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Research Article

DIAGNOSTIC PERFORMANCE OF RED CELL DISTRIBUTION WIDTH IN PREDICTING THE SEVERITY OF NEONATAL SEPSIS

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Abstract:

Background: Neonatal sepsis is a severe, life-threatening condition that arises from a systemic inflammatory response to infection in newborns. It is a significant contributor to neonatal morbidity and mortality, particularly among preterm and low-birth-weight infants.

Objective: To determine if RDW can be employed as a marker for the evaluation of newborn sepsis and the assessment of its severity.

Methods: This prospective observational study was conducted at the District Teaching Hospital, Koppal Institute of Medical Sciences (KIMS), Koppal. KIMS is a tertiary-level healthcare facility catering to the neonatal healthcare needs of the Koppal district and surrounding regions. Duration of study was conducted over a period of 18 months, from July 1st, 2023, to December 31st, 2024.

Results: Out of the 100 enrolled neonates, there were 41 males and 59 females. The study observed a higher prevalence of sepsis in male neonates (49.15%) compared to females (34.15%), whereas septic shock was slightly more prevalent in females (26.83%) than males (20.34%). Birth weight emerged as a critical factor influencing the severity of neonatal sepsis. Clinical features commonly associated with neonatal sepsis included respiratory distress, fever, lethargy, and feeding difficulties. RDW levels showed a consistent and statistically significant correlation with the severity of sepsis.

Conclusion: The potential prognostic value of RDW in neonatal sepsis, emphasizing its usefulness as a highly sensitive, readily available, and cost-effective biomarker for initial screening..

Keywords: RDW, Conventional Biomarkers, Neonatal Sepsis.

INTRODUCTION

Hematological markers are essential tools in diagnosing and managing neonatal sepsis. They help clinicians assess the presence, severity, and potential outcomes of infection, enabling timely and effective treatment decisions. One of the primary markers is the white blood cell (WBC) count. Both elevated and low WBC counts can be indicative of infection. Leukocytosis, or an increased WBC count, is commonly seen in bacterial infections, while leukopenia, a decreased WBC count, often occurs in severe sepsis or when the infection overwhelms the body's immune response. Monitoring WBC levels can provide insights into the progression of sepsis and the body's ability to mount an immune response [1].

Another important marker is C-reactive protein (CRP), which rises in response to inflammation or infection. CRP levels are often elevated in neonatal sepsis, and this increase serves as an indicator of the severity of the infection. CRP is used not only to diagnose sepsis but also to monitor the effectiveness of treatment over time. Similarly, neutrophil counts are crucial in diagnosing sepsis. An elevated neutrophil count suggests an ongoing infection, while

neutropenia, or low neutrophil levels, can be seen in severe or overwhelming infections. A notable shift toward immature neutrophils, known as band cells, is frequently observed in sepsis, further aiding diagnosis. Platelet count is another hematological parameter that often decreases during sepsis. Thrombocytopenia, or a reduction in platelet count, is common in neonatal sepsis and can be associated with more severe cases of infection, including an increased risk of complications [9]. Red Cell Distribution Width (RDW), which measures the variability in the size of red blood cells, has been shown to increase during systemic inflammation and sepsis. A rise in RDW, along with elevated CRP and WBC, can help clinicians predict the severity of neonatal sepsis and guide treatment decisions.

In neonates with sepsis, RDW can be elevated due to changes in red blood cell production. The inflammatory response triggered by infection leads to the release of cytokines such as interleukin-6 and tumor necrosis factor-alpha, which can impair the maturation of red blood cells and cause the early release of immature cells into the bloodstream. This increase in variation in RBC size, indicated by a higher RDW, has been linked to more severe forms of sepsis and complications like septic shock and multiorgan failure.

Several studies have investigated the potential of RDW as a prognostic tool in neonatal sepsis. Elevated RDW levels in neonates are associated with worse outcomes, including increased mortality and longer hospital stays [12]. RDW has been found to correlate with other biomarkers commonly used in sepsis, such as C-reactive protein (CRP) and procalcitonin, which are indicative of inflammation and infection. While RDW is not a specific marker for sepsis, its ability to reflect the overall inflammatory burden makes it a valuable adjunct in assessing the severity of infection and predicting complications.

RDW has also been studied in conjunction with other biomarkers for early detection of sepsis. When measured alongside CRP, platelet count, and other clinical signs, RDW can help identify neonates at risk of developing severe sepsis even before blood cultures yield results.

MATERIAL AND METHODS

This prospective observational study was conducted at the District Teaching Hospital, Koppal Institute of Medical Sciences (KIMS), Koppal. KIMS is a tertiary-level healthcare facility catering to the neonatal healthcare needs of the Koppal district and surrounding regions. Duration of study was conducted over a period of 18 months, from July 1st, 2023, to December 31st, 2024.

Study Design: A prospective observational study design was utilized to systematically assess the prognostic value of Red Cell Distribution Width (RDW) in neonatal sepsis.

Sample Size Determination: The sample size for this study was calculated using the standard formula for estimation of proportion in observational studies:

Sample size: l00
N: sample size. z2pq
no=-- ez
z: confidence level at 95% (standard value of 1.96). p: variance of population (0.30). q:(1-p)
e: allowable error (9%). On substituting values, we got 99.5, So sample size of l00 is taken.
Thus, the total sample size determined for this study was 100 neonates.

Inclusion Criteria:

1. Neonates aged between 1 and 28 days.
2. Neonates classified by gestational age:
   - Full-term (37 to 40 weeks),
   - Late preterm (34 to 36+6 days weeks),
   - Moderate preterm (32-33 weeks),
   - Very preterm (28-31 weeks),
   - Extreme preterm (less than 28 weeks).

3. Neonates classified by birth weight:
   - Low birth weight (<2.5 kg),
   - Very low birth weight (<1.5 kg),
   - Extremely low birth weight (<1 kg).
4. Neonates exhibiting symptoms indicative of sepsis, such as fever, respiratory distress, lethargy, decreased feeding, or other systemic infection markers.

Exclusion Criteria:

1. Neonates older than 28 days.
2. Neonates with significant congenital abnormalities.
3. Neonates experiencing perinatal asphyxia.
4. Neonates diagnosed with anemia.

Method of Data Collection: Data were collected through a structured approach consisting of detailed clinical history, physical examination, and laboratory investigations.

Clinical History:

Clinical Examination: A thorough clinical examination was conducted for all neonates enrolled in the study, which included:

- Gestational age assessment using the New Ballard Score.
- Accurate measurement of birth weight.
- Comprehensive physical examination to identify clinical signs of neonatal sepsis.
- Severity scoring of sepsis based on standard clinical parameters including vital signs (heart rate, respiratory rate, oxygen saturation), capillary refill time (CRT), and temperature monitoring.

  Laboratory Investigations: Standard laboratory procedures were meticulously followed for all enrolled neonates to ensure accuracy and reliability:
- Complete blood count (CBC) including differential leukocyte count and platelet count (PC).
  - Measurement of Red Cell Distribution Width (RDW) using automated hematology analyzers.
- C-reactive protein (CRP) assays to quantify systemic inflammatory response.
- Blood culture and sensitivity testing performed on neonates with clinical suspicion of sepsis. Neonates without sepsis served as controls and did not undergo blood culture testing.

  Sample Collection Method: Peripheral blood samples were collected aseptically through venipuncture on the first and third day of life. Sample collection procedures included: Two milliliters of blood collected into ethylene-diamine-tetra-acetic acid (EDTA) tubes for CBC, total leukocyte count (TLC), platelet count (PC), and RDW.
- One milliliter of blood collected in plain tubes for CRP analysis.
- One milliliter of blood collected under sterile conditions for blood culture analysis.
- Repeat blood samples collected to monitor the progression of the condition and the response to treatment.

  Ethical Considerations: Ethical approval for conducting the study was obtained from the Institutional Ethical Committee of KIMS. Written informed consent was obtained from the parents or legal guardians of each participating neonate before enrollment into the study.

  Statistical Analysis: Collected data were systematically recorded and analyzed using standard statistical software. Descriptive statistics to summarize demographic characteristics, clinical findings, and laboratory parameters. Independent sample 't' tests were used to compare continuous variables such as RDW between different severity groups (no sepsis, sepsis, and septic shock). Chi-square tests were applied for categorical variables such as gender, birth weight categories, and clinical

severity classification. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of RDW in predicting neonatal sepsis severity were calculated. Receiver Operating Characteristic (ROC) curve analysis was performed to determine optimal RDW cutoff values that provided maximum diagnostic accuracy.

RESULTS

Out of 100 total cases, 41 cases (41.06%) are male and 59 cases (59.94%) are female. This indicates a higher proportion of female cases compared to males. No Sepsis: Females (39.02%) have a higher proportion than males (30.51%). Sepsis: Males (49.15%) have a higher proportion than females (34.15%), indicating males are more affected by sepsis. Septic Shock: Females (26.83%) have a higher proportion than males (20.34%). Females have a higher proportion in the lowest birth weight category (1.0 - 1.5 kg). Males are more common in the normal birth weight range (2.6 - 3.5 kg). No cases were recorded in the >3.5 kg category for both sexes

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Table 1: Severity of birth weight

Variable	BIRTH WEIGHT			
	1.0-1.5 kg	**1.6-2.5 kg**	**2.6-3.5 kg**	**>3.5 kg**
No Sepsis	3 (16.67%)	8 (44.44 %)	7 (38.89 %)	0 (0.0 0%)
Sepsis	13 (56.52%)	7 (30.43 %)	3 (13.04 %)	0 (0.0 0%)
septic shock	3 (30.00%)	6 (60.00 %)	1 (10.00 %)	0 (0.0 0%)

No Sepsis cases are most common in infants weighing 1.6 - 2.5 kg. Sepsis risk is highest in infants with 1.0 - 1.5 kg birth weight. Septic Shock is most frequent in infants with 1.6 - 2.5 kg birth weight. No cases of Sepsis or Septic Shock were reported in infants weighing > 3.5 kg.

No sepsis: clinical features of sepsis present with no septic screen positive.
Clinical sepsis: clinical features of sepsis present with septic screen positive.
Culture positive sepsis: Blood culture positive with features of sepsis.
Clinical Sepsis is the most common diagnosis, higher in Late Onset Sepsis (66.67%) than Early Onset Sepsis (59.46%).
Culture Positive Sepsis rates are similar in both groups (~22-24%).
No Sepsis cases are higher in Early Onset Sepsis (16.22%) than Late Onset Sepsis (11.11%), indicating a higher likelihood of sepsis diagnosis in LOS.

Table 2: Association of Vital Signs with Severity of Illness:

Variable		Severity			
		No Sepsis	Sepsis	Septic shock	
Heart rate	Normal	20 (50.00%)	15 (37.50%)	5 (12.50%)	
	Tachycardia	14 (23.33%)	28 (46.67%)	18 (30.00%)	
	Bradycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Respiratory rate	<60cycles /mt	26 (36.62%)	26 (36.62%)	19 (26.76%)	
	>60 cycles/mt	8 (27.59%)	17 (58.62%)	4 (13.79%)	
Saturation	Normal (>92%)	32 (37.21%)	35 (40.70%)	19 (22.09%)	
	Abnormal (<92%)	2 (14.29%)	8 (57.14%)	4 (28.57%)	
CRT	< 3 sec	33 (49.25%)	27 (40.30%)	7 (10.45%)	
	> 3 sec	1 (3.03%)	16 (48.48%)	16 (48.48%)	
Temperature	Normal	21 (38.89%)	27 (50.00%)	6 (11.11%)	
	Hypothermia	1 (5.26%)	7 (36.84%)	11 (57.89%)	
	Hyperthermia	12 (44.44%)	9 (33.33%)	6 (22.22%)	

Interpretation:

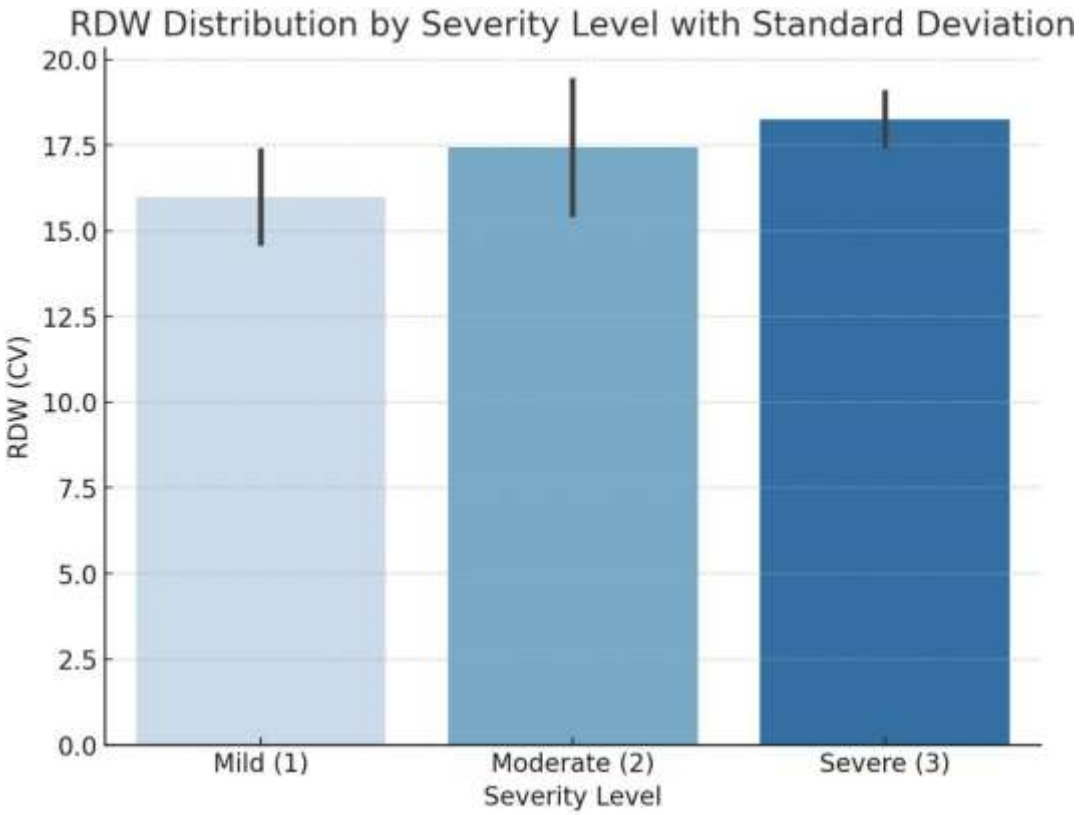
- Heart Rate: Tachycardia (46.67%) is more common in sepsis cases, while normal heart rate (50.00%) is more frequent in no sepsis.
- Respiratory Rate: Higher rates (>60 cycles/min) are associated with sepsis (58.62%), while lower rates are more evenly distributed.
- Saturation: Abnormal saturation (<92%) is more frequent in sepsis (57.14%) and septic shock (28.57%), indicating worsening severity.
- CRT (>3 sec): Strongly linked to septic shock (48.48%), suggesting poor perfusion.
- Temperature: Hypothermia (57.89%) is most common in septic shock, while hyperthermia (33.33%) is seen in sepsis.

Table 2: Relation Between RDW And Severity

SEVERITY LEVEL	AVERAGE RDW
MILD (NO SEPSIS)	15.99
MODERATE (SEPSIS)	17.43
SEVERE (SEPTIC SHOCK)	18.25

The correlation between RDW and severity is 0.49, indicating a moderate positive correlation

This suggests that as RDW increases, severity tends to be higher.



GRAPH 1:

Interpretation:

- Acinetobacter spp. and Pseudomonas aeruginosa were found only in late-onset sepsis (LOS) (100%).
- Citrobacter spp. and Klebsiella pneumoniae were detected in both early-onset sepsis (EOS) and LOS, but more frequently in LOS.
- Streptococcus was found only in EOS (100%), indicating a potential association with early infections.
- Blood culture-negative cases were more common in LOS (62.03%) compared to EOS (37.97%).
- Overall, most positive cultures were in LOS, suggesting bacterial infections are more frequent in late-onset cases.

Interpretation:

DAY1 RDW CV (Cutoff ≥ 16.00)

- AUC = 0.689 → Moderate predictor of CRP Day-1.
- High Sensitivity (88.9%) → Detects most CRP-positive cases.
- Low Specificity (51.1%) → Many false positives.
- p-value = 0.00783 → Statistically significant ($p < 0.05$).
- Conclusion: Good for detecting CRP positivity but weak in ruling it out.

DAY1 RDW SD (Cutoff ≥ 66.30)

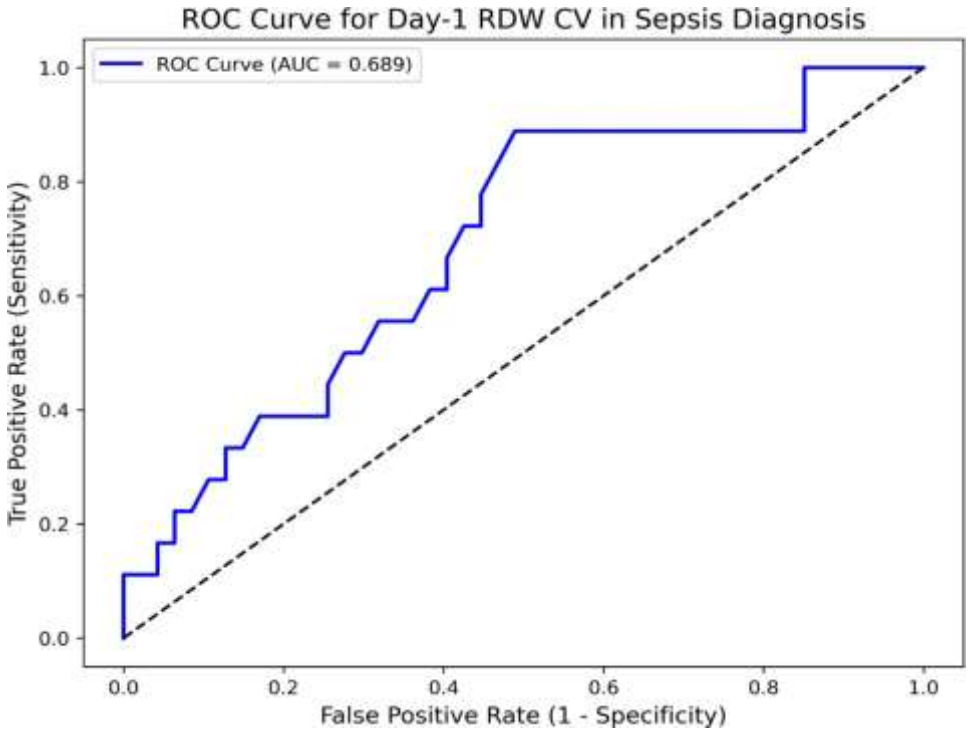
- AUC = 0.585 → Weak predictor of CRP Day-1.
- Lower Sensitivity (50.0%) → Misses many CRP-positive cases.
- Higher Specificity (78.7%) → Better at ruling out false positives.
- p-value = 0.04842 → Statistically significant ($p < 0.05$).
- Conclusion: Better at ruling out CRP-positive cases but not very sensitive.

Final Summary:

- DAY1 RDW CV is better for identifying CRP-positive cases (high sensitivity).
- DAY1 RDW SD is better for ruling out CRP-positive cases (higher specificity).
- Neither is a perfect predictor, but both are statistically significant.
- Combining RDW with other biomarkers (e.g., WBC, CRP trends) could improve prediction accuracy.

GRAPH 2:

Diagnostic Performance of Day-1 RDW CV in CRP Day-1: ROC Analysis:



GRAPGH 3:

Diagnostic Performance of Day-1 RDW SD in CRP Day-1: ROC Analysis:

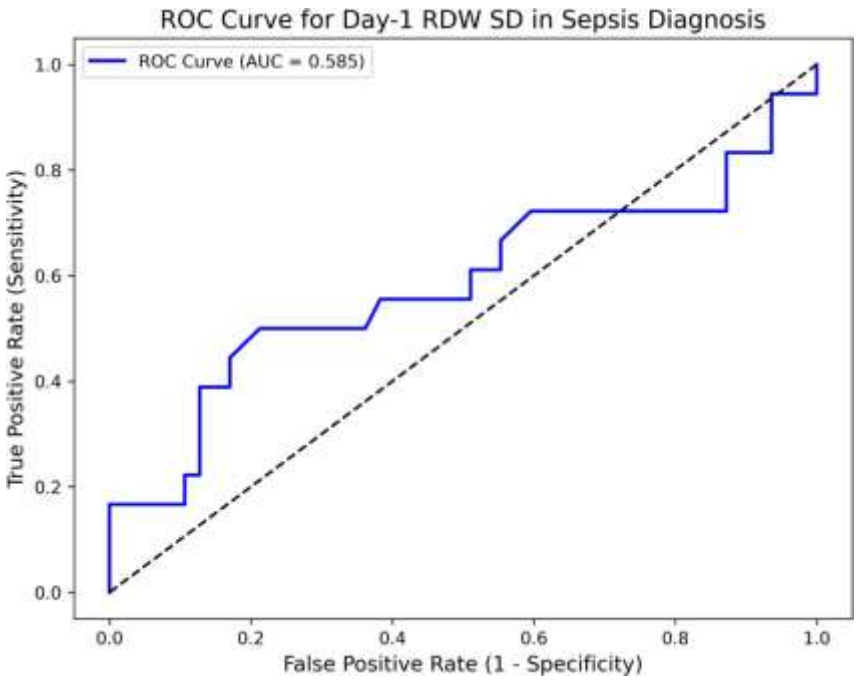


Table NO 3 : Evaluation of RDW as a Biomarker for Neonatal Sepsis Sensitivity vs. Specificity Analysis DAY 3

Variable	CRP Day3							
	Cutoff	AUC	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy	p-value
DAY3 RDW CV	≥14.80	0.471	95.60%	25.00%	74.10%	71.40%	73.80%	0.04196
DAY3 RDW SD	≥58.30	0.564	73.30%	45.00%	75.00%	42.90%	64.60%	0.24143

Interpretation:
DAY3 RDW CV (Cutoff ≥ 14.80)
AUC = 0.471 → Poor predictor (close to random).
Very high Sensitivity (95.6%) → Detects almost all sepsis cases.
Very low Specificity (25.0%) → Many false positives.
p-value = 0.04196 → Statistically significant ($p < 0.05$).
Conclusion: Good for detecting sepsis but poor at ruling it out (many false positives).

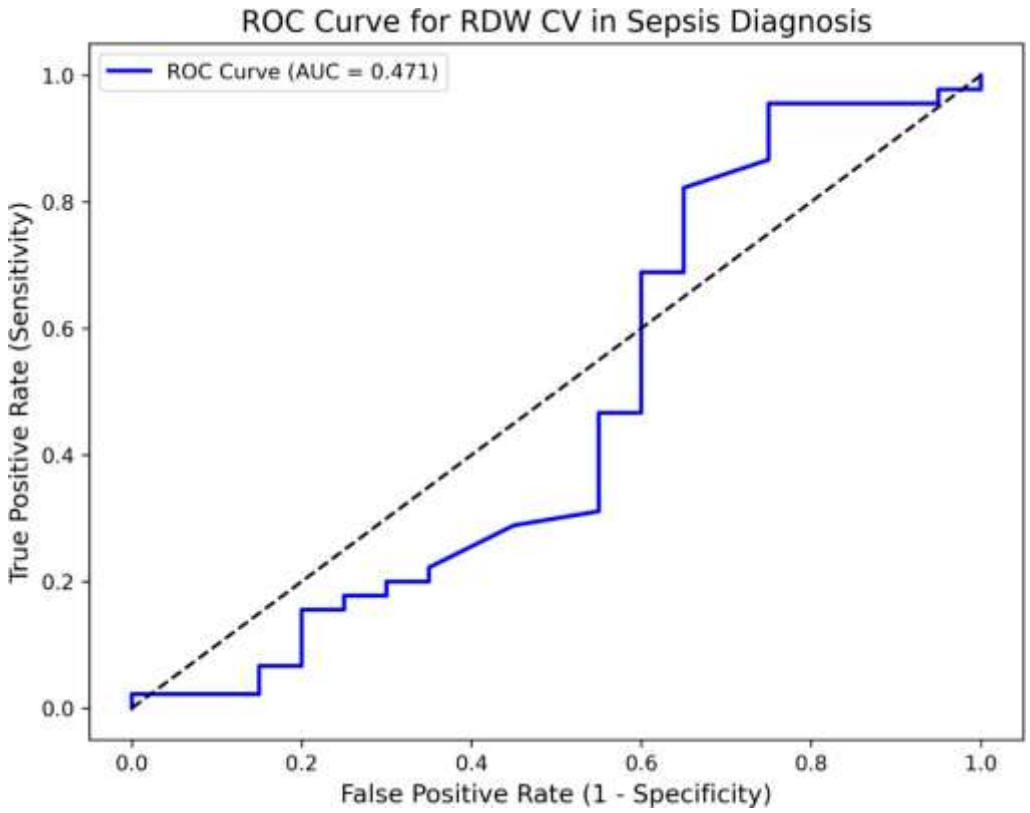
DAY3 RDW SD (Cutoff ≥ 58.30)
AUC = 0.564 → Slightly better, but still a weak predictor.
Moderate Sensitivity (73.3%) → Misses some sepsis cases.
Low Specificity (45.0%) → Still many false positives.
p-value = 0.24143 → Not statistically significant ($p > 0.05$).
Conclusion: RDW SD is slightly better than RDW CV but is not reliable for sepsis prediction (not statistically significant).

Final Summary:

- RDW CV is highly sensitive but not specific, leading to many false positives.
- RDW SD has slightly better specificity but is not a strong predictor.
- Neither RDW CV nor RDW SD alone is reliable for diagnosing sepsis.
- RDW should be combined with other biomarkers (like CRP) for better accuracy

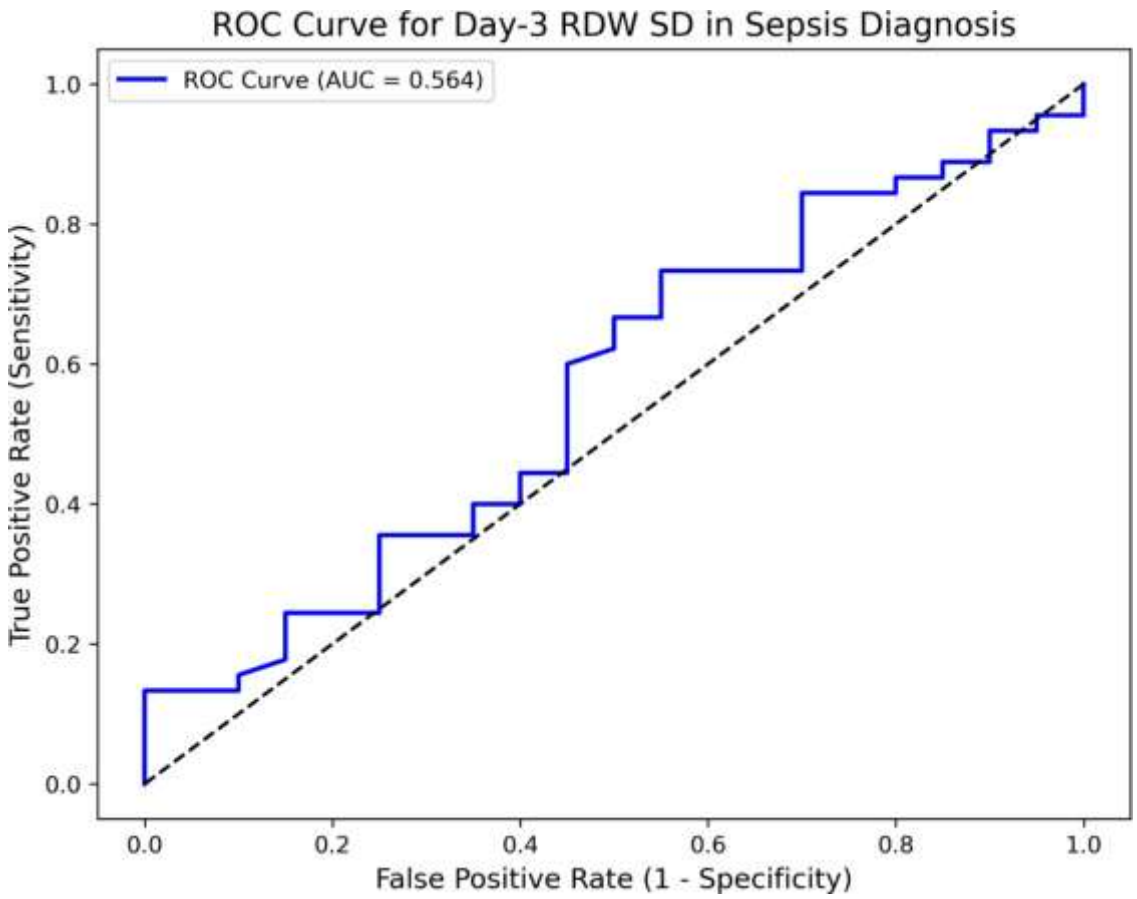
GRAPH 4:

Diagnostic Performance of Day-3 RDW CV in CRP Day-3: ROC Analysis:



GRAPH 5:

Diagnostic Performance of Day-3 RDW SD in CRP Day-3: ROC Analysis:



DISCUSSION

In Koppal District Hospital, located in a semi-rural area with limited access to advanced healthcare facilities, neonatal sepsis is a significant cause of morbidity and mortality. The hospital caters to a diverse population with varying access to prenatal care, and neonatal infections remain a leading cause of hospitalization. Given the clinical challenges and resource constraints, investigating the prognostic value of RDW in neonates with sepsis at Koppal District Hospital offers an important opportunity to assess the utility of this parameter in a real-world setting. Understanding how RDW correlates with clinical outcomes in this population could provide valuable insights into the pathophysiology of neonatal sepsis and improve patient care in similar healthcare environments [2].

The purpose of this study is to evaluate the role of RDW as a prognostic marker for neonatal sepsis at Koppal District Hospital. By analyzing the relationship between RDW levels and the severity of sepsis, as well as the correlation with patient outcomes, the study aims to provide evidence for the use of RDW as a reliable and accessible tool for early diagnosis and prognosis in neonates with sepsis. Given the importance of timely intervention in neonatal sepsis, this research holds the potential to enhance clinical practices and outcomes for neonates in resource-limited settings [3].

Out of the 100 cases included, 41 (41.06%) were male, while 59 (59.94%) were female. This indicates a higher prevalence of neonatal sepsis among female infants compared to males in the study population. The total number of cases is 100, reflecting an equal focus on both genders, though the slightly higher proportion of females suggests that neonatal sepsis may affect female neonates at a marginally higher rate in this particular setting. This distribution could be influenced by various biological, environmental, or socio-economic factors that may vary across different regions or healthcare settings.

Our study on neonatal sepsis severity reveals notable sex-based differences. Among females, 39.02% had no sepsis, 34.15% had sepsis, and 26.83% experienced septic shock. In contrast, males showed 30.51% without sepsis, 49.15% with sepsis, and 20.34% with septic shock. This suggests a higher incidence of sepsis and a lower occurrence of septic shock in males compared to females. Supporting our findings, a systematic review by **Kennedy UK et.al; 2025** indicates a higher sepsis mortality rate in boys compared to girls. [4].

Our study presents the distribution of birth weights among neonates with sepsis, highlighting differences between male and female infants. In the 1.0–1.5 kg category, 44.44% were female and 33.33% male. For 1.6 -- 2.5 kg, 38.89% were female and 42.42% male. In the 2.6–3.5 kg range, 16.67% were

female and 24.24% male. No cases were observed above 3.5 kg for either sex. Low birth weight is a significant risk factor for neonatal sepsis. A study by **Martin SL et.al; 2009** found that RDW levels were significantly higher among neonatal sepsis cases compared to controls, suggesting RDW as a potential diagnostic marker. [5].

In our study, the severity of neonatal sepsis was compared across different birth weight categories. Among neonates with birth weights between 1.0–1.5 kg, 56.52% had sepsis, while 16.67% showed no sepsis and 30.00% experienced septic shock. In the 1.6–2.5 kg range, 44.44% had no sepsis, 30.43% had sepsis, and 60.00% were in septic shock. For birth weights of

2.6–3.5 kg, 38.89% had no sepsis, 13.04% had sepsis, and 10.00% had septic shock. There were no cases above 3.5 kg in any of the categories. A study

by Alshaikh B et.al; 2013 found that lower birth weight is significantly associated with a higher incidence of neonatal sepsis and its severity. Similarly, their research supports the role of birth weight as a critical factor influencing the clinical outcomes in neonatal sepsis, with low birth weight being linked to higher mortality rates [6].

In our study, we compared provisional diagnoses with final diagnoses in neonatal sepsis cases. In the case of culture-positive sepsis, the final diagnosis of "early onset sepsis" was identified in 24.32% of cases, while 59.46% were clinically diagnosed with "clinical sepsis," and 16.22% had "no sepsis" as the final diagnosis. For late onset sepsis, 22.22% were diagnosed with "clinical sepsis," 66.67% had "no sepsis" according to final diagnosis, and 11.11% were diagnosed with early onset sepsis. A study by **Sharma D et.al; 2018** reported challenges in the diagnostic accuracy between provisional and final diagnoses, particularly in differentiating early from late-onset sepsis, with culture-negative cases often misdiagnosed as clinical sepsis. [7].

For heart rate, tachycardia was most commonly observed in septic and septic shock cases (46.67% and 30%, respectively), while only 23.33% of sepsis cases exhibited tachycardia. Bradycardia was not observed in any of the cases. Respiratory rate >60 cycles/min was significantly higher in septic (58.62%) and septic shock cases (13.79%), compared to no sepsis cases (27.59%). Oxygen saturation was abnormal (<92%) in 57.14% of septic cases and 28.57% of septic shock cases. Capillary refill time (CRT) >3 seconds was found in 48.48% of septic and septic shock cases, indicating poor perfusion. Temperature abnormalities, such as hypothermia, were particularly prevalent in septic shock (57.89%). In comparison, the study by **Fairchild KD et.al; 2017** found similar associations between abnormal vital signs and the severity of neonatal sepsis, where

tachycardia, elevated respiratory rates, and abnormal temperature regulation were strongly linked with septic shock.[8].

In our study, we observed a higher death rate among outborn infants compared to inborn infants. Among 41 inborn cases, 5 neonates succumbed, resulting in a death rate of 12.20%. Conversely, among 59 outborn cases, 12 deaths occurred, leading to a death rate of 20.34%. This suggests that outborn neonates are at a higher risk of mortality, potentially due to delays in receiving medical care, lack of early interventions, or complications during transportation. This aligns with the findings of other studies. For instance, **Yancey MK et.al; 1996** reported a higher mortality rate among outborn infants, citing factors such as delayed referral and lack of immediate medical stabilization. [9]

In our study, the evaluation of RDW as a biomarker for neonatal sepsis demonstrated that the sensitivity and specificity of RDW on Day 1 showed considerable variation depending on the parameter used. The RDW-CV cutoff of ≥16.00 had an AUC of 0.689, with high sensitivity (88.90%) but lower specificity (51.10%), indicating that it was more reliable for detecting sepsis but also yielded a higher rate of false positives. In contrast, RDW-SD with a cutoff of ≥66.30 exhibited a lower AUC of 0.585, with moderate sensitivity (50%) and higher specificity (78.70%), indicating that it was better at correctly identifying non-septic cases. The overall accuracy of RDW-CV was 61.50%, whereas RDW-SD showed a higher accuracy of 70.80%. This finding is in line with the study by **Sultana GS, et.al; 2013**, which also emphasized the utility of RDW in neonatal sepsis but noted variability in its diagnostic performance across different cutoff values. Similar to our results, their study demonstrated a higher sensitivity for RDW-CV and better specificity for RDW-SD, suggesting that RDW can be a useful but imperfect biomarker for sepsis diagnosis in neonates [9]

CONCLUSION

The potential prognostic value of RDW in neonatal sepsis, emphasizing its usefulness as a highly sensitive, readily available, and cost-effective biomarker for initial screening. Elevated RDW levels correlated significantly with increasing severity from no sepsis to septic shock, highlighting its role in early identification of severe cases.

However, due to the moderate specificity of RDW, its clinical application must be complemented by other biomarkers to optimize diagnostic accuracy. Recognizing the limitations highlighted, further extensive, multi-centered research incorporating advanced diagnostics and comprehensive biomarker panels is strongly recommended to validate these preliminary findings and translate them effectively into clinical practice, ultimately aiming to reduce neonatal morbidity and mortality associated with sepsis.

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