Section: Pathology

Original Research Article

RED CELL DISTRIBUTION WIDTH AS AN EARLY INDICATOR OF SEPSIS – AN ANALYSIS

Sharmila Annadurai[1], Sharanya Kandaswamy[2], Thiriveni Balajji G S[3], Gayathri G[4]

[1]*Consultant Pathologist, Bioline Laboratory, Coimbatore, Tamilnadu, India.*
[2]*Associate Professor, Department of Pathology, KMCH Institute of Health Sciences and Research, Coimbatore, Tamilnadu, India.*
[3]*Consultant Pathologist, Vijay Diagnostics, Coimbatore, Tamilnadu, India.*
[4]*M.Sc, MLT, Kovai Medical Center and Hospital, Coimbatore, Tamilnadu, India.*

Received *: 12/06/2025*
Received in revised form *: 05/08/2025*
Accepted *: 28/08/2025*

Corresponding Author:
Dr. Thiriveni Balajji G S,
Consultant Pathologist, Vijay Diagnostics, Coimbatore, Tamilnadu, India.
Email: thirivenib1@gmail.com

DOI: 10.70034/ijmedph.2025.3.371

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (3); 2007-2011

ABSTRAC

Background: Sepsis happens when an infection has already triggered a chain reaction throughout the body. Without timely treatment, sepsis can rapidly lead to tissue damage, organ failure, and death. In 2017, there were 48.9 million cases and 11 million sepsis-related deaths worldwide, which accounted for almost 20% of all global deaths. The aim of the study was to compare Red cell Distribution Width (RDW) in in-patients and outpatients with sepsis and relative organ dysfunction.

Materials and Methods: A retrospective analytical case-control study of 204 patients with sepsis was conducted at the KMCH Institute of Health Sciences and Research. The baseline data included demographic details, laboratory parameters, and concurrent comorbid conditions. The RDW-CV, APACHE II Score, and qSOFA score were calculated.

Results: Dependent variable analysis in the present study indicates that RDW-CV is a significant predictor of sepsis based on the qSOFA score.

Conclusion: The present study reflects similar findings of RDW-CV and qSOFA score for sepsis. High RDW-CV is associated with a score 2 (out of 3) of qSOFA, thus concluding that RDW-CV values, when elevated, would serve as an early indicator of sepsis and organ dysfunction.

Keywords: Red cell distribution width (RDW), Sepsis, Acute physiology and critical health evaluation score II (APACHE II), Quick Sequential organ failure assessment score (qSOFA).

INTRODUCTION

Sepsis is the body's extreme response to an infection. It is a life-threatening medical emergency. Infections that lead to sepsis most often start in the lung, urinary tract, skin, or gastrointestinal tract. The global burden of sepsis is difficult to ascertain, although a recent scientific publication estimated that, in 2017 there were 48.9 million cases and 11 million sepsis-related deaths worldwide, which accounted for almost 20% of all global deaths. In 2017, almost half of all global sepsis cases occurred among children, with an estimated 20 million cases and 2.9 million global deaths in children under five years of age.[1] Red blood cell distribution width (RDW) is a hematological parameter measured by hematological analyzer with a complete blood cell count. An elevated RDW indicates anisocytosis of red blood cells.[2] Present study intends to analyze Red cell Distribution Width-Coefficient of Variation (RDW-CV) in sepsis patients.The aim of the study was to compare Red cell Distribution Width (RDW) in in-patients and outpatients with sepsis and relative organ dysfunction.

MATERIALS AND METHODS

Study setting: KMCH Institute of Health Sciences and Research, Coimbatore.
Study design: Retrospective analytical case-control study.
Study period and Study population: All the patients attending Tertiary Care Centre from January 1, 2020 to Jan 31, 2021 with elevated RDW and normal Haemoglobin value.
Sample Size: 204 patients.

Inclusion Criteria

1. Age-all age groups ≥ 18 years; both gender
2. Patients with sepsis
3. Temperature (>38°C or <36°C)
4. Heart rate more than 90 beats/min
5. Respiratory rate more than 22 breaths/min
6. WBC count (>12,000 or <4,000)
7. Both In-patients and Out-patients with features of sepsis.

Exclusion Criteria

1. Anemia of all types-with/without treatment
2. Received blood transfusion within three months period
3. Ante-natal patients
4. Seropositive patients for HIV, HBsAg, HCV
5. Patients with complaints that requires surgical intervention.

Data Collection: The proposed study was conducted after getting clearance from the Institutional Research and Ethics board. Patient data only collected and confidentiality was ensured. All ethical principles were adhered throughout this study.

Study Tool

1. A semi structured proforma was used for data collection. It collects details such as baseline characteristics, medical history and physical examination.
2. RDW-CV, APACHE II Score and qSOFA score were calculated.
3. Sample 2mL of whole EDTA blood was drawn and Complete Blood Cell count was performed.

Statistical Analysis: Data was entered in Microsoft Excel format. Frequency tables and measures of central tendency (mean) and measures of dispersion (standard deviation) were calculated using the statistical package SPSS 20.0 version. For the repeated measures the Friedman test was used. To find the significance in categorical data Chi-Square test and ANOVA test were used. In all the above statistical tools, the probability value of <0.05 is considered as significant level.

RESULTS

Table 1: Age distribution

Age Category	Frequency	Percent	Cumulative percent	Mean ± SD
Below 20 years	4	2.0	2.0	46.6 ±15.37
21 – 30 years	41	20.1	22.0	
31 – 50 years	57	27.9	50.0	
51 – 70 years	94	46.1	96.1	
Above 70 years	8	3.9	100	
Total (n)	204	100		

Present study includes the patients in the age group, below 20 years – 4 patients (2%), 21 to 30 years – 41 patients (20.1%), 31 to 50 years – 57 patients (27.9%), 51 to 70 years – 94 patients (46.1%) and above 70 years – 8 patients (3.9%) and for the age category, the Mean ± SD is 46.6 ± 15.37.

Table 2: Gender Distribution

Gender	Frequency	Percent	Cumulative percent
Male	148	72.5	72.5
Female	56	27.5	100.0
Total	204	100	

Present study has 148 (72.5%) were males, 56 (27.5%) were females and the total was 204 patients.

Table 3: In-patients vs Out-patients

Sepsis	Frequency	Percent	Cumulative percent	Mean ± SD
Out-patients	87	42.6	42.6	1.57 ±0.49
In-patients	117	57.4	100	
Total	204	100		

Present study has 87 (42.6%) Out-patients and Inpatients were 117 (57.4%) and the total was 204 patients and the Mean ± SD was 1.57 ± 0.49.

Table 4: Correlation of Hemoglobin values with RDW-CV and RDW-SD

Variables	Haemoglobin in g/dl	Frequency	RDW-CV ≤14.5 (%)	RDW-CV ≥14.5 (%)	RDW-SD ≤45 (%)	RDW-SD ≥45 (%)
Male	13 to 15	65	52.3	47.7	50.8	49.2
	>15	15	53.3	46.7	26.7	73.3
Female	12 to 15	24	33.3	66.7	54.2	45.8
	>15	10	20	80	10	90
Total		204	37.7	62.3	41.7	58.3

Table 5: APACHE II Score at admission

APACHE II Score	No. of patients (%)	Mean ± SD
1 – 25	1 (16.66%)	0.91 + 6.67
26 – 35	1 (16.66%)	
36 – 71	4 (66.67%)	
Total	6 (100%)	

Out of 6 patients, 1(16.66%) patient had APACHE score II - 1 to 25; 1(16.66%) patient had APACHE score II - 26 to 35; 4 (66.67%) patients had APACHE score II. The Mean ± SD for the APACHE sore II at admission was 0.91 ± 6.67.

According to the study by Aditya Jandial et al. Mean APACHE II score of study population at admission was 22.49 ± 5.72. Out of 6 patients, 1(16.66%) patient had APACHE II - 1 to 25; 1(16.66%) patient had APACHE II score - 26 to 35; 4 (66.67%) patients had APACHE II score. The Mean ± SD for the APACHE score II at admission was 0.91 ± 6.67. 18 In comparing the above studies there is less significant of the mean value for APACHE II score.

Table 6: qSOFA Score at admission

qSOFA Score	No. of patients (%)	Mean ± SD
0	3 (2.70%)	1.992 ±1.946
1	24 (21.62%)	
2	23 (20.72%)	
3	61 (54.95%)	
Total	111 (100%)	

Out of 111 patients, 3(2.70%) patient had q SOFA score 0; 24(21.62%) patients had q SOFA score 1; 23 (20.72%) patients had q SOFA score 2. And 61(54.95%) had qSOFA score 3. The Mean ± SD for the q SOFA score at admission was 1.992 ± 1.946.

Table 7: RDW – CV with qSOFA score

ANOVA						Result
qSOFA Score						
	Sum of squares	Df	Mean Square	F#	Significance	
Between groups	0.0	2.0	0.001	0.179	0.040	Null hypothesis is rejected
Within groups	9.8	201.0	0.049			
Total	9.8	203				

fraction - ratio of variances

HO: There is no significant difference between RDW-CV with qSOFA

H1: There is a significant difference between RDW-CV with qSOFA

Based on the ANOVA table, we infer that there is a Significant difference between RDW-CV with qSOFA value. Hence, the calculated value is less than the table value. So, we can reject our null hypothesis and we conclude that the RDW-CV values are significantly different for qSOFA score category.

Out of 111 patients, 3(2.70%) patients had qSOFA score 0; 24(21.62%) patients had qSOFA score 1; 23 (20.72%) patients had qSOFA score 2 and 61 (54.95%) patients has qSOFA score 3. The Mean ± SD for the qSOFA score at admission was 1.992 ± 1.946.

Dependent variable analysis in present study indicates that RDW-CV is a significant predictor of sepsis, based on the qSOFA score, mean square is 0.001, df is 2.0 and significance is 0.040 which is statistically significant and the p value is less than the table value and interpret that the null hypothesis is rejected.

DISCUSSION

Sepsis refers to systemic inflammatory response to infection. It refers to the response of an immune system to infection. If sepsis is not diagnosed on-time and treated, it further progresses into severe sepsis, septic shock and death.[3] The most recent global estimates for sepsis incidence and mortality were based on data from seven high income countries and in 2017, there were 48.9 million cases and 11.0 million deaths were recorded worldwide.[4] From these surveys, WHO declared Sepsis as global health priority in 2017. Sepsis is categorized as primary sepsis and secondary sepsis. Primary sepsis includes: recent (<30 days) trauma/infection, ongoing systemic inflammatory or immunosuppressive disease or malnutrition. Whereas, secondary sepsis includes: recent (<7 days) trauma/infection or systemic inflammatory disease, but no immunosuppressive disease or malnutrition.[5]

Clinical laboratory report is based on evidence of infection and organ dysfunction to diagnose sepsis. From the studies reviewed, the infection starts from the lungs then followed by abdomen, genitourinary tract and blood.[4,5]

Since RDW- CV is obtained mathematically from MCV it is affected by changes in average size of RBCs.[5,26] RDW-SD is a measurement of width of RBC size distribution histogram and it is measured by calculating the width at the 20% height level of the RBC size distribution histogram. Hence RDW-SD is not influenced by the average RBC size, that is, mean corpuscular volume.[6]

Sepsis 1 Definition was developed in 1991 consensus conference in which SIRS criteria was established. Four SIRS criteria were included, namely tachycardia, tachypnea, fever or hypothermia, and leukocytosis, leukopenia or bandemia. Patients who fulfilled two or more of the criteria were said to have SIRS and SEPSIS 1 was defined as infection or suspected infection leading to the onset of SIRS.[7]

Systemic Inflammatory Response Syndrome (SIRS) fulfills two or more of the following:

a) Temperature (>38.3°C or <36°C) ; b) Heart rate (>90 beats/min) ;c) Respiratory rate (>20 breaths/min, PaCO2 <32mm Hg) ; d) WBC count (>12,000 cells /mm3 or <4,000 cells / mm3).

In 2001 a task force recognized the limitations in the previous definition and ended up expanding the diagnostic criteria which resulted in SEPSIS 2 definition. Accordingly, SEPSIS 2 refers to an individual who fulfils at least 2 SIRS criteria and with suspected or confirmed infection is said to have sepsis.[7]

According to the Third International consensus published in 2016, sepsis is defined as life threatening organ dysfunction caused by dysregulated host response to an infection (sepsis 3).[5,7] Sepsis leads to septic shock, Multiple Organ Dysfunction Syndrome (MODS) and death, if left untreated.

The most common laboratory findings that are seen in sepsis include neutrophilic leukocytosis, thrombocytopenia and hyperbilirubinemia. Urine analysis may show mild-to moderate proteinuria. Leukopenia may be seen in some individuals. Peripheral smear may reveal neutrophilia with neutrophils containing toxic granules.

Serum creatinine and blood urea nitrogen levels are commonly elevated in patients with severe sepsis and septic shock, indicating renal hypoperfusion and acute kidney injury. Arterial blood gas analysis usually reveals high anionic gap metabolic acidosis though in many patients early arterial blood gas analysis may show respiratory alkalosis as a result of hyperventilation.[8]

The Scoring systems are used to aid the physician in identifying the severity of the disease. It helps in deciding the treatment needed, saving time and money of the patients. There are several scoring systems which uses different combination of parameters that aids in assessing the severity and prognosis of the disease in patients admitted in the ICU.

APACHE II score (Acute Physiology and Critical Health Evaluation score) is one of the many scoring systems available. From 2016 this scoring system was replaced with SOFA. In 2016, the third international consensus definitions for sepsis and septic shock established the use of a sequential organ failure assessment (SOFA) score to assess the severity of the disease and to predict the prognosis. The ESICM was the first to organize a consensus meeting in Paris in October 1994 to create SOFA scoring system.[9]

The SOFA score includes laboratory variables like partial pressure of oxygen, platelet count, creatinine and bilirubin levels and clinical variables like Glasgow coma scale (GCS) and hypotension. Since SOFA requires laboratory evaluation, this delays the diagnosis and treatment, worsening the prognosis.

Thus, the latest sepsis consensus introduced a novel scoring system called quick sequential organ failure assessment (qSOFA) score for validating people with suspected sepsis. It can be performed at the bed side by the non-specialist without the analysis of any blood parameters. The score was calculated by assigning 1 point each for: Respiratory rate ≥22 breaths/min, Systolic blood pressure ≤100mm Hg, and altered mental status (GCS).

The total score was then calculated by adding the individual scores for the 3 elements. Patients with a score of 2 or more than 2 are said to be at high risk with increasing mortality rate. This scoring system is a simple, generic tool which can be calculated rapidly without the need for any laboratory or advance testing, making it potentially useful in the low resource settings.[3,8,10,11] qSOFA score includes 2 or more of the following: 1. Hypotension: Systolic Blood pressure less than or equal to 100 mmHg. 2. Altered mental status (any GCS <15) 3. Tachypnoea: Respiratory rate > or = 22/minute.[8,10,11]

The RDW-CV (Red cell Distribution Width – Coefficient of Variation) is a calculation based on both the width of the distribution curve and the mean cell size. RDW-CV is calculated by dividing the standard deviation of erythrocyte volume by the mean corpuscular volume (MCV) and multiplying by 100 to express the result as a percentage. A normal range for the RDW-CV is approximately 11.0 – 14.5%.[12,13] Since RDW- CV is obtained mathematically from MCV it is affected by changes in average size of RBCs.[6,13]

The RDW-SD (Red cell Distribution Width – Standard Deviation) is an actual measurement of the width of the red cell distribution curve in femtoliters(fL). It more accurately reflects the red cell size variance. The normal RDW-SD range for adults is 40.0 - 55.0 fL.[12,13] RDW-SD is a measurement of width of RBC size distribution. Hence, it is not influenced by the average RBC size, that is, mean corpuscular volume (MCV).

Recent studies have been focusing on evaluating RDW's prognostic value and use for the diagnostic role in sepsis. Literature reveals that as RDW is a means of evaluating the variability in size of erythrocytes it has been used widely in the differential diagnosis of anemia. Since RDW is a marker of non-specific inflammation, it can show high value in many other diseases such as heart failure, stroke, peripheral arterial disease or chronic pulmonary diseases. Red cell distribution width (RDW) represents an indicator which can vary in sepsis, under the influence of pro-inflammatory cytokines (TNFα, IFNδ, IL-1β, IL-6), released during the inflammatory process. These cytokines cause inefficient erythropoiesis resulting in structural and

functional changes of erythrocytes, with volume variations and increased RDW. Elevated value of RDW can also appear in nutritional deficiencies such as iron deficiency anemia, vitamin B12 or folate deficiency anemia, or in blood transfusions.[14]

Kim et al. evaluated the predictive role of RDW regarding the short and medium-term mortality in elderly patients with severe sepsis and septic shock and concluded that every one percent (1%) increase in RDW is equivalent to a 15% increase in the mortality rate in the first 30 days.[15]

According to Sajith Ali PI et al., there were 85 patients, the Mean RDW was 16.22 ± 0.89 (16).

According to Aditya Jandial et al., a prospective observational study was done with 200 patients with elevated RDW values and the mean RDW was 17.40 ± 3.21% (17). Present study has the mean RDW value of 15.25 ± 2.58.

From all the above studies we see that there are similarities between other studies and our present study. Hence, RDW is a useful parameter to detect and monitor sepsis.

CONCLUSION

Sepsis is a serious and common complication occurring in many patients with or without organ dysfunction. Red cell distribution width is an index of variation in RBC size or RBC volume. Present study, reflects similar findings of RDW-CV and qSOFA score for sepsis. High RDW-CV is associated with score 2 (out of 3) of qSOFA, thus concluding that RDW-CV values (Normal=11.5 to 14.5%), when elevated would serve as an early indicator of sepsis and organ dysfunction. When patients are infected with microbes, they release various toxins / lipopolysaccharides which activate inflammatory cascade via various interleukins and cytokines. This results in accelerated erythropoiesis any process that results in release of reticulocytes into the circulation will increase the RDW value. These mechanisms lead to anisocytosis and increased RDW value. Dependent variable analysis in present study indicates that RDW-CV is a significant predictor of sepsis. Further studies, including a greater number of patients can be done. Serial follow-up of RDW-CV values would help in better understanding of the utility of these values in patients with sepsis and organ dysfunction.

Declarations:

Funding: The authors declared that this study has received no funding.

Author contributions: All authors have contributed equally and reviewed and approved the final draft of the manuscript.

Conflicts of interest: The authors declare no conflict of interest.

Data availability: Data available from the authors on reasonable request.

Ethics approval: The study was approved by ethics committee of KMCH Institute of Health Sciences and Research, Coimbatore (No:16/IHEC/2021).

REFERENCES

1. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, Colombara DV, Ikuta KS, Kissoon N, Finfer S, Fleischmann-Struzek C. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. The Lancet. 2020;395(10219):200-211. doi: 10.1016/S0140-6736(19)32989-7.
2. Li N, Zhou H, Tang Q. Red blood cell distribution width: a novel predictive indicator for cardiovascular and cerebrovascular diseases. Dis Markers. 2017;7089493. doi: 10.1155/2017/7089493.
3. Brun-Buisson C. The epidemiology of the systemic inflammatory response. Intensive care med. 2000;26 Suppl 1(Suppl 1):S64-74. doi: 10.1007/s001340051121.
4. Artero A, Nogueira JM, Zaragoza R. Epidemiology of severe sepsis and septic shock. INTECH Open Access Publisher. February 10, 2012. doi: 10.5772/27208
5. Castegren S, Jonasson M, Sjölin J, Castegren M. Comparing intensive care treated primary, secondary and tertiary sepsis with respect to length of stay, organ failure and mortality: a pilot study. Crit Care. 2013;17(2):475. doi: 10.1186/cc12413
6. Caporal FA, Comar SR. Evaluation of RDW-CV, RDW-SD, and MATH-1SD for the detection of erythrocyte anisocytosis observed by optical microscopy. Jornal Brasileiro de Patologia e Medicina Laboratorial. 2013;49:324-31. https://doi.org/10.1590/S1676-24442013000500005
7. Marik PE, Taeb AM. SIRS, qSOFA and new sepsis definition. Journal of thoracic disease. 2017;9(4):943-945. doi: 10.21037/jtd.2017.03.125.
8. Faix JD. Biomarkers of sepsis. Crit Rev Clin Lab Sci. 2013;50(1):23-36. doi: 10.3109/10408363.2013.764490.
9. Askim Å, Moser F, Gustad LT, Stene H, Gundersen M, Åsvold BO, Dale J, Bjørnsen LP, Damås JK, Solligård E. Poor performance of quick-SOFA (qSOFA) score in predicting severe sepsis and mortality–a prospective study of patients admitted with infection to the emergency department. Scand J Trauma Resusc Emerg Med. 2017;25(1):56. doi: 10.1186/s13049-017-0399-4.
10. Balk RA. Severe sepsis and septic shock: definitions, epidemiology, and clinical manifestations. Crit Care Clin. 2000;16(2):179-192. doi: 10.1016/s0749-0704(05)70106-8
11. Fang L, Yuan J, Peng S, Yuan Y, Zheng J. Comparing the tested results of QBC Star and Sysmex XP-100 hematology analyzers and analyzing their operational performance. International Journal of Laboratory Medicine. 2017;38(2):204-205. doi: 10.3969/j.issn.1673-4130.2017.02.021
12. Martins EC, Silveira LD, Viegas K, Beck AD, Fioravantti G, Cremonese RV, Lora PS. Neutrophil-lymphocyte ratio in the early diagnosis of sepsis in an intensive care unit: a case-control study. Rev Bras Ter Intensiva. 2019;31(1):64-70. doi: 10.5935/0103-507X.20190010
13. Guarda LA. Anemia and severe erythrocytic morphologic abnormalities in two young patients. Laboratory Medicine. 2003;34(7):526-531.
14. Hsieh YP, Chang CC, Kor CT, Yang Y, Wen YK, Chiu PF. The predictive role of red cell distribution width in mortality among chronic kidney disease patients. PLoS One. 2016;11(12): e0162025. doi: 10.1371/journal.pone.0162025.
15. Peakman M, Vergani D. Basic and Clinical Immunology E-Book. Elsevier Health Sciences; Accessed April 24, 2009.
16. Sajith Ali Clinical significance of red cell distribution width (RDW) and circulating neutrophil-lymphocyte count ratio (NLCR) as prognostic markers in sepsis. Government Stanley Medical College, The TN Dr.MGR Medical University, Accessed 2018.
17. Jandial A, Kumar S, Bhalla A, Sharma N, Varma N, Varma S. Elevated red cell distribution width as a prognostic marker in severe sepsis: a prospective observational study. Indian J Crit Care Med. 2017;21(9):552–562. doi:10.4103/ijccm.IJCCM_208_17.