Section: Pediatrics

Original Research Article

AN OBSERVATIONAL STUDY TO EVALUATE THE ROLE OF RED CELL DISTRIBUTION WIDTH AND MEAN PLATELET VOLUME AS AN EARLY DIAGNOSTIC MARKER IN EARLY ONSET NEONATAL SEPSIS IN A TERITARY CARE CENTRE IN TELANGANA

T. Radha Kishan Thirupathi[1], Arelly Jyostna[2], Sunkari Venkata Sai Yashwant[3], Priyadarshini Theetla[4]

[1]*Associate Professor, Department of Pediatrics, Niloufer hospital, Osmania Medical College, Hyderabad, Telangana, India*
[2]*Associate Professor, Department of Pediatrics, Government Medical College Nalgonda, Telangana, India*
[3]*Postgraduate, Department of Pediatrics, Niloufer Hospital, Osmania Medical College, Hyderabad, Telangana, India*
[4]*Assosciate Professor, Department of Pediatrics, Sangareddy Medical College, Telangana, India*

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Corresponding Author:
Dr. Arelly Jyostna,
Associate Professor, Department of Pediatrics, Government Medical College Nalgonda, Telangana, India
Email: dr.jyostnaarelly@gmail.com

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ABSTRACT

Background: Neonatal sepsis is a serious infection occurring within the first 28 days of life. It is a significant cause of mortality and morbidity. Red cell distribution width (RDW) and Mean Platelet Volume (MPV) is estimated within the standard CBC profile and considered a simple tool for the diagnosis of neonatal sepsis without any additional cost. This study aimed to investigate the potential role of red cell distribution width (RDW) and MPV in the diagnosis of early-onset neonatal sepsis (EONS and prognosis of early-onset neonatal sepsis (EONS).

Materials and Methods: This is a prospective observational study conducted at the Neonatology department at a tertiary care hospital in Telangana. A total of 200 newborn babies with suspected early onset sepsis were enrolled in our study. Of which 161 were preterm babies, 39 babies were term and 7 babies were very preterm .C-reactive protein, and blood culture of all the babies were compared with Red Cell Distribution width (RDW) and Mean Platelet Volume(MPV) and Evaluated the role of Red Cell Distribution width (RDW) and Mean Platelet Volume(MPV) as an early diagnostic marker of early-onset neonatal sepsis (EONS).

Results: Considering CRP as gold standard for sepsis; at RDW cut value of ≥18- we found that Sensitivity 86%; Specificity 76%; Positive predictive value(PPV)-55%; Negative predictive value(NPV)-94%; and Accuracy-79%; Considering CRP as gold standard for sepsis; at MPV cut value of ≥8.5- we found that Sensitivity 92%; Specificity 68%; Positive predictive value (PPV)-49%; Negative predictive value (NPV)-96%; and Accuracy 74%. In Our study the mean RDW was significantly higher in CRP positive EONS cases ($p<0.001$). RDW combined with MPV has a potential role as early marker in diagnosing and predicting prognosis in early onset neonatal sepsis.

Conclusion: This study revealed that RDW and MPV have a potential role in the diagnosis and prognosis of early-onset neonatal sepsis. As they are simple, less expensive, easily available, and easily repeated, routinely done with Complete Blood count (CBC), RDW and MPV are good early diagnostic marker of Early neonatal sepsi and good indicator for prognosis of Early neonatal sepsis.

Keywords: Early Neonatal Sepsis, C Reactive Protein, Red cell distribution width (RDW), Mean Platelet Volume(MPV).

INTRODUCTION

Neonatal sepsis is characterised by signs and symptoms of infection with or without accompanying bacteremia within the first one month of life. It is the third leading cause of neonatal mortality.[1] Mortality ranges from 1% to 5% for sepsis and 9% to 20% for severe sepsis in neonates. While developed nations have a NMR of 4-5(5.82 per 1000 live births in US) as per NCHS2014 data the NMR of India is 28 per 1000 live births as per Sample registration report 2013. Neonatal sepsis most often go missed at primary and secondary care, owing to the limitations in availability of the reliable diagnostic measures thereby leading to higher mortality, morbidity and squeal.[2] There is no single laboratory test to detect neonatal sepsis with 100% sensitivity and specificity.[3]

Blood culture remains to be the gold standard test to diagnose neonatal sepsis but it takes almost about more than 3 days for the results to come, is relatively expensive and has a low positivity rate.[4]

All newborn suspected to have sepsis should undergo a septic screen which include total leucocyte count (TLC), absolute neutrophil count (ANC), immature to mature neutrophil ratio (I:T ratio), micro erythrocyte sedimentation rate (Micro ESR) and C-reactive protein (CRP).[5,6] The need of the hour is to identify the neonates who are susceptible to develop sepsis by means of a marker that is cheap, accurate, and easy to perform with quick availability of reports. When the standard deviation in red blood cell (RBC) size is divided by the mean corpuscular volume (MCV), red cell distribution width (RDW) is calculated. RDW is a simple tool for the diagnosis of neonatal sepsis.[7]

Recently, RDW can act as a prognostic factor in some life-threatening diseases such as sepsis. The same observation was also demonstrated recently in an adult population of patients being admitted to the emergency wards.[9]

Red cell distribution width (RDW) reflects the different sizes of red blood cells (RBC) during circulation. This is a simple index for inflammation, oxidative stress, and arterial underfilling in severe cases.[10]

RDW was observably higher in newborns with EONS. The pro-inflammatory cytokines released during sepsis have been found to inhibit erythropoietin induced erythrocyte maturation and proliferation and down regulate erythropoietin receptor expression, which are associated with RDW increases.

In sepsis, high oxidative stress releases reactive oxygen species that decreases red blood cell survival and leads to the release of large premature red blood cells into the peripheral circulation, so there is an increase in RDW.[11]

Mean platelet volume is the measurement of average size of platelet volume in blood and routinely available with blood counts. It is a coulter generated parameter. It is used to assess platelet function. Platelet production increases at the onset of sepsis due to accelerated destruction. However, Bone marrow is suppressed subsequently and thrombocytopenia is seen. It is proven in many studies that the level of MPV is increased in Neonatal sepsis.[12]

The aim of our study is to detect the role of red cell distribution width (RDW) and Mean Platelet Volume (MPV) in the diagnosis of early-onset neonatal sepsis (EONS).

MATERIALS AND METHODS

Around 200 neonates admitted for suspected early onset sepsis during the study period of 2 years from November 2021 to november 2024 satisfying the inclusion criteria were enrolled into the study after getting informed consent from the parents /guardians and ethical committee clearance.

The present study was a hospital based prospective observational study conducted in the Department of Neonatology, in a tertiary care hospital, Niloufer hospital, Hyderabad, Telangana.

Inclusion Criteria

For all newborns admitted in the NICU with suspected/probable sepsis

Babies with the following risk factors for sepsis

Spontaneous prematurity

Foul smelling liquor

Rupture of membranes >24 hours

Single unclean or >3 sterile vaginal examinations during labor

Prolonged labor (duration of 1st and 2nd stage of labour >24 hrs

Presence of 2 risk factors – should suspect sepsis,[13]

Exclusion Criteria

- Neonates with suspected hematological disorders
- Neonates who had received antibiotics prior to admission
- Neonates with severe birth asphyxia
- Neonates with congenital anomalies
- Mother's who have received blood transfusions in the 3rd trimester

After obtaining written informed consent from parents/guardian detailed history, physical examination and systemic examination was performed and recorded in a pre-designed proforma.

Sample collection was done under strict aseptic conditions, 2ml of blood is collected by venipuncture with a needle in an ETDA vial for RDW and MPV. 1ml of blood was collected in a clot activated vial for CRP analysis. Both the samples were sent immediately to the hospital laboratory for analysis.

The EDTA vials were evaluated by an automated cell counter from which hemoglobin, total white cell count, total neutrophil count, MPV, RDW were noted.

For the neonates who turned out CRP positive, 1-2 ml of blood was inoculated aseptically into the blood

culture media, after which the bottles were incubated at 37 degrees Centigrade for 5-7 days.
The details were plotted and the results were analysed.[14]
The RDW-CV is a calculation based on both the width of the distribution curve and the mean cell size. It is calculated by dividing the standard deviation of the mean cell size by the MCV of the red cells and multiplying by 100 to convert to a percentage. A normal range for the RDW-CV is approximately 11.0 - 15.0%. Because it is a calculation, the RDW-CV is dependent not only on the width of the distribution curve but also the MCV of the red cell population and may not always reflect the actual variation in red cell size. Be aware that:

- A homogenous population of red cells with a narrow distribution curve and low MCV may have an elevated RDW-CV
- A heterogeneous population of red cells with a broad distribution curve and a high MCV may have a normal RDW-CV.

The RDW-SD is an actual measurement of the width of the red cell distribution curve in femtoliters (fL). The width of the distribution curve is measured at the point that is 20% above the baseline. Since the RDW-SD is an actual measurement, it is not influenced by the MCV and more accurately reflects the red cell size variance. The normal RDW-SD range for adults is 40.0 - 55.0 fL

Mean Platelet Volume

The Mean Platelet Volume (MPV) parameter, the average volume of individual platelets, is derived from the PLT histogram. A high MPV, indicating larger platelets, is indicative of more young platelets in the blood. Following blood loss or destruction of platelets, the bonemarrow releases more megakaryocytes, which inturn, are fragmented into large platelets. Coupling the platelet count with the MPV can indicate different associated conditions.

Like a high MPV indicates younger platelets a low MPV indicates older platelets and can be indicative of disease. For example, low MPV has been associated with diseases including systemic lupus erythematosus, hypothyroidism, and HIV infection. Low MPV may also simply be a response to medications such as heparin.

Statistical Analysis: Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov - Smirnov test. If the normality is rejected then non parametric test were used.
Statistical tests were applied as follows-

- Quantitative variables were associated using Unpaired t-test/Mann Whitney Test (when the data sets were not be normally distributed).

Qualitative variables were associated using Chi-Square test /Fisher's exact test. A p value of <0.05 was considered statistically significant. Predictive analysis was done to estimate the sensitivity; specificity; negative predictive value; positive predictive value and accuracy for MPV and RDW to diagnosis EONS. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 25.0.

RESULTS

A total of 200 newborn babies with early onset sepsis were enrolled in our study. The mean age was 20.88 Hours of life (HOL) (min.2 HOL; Max.62 HOL). Majority of babies belonged to 12-24 HOL (45.5%) followed by 24-48 HOL (32%).

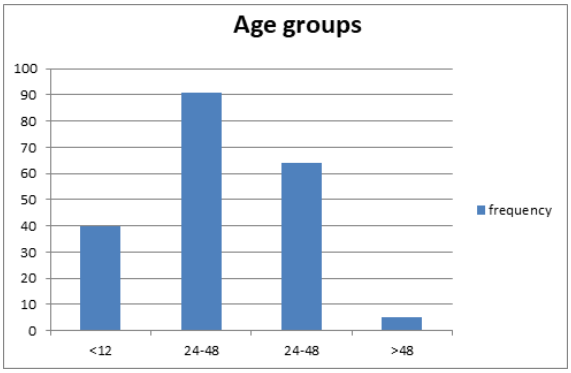

Figure 1: Age of Presentation

Among 200 babies; 161 were preterm babies (80.5%). Most of the babies belonged to late pre-term 35 weeks (28.5%) followed by late preterm 36 weeks (20.5%). 39 babies (19.5%) were term 38 weeks and 7 babies were very preterm 29 weeks (3.5%). Among 200 babies; CRP positivity were 25.5% (51/200).

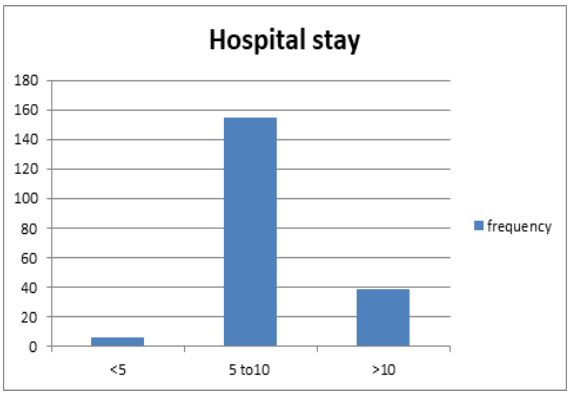

Figure 2: Hospital Stay of Study Population

The mean hospital stay was 9.20 days (Min. 2 days; Max.44 days). Most of the babies had hospital stay of between 5—10 days (77.5%). 39 babies had hospital stay of >10 days (19.5%).
Blood culture was not done among 158 babies (79%). 22 babies were found to be blood culture positive (11%) and 20 babies had blood culture negative report (10%). Among 200 babies; 7 babies were died in our study period. The mortality rate was 3.5%. The positivity of blood culture was found to be significantly correlated with CRP positivity (p<0.001). All 22 cases of blood culture positive babies also had CRP positive report. CRP positivity

was found to be strongly correlated with mortality among babies with sepsis (p<0.001). 6 cases of CRP positive were found died in our study. Mortality among CRP positivity was 11.8%.

Table 1: Association between blood culture and CRP.

		CRP			
		Negative		Positive	
		Count	Row N%	Count	Row N%
Blood Culture	Negative	2	10.0%	18	90.0%
	Not Done	147	93.0%	11	7.0%
	Positive	0	0.0%	22	100.0%
P value<0.001					

Table 2: Correlation between CRP with RDW and MPV.

Report			
CRP		RDW	MPV
Negative	N	149	149
	Mean	17.3040	8.4282
	Std deviation	1.06827	.46209
Positive	N	51	51
	Mean	19.3784	10.0255
	Std deviation	1.37974	1.17232
Total	N	200	200
	Mean	17.8330	8.8355
	Std deviation	1.46583	.99861
P value		<0.001	<0.001

The mean value of RDW (17.3 v/s 19.3;p<0.001) and MPV (8.42 v/s 10.02;p<0.001) were significantly higher among CRP positive babies as compared to CRP negative babies.

Table 3: Predictive ability of RDW.

RDW		CRP		
		Negative	Positive	Total
< 18	Observed	113	7	20
	% within row	94%	6%	100%
>= 18	Observed	36	44	80
	% within row	45%	55%	100%
Total	Observed	149	51	200
	% within row	74%	26%	100%
Sensitivity 86%; Specificity 76%; PPV 55%; NPV94%; Accuracy 79%.				

Considering CRP as gold standard for sepsis; at RDW cut value of ≥18- we found that Sensitivity 86%; Specificity 76%; PPV-55%; NPV-94%; and Accuracy-79%.

Table 4: Predictive ability of MPV

MPV		CRP		Total
		Negative	Positive	
>= 8.5	Observed	48	47	95
	% within row	51%	49%	100%
< 8.5	Observed	101	4	105
	% within row	96%	4%	100%
Total	Observed	149	51	200
	% within row	74%	26%	100%
Sensitivity 92%; Specificity 68%; PPV49%; NPV96%; Accuracy74%				

Considering CRP as gold standard for sepsis; at MPV cut value of ≥8.5- we found that Sensitivity 92%; Specificity 68%; PPV-49%; NPV-96%; and Accuracy-74%. High MPV and RDW were independent risk factors of morbidity and mortality in neonates with sepsis. With the above results, Comparing CRP with RDW, MPV has a strong correlation for early neonatal sepsis. Hence we consider RDW combined with MPV has a potential role as early marker in diagnosing and predicting prognosis in early onset neonatal sepsis

DISCUSSION

Early-onset sepsis is a significant cause of morbidity often complicated by meningitis or pneumonia. Most newborns with early-onset infection present within 24 hrs, few neonates may present at 24–48 hrs, and rarely, neonates with early-onset sepsis may present between 48 h and 6 days of life.[14]

When the standard deviation in red blood cell (RBC) size is divided by the mean corpuscular volume (MCV), red cell distribution width (RDW) is calculated. RDW is a simple tool for the diagnosis of

neonatal sepsis.[15] Although the exact mechanisms that explain the association between RDW and mortality are unknown, high RDW is associated with the presence of an ongoing disease process, such as inflammation, tissue hypoperfusion oxidative stress, or renal failure.[16] Recently, RDW can act as a prognostic factor in some life-threatening diseases such as sepsis. Neonatal sepsis is manifested by bacteremia and clinical manifestations due to microorganism invasion and their toxins. Neonatal sepsis diagnosis should include infection establishment with a systemic illness in which non-infectious explanations for pathophysiologic abnormality are excluded.[17]

Accurate diagnosis is made by blood culture which is a time-consuming method. For this cause, a number of other biochemical markers for accurate diagnosis of sepsis in the shortest time as red cell distribution width (RDW) which is an early cheap and available biomarker for diagnosis of neonatal sepsis.[18,19]

MPV describes the average size of platelets in a blood sample, which is a simple, economical, and useful diagnostic marker for neonatal sepsis. Elevated MPV may be indicative of oxidative stress in newborns elevated MPV in preterm newborns can inform clinicians of possible hypercoagulative states, increased inflammatory response, and oxidative stress. Among these, the most possible explanation for the relationship between MPV and mortality is an inflammatory response.[20,21]

Our study find that the mean RDW was significantly higher in CRP positive EONS cases ($p<0.001$) RDW showed Sensitivity 86%; Specificity 76%; PPV 55%; NPV-94%; and Accuracy-79% for detection of EONS. Considering CRP as gold standard for sepsis; at MPV cut value of ≥8.5- we found that Sensitivity 92%; Specificity 68%; PPV-49%; NPV-96%; and Accuracy-74%.[22,23]

CONCLUSION

In our country, where neonatal sepsis is one of the leading causes of morbidity and mortality in neonates, early diagnosis of neonatal sepsis is very important and RDW is a very promising test in serving this purpose.

This study proved the efficacy of RDW in the diagnosis of early neonatal sepsis. Further large trials are needed to prove the usefulness of this simple test which can have a large impact in reducing the morbidity and mortality of neonatal sepsis.

MPV which is a platelet index obtained from complete blood count can be used an adjuvant marker along with established septic screen to ensure early diagnosis and treatment with no additional expense. However further studies in large scale populations maybe needed to firmly establish the role MPV in neonatal sepsis.

MPV and RDW were independent predictors of prognosis and the combination of the two helps in predicting the prognosis of neonates with early-onset sepsis in the early stage.

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