) selected using purposive sampling. Inclusion criteria consisted of term neonates with a gestational age of 37-42 weeks, normal birth weight (2,500-3,999 grams), meeting the National Neonatology Forum (NNF) clinical criteria for neonatal sepsis, with significant predisposing factors for EONS, and at least two positive laboratory findings such as abnormal WBC count, thrombocytopenia, CRP >10 mg/L, or a positive blood culture. Exclusion criteria included neonates with low birth weight, preterm births, congenital anomalies, Hypoxic Ischemic Encephalopathy, history of RBC transfusion, congenital infections, severely ill conditions, or those with prior antibiotic exposure. Following informed consent, neonates were evaluated, and data were collected using a structured form. Blood samples were drawn for complete blood count (CBC), CRP levels, and blood cultures using standardized techniques. RDW was measured using an automated hematology analyzer, with RDW >20% considered high and <15% low. Data were analyzed using SPSS version 21. Continuous variables were described as mean ± SD, while categorical variables were presented as frequencies or percentages. Statistical significance was determined using the chi-square test for categorical variables and t-tests for quantitative data, with a p-value of <0.05 considered significant. Receiver Operating Characteristic (ROC) analysis was employed to evaluate the sensitivity and specificity of RDW as a biomarker for EONS. Ethical considerations included obtaining informed consent from the parents, maintaining confidentiality, and assuring that participation would not affect the treatment of their newborns. Participants were informed of their right to withdraw from the study at any time. This structured approach aimed to identify the association between RDW and early-onset neonatal sepsis in neonates.

RESULTS

Table I: Distribution of the respondents according to Age (n=90)

Age	Case	Control	P value
	mean±SD	mean±SD	
Postnatal age (days)	1.86±0.730	1.88±0.738	**0.860***
Gestational age (weeks)	38.83±1.59	39.06±1.78	**0.266***
Maternal Age (years)	28.43±1.13	25.80±1.52	**<0.01***

***P value was determined by independent sample t test.**

Table I shows mean postnatal age was 1.86±0.730days and gestational age was 38.83±1.59weeks in case group besides mean postnatal age was 1.88±0.738days and gestational age was 39.06±1.78weeks in control group. Mean maternal age was 28.43±1.13years in case group and 25.80±1.52years in control group. There was highly significant difference has been found between both groups with maternal age.

Table II: Distribution of the respondents according to Antepartum hemorrhage (n=90)

	Case	Control	P value
Present	11 (36.7)	7 (11.7)	
Absent	19 (63.3)	53 (88.3)	**0.005***

*P value was determined by chi square test.

Table II shows 36.7% mothers had antepartum hemorrhage in case group besides 11.7% had antepartum hemorrhage in control group. There was significant difference has been found between both groups with antepartum hemorrhage.

Table III: Distribution of the respondents according to Parity (n=90)

Parity	Case	Control	P value
Primiparous	21 (70)	10 (16.3)	
multiparous	9 (30)	50 (83.7)	**<0.01***

*P value was determined by chi square test.

Table III shows 70% women was primiparous and 30% was multiparous in case group whereas 16.3% women primiparous and 83.7% was multiparous in control group. There was highly significant difference has been found between both groups with parity.

Table IV: Distribution of the respondents according to Mode of delivery (n=90)

Mode of delivery	Case	Control	P value
Cesarean section	20 (66.7)	10 (16.7)	**<0.01***
NVD	10 (33.3)	50 (83.3)	

*P value was determined by chi square test.

Table IV shows 66.7% undergoes cesarean section in case group and 16.7% undergoes cesarean section in control group. There was highly significant difference has been found between both groups.

Table V: Distribution of the respondents according to neonate's APGAR score (n=90)

APGAR score	Case	Control	P value
≥7	8 (26.7)	50 (83.3)	
<7	22 (73.3)	10 (16.7)	**<0.01***

*P value was determined by chi square test.

Table V shows 26.7% neonates APGAR score was ≥7 and 73.3% was <7 in case group whereas 83.3% APGAR neonates was ≥7 and 16.7% was <7. There was highly significant difference has been found between both groups.

Table VI: Distribution of the neonate according to Clinical feature of neonatal sepsis (n=30)

Clinical feature	Present	Absent
	Frequency (%)	Frequency (%)
Fever	6 (20)	24 (80)
Jaundice	19 (63.3)	11 (36.7)
Cyanosis	17 (56.7)	13 (43.3)
Hypotension	22 (73.3)	8 (26.7)
Respiratory distress	19 (63.3)	11 (36.7)

Table VI shows 20% had fever and 80% had no fever, 63.3% had jaundice and 36.7% was free from jaundice, 56.7% had cyanosis and 43.3% had no cyanosis, 73.3% had hypotension and 26.7% had no hypotension, 63.3% had respiratory distress and 36.7% had no respiratory distress in case group.

Table VII: Distribution of the respondents according to Hematological findings (n=90)

Hematological findings	Case	Control	P value
	mean±SD	mean±SD	
Hb (gm/dl)	12.76±0.85	12.86±0.83	**0.727***
WBC (10^3/mm^3)	20.12±1.27	14.81±1.23	**<0.01***
RBC (million/mm^3)	4.63±0.77	4.85±0.71	**0.185***

MCV (fl)	85±0.97	82.23±1.19	**<0.01***
Platelet (10^3/mm^3)	232±11.86	280±14.26	**<0.01***
CRP (mg/dl)	21±0.77	3.55±0.70	**<0.01***
RDW (%)	21.83±2.39	15.23±1.85	**<0.01***

*P value was determined by independent sample t test.

Table VII shows mean heamoglobin was 12.76±0.85, WBC was 20.12±1.27, RBC was 4.63±0.77, MCV was 85±0.97, platelet was 232±11.86, CRP was 21±0.77 and RDW Percentage was 21.83±2.39 in case group whereas mean heamoglobin was 12.86±0.83, WBC was 14.81±1.23, RBC was 4.85±0.71, MCV was 82.23±1.19, platelet was 280±14.26, CRP was 3.55±0.70 and RDW Percentage was 15.23±1.85 in control group. There was highly significant difference has been found between both groups with WBC count, platelet count, MCV count, CRP count and RDW percentage.

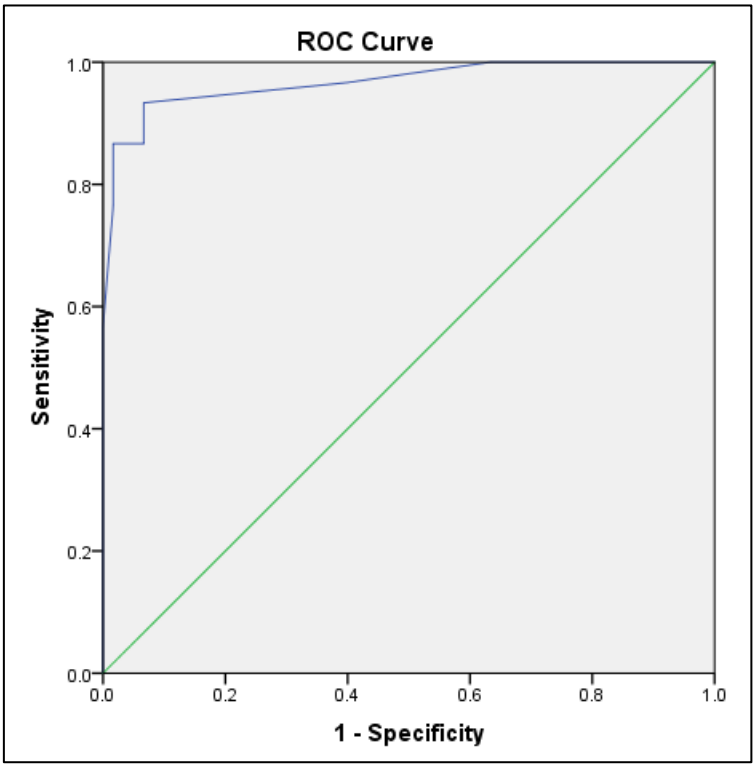

Figure 1: ROC curve analysis RDW% in the diagnosis of EONS

Figure 1 shows ROC analysis of RDW% in the diagnosis of neonatal sepsis found a AUC of 0.967 (95%CI 0.867- 0.017) which is statistically significant ($p<0.001$). A cut-off value of ≥ 20.60 showed an 86.6% sensitivity and 95% specificity.

DISCUSSION

Neonatal sepsis is a major cause of mortality in the developing countries. The incidence of EONS was previously reported as 3-4 cases in 1000 live births [15]. Early identification and timely treatment of sepsis in children is particularly critical in reducing the mortality. RDW is calculated by dividing standard deviation of red blood cell (RBC) volume by mean corpuscular volume (MCV) and multiplying the product by 100. Red cell distribution width can be used as a cheap, easy, rapid and accurate marker for rapid identification of early onset neonatal sepsis.

This study was a case control study where 30 were neonatal sepsis group (case) and 60 healthy neonates (control). The purpose of this study was to find out the association between RDW and EONS.

This study showed mean postnatal age was 1.86±0.730 days and gestational age was 38.83±1.59 weeks in case group whereas mean postnatal age was 1.88±0.738 days and gestational age was 39.06±1.78 weeks in control group. Mean birth weight of case group was 3240±135.44 gm and control group was 3346.66±139.57gm. There was no significant difference was found between both groups. Previous study showed that 43 new-born with the diagnosis of EONS and 45 healthy new-born were analyzed prospectively. Significant intergroup difference was not detected regarding postnatal and gestational age & birth weight [15].

Mean maternal age was 28.43±1.13 years in case group and 25.80±1.52 years in control group. Highly significant difference was found between both groups with maternal age. Cosar H *et al.,* had similar observation where maternal age was significantly higher in the early-onset neonatal sepsis group (28.78 ± 6.25 years vs. 26.29 ± 5.17 years; p=0.049) [15].

In this study 36.7% mother had antepartum hemorrhage disorder in case group besides 11.7% had antepartum hemorrhage disorder in control group. There was significant difference between both groups with antepartum hemorrhage. P. Adatara *et al.,* also observed antepartum hemorrhage during pregnancy was significantly related to the risk of neonates developing sepsis (p<0.001) [16].

We found that 70% women was primiparous and 30% was multiparous in case group whereas 16.3% women primiparous and 83.7% was multiparous in control group. There was highly significant difference between both groups with parity. In a previous study Maternal parity was strongly related to the risk of neonatal sepsis (p<0.027). It was further noted that primiparous women had 1.89 times higher chance of sepsis as compared to multiparous women [16].

Here 66.7% of mothers underwent cesarean section in case group and 16.7% in control group. Highly significant difference was found between both groups. P. Adatara *et al.,* found that mode of delivery to be statistically associated with neonatal sepsis (p<0.001). The study also showed that CS deliveries were the majority among the cases, 67 (65.0%) [16]. Another study showed that sepsis was high in neonates born by cesarean section than by vaginal delivery with no statistical significant difference [17].

In this study 73.3% neonates APGAR score was <7 in case group whereas 83.3% neonates APGAR score was ≥7. There was highly significant difference between both groups. Adatara P *et al.,* observed that the proportion of neonates who had an APGAR score <7 at the first minute were higher in the cases, 47 (45.6%), than controls, 231 (29.0%) [16].

We found that 20% neonates had fever, 63.3% had jaundice, 56.7% had cyanosis, 73.3% had hypotension and 63.3% had respiratory distress in case group. Among them mortality was only 6.7%. In a previous study they demonstrated that respiratory distress was the main clinical feature of neonatal sepsis. Hypotension in septic neonates is a sign of severe sepsis or septic shock according to the International Consensus Conference on Pediatric Sepsis. In previous study they observed mortality rate was 30.9% [18].

In this study mean heamoglobin was 12.76±0.85, WBC was 20.12±1.27, RBC was 4.63±0.77, MCV was 85±0.97, platelet was 232±11.86, CRP was 21±0.77 and RDW Percentage was 21.83±2.39 in case group whereas mean heamoglobin was 12.86±0.83, WBC was 14.81±1.23, RBC was 4.85±0.71, MCV was 82.23±1.19, platelet was 280±14.26 and CRP was 3.55±0.70. RDW Percentage was 15.23±1.85 in case group. WBC count, MCV count, CRP count and RDW percentage was significantly higher in case group and platelet count is significantly lower in case group. In a previous study by C.H *et al.,* they observed in new-born in the EONS group significantly higher levels of WBC (19.60 ± 6.30 103/mm3 vs. 15.48 ± 5.46 103/mm3; p=0.002), RDW (22.35 ± 5.27% vs 15.33 ± 1.87%; p<0.001) and CRP (21.2 ± 19.06 mg/L vs. 2.71 ± 0.76 mg/L; p<0.001), while platelet counts were significantly lower (226.09 ± 71.79 × 103/mm3 vs. 291.56 ± 70.99 × 103/mm^3; p<0.001) [15].

In another study they observed the mean RDW level was significantly higher in neonatal sepsis cases (21.31±3.08%) as compared controls (16.23±1.16%) [19]. S. Martin *et al.,* also observed RDW levels were significantly higher among the neonatal sepsis cases (19.90%) as compared to the controls (18.90%) [20].

In our study the ROC analysis of RDW% in the diagnosis of neonatal sepsis found an AUC of 0.967 (95%CI 0.867- 0.017) which is statistically significant (p<0.001). A cut-off value of RDW% ≥20.60 showed respectively 86.6%, 95%, 89.66%, 93.44% and 92.22% sensitivity, specificity, PPV, NPV and accuracy. Choudhary *et al.,* observed a cutoff of 18.5, RDW had 94.55% sensitivity and 96.36% specificity for diagnosis of EONS [19].

Limitations of the study

This study had some limitations, including its single-center design, which may limit generalizability, and a relatively small sample size, which may not be fully representative. Additionally, we were unable to establish a clear correlation between RDW and early-onset neonatal sepsis, likely due to these factors. Larger, multicenter studies are needed to confirm these findings.

Recommendations

RDW should be considered as a valuable factor in the diagnostic assessment of early-onset neonatal sepsis (EONS), alongside other clinical and laboratory indicators, to enhance early detection and treatment.

CONCLUSION

RDW indices were observably higher in neonate present with early onset of neonatal sepsis. Besides these there is a strong correlation between RDW and CRP in the early onset of neonatal sepsis. Moreover, a cut-off value of RDW≥ 20.60 showed an 86.6% sensitivity and 95% specificity. However, further studies investigating the correlations between RDW and EONS are required for finalization of the comment.

Acknowledgment

I sincerely thank the staff, participants, and my co-authors/colleagues for their invaluable support and cooperation in this study.

Financial support and sponsorship: No funding sources.

Conflicts of interest: There are no conflicts of interest.

Ethical approval: The study was approved by the Institutional Ethics Committee.

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