RED CELL DISTRIBUTION WIDTH AS A
DIAGNOSTIC AND PROGNOSTIC MARKER IN
NEONATAL SEPSIS

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INTRODUCTION
• Neonatal sepsis refers to systemic infections affecting infants within 28 days of life.

• Neonatal sepsis is one of the major causes of morbidity and mortality in newborns and thus an early diagnosis is very important.

• A single sepsis screen may be negative early in neonatal sepsis.

• Studies have found Red cell Distribution Width (RDW) to vary significantly in pathological conditions associated with inflammation and infection.
• Red Cell Distribution Width (RDW) is the quantitative assessment of the variation in red cell volume and corresponds to the degree of anisocytosis.

• RDW could be found increased in sepsis because of the effect of proinflammatory cytokines on red cell production.

• There is a paucity of studies on RDW in the newborns and its association with neonatal sepsis.
AIMS AND OBJECTIVES
1. To find out the **normal range of RDW** in healthy newborns.

2. To investigate the **role of RDW in**

   I. The **diagnosis of neonatal sepsis**

   II. Prediction of the **severity** of neonatal sepsis

   III. Prediction of **mortality** in neonatal sepsis
MATERIALS AND METHODS
• This study was a **prospective analytical study**.

• It was conducted in Silchar Medical College from August to October 2019.

• A total of **100 newborns** (50 normal and 50 neonatal sepsis) were taken for the study.

• The **normal newborns group** consisted of healthy neonates without any associated health problems / symptoms of clinical sepsis with **negative sepsis screens**.
• The **neonatal sepsis group** consisted of neonates with (i). **Positive sepsis screen** with/without clinical features of neonatal sepsis (or) (ii). **Blood, urine or csf culture positive** or signs of pneumonia on chest xray.

• Neonates with severe birth asphyxia, meconium aspiration syndrome, congenital malformations, metabolic disease & ABO/Rh isoimmunisation are **excluded from study**.

• The **neonatal sepsis group** was subdivided into **3 groups** (sepsis, severe sepsis and septic shock).
68 neonates with maternal history or symptoms and signs suggestive of neonatal sepsis

15 sepsis screen positive
- 8 blood c/s positive
  - 1 meningitis
  - 1 pneumonia
  - 1 UTI
- 7 blood c/s negative
  - 4 - only sepsis screen positive

53 sepsis screen negative
- 23 blood c/s positive
  - 22 – only blood c/s +ve
    - 1 pneumonia
    - 10 pneumonia
    - 2 meningitis
- 30 blood c/s negative
  - 18 - no evidence of sepsis

EXCLUDED
• **Informed consent** was obtained from the parents before the delivery of the baby for the study.

• **Ethical clearance** was obtained from the institutional research board of Silchar Medical College and Hospital.

• The collected data were analysed with **IBM.SPSS** statistics software **25.0 Version**.
RESULTS
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal newborns group (n=100)</th>
<th>Neonatal sepsis group (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in days</td>
<td>1.94 ± 0.81</td>
<td>2.34 ± 1.43</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>NVD = 30, CS = 20</td>
<td>NVD = 31, CS = 19</td>
</tr>
<tr>
<td>Gender</td>
<td>Females = 25, Males = 25</td>
<td>Females = 20, Males = 30</td>
</tr>
<tr>
<td>Gestational age in weeks</td>
<td>38.9 ± 0.88</td>
<td>37.88 ± 2.46</td>
</tr>
<tr>
<td>Birth weight in kg</td>
<td>3.05 ± 0.33</td>
<td>2.50 ± 0.58</td>
</tr>
<tr>
<td>Platelet count</td>
<td>196x10³/µL ± 87x10³/µL</td>
<td>159x10³/µL ± 109x10³/µL</td>
</tr>
<tr>
<td>RDW %</td>
<td><strong>Mean</strong> 16.18 ± 1.23</td>
<td><strong>Mean</strong> 18.40 ± 1.18</td>
</tr>
<tr>
<td></td>
<td>Median 16.45</td>
<td>Median 18.20</td>
</tr>
<tr>
<td></td>
<td>Minimum 12.80</td>
<td>Minimum 16.70</td>
</tr>
<tr>
<td></td>
<td>Maximum 18.30</td>
<td>Maximum 21.90</td>
</tr>
</tbody>
</table>

*p value = 0.000*
42 neonates had Early Onset Sepsis and 8 neonates had Late Onset Sepsis
Relationship between RDW and the diagnosis of Neonatal Sepsis

Relationship between RDW and the diagnosis of Neonatal Sepsis (n = 200) :
Significant (p value = 0.000)
Mean RDW and outcome in the subgroups of neonatal sepsis

<table>
<thead>
<tr>
<th>RDW %</th>
<th>Sepsis (n = 25)</th>
<th>Severe Sepsis (n = 16)</th>
<th>Septic Shock (n = 9)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>17.89 ± 0.94</td>
<td>18.60 ± 0.90</td>
<td>19.47 ± 1.45</td>
<td>0.001</td>
</tr>
<tr>
<td>Dead</td>
<td>0 (0%)</td>
<td>4 (25%)</td>
<td>7 (77.78%)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Outcome in Sepsis group
### Relationship between RDW and mortality in neonatal sepsis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number</th>
<th>Mean ± SD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dead Neonates</td>
<td>11</td>
<td>19.31 ± 1.51</td>
<td>0.003</td>
</tr>
<tr>
<td>Living Neonates</td>
<td>39</td>
<td>18.14 ± 0.93</td>
<td></td>
</tr>
</tbody>
</table>

Relationship between RDW and mortality in Neonatal Sepsis (n = 50) : Significant (p value = 0.001)
• In the neonatal sepsis group (n=100), **RDW had a significant relationship with**

  1. **Sepsis screen (atleast any 2 of 5 parameters positive)** (p value = 0.023)

  2. **CRP** (p value = 0.037)

  3. **Sclerema neonatorum (n = 5)** (p value = 0.028)
ROC curve for the diagnosis of neonatal sepsis by RDW

An RDW cut off of 16.95% has a 96% sensitivity, 95.23% NPV, 93.8% accuracy, 82.75% PPV and 80% specificity in the diagnosis of neonatal sepsis.
An RDW cut-off level 19% predicted mortality in neonatal sepsis with 89% NPV, 82% specificity, 73% accuracy, 64% sensitivity and 50% PPV.

Diagonal segments are produced by ties.
DISCUSSION
Comparison of RDW in normal and sepsis neonates in other studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean RDW (%)</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Normal neonates</td>
<td>Sepsis neonates</td>
<td>P value</td>
</tr>
<tr>
<td>Cosar H et al. 2017</td>
<td>15.33±1.87</td>
<td>22.35±5.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Martin SL et al. 2018</td>
<td>18.90</td>
<td>19.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dr. Monu Singh et al. 2019</td>
<td>16.23±1.16</td>
<td>21.31±3.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Our study 2019</td>
<td>16.18± 1.23</td>
<td>18.40±1.18</td>
<td>0.000</td>
</tr>
</tbody>
</table>

In a study by Ellahony DM et al., RDW was significantly higher in non-survivors compared with survivors (p value<0.0001) and also significantly higher in septic shock compared with sepsis and severe sepsis (p value 0.000). Our study agrees with the above study.
Comparison of RDW Cut offs for the diagnosis of neonatal sepsis in other studies

<table>
<thead>
<tr>
<th>RDW</th>
<th>Abdullah et al. 2018</th>
<th>Dr. Monu Singh et al. 2019</th>
<th>Our study 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut off</td>
<td>&gt;14.3%</td>
<td>≥18.55%</td>
<td>≥16.95%</td>
</tr>
<tr>
<td>Area Under Curve</td>
<td>0.924</td>
<td>0.988</td>
<td>0.935</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.000</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>85%</td>
<td>94.55%</td>
<td>86%</td>
</tr>
<tr>
<td>Specificity</td>
<td>100%</td>
<td>96.36%</td>
<td>87%</td>
</tr>
<tr>
<td>PPV</td>
<td>-</td>
<td>96.3%</td>
<td>86.86%</td>
</tr>
<tr>
<td>NPV</td>
<td>-</td>
<td>94.64%</td>
<td>86.13%</td>
</tr>
<tr>
<td>Diagnostic accuracy</td>
<td>-</td>
<td>95.45%</td>
<td>93.5%</td>
</tr>
</tbody>
</table>

Comparison of AUC of RDW in ROC curve for the prediction of mortality in neonatal sepsis

<table>
<thead>
<tr>
<th>RDW</th>
<th>Ellahony DM et al. 2017</th>
<th>Our study 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut off</td>
<td>-</td>
<td>19%</td>
</tr>
<tr>
<td>Area Under Curve</td>
<td>0.75</td>
<td>0.728</td>
</tr>
</tbody>
</table>
LIMITATIONS
• RDW is also elevated in other conditions like Iron Deficiency Anemia, B12 and Folate deficiencies and also due to blood transfusions.

• Serial RDW measurements after initiation of antibiotics is not done.

• The sample size is small in our study.

• Follow up after discharge of the sepsis neonates to study the morbidity is not done.
CONCLUSION
• **RDW** is a cost effective **simple test useful in the diagnosis of neonatal sepsis** that is readily available in the print out of **CBC report**.

• **RDW** can be elevated early in sepsis even before sepsis screen becomes positive.

• **RDW** can be used as an **adjunctive test in the early diagnosis of neonatal sepsis**.
• Higher RDW (≥19.75%) is significantly associated with mortality in neonatal sepsis.

• Further large trials are needed to prove the usefulness of this simple test in neonatal sepsis.
REFERENCES


• 9. Brahm Goldstein, MD; Brett Giroir, MD; Adrienne Randolph, MD; and the Members of the International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics. Pediatr Crit Care Med 2005 Vol. 6, No. 1


THANK YOU