

RED CELL DISTRIBUTION WIDTH (RDW) AS A PROGNOSTIC MARKER IN SEPSIS : A PROSPECTIVE OBSERVATIONAL STUDY

General Medicine

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ABSTRACT

AIMS AND OBJECTIVES: The aim of the study is to investigate whether changes in RDW during the first week correlates with the severity of sepsis and to assess the efficiency of RDW in predicting the clinical outcome after 28 days as assessed by SOFA score in patients with sepsis and septic shock.

MATERIAL AND METHODS: In prospective observational study, 80 adult patients of both sex with a diagnosis of sepsis and admitted in the General ward, emergency wards and Intensive medical Care unit in the MBS Hospital, KOTA under the Department of Medicine were included in the study. The source of infection, complications, duration of in-hospital stay, RDW was compared between the survivors and non-survivors groups.

RESULTS: Out of 80 patients 47 males and 33 were females. Males showed a high rate of mortality. The occurrence of comorbid conditions like Diabetic mellitus, Hypertension, Ischemic heart disease showed higher risk of death outcome. At time of admission mean RDW 16.59 ± 1.36 in the case of survivors and 19.32 ± 1.15 in the case of non-survivors which was statistically significant ($p < 0.001$). RDW had a significant and positive correlation with SOFA score.

CONCLUSION: RDW measured on admission can be used as prognostic markers in patients with sepsis and septic shock.

KEYWORDS

RDW, SOFA score, sepsis, septic shock, prognostic markers.

INTRODUCTION

Sepsis is a major cause of morbidity and mortality worldwide^[1]. The mortality rate accounting for about 30–50% of hospital deaths^[2]. It is estimated to affect more than 30 million people worldwide every year, potentially leading to 6 million deaths^[3]. Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection^[4]. The definition of sepsis was updated in 2016 following publication of the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)^[4]. "Sepsis-3" clinical criteria for the diagnosis of sepsis include : (a) a suspected infection and (b) acute organ dysfunction, defined as an increase by two or more points from baseline (if known) on the sequential (or sepsis-related) organ failure assessment (SOFA) score^[4,5]. The 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 the literature. The Red Cell Distribution width (RDW) is one of the various biomarkers which have been shown to predict the mortality and morbidity of sepsis. The Red Cell Distribution Width (RDW) is the coefficient of variation of Red Blood Cell (RBC) volume and is a representation of the RBC size heterogeneity of an individual patient^[6].

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The aim of the study is to investigate whether changes in RDW during the first week correlates with the severity of sepsis and to assess the efficiency of RDW in predicting the clinical outcome after 28 days as assessed by SOFA score in patients with sepsis and septic shock.

MATERIALS AND METHODS

STUDY DESIGN

The study was conducted in govt. medical college, MBS hospital kota. In prospective observational study, 80 adult patients of both sex with a diagnosis of sepsis and admitted in the General ward, emergency wards and Intensive medical Care unit in the MBS Hospital, KOTA under the Department of Medicine were included in the study. The source of infection, complications, duration of in-hospital stay, RDW was compared between the survivors and non-survivors.

INCLUSION CRITERIA

- 1) Patients admitted to the emergency ward and intensive medical care unit who meet the criteria of sepsis and septic shock.
- 2) Patients of Age > 18 years
- 3) Patients having a hospital stay of at least 72 hours.

EXCLUSION CRITERIA

- 1) Patients of Age < 18 years
- 2) Patients diagnosed with anemia or with hematological disorders
- 3) Patients with diseases causing trauma, intoxication
- 4) Patients with immuno-suppressive disease, receiving immuno-suppressive therapy or using drugs that can change the morphology of red blood cells
- 5) Patients with bleeding > 10% volume
- 6) Patients who had received recent transfusion of blood products
- 7) Patients with malignancies and on chemotherapy (within the last 6 months)
- 8) Pregnant individuals.

METHODOLOGY

All the patients who fulfill the inclusion / exclusion criteria were selected from indoor patient from the M.B.S. Hospital Kota.

Patients will be assessed for sepsis and septic shock according to new criteria in 2016 "SEPSIS-3". Blood samples were collected and analysed within 3hrs from the time of presentation. Clinical, and laboratory data were obtained and blood culture were studied before administration of broad spectrum antibiotics. RDW was obtained from complete hemogram.

The principles of initial resuscitation (fluid therapy, vasopressors, inotropic support) and infection issues (source identification and control, appropriate antibiotic therapy) were followed regularly and the outcome studied. SOFA score was recorded at admission. The correlation studies of RDW and SOFA score were done.

All patients were undergone:-

1. Detailed history and scrutiny of previous medical record
2. Clinical examination
3. Complete laboratory work up at time of admission - Complete Blood Count Renal function test, Peripheral smear, Serum electrolytes, Liver function test, Blood sugar, ABG, ECG, Chest X Ray PA view, USG Abdomen, Blood culture, Urine complete & culture, Pus culture, Sputum culture, Prognostic scores for sepsis (APACHE-II, SOFA score, qSOFA).

STATISTICAL ANALYSIS

Two groups were made survivors and non-survivor. Frequency tables and measures of central tendency (mean) and measures of dispersion

(standard deviation) were calculated using the statistical package SPSS 2.0 version. To find the significance in categorical data unpaired t test, Chi-Square test and single factor ANOVA test were used. In all the above statistical tools, the probability value <0.05 is considered as significant level. Pearson's Correlation coefficient and R squared were tested statistically for correlation.

RESULTS

A total number of 80 patients with diagnosis of sepsis who were admitted in MBS hospital were included in this study. The population was divided into two groups into survivors and non-survivors on basis of outcome treatment. The mean age of survivor group was 50.68 years. The maximum numbers of survivors were in age group 41-60 years i.e.44.26%. The mean age of non-survivors group was 68.17. The maximum numbers of non-survivor were in age group 61-80 years i.e.73.68%. The male-female survivors ratio was 59.02:40.98. Among the non-survivors, males showed a high rate of mortality (57.89%) and female 42.11%.

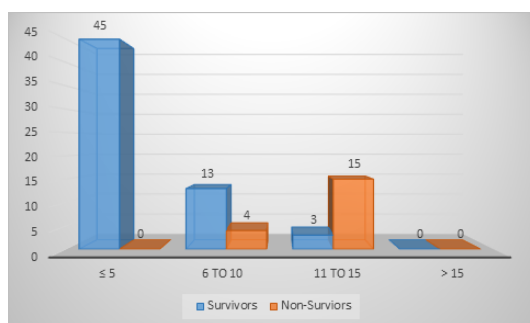
Diabetes mellitus and hypertension were the most common comorbid conditions in both groups followed by ischemic heart disease. It may be concluded that the occurrence of comorbidities like diabetes mellitus, hypertension and ischemic heart disease pose a higher risk of death outcome. Among the survivors group, respiratory tract infection, urinary tract infection, blood stream, soft tissue and abdominal infection were found to be common source of infection (31.15%, 29.50%, 13.11%, 9.84%, 9.84%). Respiratory and urinary tract infection (68.42% & 26.32%) were observed common source of infection in non-survivors group.

TABLE NO.1 CAUSATIVE AGENTS DISTRIBUTION

Causative Agent	Survivors	%	Non-Survivors	%
Not Isolated	17	27.87	2	10.53
Gram+ve	12	19.67	5	26.32
Gram-ve	32	52.46	12	63.16
Total	61	100	19	100

The majority of study subjects in survivors group had sepsis 78.69% and 21.31% had septic shock. In non-survivors group all subjects had septic shock i.e.100%. In our study, the mean SBP was 98.19 ± 17.17 mmHg in survivors group and 62.63 ± 9.33 mmHg in the non-survivors group. The mean diastolic blood pressure was 61.47 ± 13.52 mmHg in survivors group and 30 ± 7.45 mmHg in non-survivor group.

CHART NO.1 SOFA SCORE DISTRIBUTION



The mean of SOFA score was found 4.39 ± 2.38 in survivors. In non-survivors, the mean of SOFA score was 11.52 ± 1.77 . The unpaired t test showed high significance ($P < 0.05$) of SOFA score in predicting the outcome of patients during in hospital stay, higher the SOFA score, higher would be mortality rate.

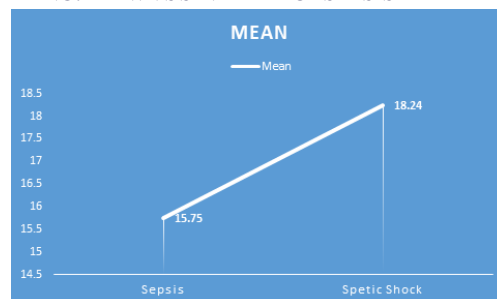
Mean duration of in-hospital stay was 10.83 ± 4.05 in the survivors group and the non-survivors group, mean duration of in-hospital stay was 5.47 ± 2.24 . Among the survivors group, only a few (i.e.21.31%) needed inotropic support. Inotropic support was given to all the 19 non-survivors (i.e.100%). Above results showed that increase in the need for inotropic support in sepsis subjects is associated with a significant increase in death outcome. Majority of subjects in both the survivors and non-survivors were presenting with multiple complications like acute kidney injuries (39.34%; 73.68%), thrombocytopenia (54.09%; 31.57%), Coagulopathy (11.48%; 26.31%), metabolic acidosis (24.59%; 36.84%), encephalopathy (21.31%; 73.68%), jaundice (21.31%; 15.78%), and ARDS (4.91%, 57.89%).

TABLE NO.2 ANALYSIS OF VARIATION OF RDW FROM DAY 1 TO DAY 7

RDW		At Admission	After 72 Hours	After 7 Days
Survivors	Mean	16.59	16.15	15.45
	SD	1.36	1.36	1.32
Non Survivors	Mean	19.32	18.97	17.85
	SD	1.15	0.92	1.56

Among survivors group, means of RDW at time admission, after 72 hours and after 7 days were 16.59 ± 1.36 , 16.15 ± 1.36 and 15.45 ± 1.32 . Means of RDW at time of admission, after 72 hours and after 7 days were 19.32 ± 1.15 , 18.97 ± 0.92 and 17.85 ± 1.56 in non-survivors group.

CHART NO.2 RDW VS SEVERITY OF SEPSIS



From the RDW Vs Sepsis table, it was evident that the study subjects with sepsis had a mean RDW of 15.75 ± 1.30 , and with septic shock had a mean RDW of 18.24 ± 1.43 . When compared statistically using single factor ANOVA test, the difference in mean RDW between various stages of sepsis was found to be significant ($p < 0.05$). Most of study subjects with RDW at admission above 18.24 will have septic shock as outcome.

TABLE NO.3 PREDICTION OF MORTALITY

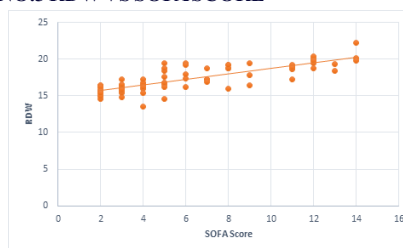
Independent variable	Dependent variable	Cut off	Odds ratio	95% confidence interval(CI)	P value
RDW	28 days mortality	18	38.6	8.5 to 175.2	<0.001

The cut off value suggested that sepsis patients with RDW >18 had 38 times more risk of death after 28 days compared to sepsis patients with RDW ≤ 18 .

TABLE NO.4 CORRELATION OF RDW WITH SOFA SCORE

RDW vs SOFA Score correlation	
Pearson's correlation coefficient	0.86
R Squared	0.68
P value	<0.001

CHART NO.3 RDW VS SOFAScore



In sepsis patients, when RDW was cross matched against SOFA score, a positive correlation with Pearson's correlation coefficient of $r=0.86$ was found. In sepsis patients, the increase in levels of RDW correlates with the increase in SOFA score 86% of times. The statistical significance was found to be p value is <0.001 .

DISCUSSION

Cell distribution width was highest among patients with septic shock followed The SOFA score was calculated with the available laboratory parameters during admission. The SOFA scores during admission correlated well with the outcome of the patients. Those patients with scores less than 5 had a better survival rate and short duration of hospital stay. Those patients with the SOFA scores above 10 had a high mortality rate. In the survivors group, SOFA scores more than 10

during admission had a prolonged duration of hospital stay and also developed complications. These patients needed vigorous intervention compared to those with a SOFA score of less than 10 during admission. 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 poor survival. These patients also developed associated complications like acute kidney injury, coagulopathy and encephalopathy. RDW (Mean 18.24, 15.75). These parameters showed strong statistically significant correlation of red cell distribution width with the severity of sepsis. 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 16.59 at admission, 16.15 after 72 hours and 15.45 after 7 days. In the non-survivors group, the red cell distribution width were 19.32 during admission, 18.97 after 72 hours, and 17.85 after 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.

CONCLUSION

In our study, the efficiency of RDW used as biomarkers of sepsis and septic shock has been made and the correlation of the SOFA score with RDW in predicting the outcome of patients has been studied. In sepsis patients when SOFA score was cross matched with RDW the increase in their values strongly and positively correlated with increase in SOFA score, thus elucidating the usefulness of RDW as prognostic markers in the study of severity of sepsis and the outcome. However, there are certain limitations of the study :-

1. RDW level is affected by many conditions, RDW level without other inflammatory indicators such as C-reactive protein, gamma-glutamyl transferase and albumin, may not give exact information about patients' inflammatory status.
2. Only the circulating neutrophil and lymphocyte counts were analyzed but the different subpopulations of the lymphocytes had not been explored.
3. The study is a prospective observational study in a single institution in a short duration with less sample size of 80. For validation of the results, the sample size should be large.
4. The time elapsed between the blood sampling and the measuring of RDW may significantly affect the RDW levels. Intra-day cell count variations also may be considered. All these necessitate future prospective clinical research.

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