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Study Of Red Cell Distribution Width As A Prognostic Indicator In Sepsis

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Abstract

Background: Sepsis is one of the leading causes of death worldwide. Rapid and precise diagnosis and appropriate antibiotic therapy is necessary to reduce mortality and morbidity in patients with sepsis. Though several biomarkers and scoring systems have been evaluated, prognostic markers to quickly and precisely establish the diagnosis or prognosis of patients with sepsis and septic shock are yet to be evaluated.

Aim And Objectives

1. To study the role of Red Cell Distribution Width as a prognostic indicator in sepsis
2. Comparison of RDW values between survivors & non-survivors

Methodology: This is prospective observational study conducted in Mysore Medical college and ResearchInstitute, Mysore, on 100 adult patients of both sex with diagnosis of sepsis and admitted in the emergency wards and Intensive Medical Care unit. We have studied Red cell Distribution Width in patients with sepsis and the values were compared among survivors and non-survivors groups. SOFA score and RDW were correlated in predicting mortality

Results: A total of 100 subjects were selected among which 75 were survivors and 25 were non-survivors. The mean RDW of survivors was 15.97 at the time of admission whereas in non-survivor group it was higher with mean RDW is 19.97 and was found statistically significant(p=0.0001).Positive correlation with Pearson's correlation coefficient of r=0.80 was found when RDW was cross matched against SOFA score. High RDW was associated with increased mortality in patients with sepsis

Conclusion: Red Cell Distribution Width can be used as a simple, inexpensive and a novel prognostic marker in patients with sepsis.

Keywords: Sepsis, prognostic markers, RDW, SOFA Score

Introduction

Sepsis is a life-threatening organ dysfunction resulting from dysregulated host responses to infection.[1] Data from the centre for Disease Control and Prevention reveals that sepsis is the leading cause of death in noncoronary intensive care unit patients and the tenth most common cause of death worldwide, the first being heart disease.[1]

Despite advances in intensive care and antimicrobial therapy, the incidence of sepsis and related mortality

rate has increased over the last thirty years.[2] The mortality rate is estimated at 30% in sepsis and 80% in septic shock in the USA 3 and at 12.8% in sepsis and 45.7% in septic shock in Europe.4 Reduced rates of reporting may affect estimations in developing countries.

The incidence of sepsis and septic shock continues to increase worldwide. The mortality increase has been attributable to patients' advanced age, pre-existing comorbidity, immunosuppressive diseases and therapies or infections with multi-drug resistant bacteria, patients with chronic diseases for a long period, and those on medical treatment that circumvent host defences viz. in-dwelling catheters and mechanical devices.[4,5] Invasive bacterial infections are a prominent cause of death around the world-especially among children.[5]

Without consistent and reproducible criteria the extensive pathophysiology associated with sepsis is difficult to diagnose and treat. A delay in the diagnosis and treatment of sepsis will result in the rapid progression of circulatory failure, multiple organ dysfunction and eventually death. Treatment guidelines are ambiguous. It involves a prolonged hospital stay for patients, while receiving complex therapy.

The in-hospital mortality risk of 10% in patients diagnosed with sepsis is widespread and those who develop septic shock increase their mortality risk greater than 40%.

Early diagnosis of severity of sepsis and appropriate treatment is essential for the survival of the patients. There are many biochemical markers, clinical parameters and scoring systems used to assess the severity and in predicting the mortality in patients with sepsis some of which include- estimating serum procalcitonin levels, clinical scoring systems like Sequential Organ Failure Assessment (SOFA), quick SOFA (qSOFA), Acute Physiology and Chronic Health Evaluation (APACHE II) scoring systems. The degree of severity is most often quantified by the Sequential Organ Failure Assessment (SOFA) score, which can predict the severity and outcome of multiple organ failure. However, calculating SOFA score is cumbersome. Moreover, assessment of the septic patient outcome during treatment needs to be focused on, as currently used clinical and biological criteria are undefined and inadequate for this purpose. The need for simple, cost effective and easily available, yet reliable markers has pushed researchers in identifying such markers for assessing the severity and predicting the prognosis of sepsis. Several inflammatory biomarkers have been evaluated in recent years with the high sensitivity, specificity, positive and negative predictive values for the early diagnosis of sepsis as available in literature. One such biomarker is the Red Cell Distribution width (RDW).

In this work, the haemogram parameter RDW which is a part of a complete blood count, easy to evaluate and which do not incur additional costs to routine analysis are studied in assessing prognosis in patients with sepsis

Objectives Of The Study

1. To study the role of Red Cell Distribution Width as a prognostic indicator in sepsis
2. Comparison of the values between survivors & non-survivors

Materials & Methods

A Prospective observational study was performed at Mysore medical college and Research Institute after obtaining approval from the ethical committee. Study period was one year from January 2018 to December 2018. Patients admitted with Sepsis in the Emergency department & various wards at K.R. Hospital Mysuru were included.

Sampling Procedure:

Patients with sepsis according to 'The Third International Consensus Definition 2016' satisfying the inclusion and exclusion criteria are recruited in the study. This includes a detailed clinical history, complete physical examination and baseline laboratory test. Blood samples were collected in two separate containers and sent for investigations including RDW. Blood cultures sent before administration of antibiotics. SOFA Score was recorded at the time of admission in ward or in ICU. RDW was done at the time of admission, after 72hrs, after 7 days. Major adverse events during course were recorded including death. Correlation studies of RDW and SOFA Score was done. The data obtained was statistically analyzed Friedman test for the repeated measures, Chi square test to find the

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significance in categorical data and probability value <0.05 is considered significant.

Inclusion Criteria

1. Patients admitted to ICU and Emergency ward who meet the criteria of Sepsis and Septic Shock
2. Age more than 18yrs.
3. Subjects who give valid informed written consent for the study

Exclusion Criteria:

1. Bleeding >10% blood volume.
2. Patients with anemia & other hematological disorder
3. Patients with known chronic diseases
4. Blood product transfusion in the previous week of admission.
5. Patients with malignancies on Chemotherapy.
6. Use of drugs known to change Morphology and Rheology of Red Blood Cells and platelets
7. Pregnancy

Results And Analysis

A total of 100 subjects were selected among which 75 were survivors and 25 were non-survivors. Majority of subjects in survivors belonged to age group of 41-60 years whereas in non-survivors belonged to age group beyond 60yrs (Table 1)(Figure1). The mean age was 52.61 years in survivors group and 64 years in non survivors group. When compared statistically using unpaired t test, the difference in mean age between study groups was found to be significant ($p<0.05$). It showed that increase in age in sepsis patients is associated with increase in mortality.

Out of 100 subjects, 57 were males, 43 were females with male to female ratio of 1.3:1 (Table 2)(Figure 2). Respiratory tract infection, urinary tract, blood stream were found to be the common source of infection both in survivor and non-survivor groups. . Respiratory tract was observed the most common in both the group.(Table 3)(Figure 3)

SOFA score analysis showed that the SOFA score was ≤ 5 for 85.3% of the survivors, the mean SOFA score being 3.86. The SOFA score for non-survivors was found to be high (between 10 and 15) and the mean was 10.64, higher the SOFA score, higher would be the mortality rate (Table 4 and 5)(Figure 4 and 5)

It is evident that majority of the study subjects in the survival group had a mean RDW of 15.97 at admission whereas in non-survivor group it was higher with mean RDW is 19.97 (Table 6).The mean red cell distribution width on the day of presenting the illness was significantly higher in non survivors than survivors. Those patients who had a high red cell distribution width during admission were associated with poor survival. In sepsis patients, when RDW was cross matched against SOFA score, a positive correlation with Pearson's correlation coefficient of r=0.80 was found. In sepsis patients, the increase in levels of RDW correlates with the increase in SOFA score 80% of times The statistical significance was found to be p value is < 0.0001.(Table 7) Higher RDW was observed in patients with sepsis among non-survivors when compared with survivors.

Discussion

Sepsis is a complex and deadly disease1. It is associated with acute organ dysfunction and high risk of mortality[1]. This syndrome requires urgent treatment and awareness[3] Incidence of sepsis is high and remains one of the leading cause of death globally[1]

Our study was conducted in 100 patients admitted to the Emergency ward ICCU and the mean age in both sex is 64 years. Study conducted by Aditya et al the mean age is 51.32 years, study by Sejin Kim et alet al mean age is 78 years and study by Farid Sadaka et al et al is 67.4 years.The most common source of infection was respiratory tract which accounts for 33% followed by urinary tract infections in our study which is comparable with other studies conducted by Aditya et al , Sejin kim et al, Farid sadak et al wherin most common source of infection is respiratory tract followed by urinary tract.

In our study Mean sofa score is 3.86 in survivors and 10.6 among non survivors which is comparable with study conducted by Sejin kim et al where it was 6 among survivors and 9 among non survivors. In study conducted by Farid sadak et al mean sofa score among survivors was 5 and 10 among non survivors

Those patients with scores less than 5 had a better survival rate and short duration of hospital stay.

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Those patients with the SOFA scores above 10 had a high mortality rate.

In our study Mean RDW among survivors was 15.97 and 19.97 among non survivors which is comparable with other studies conducted by Aditya et al where it was 16.84 among survivors and 17.84 among non survivors. In a study conducted by Sejin kim et al mean RDW among survivors it was 16.84 in survivors and 17,84 among non survivors. In study conducted by Farid sadak et al mean RDW among survivors was 15.6 and 17.6 among non survivors. In our study, the mean red cell distribution width on the day of presenting the illness was significantly higher in non survivors than survivors. Those patients who had a high red cell distribution width during admission were associated with increased mortality.

Based on the changes in red cell distribution width during admission, after 72 hours and after 7 days it was evident that majority of the study subjects in the survival group had a mean RDW of 16.22 at admission,15.94 after 72 hours and 15.79 after 7 days. In the non survivors group, the red cell distribution width was 19.08 during admission, 18.93 after 72 hours, and 18.87after 7 days. From this we might conclude that the increase in red cell distribution width at admission in septic patients is associated with a significant increase in death outcome. No statistical significant conclusion could be made among these group as far as change in red cell distribution width from baseline to 72 hours and after 7 days of hospitalization is concerned This result correlates with the study of Mahmood et al., in which RDW greater than 16 was concluded to be associated with increase in severity of illness.

Red Cell Distribution Width is an indicator which can vary in sepsis under the influence of TNF-α, IFN-δ, IL-1β, IL-6, the pro inflammatory cytokines which are released during the inflammatory process.

These cytokines cause inefficient erythropoiesis resulting in structural and functional changes of erythrocytes with volume variation. This may be accounted for an increased value of RDW7

Conclusion

RDW was found to be higher in patients with sepsis. On comparing these values RDW was found to be significantly higher in non-survivors than in survivors. High RDW is associated with high SOFA score and increased mortality.

Hence this can be simple, inexpensive and a novel prognostic marker of sepsis and its associated mortality

Table 1: Age distribution

Age groups	Survivors	%	Non- survivors	%
18-40	14	18.7	0	0
41-60	44	58.7	12	52
>_60	17	22.7	13	48
TOTAL	75	100	25	100

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Figure 1: Age distribution

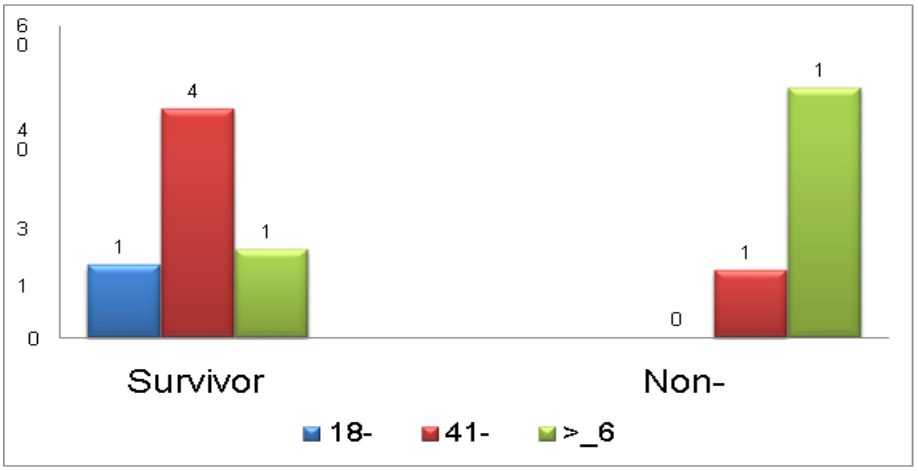

Table 2: Gender status

Gender Status	Survivors	%	Non-survivors	%
MALE	40	53.3%	17	68
FEMALE	35	46.7%	8	32
TOTAL	75	100%	25	100%
P value Chi square test		0.2		

Figure 2: Gender status

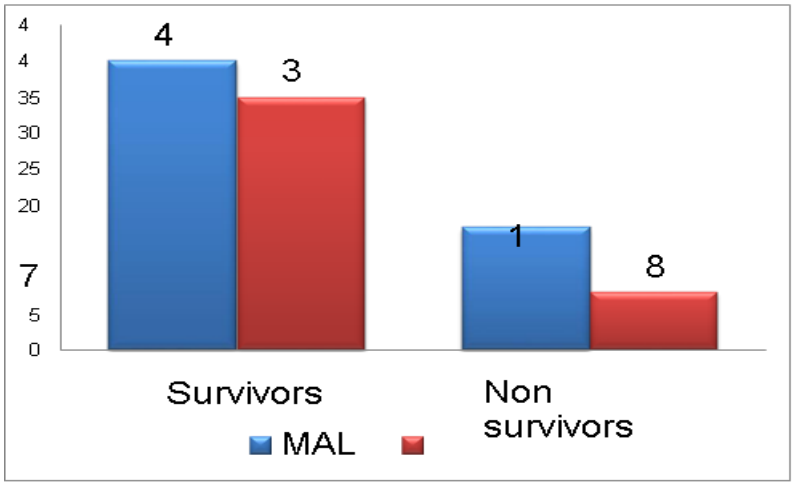

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Table 3:Source of infection

Source of Infection	Survivors	%	Non-survivors	%
Respiratory	24	32	9	36
Urinary Tract	18	24	5	20
Abdominal	13	17.3	3	12
Soft tissue	7	9.3	6	34
Blood Stream	13	17.3	2	8
TOTAL	75	100%	25	100%

Figure 3:Source of infection

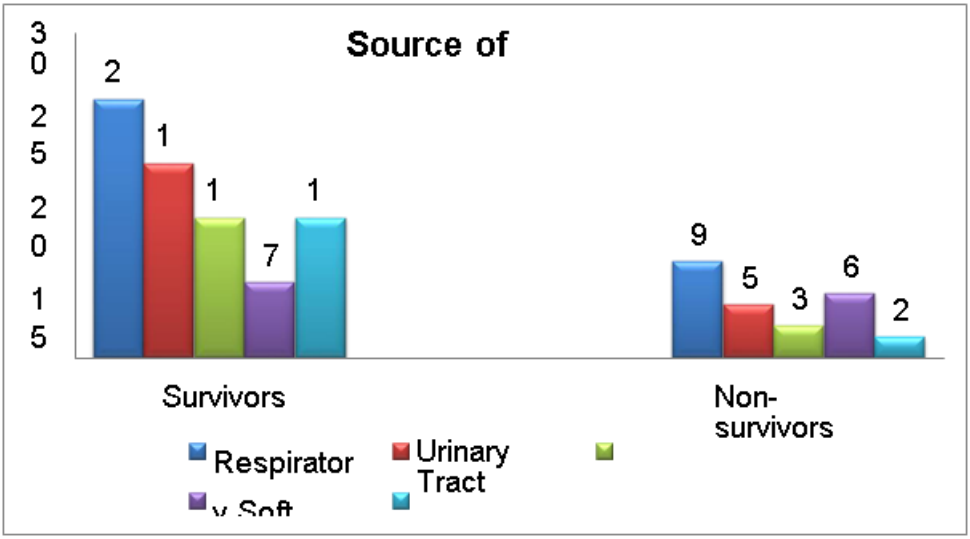

Table 4:SOFA Score

SOFA SCORE	Survivors	Percentage	Non survivors	Percentage
<_5	64	85.3	2	8
6-10	11	14.7	8	32
11-15	0	0	15	60
>15	0	0	0	0

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Total	75	100%	25	100%

Figure 4: SOFA SCORE

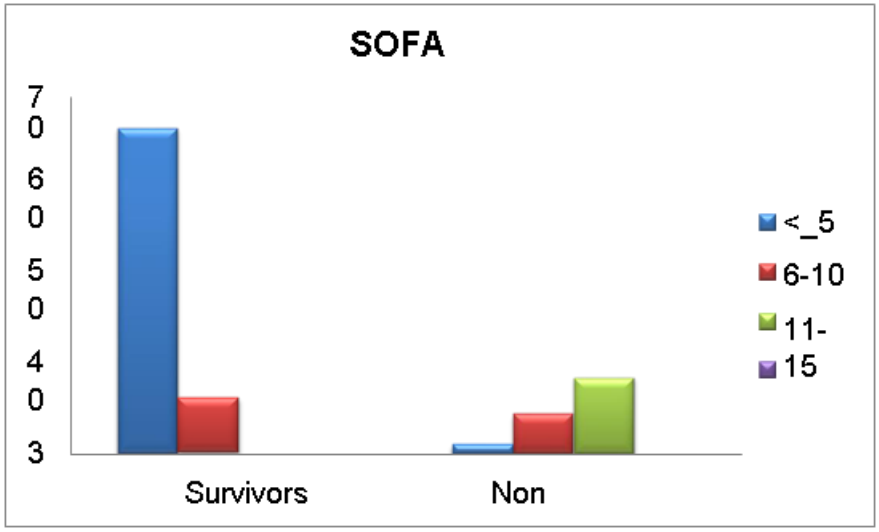

Table 5:SOFA Score distribution

SOFA SCORE	Survivors	Non survivors
Mean	3.86	10.64
SD	1.44	3.03
P value	<0.0001	

Figure 5: SOFA Score distribution

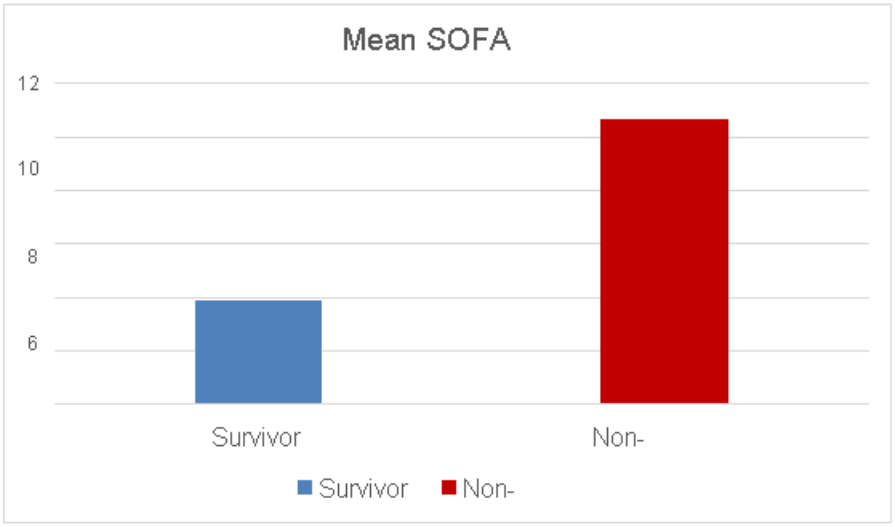

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Table 6: Variation of RDW

		At admission	After 72hrs	After 7days
Survivors	Mean	15.97	15.83	15.57
	SD	0.65	0.67	0.73
Non Survivors	Mean	19.97	19.81	19.44
	SD	1.21	1.23	1.43
P value		< 0.0001		

Figure 6:Variation of RDW

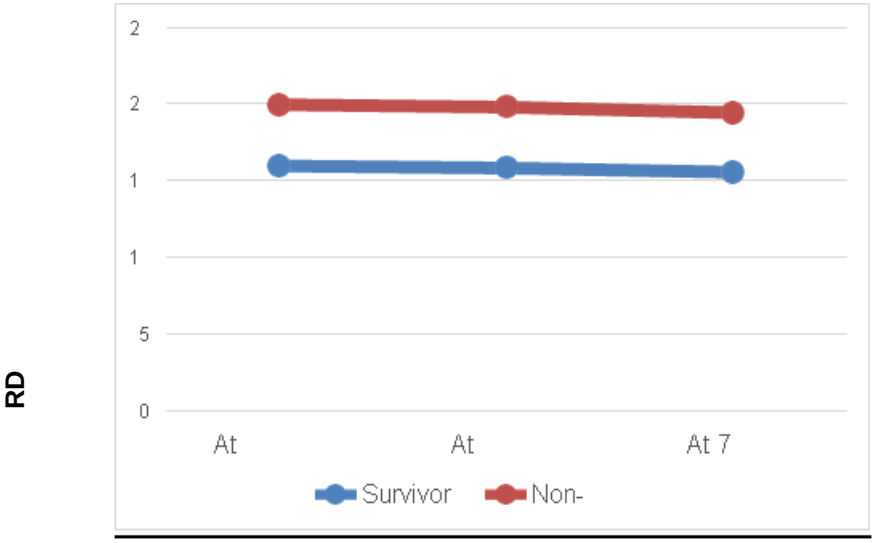

Table 7:Correlation of RDW with SOFA score

RDW Vs SOFA Score Correlation	
Pearson's R	**0.80**
R Square	**0.64**
F statistic	**155.57**
P value	**<0.0001**

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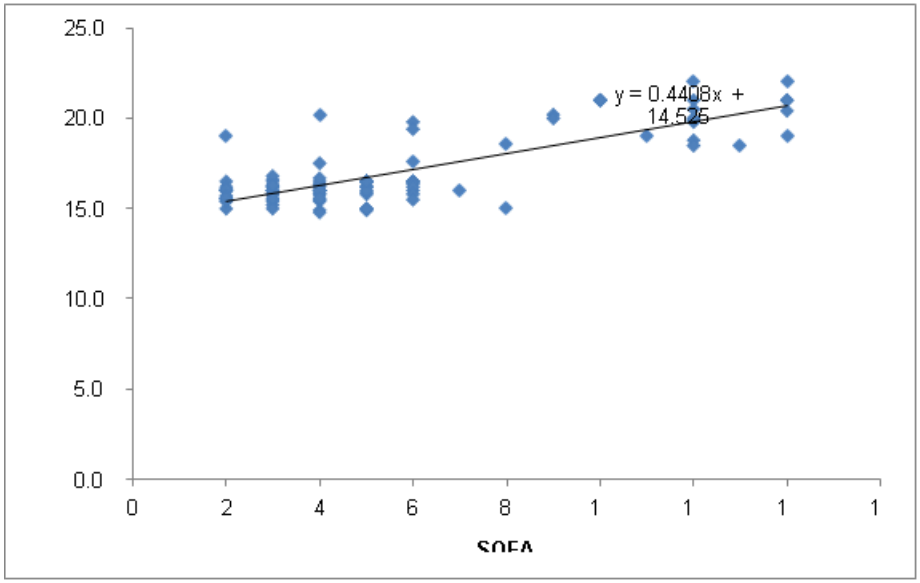
Figure 7: Correlation of RDW with SOFA score



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