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Original Research Article

Red cell distribution width as a prognostic marker in septic neonates versus healthy term newborns

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ABSTRACT

Background: We evaluated the usefulness of RDW (red cell distribution width) as a diagnostic tool in newborn sepsis. Several biomarkers for sepsis have been studied including CRP (C-reactive protein), procalcitonin, interleukins, total WBC count (TC) absolute neutrophil count (ANC), ratio of immature neutrophils to total neutrophils (I/T ratio). An ideal biomarker for sepsis is still elusive. Hence we evaluated RDW as a sepsis marker as it was cheap and available. The objective of the study was to evaluate the role of RDW as a prognostic marker in newborn sepsis compared to healthy newborns.
Methods: The study sample comprised of two groups (cases and control group) each with 40 neonates. Group 1 (cases group) comprised 40 newborns with suspected/probable sepsis based on clinical or laboratory parameters. In group 1 (suspected/probable sepsis) RDW was done at the time of suspicion of sepsis along with other relevant investigations. According to the clinical course these parameters were repeated 24-48 hrs after first value. Group 2 (control group) comprised 40 normal newborns in the postnatal ward. For the control group blood sampling for CBC and RDW was done simultaneously along with blood sampling for newborn screening.
Results: On comparing the baseline variables there is no significant difference among cases and control group with respect to gender distribution, age in days, gestational age in weeks and birth weight. The mean RDW among the cases group was significantly higher than among the control group. In ROC analysis we obtained a cut off value of RDW of 17.25 is helpful to diagnose sepsis with reasonable sensitivity (70%) and specificity (60%).
Conclusions: This study revealed that RDW may also be included in the diagnosis of sepsis in newborns as it is a simple, inexpensive, available and easily repeated test as it is routinely done with a complete blood count.

Keywords: Red cell distribution width, RDW, Neonatal sepsis

INTRODUCTION

Sepsis is an infection-induced systemic inflammatory response syndrome and can further lead to severe sepsis, septic shock and multiple organ dysfunction syndrome or multiple organ failure.[1] Neonatal sepsis can broadly be classified into early onset neonatal sepsis (EONS) (<72 hours) and late onset neonatal sepsis (LONS) (>72 hours).

Neonatal sepsis represents one of the most common causes of morbidity and mortality in both term and preterm infants. Reports show that the incidence of neonatal sepsis ranges from 1 to 5 cases per 1000 live births in developed countries and 49-170 cases per 1000 livebirths in developing countries.[2]

Early diagnosis of severity of sepsis and appropriate treatment is essential for the survival of patients.

Laboratory evaluation of the symptomatic neonate suspected of EONS includes complete blood count (CBC) with differential count, ANC, the absolute band sensitivity especially if measured early in the course of sepsis3 and isolation of causative organisms from microbial cultures upto 72 hours does not identify most infants in view of low culture yield.[4]

Hence a number of other tests have been evaluated for their ability to predict which high risk neonates will go on to develop symptomatic or culture proven sepsis. Apart from CBC and blood culture, this included the measurement of CRP and procalcitonin.

The need for simple, cost effective and easily available, yet reliable markers has pushed researchers into identifying such markers for assessing severity and predicting the prognosis of sepsis.

RDW indicates heterogenicity of erythrocyte volume in circulation, that is reported as a part of standard CBC.[5] RDW is calculated by dividing standard deviation of red blood cell (RBC) volume by mean corpuscular volume (MCV) and multiplying the product by 100.[6] Most automated instruments produce a quantitative assessment of the variation in red cell volume indicated by RDW which corresponds to the microscopic analysis of the degree of anisocytosis. All samples were from 1st day of life.

Table 1: Normal range of RDW in neonates according to gestational age at birth.[7]

Gestational age (in weeks)	<30	31-32	32-34	35-36	37-42
RDW (mean±SD)	17.67±2.28	16.9±1.98	17.86±2.23	16.81±1.82	16.65±1.81

New studies have shown that RDW increase can be used as an important and independent predictive factor for the incidence of death caused by various diseases. Meanwhile, RDW values can reflect the degree of overall inflammation and oxidative stress.[1]

There are other biomarkers for sepsis like CRP and procalcitonin. CRP is however non-specific and can be increased in many other causes other than sepsis like inflammation, surgery, meconium aspiration syndrome. On the other hand, use of procalcitonin is limited in that it spikes within less than 6 hours of onset of sepsis and has little use thereafter. Hence the advantage of RDW over these markers. It could help in the diagnosis of sepsis and also be repeated serially to assess the course of sepsis to see whether sepsis is improving or worsening. As RDW can be checked in the same sample taken for complete blood count, it does not involve additional effort, additional blood volume or additional cost.

In this study we tried to assess the role of RDW as a prognostic marker in newborn sepsis.

The objective of the study was to evaluate the RDW among neonates with sepsis and healthy newborns and establish a cut off value for RDW as a prognostic marker.

METHODS

The study was a case control study conducted in the department of neonatology, Rajagiri hospital, Chunangamvely, Aluva, Kerala from January 2019 to November 2019. All neonates who satisfy the inclusion and exclusion criteria were enrolled in the study. The study sample comprised of two groups (cases and control group) each with 40 neonates. Group 1 (cases group) comprised newborns with suspected/probable sepsis based on clinical or laboratory parameters. In our study suspected /probable sepsis was defined as: suspected sepsis: any 1 of the clinical features of sepsis or >3 maternal risk factors/lab criteria; probable sepsis: features of suspected sepsis and CRP positivity (>10 mg/dl).

All suspected/probable cases having blood/urine/CSF (cerebrospinal fluid) culture positivity were defined as cases of confirmed sepsis.

Laboratory parameters of sepsis included raised CRP, increased ratio of immature neutrophils to total neutrophils (I/T ratio) more than 0.2, decrease in ANC less than 100 per cubic mm and a positive blood, urine or CSF culture.

Inclusion criteria

For cases, all, newborns ≥35 weeks gestation admitted in the NICU/postnatal ward with suspected/probable sepsis were included in the study.

For controls, normal healthy term newborns admitted in the postnatal ward were in included.

Preterm babies ≤34+6/7 weeks of gestation and neonates having hematological disorders, hemolytic anemias, isoimmune hemolytic anemias and jaundice were excluded from the study. Neonates with confirmed or suspected sepsis who had received antibiotics prior to admission were also excluded.

In group 1 (suspected/probable sepsis) RDW, CRP, total WBC count, ANC, I/T ratio and platelet count (PLT) measurement was done on suspicion of sepsis. According to the clinical course these parameters were repeated 24-48 hrs after first value. RDW value was obtained from CBC by 5 part automated hematology analyser ADVIA2120i by electrical impedance method.

Group 2 (control group) comprised 40 normal healthy newborns in the postnatal ward who did not have any risk factors for sepsis. These healthy control babies are normally subjected to a blood sampling for their newborn screening test which is a universally accepted test for all newborns. We took the sample for complete blood count (RDW included in the automated result for CBC) at the same time the samples for newborn screening tests were taken. This did not involve any additional/unwanted prick for the babies concerned and the cost for such a complete blood count (RDW included) was borne by the investigator.

Data management and statistical analysis plan

The data collected using the proforma were entered and analysed by using the Microsoft office excel version 10 and SPSS version 25. Level of significance was fixed at 95% (p value of <0.05 was considered to be statistically significant). Comparison of categorical variables were done by Chi-square or Fisher's exact test. Comparison of continuous variables were done by independent sample t test. RDW was compared between the 2 sets of population using independent sample t test.

RESULTS

We enrolled 40 newborns who were admitted in the department of neonatology at Rajagiri hospital with suspected/probable sepsis as cases group (group 1) and 40 healthy newborns were taken as control group (group 2).

Table 2: Comparison of RDW width among cases group and control group.

Variables	Group 1 (cases)		Group 2 (controls)		P value
	Mean	SD	Mean	SD	
RDW1	18.39	1.73	17.24	0.89	<0.001

Table 3: Distribution of RDW within cases group in babies evaluated for early and late onset sepsis.

Diagnosis	N	Mean RDW 1	SD	P value
Babies evaluated for early onset sepsis	33	18.58	1.71	0.130
Babies evaluated for late onset sepsis	7	17.48	1.65	

Table 4: Area under the curve.

Area under the curve				
Area	Standard error	P value	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.712	0.061	0.001	0.593	0.832

Table 5: ROC analysis results for diagnosis of neonatal sepsis if RDW cut off value >17.25.

RDW cut off	Group		Total	P value
	Group A (cases)	Group B (control)		
≥17.25	28	16	44	0.007; O =3.5; 95% C.I.=1.386-8.835
	63.6%	36.4%	100.0%	
<17.25	12	24	36	
	33.3%	66.7%	100.0%	
Total	40	40	80	
	50.0%	50.0%	100.0%	

On comparing baseline variables, there was no significant difference among cases and control group with respect to gender distribution, age in days, gestational age in weeks and birth weight.

Among the cases group, 57.5% were males and remaining 42.5% were females. Among the control group, 37.5% were males and 62.5% were females (p=0.073). The mean age (SD) in days among cases was

3.45 (6.35) and among controls, the mean age (SD) in days was 2 (0) (p=0.153). The mean (SD) gestational age in weeks among cases was 38.30 (1.35) and among controls, the mean (SD) gestational age was 38.14 (1.02) (p=0.576). The mean (SD) birth weight in grams among cases was 2920.15 (562.81) and among controls, mean (SD) birth weight in grams was 3024.15 (346.00) (p=0.323). Among cases, 82.5% (33/40) were babies evaluated for early onset sepsis and remaining 17.5% (7/40) were babies evaluated for late onset sepsis.

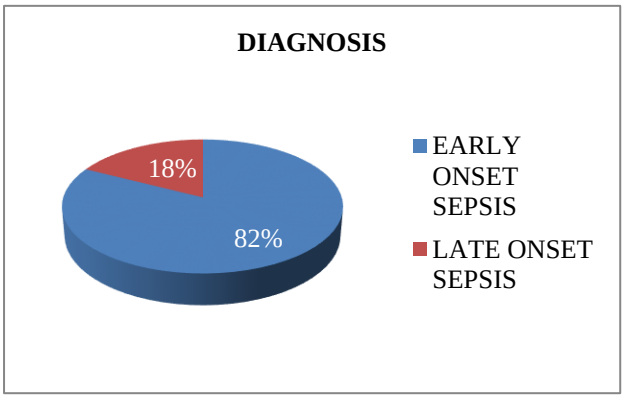

Figure 1: Percentage of babies evaluated for different types of sepsis among cases group n=40 (cases).

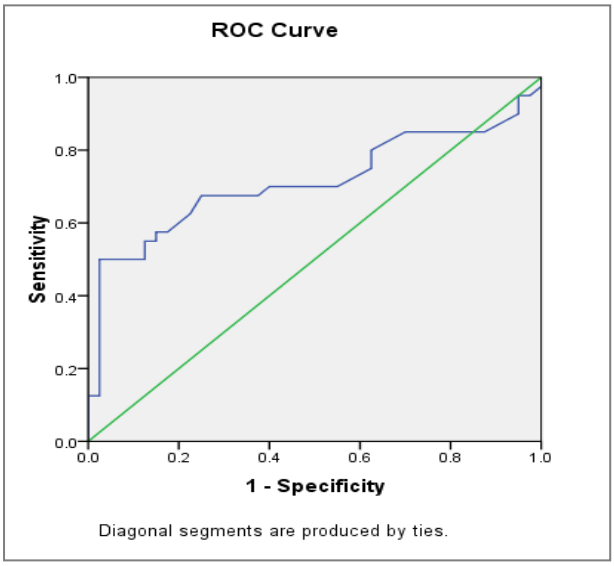

Figure 2: ROC (receiver operating characteristic curve) analysis.

Babies evaluated for early and late onset sepsis

Among cases, 82.5% were babies evaluated for early onset sepsis and remaining 17.5% were babies evaluated for late onset sepsis.

Among the cases group, mean RDW was 18.39 with a standard deviation of 1.73 and among the control group, mean RDW was 17.24 with a standard deviation of 0.89. This difference in the mean of RDW among cases and controls was 1.15 with standard error of 0.31 was highly significant with p value of <0.001. This showed that there was a significant difference in RDW between cases group and control group.

Among the cases group, the mean RDW in babies evaluated for early onset sepsis was 18.58 with a standard deviation of 1.71 and the mean RDW in babies evaluated for late onset sepsis was 17.48 with a standard deviation of 1.65. The p value obtained was 0.130 (>0.05). This showed that there was no significant difference in RDW between babies evaluated for early versus late onset sepsis.

In ROC analysis, the area under the curve obtained was 0.712 with a p value of 0.001 which was highly significant. The cut off value for RDW identified based on ROC analysis was 17.25 with a p value of 0.007 which was highly significant. The cut off was derived using Youden's index.

If a cut off value of 17.25 was used for diagnosing neonatal sepsis, the p value obtained was 0.007 with a sensitivity of 70%, specificity of 60.0%, positive predictive value of 63.6% and negative predictive value of 66.7% was obtained.

DISCUSSION

The primary objective of the study was to evaluate the role of RDW as a prognostic marker in newborn sepsis compared to healthy newborns.

The mean RDW among cases group was significantly higher than among control group(18.39±1.73 versus 17.24±0.89 respectively) (p<0.001). This finding was in agreement with Jianping et al 2015 who reported that RDW value of sepsis group (19.61±1.48) was much more higher than that of normal control group (16.04±1.25) and there was a significant difference (F=15.6, p=0.0001).[1] Our finding was also in agreement with Saleh et al 2017 who reported that the mean RDW was higher among sepsis cases than controls (18.35±1.79 and 12.95±2.23 respectively) (p<0.001).[6] Our finding was also in agreement with Cosar et al5 who reported that the mean RDW in sepsis cases was significantly higher in cases than in controls (22.35±5.27 versus 15.33±1.87, p<0.001).

In ROC (reciever operating characteristic curve) analysis of RDW, the area under the curve obtained was 0.712 (p=0.001). This result was in agreement with Abdullah et al study in which the area under the ROC curve obtained was 0.739 (p<0.001).[2] He got a RDW cut off value of 18 for diagnosis of neonatal sepsis with a sensitivity of 64.3% and specificity of 84.6%. In our study we found that in ROC curve when a cut off value of 17.25 for RDW was used for diagnosis of neonatal sepsis, we got 70% sensitivity and 60% specificity.

In view of these results RDW may be used as an additional diagnostic/prognostic marker to supplement the existing biomarkers in neonatal sepsis. RDW may be used along with other inflammatory markers in diagnosing sepsis. Previous studies regarding RDW and sepsis were limited in number and there were no Indian studies in this regard. RDW was easily available and easily repeated as it was routinely done with a complete blood count.

The main limitation of our study was a relatively small sample size. Mothers receiving antibiotics antenatally can potentially affect the RDW of babies. Clinical course of the baby and its relation to RDW was not included in our study. This may be important from a clinician's point of view. Majority of our babies were suspected cases of early onset sepsis. During early newborn period several normal physiological clinical symptoms may mimic sepsis. Further studies investigating the correlation between RDW and sepsis were needed.

This study revealed that RDW may also be included in the diagnosis of sepsis in newborns as it was a simple, inexpensive, available and easily repeated test as it was routinely done with a CBC.

CONCLUSION

We found that RDW was significantly high in cases when compared to controls. From our study ,we suggest that a cut off value of RDW of 17.25 is helpful to diagnose sepsis with reasonable sensitivity (70%) and specificity(60%) .This study revealed that RDW may also be included in the diagnosis of sepsis in newborns as it is a simple, inexpensive, available and easily repeated test as it is routinely done with a complete blood count.

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

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