

Original Research Article

Red cell distribution width as predictor tool in critically ill neonate

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ABSTRACT

Background: Neonatal sepsis is one of the most common causes for critically ill neonate. Early recognition and prompt treatment are crucial. Red cell distribution width (RDW) varies significantly in such conditions. This study aims at finding the relation between RDW and critically ill neonate.

Methods: This hospital based prospective cohort study was conducted on 60 neonates with suspected sepsis. The RDW values were collected at admission and after 72 hours of admission. The primary outcome measures were mortality and recovery from illness. Statistical analysis was done using statistical package for the social sciences (SPSS) 22 version software with appropriate statistical methods applied.

Results: The mean RDW in our study group was 14.788 ± 2.138 . Receiver operating characteristic (ROC) curve for RDW at 72 hours of admission revealed area under curve (AUC) 0.810 at 14% cut-off with sensitivity of 81.25%, specificity of 72.73%, positive predictive values (PPV) 52% and negative predictive values (NPV) 91.4% with $p < 0.0001$.

Conclusions: RDW is a simple, easily available, rapid test to predict the outcome in critically ill neonate.

Keywords: Critically ill, Neonatal sepsis, RDW

INTRODUCTION

The neonatal period - first 28 days of life is the most vulnerable time as neonatal deaths are still the leading cause of infant mortality. As per United Nations International Children's Emergency Fund (UNICEF) 2018 data, India stands 12th amongst 52 lower middle income countries with newborn mortality rate (NMR) of 25.4 deaths per 1000 live births.¹ More than 80 per cent of newborn deaths are the result of premature birth, complications during labour and delivery and infections such as sepsis, meningitis and pneumonia.²

During inflammatory process in body there is oxidative burst which hinders the survival of cells, leading to release of immature cells into circulation.³ The inflammatory process can cause inhibition of erythropoietin (EPO) production, resistance to EPO, lack of bioavailability of iron

and stimulation of apoptosis and phagocytosis of red blood cells (RBC).⁴⁻⁸ Due to decreased survival of RBCs in peripheral circulation, a surge in immature RBCs which are larger in size occurs into the peripheral circulation.⁹ The ROS cause significant harm to RBCs by altering the glycoproteins and ion channels in the RBC membrane.¹⁰⁻¹³

Red cell distribution width (RDW) basically analyses the amount of anisocytosis.¹⁴ This measurement is subject dependent objective analysis of variation in the cell size.¹⁵ Increased RDW indicate how uneven the RBCs are.¹⁶ As a response to inflammatory process in the body RDW increase.¹⁷ RBC maturation suppression leads to increased half-life of immature RBCs leading to varied sized cells.¹⁸ RDW is obtained after consideration of erythrocyte histograms.¹⁹⁻²⁰ Electronic counters give the RDW values in terms of co-efficient of variation, and are different in neonate in comparison to that of child and adult.²¹ Level of

inflammation in patients with sepsis is reflected in RDW value.²² So far no extensive study has been conducted about RDW in neonatal population, especially in neonatal sepsis. Hence this study is taken up to meet the need of hour.

METHODS

This hospital based prospective cohort study was conducted in neonatal intensive care unit department of paediatrics, Adichunchanagiri Institute of Medical Sciences, BG Nagara, Mandya from January 2019 to June 2020 (18 months). Term neonates (≥ 37 weeks) delivered via lower segment caesarean section (LSCS) or vaginal delivery with sepsis, sepsis like illness, respiratory distress, meningitis were included in the study. The neonates with ABO incompatibility, neonatal hyperbilirubinemia, post term (≥ 42 weeks), pre term (< 37 weeks), large/small for gestation, neonates with cardiac conditions, congenital anomalies, neonate with metabolic disorder, neonates given blood transfusion, neonates with maternal history of significant antepartum hemorrhage/severe anemia (hemoglobin < 7 mg/dl)/multiple pregnancies, family history of blood disorders like thalassemia were excluded. The study was approved by institutional ethical committee.

Details of the study protocol were explained to the patient relatives. A written consent was taken. A complete maternal history which included maternal age, parity and medical and obstetric history, events during labor like pre-eclampsia, premature rupture of membranes (PROM), antepartum hemorrhage, fever, uterine tract infection (UTI), chorioamnionitis was taken. Significant perinatal history like gestational age, mode of delivery was also taken.

A detailed clinical examination was undertaken. Resident doctor under strict aseptic precaution, 2 cc blood sample was collected in an ethylenediaminetetraacetic acid (EDTA) vacutainer at admission and A-RDW is noted within 2 hours of sample collection. No additional pricks were made. Analysis was made in the same sample for the sepsis screening as per the NICU protocol; a repeat sample was taken at 72 hours of admission under above mentioned conditions (R-RDW). The EDTA blood sample was put into automated cell counter (PENTRA ES 60 (HORIBA)) which works on the principle of electronic impedance and light scatter.

Blood culture, chest X-ray, ABG was done at the time of admission. Hematological sepsis scoring (HSS) also aided in diagnosis.²³ As neonatal population lack a single reference range for RDW.²⁴ 60 neonates, age and sex matched with cases were considered to obtain a normal reference range for the neonates admitted in our setup and hematological analyzers. Outcome measures for this study were mortality of the neonate and recovery from illness. Data was analyzed using statistical package for the social

sciences (SPSS) 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables and qualitative variables respectively. P value of < 0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

Among the 60 infants included in our study, the mean age was 3.35 ± 3.063 days. The most common presentation of neonate with suspected sepsis was tachypnea (21.7%) followed by decreased activity, asphyxia and seizures. 5% of the sepsis neonates presented with abdominal distension. The mean duration of stay of our study subjects in NICU was 6.86 ± 3.46 days. Slight female preponderance was seen in our study (Table 1).

Statistically significant difference was seen heart rate (HR), respiratory rate (RR), C-reactive protein (CRP), RDW taken at admission and after 72 hours with $p < 0.001$, $p < 0.001$, 0.03 and 0.004 respectively (Table 2). Most of neonates with sepsis recovered without any complications (73.3%). Death followed by shock and feed intolerance were the most common complications seen in our study subjects.

Majority of the cases required oxygen therapy (60%), but artificial ventilation was needed only in 18.3% of the study population. Inotrope support was necessary in 21.7% of the neonates (Table 3). Highest RDW value was seen in neonate with complication of intraventricular hemorrhage (19.0). P value (0.002*) was statistically significant between RDW values in neonates with different outcomes.

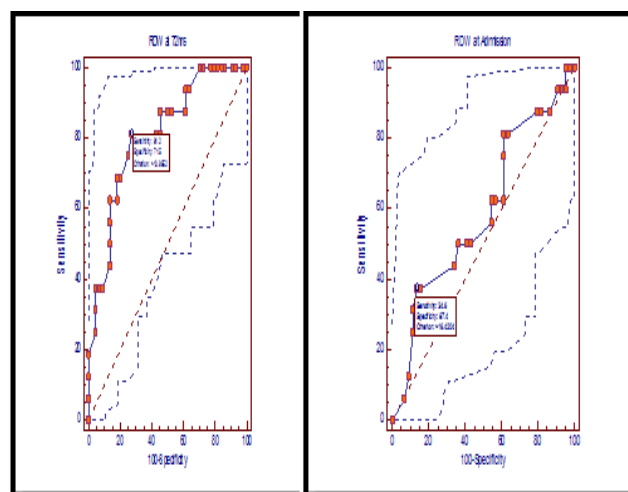


Figure 1: ROC curve 1 and 2 for RDW at admission and at 72 hours respectively.

Table 1: The baseline characteristics among the study subjects were as follows.

Baseline characteristics	Percentage (%)	RDW (mean±SD)	P value
Gender			
Male (n=26)	43.3	12.7±2.8	0.038*
Female (n=34)	56.7	14.1±2.4	
Mode of delivery			
Instrumental (n=14)	23.3	14.1±2.2	0.695
LSCS (n=20)	33.3	13.5±2.7	
NVD (n=26)	43.3	13.3±3.0	
PROM			
No (n=39)	66.7	13.6±2.8	0.751
Yes (n=20)	33.3	13.4±2.5	
Intrauterine complications			
Yes (n=24)	40	13.9±2.6	0.455
No (n=36)	60	13.3±2.7	
Maternal comorbidities			
Yes (n=26)	43.3	12.4±2.3	0.004*
No (n=34)	56.7	14.4±2.6	
Need for resuscitation			
Present (n=33)	55	14.2±2.4	0.139
Absent (n=27)	45	13.1±2.8	

Table 2: Comparison of vital parameters, CRP, HSS and RDW at admission and at 72 hours of admission.

Vital parameters	N	Mean	SD	P value
HR				
At admission	60	139.38	20.16	<0.001*
At 72 hours	60	119.77	14.54	
RR				
At admission	60	68.43	13.63	<0.001*
At 72 hours	60	54.80	11.23	
CRP				
At admission	60	7.45	3.54	0.03*
At 72 hours	60	6.30	3.88	
HSS				
At admission	60	3.98	1.09	0.274
At 72 hours	60	3.77	1.41	
RDW				
At admission	60	14.78	2.13	0.004*
At 72 hours	60	13.56	2.72	

Table 3: Parameters and relation to RDW.

Parameter	RDW (mean±SD)	P value
Oxygen requirement		
Yes	14.8±2.4	<0.001*
No	11.6±1.8	
Mechanical ventilation		
Yes	16.1±2.1	<0.001*
No	12.9±2.5	
Inotrope requirement		
Yes	15.6±2.3	0.001*
No	12.9±2.5	
Blood culture		
Growth present	14.3±2.7	0.132
Growth absent	13.2±2.6	

DISCUSSION

In our study a statistically significant difference was seen in pulse rate and respiratory rate recorded at admission and at 72 hours of admission ($p < 0.001$). Hence these were considered as the clinical indicators of prognosis. According to a study, hematological sepsis score ≥ 3 confirmed neonatal sepsis.²⁵ In our study, the mean HSS value was 3.98 ± 1.09 and 3.77 ± 1.41 at 72 hours of admission ($p = 0.274$), which implies there is no prognostic role of this scoring system. The mean CRP at admission was 7.45 ± 3.54 mg/dl and at 72 hours of admission 6.30 ± 3.88 mg/dl with statistical difference of $p = 0.03$, which can also aid in prognosis.^{16,26} The normal range for RDW in normal neonatal population obtained in our hematological analyzer was 11.345 ± 0.792 and mean RDW in sepsis neonates was 14.788 ± 2.138 [PENTRA ES 60 (HORIBA)]. Mean RDW in neonatal sepsis group in few other studies were 16.4 ± 3.8 ($p < 0.001$), 15.65 ± 1.18 .^{2,27} ROC curve at 72 hours of admission in our study revealed AUC 0.810 at 14% cut-off with sensitivity of 81.25%, specificity of 72.73%, PPV 52% and NPV 91.4% (Figure 1 and 2) similar to that in a study by Mousa et al.^{28,29} In our study the mean value of RDW at admission of the study group was 14.78 ± 2.13 and at 72 hours of admission was 13.56 ± 2.72 with statistically significant difference of $p = 0.004$ similar to some studies where in 0.2 change in RDW from baseline at 72 hours of admission was implicated in higher mortality.^{30,31} Change in RDW between 1st and 3rd day was statistically significant. Hence RDW change is associated with prognosis in our study.

Limitations

As our study was conducted on a small population, larger study is required to prove the prognostic role of RDW in critical neonates.

CONCLUSION

This study has revealed that RDW has all the potential of a prognostic indicator in a critically ill neonate. The study has also conveyed the positive correlation between higher RDW value and early onset neonatal sepsis. RDW is an ideal marker of sepsis due to its simplicity, cost effective and easy repetition as it is routinely done with complete blood count (CBC), especially when combined with clinical scoring. This easily available tool has proved its efficacy in predicting the outcome in a sick neonate, especially when done at 72 hours of admission. As this study is a prospective observational study in an institution conducted in a short duration, for validation of current results a larger sample and multi-centric trial is necessary.

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Conflict of interest: None declared

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

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