Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/dpfx4s89

DIAGNOSTIC UTILITY OF RED CELL DISTRIBUTION WIDTH IN NEONATAL SEPSIS – AN OBSERVATIONAL STUDY

Dr Divya Prakash[1*]

[1*]Senior resident, Department of Paediatric, M S Ramaiah Medical College

***Corresponding Author:** Dr Somashekar A R
*Professor, Department of Paediatric, M S Ramaiah Medical College

ABSTRACT

Neonates with sepsis usually present with nonspecific symptoms making the diagnosis difficult. The gold standard for diagnosis of sepsis is blood culture but it's positive only in 40% of the cases. The investigations complete blood count and C reactive protein are used for early diagnosis, but they are not as conclusive as blood culture. Red cell distribution width is defined as the variation in red blood cell volume. It is a measure of erythrocyte size. Recent studies show that RDW is raised significantly in sepsis.

Objective: To assess the diagnostic utility of red cell distribution width in neonates with sepsis.
Methods: we conducted an observational, cross sectional, descriptive study over a period of 18 months. All neonates who underwent sepsis screen during the study period were included in this study.
Results: The mean RDW in the no sepsis and probable sepsis and culture proven sepsis were 15.019% (14.78% - 15.25%), 15.87% (15.56% - 16.19%), and 16.30% (15.84% - 16.76%) respectively. The comparison of the mean values of RDW in three study groups was significant with a p-value < 0.001. No correlation was found between RDW and CRP (r= 0.128, p =0.085). For the RDW cutoff value of 14.95%, sensitivity was 88.6% and specificity was 54.8%. The positive predictive value of RDW in predicting neonatal sepsis was 66.9%, and the negative predictive value was 72.6%.

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first 28 days of life.[1]. According to a survey by World Health Organization (WHO) in 2019 neonatal mortality accounted for 17 deaths per 1000 live birth.[2] Septicemia in neonates is the third most leading cause of death in neonates accounting for 13.81% globally and 12.36% in India.[2]

The Red Cell Distribution Width (RDW) is defined as the variation in red blood cell volume. It is a measure of erythrocyte size i.e. anisocytosis.[3] RDW is calculated as the standard deviation of the red cell volume distribution curve in femtoliter. It is usually reported as a percentage relative to mean red cell volume. RDW is commonly used to differentiate the different types of anemia. Recent studies show that RDW is raised significantly in sepsis. Other than sepsis, it is reported to be raised in cardiac condition and critically ill children.[4-6] In sepsis, the inflammatory reaction alters both erythropoiesis and erythrocyte maturation thus there is a raise in RDW.[7] The increased RDW reflects the severity of the underlying inflammatory state. It may provide useful prognostic information about the risk of mortality.

RDW estimation needs no extra sample for analysis. It is cost effective and in line with the point of care principle.

Methods:
Observational, cross sectional, descriptive study is conducted in a teaching hospital over a period of 18 months after obtaining the clearance from the institutional ethics committee. All neonates who underwent sepsis screen during the study period were included in this study. A total of 165 neonates were included in this study. Based on the clinical condition investigations were repeated for 16 babies and their respective values were recorded. Blood investigation reports were analyzed for a total of 182 samples. The demographic data like gestational age, gender of infant, maturity, birth weight, perinatal risk factors for sepsis were entered in a predetermined perform. The clinical details like signs and symptoms at presentation and laboratory data like Hb, TLC, ANC, IT ratio, platelet count, CRP, RDW-CV, blood culture, or body fluid culture like CSF were entered in the perform. Newborns were classified into two groups i.e. no sepsis and sepsis based on clinical presentation and sepsis screen. The sepsis group was further classified into probable sepsis, and culture proven sepsis based on the culture.

Statistical analysis: SPSS software, version 20 was used for data analysis. Comparison of RDW in the categories of neonates with no sepsis, probable sepsis, and culture proven sepsis is done by the Anova test. RDW and CRP were correlated by Pearson or Spearman correlation test based on normality of distribution. Post hoc analysis was done using Tukey for sepsis screen parameters. The receiver operator curve was generated for RDW, and sensitivity, specificity, and predictive value of RDW were calculated for diagnosing neonatal sepsis.

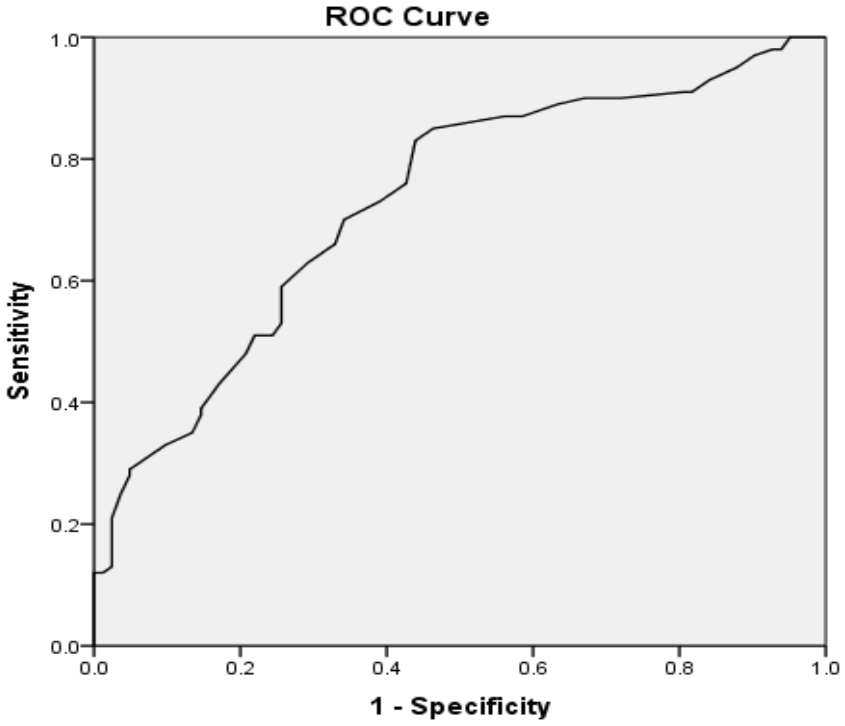
Results:
Based on the sepsis screen 55% of newborns had no sepsis (n=82) and 45% had sepsis (n=100). Based on the culture report in the sepsis group 63% were grouped into probable sepsis (n=63) and the rest 37% in culture proven sepsis (n=37). 19% of newborns showed no signs or symptoms of sepsis (n=34). The majority of the newborns presented with respiratory distress as the main presenting feature accounting for 40% (n=73). Other presenting symptoms noted were jaundice, hypoglycemia, fever, and vomiting accounting for 24% (n=43), 8% (n=14), 6% (n=12), and 3% (n=6) respectively.
Risk factors for the final diagnosis of sepsis and no sepsis were analyzed using the chi-square test, and the odds ratio for the same was calculated. Prematurity was at 2.7 times at higher risk than term neonates for sepsis with an odds ratio of 2.72 ($r = 7.34$, p-value = 0.0074). Pearson chi-square test showed significant values for low birth weight infant and neonatal sepsis as their odds of sepsis increased by 3.2 times as compared to normal weight neonates ($r = 12.7$, p-value <0.001). Maternal risk factors like PROM, maternal fever, maternal UTI, and maternal fever were significantly associated with sepsis ($r = 23.2$, p-value <0.001, odds ratio = 5.12)
The range of RDW noted in the study population was 11.6% to 20.6%. The mean RDW in the study population was 15.57% (95% CI: 15.38 - 15.76). Mean RDW in the three study groups i.e, no sepsis, probable sepsis, and culture proven sepsis group was 15.019% (14.78 - 15.25), 15.87% (15.56 - 16.19), and 16.30% (15.84 - 16.76) respectively with 95% CI. The comparison of the mean values of RDW in three study groups were significant with p-value < 0.001 ($f=17.861$). Post hoc analysis showed significance between no sepsis and probable sepsis and between no sepsis and culture proven sepsis with a p-value of < 0.001. However, there was no significance noted between probable sepsis and culture proven sepsis. RDW showed no correlation with TLC, IT ratio, and platelets as Pearson correlation was -0.073 ($p = 0.32$), 0.022 ($p = 0.764$), and -0.174 ($p = 0.019$) respectively. No correlation was found between RDW and CRP as Pearson correlation was 0.128 ($p =0.085$). The sensitivity of RDW for diagnosis of neonatal sepsis at an RDW cut off of 14.95 was 88.6% and specificity was 54.8%. The positive predictive value of RDW in predicting neonatal sepsis was 66.9%, and the negative predictive value was 72.6%.

Table 1: Comparison of mean values of sepsis screen and RDW

Variables	f	p-value	95% Confidence Interval
RDW	3.947	0.048	0.66 to 1.36
CRP	38.655	<0.001	13.50 to 26.26
ANC	0.062	0.804	-1571.86 to 1161.35
Platelet	12.703	<0.001	-60356.31 to -8351.98
IT ratio	1.216	0.272	0.09 to 0.23749
TLC	3.191	0.076	-1328.70 to 2473.25

(RDW- Red Cell Distribution Width, TLC- Total Leucocyte Count, IT ratio- Immature To Total Leucocyte ratio, ANC- Absolute Neutrophil Count, and CRP- C Reactive Protein)

Figure 1: Receiver operator curve of Red Cell Distribution Width.



At a RDW cutoff of 14.95%, sensitivity was 88.6% and specificity was 54.8%.

Discussion

The risk factors for neonatal sepsis noted in the study were preterm neonates (odds ratio=2.7, r=7.34, p= 0.0074), Low birth weight newborns (odds ratio=3.2, r=12.7, p<0.001), and maternal risk factor like premature rupture of membranes (odds ratio=5.12, r=23.2, p=<0.001). No culture isolate noted in 80% (n=145), culture isolate were noted in 20% (n=37). The most common organism isolated was enterococcus accounted to 31% (n=12), other isolates noted were Methicillin-resistant Staphylococcus aureus (MRSA), Klebsiella pneumonia, Serratia marcescens, Staphylococcus species, fungal isolate accounted to 15% (n=6), 13% (n=5), 10%(n=4), 18%(n=7), 10%(n=4) respectively.

The comparison of the mean values of RDW in three study groups were significant with p-value < 0.001 (f=17.861). Post hoc analysis showed significance between no sepsis and probable sepsis and between no sepsis and culture proven sepsis with a p-value of < 0.001. But, there was no significance noted between probable sepsis and culture proven sepsis. RDW showed no correlation with TLC, IT ratio, and platelets and CRP. In a study by **Ellhony et al**.[8], for an RDW cutoff value of 16.35%, the sensitivity of RDW CV for diagnosis of neonatal sepsis was as high as 70% and specificity was 66%. In our study, the cutoff value was 14.95% which is much lesser as compared to other studies as we included a wide range of neonates with different gestational age and birth weight. There was no matching done for gestational age, gender, and birth weight. Most of the studies done were comparing RDW-CV values in the surviving group with sepsis with the non-surviving group. It was found that nonsurvivors with sepsis had a higher mortality rate as compared to the surviving group with sepsis. Most of the studies done on RDW are either in critically ill adults or very sick pediatric population. They have analyzed the correlation of RDW values with mortality. The studies using RDW as a marker for sepsis are less in number. In our study, we have included all the neonates who underwent sepsis screen without any bias. We have studied the correlation of RDW-CV with other sepsis screen parameters like CRP, TLC, IT ratio, and platelets. However, it showed no correlation except for platelet count. Thus RDW can be used as a separate single marker for sepsis.

Reference

1. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. The Lancet. 2017 Oct;390(10104):1770–80.
2. Neonatal mortality 2019, WHO - UNICEF data. Available on htmlhttps://data.unicef.org/topic/child-survival/neonatal-mortality/.
3. Christensen RD, Yaish HM, Henry E, Bennett ST. Red blood cell distribution width: reference intervals for neonates. J Matern Fetal Neonatal Med. 2015 May 24;28(8):883–8
4. DeBari V, Mahmood N, Mathew J, Kang B, Khan M. Broadening of the red blood cell distribution width is associated with increased severity of illness in patients with sepsis. Int J Crit Illn Inj Sci. 2014;4(4):278.
5. Said AS, Spinella PC, Hartman ME, Steffen KM, Jackups R, Holubkov R, et al. RBC Distribution Width: Biomarker for Red Cell Dysfunction and Critical Illness Outcome?*. Pediatr Crit Care Med. 2017 Feb;18(2):134–42.
6. Khanbabaee G, Hashemi SM, Salarian S, Fariborzi MR, Kiumarsi A. Red Cell Distribution Width Elevation and Sepsis in Pediatric Critically Ill Patients. Arch Pediatr Infect Dis. 2018 Mar 11.
7. 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. 2018 Jan 8;1–6
8. Ellahony DM, El-Mekkawy MS, Farag MM. A Study of Red Cell Distribution Width in Neonatal Sepsis. Pediatr Emerg Care. 2020 Aug;36(8):378-383