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Original Research Article

Role of Admission RDW-CV in Patients with Sepsis as In-Hospital Prognostic Marker

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Conflict of interest: Nil

Abstract

Background: In an effort to find a quick and reliable prognostic marker for sepsis, scientists have done several researches. A simple haematology parameter RDW-CV as a in-hospital prognostic marker in patients with sepsis in a resource limited setting has been widely studied and this present study evaluates the same.

Objective: The present study aimed to study the distribution of RDW-CV in patients with sepsis and its role as a prognostic marker in sepsis.

Methods: It was a hospital based prospective observational study conducted over a period of one year from June 2021 to May 2022 in Department of Medicine of a tertiary care teaching hospital in Assam, India in which 280 sepsis patients aged 18 year and above were enrolled.

Results: Respiratory infections was the most common cause of sepsis (42.8%), followed by intra-abdominal infections (23.9%) and genito-urinary infections. The mean RDW-CV in survivors were 14.23±1.59 and it was 17.66 ±3.81 in those who died.

Conclusion: High RDW-CV is an independent prognostic marker in sepsis.

Keywords: Red Cell Distribution Width, Sepsis, Prognostic Marker.

Introduction

The cornerstone of sepsis management worldwide is the search for a rapid, low-cost biomarker for early diagnosis of sepsis as it is a major source of morbidity and mortality. Sepsis was initially believed to be a purely pro-inflammatory condition. Leucocyte count was therefore relied upon for sepsis diagnosis, however it was found to be an inconsistent sign of infection, let alone sepsis. As our knowledge of the pathophysiology of sepsis increased, it became clear that it is more of an immune response that is dysregulated, with both pro- and anti-inflammatory immune responses

occurring simultaneously in varying degrees. Periodically, new molecules were found.[1]

Serum procalcitonin (PCT) has recently proven itself as a reliable diagnostic and prognostic indicator of bacterial sepsis. Unlike Procalcitonin, C-Reactive Protein (CRP) is a well-known inflammatory marker but is less selective for bacterial sepsis. In several of the world's leading institutions for the treatment of sepsis, the increase and fall of certain interleukins are now being tracked. However, these tests are costly, add to the strain on the public health system, and are not included in routine blood tests. Therefore, the urgent need has been to identify a blood marker that could both diagnose and prognosticate sepsis, especially one that is included in a standard blood test like a full blood count.

Therefore, studies on RBC production, shape, size, release from the bone marrow, function, and survival in the context of sepsis have been conducted all over the world. It has been discovered that sepsis reduces RBC deformability because of the body's dysregulated immune response. As a result, in this scenario of multisystem involvement with broad cytokine release and oxidative stress, anisocytosis is very likely to increase. Red Cell Distribution Width (RDW) increases in sepsis due to unfavourable effects on RBC creation, maturation, and survival that may result in the release of immature or malformed RBCs into circulation from the bone marrow. The degree of variation in RBC cell size is shown by RDW in [1].

A higher RDW denotes a wide range of variation in RBC cell size. RDW can be expressed as a standard deviation or a coefficient of variation, or RDW-CV or RDW-SD, respectively. The current study aims to investigate RDW-CV distribution in sepsis patients and its function as a predictive factor in sepsis. Sepsis is a leading cause of morbidity and mortality in the world, and incidence is increasing[2-4], possibly as a result of increased comorbidities brought on by longer life expectancies.[5]

Material and Methods

Study design, settings and participants:

It was a hospital based prospective observational study conducted over a period of one year from June 2021 to May 2022 in Department of Medicine of a tertiary care teaching hospital in Assam, India. Patients above 18 years of age and diagnosed with sepsis as per SOFA score were included in the study. Pregnant females, Patients who were on recent chemotherapy, Known haematological disorders, subjects with immunosuppression and Post splenectomy patients were excluded from the study. 280 sepsis patients were enrolled serially for the study, after fulfilment of inclusion and exclusion criteria.

Data collection

After obtaining clearance and approval from the institutional ethics committee and written informed consent of the patient/legal guardian, all the patients admitted in the Department of Medicine, Silchar Medical College & Hospital, during the study period were screened for eligibility criteria and enrolled in the study. The purpose of the study was explained to the participants in English, Hindi and/or local language they understood.

Information was collected through a pre-formed proforma (Annexure) and the qualifying patients were subjected to a detailed history, clinical examination and investigations. Clinical features such as fever, tachypnoea, tachycardia, hypotension, history of altered mentation, burning micturition, cough with expectoration, loose tools, abdominal pain with guarding/rigidity i.e, patients suspected of underlying infection were evaluated for risk for sepsis. Patients at

risk for sepsis were triaged using qSOFA at bedside. Any patient with qSOFA ≥ 2 were promptly identified to be at risk for sepsis. The patients were admitted either under ward or sent to ICU as per their clinical condition.

These patients were immediately treated empirically and stabilized. Routine investigations which included complete blood count including all red cell indices, random blood sugar, serum creatinine, serum sodium, serum potassium, serum urea, serum Total bilirubin and fraction, ALT, AST, arterial blood gas analysis, ECG, blood culture were done in all cases.

Chest Radiograph, ultrasonography of the abdomen, Urine microscopic examination, CT scan were done in certain patients to localize the site of infection or for diagnosis of the primary disease. Study of CSF, ascitic fluid, pleural fluid, urine culture, pus culture were done in selected cases as per the suspected system involved in origin of sepsis.

For diagnosis of sepsis, SOFA score was used. SOFA score of ≥ 2 consequent to infection was defined as sepsis.

Glasgow Coma Scale is a clinical score which assesses patients according to three aspects of responsiveness: eye-opening, motor, and verbal responses. Maximum score is 15 and minimum score is 3.

PaO2 was obtained from arterial blood gas analysis. In cases where ABG is not possible, PaO2 can be calculated from SpO2 reading. Fraction of Inspired Oxygen (FiO2) was calculated based on the oxygen flow patient is receiving via nasal canula or face mask. The calculation was : FiO2 = 0.20 + (0.04 x oxygen flow in L/min)

Statistical Analysis

The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analysed and statistically evaluated using Epi Info Software. Normal distribution of different parameters was tested by the Shapiro-Wilk normality test. Quantitative data was expressed in mean ± standard deviation or median with interquartile range and depends on normality difference between mean of two groups were compared by student t test or Mann Whiney U test while. Qualitative data were expressed in frequency and percentage and statistical differences between the proportions were tested by chi square test or Fisher's exact test. ROC Curve using RDW was calculated to predict outcome in sepsis subjects. Cut off was calculated using Youden index and sensitivity, specificity, positive predictive and negative predictive value was calculated. P' value less than 0.05 was considered statistically significant.

Ethical Issues

All participants were explained about the purpose of the study. Confidentiality was assured to them. Informed written consent was taken from them or their parents or caregivers. The study was approved by the Institutional Ethical Committee.

Observation & Results

Out of 280 cases selected for this study, range of age was 18-89 years and majority of the subjects were in the age group of 26-45years (31.07%). The least number of subjects were seen between the ages of 18-25 years (15.4%). Out of the 280 cases selected for this study, 148/280 (52.9%) were males and 132/280 (47.1%) were females. Most common comorbidity was hypertension followed by diabetes.

In this study among 280 patients, 184 (65.7%) survived while 96 (34.2%) expired. Blood culture was positive in 90 of 280 patients, i.e., 32.2 % of sepsis patients were blood culture positive. The gram-negative bacteria formed a major proportion followed by gram positive bacteria. E. coli and Methicillin sensitive Staphylococcus aureus

(MSSA) made up 7.8 % and 6.4 % were the top two bacteria most commonly associated sepsis (table 1). Respiratory infections was the most common cause of sepsis (42.8%), followed by intra-abdominal infections (23.9%) and genito-urinary infections (15.7%).

Table 1: Blood culture finding in Sepsis subjects

Blood culture	**No.**	**%**
Negative	190	67.8
Gram Negative (n=56; 20%)		
E Coli	22	7.8
K. Pneumoniae	10	3.6
Pseudomonas	12	4.3
Acinetobacter Baumanii	4	1.4
K. Oxytoca	8	2.8
Gram positive (n=34; 12.1%)		
MRSA	16	5.7
MSSA	18	6.4

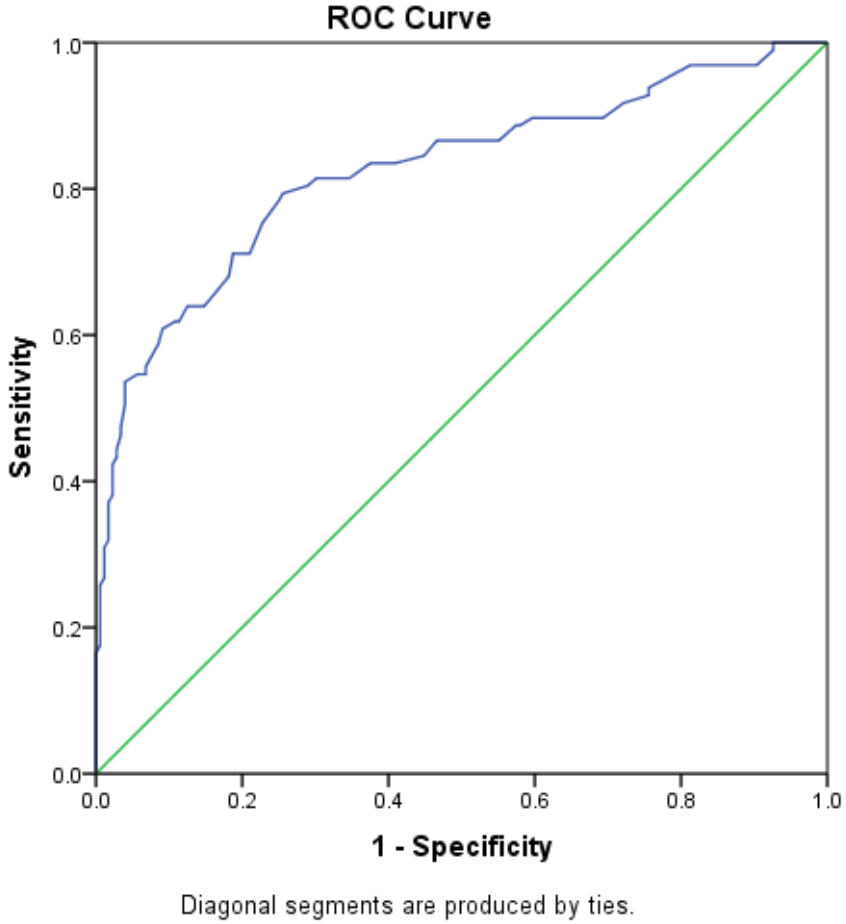

Figure 1: ROC curve using RDW for prediction of mortality in Sepsis subjects

The mean RDW-CV in survivors were 14.23±1.59 and it was 17.66 ±3.81 in those who died with a p-value of <0.001 showing statistical significance. Area under the curve using RDW was 0.82 (95% CI: 0.76-0.88) for prediction of mortality in Sepsis subjects. Best cut off value was 15.1 which gave 79.4% sensitivity, 74.4% specificity, 63.11% positive predictive value and negative predictive value of 86.67%. In the present study, higher SOFA Score at admission was associated with higher RDW at admission. P value was < 0.001. A staggering 44.5% of patients in the RDW>15 group fell under SOFA Score range of 11-15. Therefore, higher RDW seems to have association with higher SOFA Score at admission. (table 2)

Table 2: Association of SOFA score with RDW in sepsis subjects

SOFA score	RDW	
	RDW ≤15	RDW >15
1-5	66 (43.4%)	16 (12.5%)
6-10	76 (50.6%)	34 (26.6%)
11-15	10 (6.6%)	57 (44.5%)
16-20	0	21 (16.4%)

Chi square value = 99.16; p value <0.001

Discussion

The goal of the current study is to better understand RDW's function as a sepsis prognostic marker. The majority of the sepsis cases, or 31.07% of the 280 sepsis cases in our study, occurred in the age ranges of 26 to 45. With a male to female ratio of 1.12:1, there were 148 (52.9%) more male patients than female patients. The mean age of 203 sepsis patients in Moreno-Torres *et al*.'s [6] study was 63.1 years (SD - 14.3%), which is older than 45 as is the case in 85% of cases in the current study. Their study's distribution of men and women was consistent with ours.

The mortality rate in the current study was 34.2%. With only 7 deaths in the ward and the remaining 89 in the ICU, the majority of deaths occurred in ICU patients. The results of our study agreed with those of Moreno-Torres *et al*.'s[6] study, which indicated that in-hospital mortality was 31.5% for 203 patients admitted to the intensive care unit. In their 2014 prospective analysis of 297 severely septic patients, Lorente L *et al*.[7] discovered a mortality of 35.01%. Another study by Jandial A *et al*.[8] that was released in 2017 discovered that 200 patients had a 30-day mortality rate of 57%. greater RDW was discovered to be related to greater sepsis mortality in our study. The results of our investigation were correlated with those of studies by Lorente *et al*[7], Sadaka F *et al*,[9] and Moreno-Torres *et al*.[6] According to Jandial *et al*.'s study[8], the 30-day death rate was 30% in the group of patients with RDW 14.5%, 53.4% in the group with RDW 14.6%-17.3%, and 68.8% in the group with RDW >17.3%.

Higher RDW at admission was linked in the current study to a higher SOFA Score at admission. 0.001 was the P value. Therefore, it appears that a greater SOFA Score at admission is associated with a higher RDW.

The AUC for the sequential organ failure assessment (SOFA) and the Acute Physiologic and Chronic Health Evaluation II (APACHE II) were both 0.69 in the study by Sadaka F *et al*[9]. The RDW performed better than SOFA or APACHE II, and the two together were a greater predictor of death than either one was by itself. RDW and SOFA score showed a positive connection at day 1 (p = 0.007), day 4 (p = 0.002), and day 8 (p, 0.001). According to RDW tertiles, the

APACHE II and SOFA scores also increased, according to a different study by Yo YH *et al*.[10]

Conclusion

Based on the finding of our study it was concluded that a high Red Cell Distribution Width (RDWCV) is an independent prognostic marker in sepsis. In the present study, respiratory infection was the most common cause of sepsis and male population was affected more than the female population.

SOFA Score at admission, need for mechanical ventilation, inotrope support and hypertension, blood culture positivity was positively associated with RDW-CV at admission.

Recommendations

Although, conduction of this study in a sole institution with paucity of time and resources highlighted the role of RDW-CV in influencing the course of sepsis, a more elaborate multi centric study would be needed to precisely establish the role of RDW-CV as prognostic marker in sepsis.

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