VOLUME - 13, ISSUE - 08, AUGUST - 2024 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Medicine

RED CELL DISTRIBUTION WIDTH AS A PROGNOSTIC INDICATOR IN SEVERE SEPSIS: A PROSPECTIVE STUDY

Dr Varun Mishra

Dr Nidhi Anam

Dr Amrit Kejriwal

ABSTRACT

Introduction: Sepsis is a systemic condition recognized as dysregulated host response to infection. Red cell distribution width (RDW) has emerged as a promising prognostic marker in sepsis, especially when elevated early in hospitalization. This study aims to investigate the correlation between RDW and mortality in patients, assessing its utility as a prognostic indicator & potential for sequential monitoring to guide treatment decisions & improve patient outcomes. **Methods:** This prospective observational study was conducted in patients aged over 18 diagnosed with sepsis & admitted to the (MEDICAL INTENSIVE CARE UNIT) MICU at a tertiary care hospital. The study involved 100 subjects, with data collection through a structured proforma & analysis performed using MS Excel & IBM SPSS Statistics 26.0, employing descriptive statistics & statistical tests such as t-test & chi-square test, with significance set at $p < 0.05$. **Results:** The result indicates no significant difference in Hb, PCV, MCV, TLC, DLC, Platelets, & RBC count between survivors and non-survivors ($p > 0.05$), but a significant difference in the mean RDW-CV values was observed ($t = -23.865$, $p < .001$), indicating its potential as a prognostic marker. Additionally, renal, liver function test parameters showed no significant differences between survivors and non-survivors ($p > 0.05$). **Conclusion:** The study concludes RDW's potential as a cost-effective prognostic biomarker in sepsis, effectively predicting mortality, aiding in treatment decisions. RDW shows high accuracy in mortality prediction, with notable associations with age groups among non-survivors, suggesting its relevance across demographics, maintaining independent prognostic value, unaffected by renal or liver function test results.

KEYWORDS :

INTRODUCTION:

Sepsis, a historically recognized yet still common and mortal condition, has evolved in its understanding over millennia. Initially described by Hippocrates and later conceptualized by Galen, sepsis was traditionally viewed as a manifestation of local infection spreading through the bloodstream. (1,2) However, the advent of germ theory in the nineteenth century provided a new perspective, linking sepsis to systemic infection and pathogen invasion. Despite this advancement, many patients continued to succumb to sepsis even after successful pathogen eradication, indicating a deeper complexity. Recent research, spanning the past two decades, has revealed that sepsis involves a dysregulated host response to infection, often leading to acute organ dysfunction. The 2016 Third International Consensus Definitions redefined sepsis as such, distinguishing it from uncomplicated infection and emphasizing the role of organ dysfunction in its diagnosis.(3,4) Within this evolving understanding of sepsis, red cell distribution width (RDW) has emerged as a potential prognostic marker. RDW, a measure of the variation in size of red blood cells, has shown promise in predicting adverse clinical outcomes in septic patients, particularly when elevated within the first 72 hours of hospitalization. This simple and readily available investigation offers a valuable tool for assessing severity and guiding treatment strategies early in the course of severe sepsis or septic shock. By incorporating baseline RDW values and monitoring changes over time, healthcare providers can better anticipate patient outcomes and tailor management protocols accordingly, thus potentially improving patient care and survival rates.(5–8).

The aim of this study is to investigate the correlation between red cell distribution width (RDW CV) and mortality among patients diagnosed with sepsis. Through this research, we aim to discern the usefulness of elevated RDW as a prognostic indicator for the severity of sepsis. Furthermore, our objectives include evaluating the potential of sequential elevation in RDW levels throughout the entire duration of hospitalization as a predictive marker for the severity of sepsis. By achieving these objectives, we seek to contribute valuable insights into the clinical utility of RDW in prognosticating outcomes and guiding therapeutic decisions for patients with sepsis.

REVIEW OF LITERATURE:

Sepsis is a severe medical condition characterized by a dysregulated immune response to infection, often resulting in multiple organ failure and high mortality rates. The global incidence of sepsis has been increasing, with approximately 31 million cases and 5 million deaths annually. Despite advancements in medical care, mortality rates among sepsis patients remain high. Various biomarkers and scoring systems have been studied to aid in the early identification and prognosis of sepsis. Red cell distribution width (RDW), a component of the complete blood count (CBC), has emerged as a potential prognostic marker for sepsis. RDW reflects the variability in the size of red blood cells and is associated with inflammation and oxidative stress. Elevated RDW levels have been linked to increased mortality and morbidity in sepsis patients (Stojkovic et al., 2020; Wang et al., 2019).(9,10)Traditional prognostic indicators such as Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores can be complex to calculate and may not be readily available, especially in resource-limited settings. RDW, being a part of routine CBC testing, offers a simple, cost-effective, and easily accessible alternative for predicting outcomes in sepsis patients (Piva et al., 2020; Zhang et al., 2020).(11,12) RDW has shown promise in predicting mortality and morbidity in various other diseases, including cardiovascular disorders, pulmonary embolism, and critical illnesses. Its association with adverse outcomes in sepsis underscores its potential utility as a prognostic tool in identifying patients at higher risk of poor outcomes (Furuncuoglu et al., 2016; Huang et al., 2017).(13,14).

In case of severe sepsis, the prognostic factors like co-morbidities, biomarkers, severity of disease, age of subject, sex of subject etc., have been seen to be associated with the outcome of severe sepsis. These prognostic factors may allow aggressive management of among particular group of patients.(15,16) Deteriorating sepsis is related to the high mortality as multiple organ systems fail. APACHE II score quantifies the degree of severity and can predict the severity

and outcome of multiple organ failure.(17) However, calculating APACHE II scores is not a simple task.(18) Instead, it is better to identify a biomarker which may be is associated with the degree of severity in patients with sepsis. (19,20)

In summary, RDW has emerged as a valuable prognostic marker for sepsis, offering a simple and cost-effective means of assessing severity and guiding treatment decisions, particularly in settings with limited resources. Further research and validation studies are warranted to establish its utility across different patient populations and clinical settings.

MATERIAL AND METHODS:

This prospective observational study was carried out at the Department of Medicine, MGM Institute of Health Sciences, Navi Mumbai, spanning from June 2021 to November 2022. The study includes patients over 18 years old who were diagnosed with sepsis and admitted to the Medical Intensive Care Unit (MICU) at MGM Hospital Kamothe. Criteria for inclusion were patients diagnosed with sepsis for more than 24 hours, aged over 18, and sepsis defined by SOFA scoring. Exclusion criteria encompassed patients admitted in SICU with sepsis, those with a recent history of packed cell transfusion, known hematological disorders, recent chemotherapy, immunosuppression, solid organ transplantation, post-splenectomy, or those using drugs that alter the morphology and rheology of RBCs. Patients who had received primary treatment elsewhere or whose relatives denied consent were also excluded. The study consisted a sample size of 100 subjects, calculated with a 95% confidence interval, 90% power, and accounting for the prevalence of sepsis at 14%, to achieve a desired precision of 12%. Data collection was done using a pre-tested and structured proforma, including detailed patient histories, clinical examinations, and laboratory investigations, without follow-up beyond 7 days.

The collected data was entered into MS-Excel for organization and subsequently analyzed with IBM SPSS Statistics 26.0 (Statistical Package for the Social Sciences) version 26.0. For continuous variables, the mean and standard deviation were utilized for descriptive purposes, while graphical representations followed by statistical analysis using tests like t-test, chi-square test and ROC curve. A p-value below 0.05 was deemed to indicate statistical significance.

RESULTS:

Table 1. Distribution of study subjects according to gender, age and outcome

Variable		Outcome				Total (n=100)		p-value
		Survived (n=46)		Not survived (n=54)				
		n	%	n	%	n	%	
Gender	Male	32	50.8%	31	49.2%	63	63.0%	>0.05, NS
	Female	14	37.8%	23	62.2%	37	37.0%	<.05*
Age (years)	18-30	4	40.0%	6	60.0%	10	10.0%	>.05, NS
	31-40	4	50.0%	4	50.0%	8	8.0%	1.000
	41-50	6	33.3%	12	66.7%	18	18.0%	<.05*
	51-60	18	60.0%	12	40.0%	30	30.0%	>.05, NS
	61-70	6	40.0%	9	60.0%	15	15.0%	<.05*
	71-80	6	40.0%	9	60.0%	15	15.0%	<.05*
	>80	2	50.0%	2	50.0%	4	4.0%	>0.05, NS

*NS: Not significant, *: Significant at 5% level of significance*

This prospective observational study was conducted with an aim to discern the usefulness of elevated RDW as a prognostic indicator for the severity of sepsis. Furthermore, our objectives include evaluating the potential of sequential elevation in RDW levels throughout the entire duration of hospitalization as a predictive marker for the severity of sepsis. For this purpose, a sample of 100 study subjects, diagnosed with sepsis, and admitted in ICU were included in the study, out of which 63 (63%) were male and 37 (37%) were female. The majority of the study subjects belong to age group 40-80 years with a mean age of 56.98 (SD=15.74). At the end of day 7, out of 100 study subjects, 46 (46%) survived and 54 (54%) did not survive. The mortality was significantly higher among females (p<.05) and in the age group 60 and above (p<.05). (Table 1) No significant difference in the average age of survived (55.217 (SD=15,329)) and non-survived (55.352 (SD=16.804)) subjects was observed (p=0.967) (Table 2).

Table 2. Mean age according to outcome

Outcome		N	Mean	SD	Sem	t-stat	p-value
Age	Survived	46	55.217	15.793	2.329	-0.041	0.967
	Not survived	54	55.352	16.804	2.287		

Table 3 indicates the comparison of various study parameters according to the outcome. No significant difference was observed in the study variables Hb, PCV, MCV, TLC, DLC, Platelets, and RBC count among survivors and non-survivors (p > 0.05). The mean RDW CV was 14.537 (±0.491) for survivors and 18.896 (±1.153) for non-survivors. Significant difference in mean RDW-CV values was evident between survivors and non-survivors (t = -23.865, p < .001). No significant differences were observed in the RFT parameters like Urea, Creatinine, BUN, Uric acid, Na, K, and Cl between survivors and non-survivors (p > 0.05). No significant differences in the LFT parameters were observed in the study variables BILI(T), BILI(D), SGOT, SGPT, ALPO4, TPR, and ALBUMIN between survivors and non-survivors (p > 0.05).

Table 3. Comparison Of Study Parameters At Day 0 According To Outcome

Parameter		Survived		Not survived		t-stat	p-value
		Mean	SD	Mean	SD		
CBC	Hb	12.478	9.77	9.7	2.679	2.005	0.048
	PCV	32.926	14.013	30.235	10.8	1.078	0.284
	MCV	81.854	10.628	82.309	13.896	1.104	0.272
	TLC	17031.3	10449.84	17471.22	13583.49	-0.179	0.858
	DLC-N	84.609	9.248	83.093	9.521	0.804	0.423
	DLC-L	10.457	7.133	12.907	13.529	-1.104	0.272
	Platelet	24.183	149.643	20.732	138.138	0.12	0.905
	RBC count	11.038	47.681	3.542	1.075	1.156	0.251
	RDW-CV	14.537	0.491	18.896	1.153	-23.865	0
RFT	Urea	80.514	52.621	104.466	95.474	-1.516	0.133
	Creatinine	4.743	9.191	3.866	6.033	0.571	0.569
	BUN	37.196	24.609	51.674	43.022	-2.018	0.046
	Uric acid	11.263	16.666	13.366	24.951	-0.486	0.628
	Na	132.109	20.863	129.735	26.143	0.496	0.621
	K	4.687	1.409	4.593	1.048	1.089	0.279
	Cl	95.565	20.92	96.139	15.08	-0.159	0.874
LFT	BILI(T)	2.4	3.028	2.883	5.839	-0.506	0.614
	BILI(D)	1.463	2.815	1.585	2.699	1.089	0.279
	SGOT	541.522	313.276	522.444	320.782	1.616	0.109
	SGPT	345.478	838.468	389.148	892.338	1.088	0.279
	ALPO4	112.526	84.197	107.198	80.248	0.323	0.747
	TPR	5.817	1.545	5.97	1.471	-0.507	0.614
	ALBUMIN	2.673	0.869	2.766	0.778	-0.562	0.575

Table 4 shows an association between RDW-CV and outcome. The Chi-square analysis indicates a significant association between RDW-CV and outcome. Subjects with RDW-CV below 15% exhibited higher survival rates compared to those with RDW-CV values equal to or greater than 15%.

Table 4. Association between RDW-CV and Outcome

RDW	Outcome				Total	
	Survived		Not survived			
	n	%	n	%	n	%
<15	40	100.00%	0	0.00%	40	40.00%
>=15	6	10.00%	54	90.00%	60	60.00%
Total	46	46.00%	54	54.00%	100	100.00%

Chi-square = 78.261, df=1, p<.001, highly significant

Table 5. Comparison of study parameters at day 0 and Day 3 according to outcome

Variable	Day1					Day 3				
	Survived		Not survived		p	Survived		Not survived		p
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Hb	10.40	3.83	9.12	2.27	0.07	10.39	4.03	9.26	2.39	0.30
PCV	31.89	13.10	28.86	14.05	0.31	32.66	15.87	27.33	6.70	0.21
MCV	205.98	816.03	332.01	1544.61	0.63	86.01	12.07	89.29	10.83	0.35
TLC	15947.7	8955.7	16760.72	9459.2	0.68	15400.2	7906.92	16641.33	9070.84	0.61
DLC_1	87.00	5.45	82.10	12.83	*0.02*	84.85	13.45	84.60	8.16	0.94
DLC_2	8.82	4.58	13.08	12.57	*0.03*	9.06	4.04	10.60	6.40	0.27
Platelet	893.09	4238.21	1463.37	6540.33	0.63	1.99	1.32	1.51	1.21	0.22
RBC	4.12	2.68	3.32	0.90	0.08	3.71	2.22	3.08	0.91	0.28
RDW-CV	14.46	0.50	19.11	1.23	*0.01*	14.361	0.531	18.887	1.352	*<0.01*

Table 6. Descriptive statistics for study variables at day 7 (Survived)

Variable	N	Mean	SD
Hb (gm %)	46	10.165	3.732
PCV (%)	46	37.092	40.236
MCV (μm^3)	46	288.107	1367.44
TLC (cells/μL)	46	15251.8	8165.67
DLC1(%)	46	84.343	13.646
DLC2 (%)	46	9.539	4.187
Platelets (per mcL)	46	1937.14	13122
RBC (million/mm^3)	46	3.733	1.983
RDW-CV (%)	46	14.278	0.551

The table above shows comparison of study parameters among survived and non-survived subjects on day 1. There were no significant differences found in parameters such as Hb, PCV, MCV, TLC, Platelets, RBC count, and DLC between survived and non-survived subjects ($p > .05$). However, a significant difference was observed in the study parameters DLC and RDW-CV among survived and non-survived subjects ($p < .05$). On day 7, no significant differences were found in parameters such as Hb, PCV, MCV, TLC, Platelets, RBC count, and DLC between survived and non-survived subjects ($p > .05$). However, on day 7, a significant difference was observed in RDW-CV among survived and non-survived subjects ($p < .001$).

Table 5. Diagnostic test result

Statistic	Value	95% CI
Sensitivity	86.96%	73.74% to 95.06%
Specificity	100.00%	94.04% to 100.00%
Positive Predictive Value (*)	100.00%	---
Negative Predictive Value (*)	90.91%	82.58% to 95.47%
Accuracy (*)	94.34%	88.09% to 97.89%

Table 6 presents descriptive statistics for study variables at day 7 among subjects who survived. The mean hemoglobin (Hb) level was 10.165 (SD= 3.732) gm%. Packed Cell Volume (PCV) had a mean of 37.092% (SD= 40.236), while MCV had a mean of 288.107 (SD= 1367.44) μm^3. Total Leukocyte Count (TLC) showed a mean of 15251.8 (SD= 8165.67) cells/μL. Differential Leukocyte Count 1 (DLC1) showed a mean of 84.343% (SD= 13.646), and Differential Leukocyte Count 2 (DLC2) had a mean of 9.539% (SD=4.187). Platelet count averaged at 1937.14 (SD=13122) per mcL, and Red Blood Cell (RBC) count had a mean of 3.733 (SD of 1.983) million/mm^3. Red Cell Distribution Width (RDW-CV) exhibited a mean of 14.278% with (SD= 0.551).

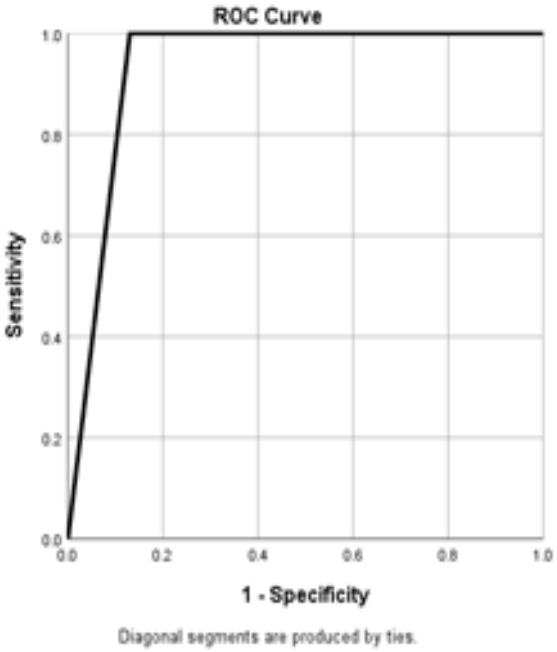

Figure 1. ROC Curve

The RDW-CV showed a sensitivity of 86.96% (95% CI: 73.74% to 95.06%) in predicting mortality, with a specificity of 100.0%. The positive predictive value was also 100.0%, while the negative predictive value stood at 90.91 (95% CI: 82.58% to 95.47%). The overall accuracy of RDW-CV as a predictor of mortality was determined to be 94.34% (95% CI: 88.09% to 97.89%). (Table 5)

The figure 1indicates ROC Curve. The area under ROC curve was 0.935 which indicates the ability of RDW-CV as a predictor of mortality. RDW-CV has high sensitivity, specificity, negative predictive value and positive predictivity value (Figure 1).

DISCUSSION:

The study aimed to evaluate the efficacy of Red Cell Distribution Width (RDW) as a diagnostic and prognostic tool for sepsis in a tertiary care hospital in Navi Mumbai. Recruiting 100 MICU patients aged above 18, the research analyzed various parameters alongside RDW to gauge its potential in early sepsis diagnosis and outcome prediction. Among the subjects, 63% were male and 37% female, exhibiting a male preponderance consistent with previous studies, contrasting with studies showing female preponderance.(21,22)The average age of subjects was 55.337 ± 16.42 years, with non-survivors notably prevalent in age groups 41-50, 61-70, and 71-80 years. This contrasts with other studies where subjects were slightly younger. The study compared RDW with other parameters across several days, revealing significant differences in RDW between survivors and non-survivors. The RDW diagnostic test demonstrated a significant area under the ROC curve, aligning with similar findings from other studies.(21,22)

The results of the current study indicated that there was a significant difference in the mean RDW at day 0, day 1 day 3 and day 7 between survivors and non survivors. The results are in line with several other studies which showed the significant difference in the average RDW values over the period. The diagnostic test results of the RDW concluded that, the area under the ROC curve was 0.762 (95% CI: 0.717 to 0.807). Kavita Jain et al. conducted a study at Ujjain, India, found that the RDW value was significantly higher in patients with severe sepsis and in non-survivor patients than in survivors (P<0.0001). Large multicenter prospective studies can confirm the utility of this routinely available marker for patients with sepsis.(23) According to this study, clinical symptoms such as fever, laboratory parameters such as mean haemoglobin concentration and serum sodium were significantly lower in non survivors as compared to survivors. They found that haemoglobin, Na+, and bilirubin were highly significant indicating their role in severe sepsis, however no such association was found in our study. While no significant changes were shown with the MCV, MCH, MCHC, RBS, serum K+, SGOT, SGPT, ALP and albumin/globulin ratio which is consistent with our study.

Nader A Mahmood et al conducted a study from January 2007 to December 2008 in New Jersey involving a cohort of 349 patients with sepsis concluded that a prognostic biomarker for sepsis in the form of a routine blood test may be of considerable clinical utility. The results of the study suggest that RDW may have value in differentiating between more severe and less severe cases of sepsis. Future studies with larger samples are needed to confirm these findings.(24)

The diagnostic power of RDW for early diagnosis of sepsis is comparable to that of conventional scores viz. SIRS, qSOFA and MEWS. It was found that for early clinical deterioration RDW outperforms all these bedside scores. The study results are similar to the previous studies, which concluded the independent prognostic value of RDW in sepsis and comparable Area Under the Receiver Operative Curve (AUROC). The previous studies included more homogeneous and defined patient groups like diagnosed sepsis or septic shock, and critically ill patients. Among patients with already established diagnosis of severe sepsis or septic shock, non-survivors showed the significantly higher levels of RDW.(16,25) The results of our study indicated that the higher sepsis scores are correlated with higher levels of RDW which suggests that critically ill study subjects have increased level of RDW. This indicates the significant association between RDW and high scores, but RDW act as an independent predictor for mortality after correction for disease severity. This study was conducted among the heterogeneous population including the subjects from all age groups and gender. The study population consisted of patients above age 18 years and who were suspected for infection and were admitted to the MICU.

In a study performed by Huabin Wang et al. where patients with sepsis, admitted to intensive care unit between 2008-2012, with 24 hrs of admission were included. An approximately increasing linear relationship was found between RDW and mortality. When the RDW was in the range of 19.0%–19.5%, the 90-day mortality rate was as high as 67%, and the 30-day Mortality rate was 60% here they compared the interaction between RDW and degree of ARDS, use of vasopressors and anaemia and there was no obvious difference between the RDW and mortality among patients with different degree of ARDS, whether vasopressin was used and whether anaemia was present. Since our study did not follow up patients after 7 days, the further outcomes of those who did not survive after 7 days weren't compared.

Currently the association between raised RDW and mortality in septic subjects is not yet fully understood, numerous probable clarifications have been suggested in previous studies. Systemic inflammation in RDW has proved to predict the cardiovascular mortality+, progressive illness, and death in ICU patients. The bone marrow function and iron metabolism are impacted due to the Systemic inflammation response (26), and proinflammatory cytokines have been found to inhibit erythropoietin-induced erythrocyte maturation and proliferation, and to downregulate erythropoietin receptor expression, which are associated with RDW increases.(28) Many studies have stated that the by reducing the RBC survival, the oxidative stress induces an increase in RDW and increases the release of large premature RBCs into the peripheral circulation.(29)

CONCLUSION:

The study highlights the potential of Red Cell Distribution Width (RDW) as a prognostic biomarker in sepsis, suggesting its utility in differentiating between severe and less severe cases and predicting mortality. Unlike other prognostic markers which may be costly and not readily available, RDW derived from routine blood tests is easily accessible and cost-effective, aiding in early prediction of outcomes and guiding treatment decisions. The study underscores the significance of RDW in predicting mortality and inflammation markers in sepsis patients, particularly noting its high accuracy in mortality prediction and its potential for further research in this area. Additionally, while RDW showed no significant relationship with sex, it exhibited notable associations with age groups among non-survivors, emphasizing its relevance in prognosis across different patient demographics. Moreover, no significant correlation was observed between RDW and other parameters such as renal or liver function tests in both survivors and non-survivors, highlighting its independent prognostic value.

REFERENCES:

1. Geroulanos S, Douka ET. Historical perspective of the word "sepsis." Intensive Care Med. 2006 Dec;32(12):2077.
2. Vincent JL. Evolution of the Concept of Sepsis. Antibiotics. 2022 Nov 9;11(11):1581.
3. Mayr FB, Yende S, Angus DC. Epidemiology of severe sepsis. Virulence. 2014 Jan 1;5(1):4–11.
4. Bone RC, Sibbald WJ, Sprung CL. The ACCP-SCCM consensus conference on sepsis and organ failure. Chest. 1992 Jun;101(6):1481–3.
5. Hou H, Sun T, Li C, Li Y, Guo Z, Wang W, et al. An overall and dose-response meta-analysis of red blood cell distribution width and CVD outcomes. Sci Rep. 2017 Feb 24;7:43420.
6. Zorlu A, Bektasoglu G, Guven FMK, Dogan OT, Gucuk E, Ege MR, et al. Usefulness of admission red cell distribution width as a predictor of early mortality in patients with acute pulmonary embolism. Am J Cardiol. 2012 Jan 1;109(1):128–34.
7. Bazick HS, Chang D, Mahadevappa K, Gibbons FK, Christopher KB. Red cell distribution width and all-cause mortality in critically ill patients. Crit Care Med. 2011 Aug;39(8):1913–21.
8. Braun E, Domany E, Kenig Y, Mazor Y, Makhoul BF, Azzam ZS. Elevated red cell distribution width predicts poor outcome in young patients with community acquired pneumonia. Crit Care Lond Engl. 2011 Aug 11;15(4):R194.
9. Stojkovic Lalosevic M, Pavlovic Markovic A, Stankovic S, Stojkovic M, Dimitrijevic I, Radoman Vujacic I, et al. Combined Diagnostic Efficacy of Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Mean Platelet Volume (MPV) as Biomarkers of Systemic Inflammation in the Diagnosis of Colorectal Cancer. Dis Markers. 2019;2019:6036979.
10. Wang W, Xu X, Tian B, Wang Y, Du L, Sun T, et al. The diagnostic value of serum tumor markers CEA, CA19-9, CA125, CA15-3, and TPS in metastatic breast cancer. Clin Chim Acta Int J Clin Chem. 2017 Jul;470:51–5.
11. Piva E, Zuin J, Pelloso M, Tosato F, Fogar P, Plebani M. Monocyte distribution width (MDW) parameter as a sepsis indicator in intensive care units. Clin Chem Lab Med. 2021 Jun 25;59(7):1307–14.
12. Zhang H, Liang K, Ke L, Tang S. Clinical application of red cell distribution width, mean platelet volume, and cancer antigen 125 detection in endometrial cancer. J Clin Lab Anal. 2020 Mar 20;34(8):e23309.
13. Furuncuoğlu Y, Tulgar S, Dogan AN, Cakar S, Tulgar YK, Cakiroglu B. How obesity affects the neutrophil/lymphocyte and platelet/lymphocyte ratio, systemic immune-inflammatory index and platelet indices: a retrospective study. Eur Rev Med Pharmacol Sci. 2016 Apr;20(7):1300–6.
14. Li S, Hu X, Xu J, Huang F, Guo Z, Tong L, et al. Increased body mass index linked to greater short- and long-term survival in sepsis patients: A retrospective analysis of a large clinical database. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2019 Oct;87:109–16.
15. Afessa B, Keegan MT, Mohammad Z, Finkielman JD, Peters SG. Identifying potentially ineffective care in the sickest critically ill patients on the third ICU day. Chest. 2004 Dec;126(6):1905–9.
16. Annane D, Bellissant E, Cavaillon JM. Septic shock. Lancet Lond Engl. 2005 Jan 1;365(9453):63–78.
17. Angus DC, van der Poll T. Severe sepsis and septic shock. N Engl J Med. 2013

Aug 29;369(9):840–51.
18. Fleischmann C, Scherag A, Adhikari NKJ, Hartog CS, Tsaganos T, Schlattmann P, et al. Assessment of Global Incidence and Mortality of Hospital-treated Sepsis. Current Estimates and Limitations. Am J Respir Crit Care Med. 2016 Feb 1;193(3):259–72.
19. Kim CH, Park JT, Kim EJ, Han JH, Han JS, Choi JY, et al. An increase in red blood cell distribution width from baseline predicts mortality in patients with severe sepsis or septic shock. Crit Care Lond Engl. 2013 Dec 9;17(6):R282.
20. Cho WH. Update of Sepsis: Recent Evidences about Early Goal Directed Therapy. Tuberc Respir Dis. 2015 Jul;78(3):156–60.
21. 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 Peer-Rev Off Publ Indian Soc Crit Care Med. 2017 Sep;21(9):552–62.
22. Red Cell Distribution Width as a Predictor of Mortality in Patients With Clinical Sepsis: Experience From a Single Rural Center in Central India - Kavita Jain, Darshita Sharma, Mala Patidar, Shirish Nandedkar, Ashish Pathak, Manju Purohit, 2022 [Internet]. [cited 2024 Mar 15]. Available from: https://journals.sagepub.com/doi/full/10.1177/2632010X221075592
23. Jain K, Sharma D, Patidar M, Nandedkar S, Pathak A, Purohit M. Red Cell Distribution Width as a Predictor of Mortality in Patients With Clinical Sepsis: Experience From a Single Rural Center in Central India. Clin Pathol Thousand Oaks Ventura Cty Calif. 2022;15:2632010X221075592.
24. Mahmood NA, Mathew J, Kang B, DeBari VA, Khan MA. 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):278–82.
25. Seymour CW, Angus DC. Sepsis and Septic Shock. In: Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, editors. Harrison's Principles of Internal Medicine [Internet]. 20th ed. New York, NY: McGraw-Hill Education; 2018 [cited 2024 Mar 15]. Available from: accessmedicine.mhmedical.com/content.aspx?aid=1159155638
26. Pierce CN, Larson DF. Inflammatory cytokine inhibition of erythropoiesis in patients implanted with a mechanical circulatory assist device. Perfusion. 2005 Mar;20(2):83–90.
27. Oxidative stress in sepsis: a redox redux - PMC [Internet]. [cited 2024 Mar 15]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1421363/
28. Kolls JK. Oxidative stress in sepsis: a redox redux. J Clin Invest. 2006 Apr 3;116(4):860–3.
29. S G. Oxidative stress in the regulation of normal and neoplastic hematopoiesis. Antioxid Redox Signal [Internet]. 2008 Nov [cited 2024 Mar 15];10(11). Available from: https://pubmed.ncbi.nlm.nih.gov/18707226/