

RED CELL DISTRIBUTION WIDTH IN CORRELATION WITH SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORE AS A PROGNOSTIC MARKER OF SEPSIS

ABSTRACT :

INTRODUCTION : Sepsis is a dysregulated host response to infection resulting in potentially life-threatening organ dysfunction. Elevation in red cell distribution width (RDW), a simple routinely done investigation, can be a prognostic marker in these sepsis patients. Although many studies were lacking to find the relationship between RDW and other severity sepsis markers.

AIM : To determine the significance of red cell distribution width as prognostic marker in patients with sepsis. To assess the clinical outcome by correlating red cell distribution width with SOFA score in patient with sepsis.

METHODS : This was a prospective study, which was conducted at tertiary care hospital , Pondicherry where we enrolled 71 patients above 18 years of age who had sepsis symptoms admitted in the medical ward/ICU. Patients with sepsis at admission were prospectively evaluated for correlation between RDW value, SOFA score both at admission , day 3 and day 7 with survivors and non-survivors. Besides the groups of raised and normal RDW, study population was further analyzed after categorizing into three RDW groups as follows: $\leq 14.2\%$, $14.2-15.2\%$, and $>15.2\%$ as well.

RESULTS: 71 sepsis patient's age ranged from 25 to 91 years with a mean age of 60.39 years. The male gender was predominant. The causes of sepsis were multifactorial and pneumonia was the prime cause of sepsis. 41-60 and 61-80 years were predominant age groups and equal number of major non- survivors were also belongs to this age groups (14.08 % each). The RDW showed highly significant difference between survivors and non-survivors ($P < 0.0001$). The mortality rate was highly significant in moderate and higher RDW groups ($P < 0.0001$). While the RDW values increased, the mortality rate was also increased in the present study. There was a significant association between RDW levels and severity of sepsis that leads to mortality. Comparison of diagnostic accuracy of both RDW and SOFA at the time of admission showed that RDW had 100 % sensitivity and specificity whereas SOFA showed 100 % and 50 % sensitivity and specificity respectively.

CONCLUSION : By this study we could measure RDW value which is a part of an automated CBC which is a done routinely, which is cheap, easily available parameter on admission can be used as a prognostic marker in patients in sepsis.

Key words: Sepsis, RDW value, SOFA Score

INTRODUCTION:

Sepsis and its complications are a common cause of infectious diseases and death worldwide.(1) Sepsis refers to the systemic inflammatory response syndrome (SIRS) caused by infection.(2,3) But, the infection can be challenging to confirm. Diagnosis of the infections, there is no existing gold standard method, and although blood cultures processed using standard microbiological techniques are a common diagnostic step need a certain amount of time, usually at least 24-48 hours to obtain results. Delays in empirical treatment of sepsis and bacteremia increase mortality(4) also a length of hospitalization(5) and price(6) which makes timely identification of infections and initiation of appropriate treatment important goals. Pneumonia is the predominant cause of the infection that causes sepsis, accounting for half of all sepsis cases, followed by intra-abdominal and urinary tract infections. Literature survey revealed that the leading site of infection affects the risk of death associated with intra-abdominal infection. The highest risk of in-hospital death after sepsis and urinary tract infection is the lowest.(7) While the pathogen causing the infection is also an important determinant for sepsis outcome,(8) in 30% of all sepsis cases no microorganism can be cultured from any bodily site.(9)

India has a population of 1.2 billion, one of the countries with the highest burden of infectious diseases in the world.(10) Although there is a lack of systematic data on the manifestations of acute febrile illness, 12% of adults with acute febrile illness (1–51%) will

develop bacteraemia. (11) Sepsis causes a systemic host reaction, containing hundreds of mediators, which can potentially be used as a diagnostic and prognostic biomarker. Early diagnosis of sepsis and initiation of appropriate treatment is essential for the lifesaving of the patients, severity of sepsis patients and predict mortality-some of them include-to assess serum procalcitonin levels, clinical scoring systems (such as sequential organ failure assessment (SOFA), quick SOFA (QSOFA), Acute Physiology and Chronic Health Assessment (APACHE II) scoring system. However, calculating the SOFA score is troublesome.

RDW is a haematological parameter, which is frequently measured at every complete blood count. Its utility in daily practice is primarily in the differential diagnosis of anaemia, but currently, investigators are aiming at different methods for red blood cell function and morphological changes. RDW has also been studied as an independent variable in different predictive scores. Some studies have shown that it should be included in the scores used daily in intensive care institutions and emergency departments.(12) This study and our aim is to determine the significance of red cell distribution width in correlation with SOFA score as prognostic marker in patients with sepsis.

MATERIALS AND METHODS :

This was a prospective study, conducted at a tertiary care hospital, in Puducherry, India. The Institutional Human Medical Ethics Committee(IHEC) approved this study from February 2019 for 18 months. All the patients with sepsis symptoms as per the International Guidelines for Management of Sepsis and Septic Shock with age more than 18 years irrespective of genders admitted in the medical ward/ICU were enrolled in the study. Patients diagnosed with sepsis Participants with the following clinical conditions Haematological disorders, Anaemia, Disease causing trauma (Road traffic accident), Intoxication, Immuno-

suppressive disease, Receiving immune-suppressive therapy or drug that can change the morphology of red blood cells, Received recent transfusion of blood products, Malignancies /on chemotherapy, Bleeding >10 % volume and Pregnant women were excluded from the study.

All patients who fulfilled the inclusion criteria and consented to participate in the study were included. Demographic details such as age (in years), and Medical details (co-morbidities) were collected. Laboratory analysis such as RDW was done within 3 hours of admission and the same was analysed with frequent intervals. RDW value was measured as a part of Automated Complete blood count using (PENTRA ES60, YUMIZEN-1500). Severity of sepsis was determined by calculating SOFA score (< 5-Mild; 6-10- Moderate; 11-15-Severe; >15-more severe). Major adverse cardiovascular events in the form of cardiogenic shock requiring inotropic support, pulmonary oedema and death was recorded. Patients were treated as per hospital protocol. RDW, SOFA score were assessed at the time of admission, after 72 hours and after 7 days of treatment and was study the in-hospital outcome. All categorical variables were expressed as percentages and the continuous variables were expressed as mean \pm standard deviation. Association between age, sex, comorbidities, SOFA score, RDW at admission, day 3 and day 7, inotrop support, mechanical ventilator, cause of sepsis, survivor. Comparing RDW and SOFA score at admission, day 3 and day 7 with non-survivor. The statistical significance of mean differences was compared using unpaired t-test, chi-squared analysis. The estimated sample size was calculated as 71.

STATISTICAL METHODS

The data was entered with an excel sheet. Data was exported to Medcalc version 19.0 for further processing. All categorical variables were expressed as percentages and the continuous variables were expressed as mean \pm standard deviation. Association between age, sex, comorbidities, SOFA score, RDW at admission, day 3 and day 7, inotrop support, mechanical ventilator, cause of sepsis, survivor. Comparing RDW and SOFA score at admission, day 3 and day 7 with non-survivor. The statistical significance of mean differences was compared using unpaired t-test, chi-squared analysis. All values were considered significant if the *P*-value was < 0.05 .

RESULTS:

Totally 71 sepsis patient's age ranged from 25 to 91 years with a mean age of 60.39 years. The male gender was predominant. Diabetes mellitus and hypertension were the major comorbidities observed in the present study participants. The causes of sepsis were multifactorial and pneumonia was the prime cause of sepsis which covered more than half of the causes of sepsis in the study. The inotrope support was required by 43.66 % and mechanical ventilator support was provided to 64.78 % of the present study patients. The study patients were categorized in to four groups based on the age such as 21-40 years, 41-60 years, 61-80 years and >80 years. 41-60 and 61-80 years were predominant age groups and equal number of major non-survivors were also belonging to this age groups (14.08 % each). A significant association ($P < 0.0001$) with the causes of sepsis and non-survivors. Pneumonia-severe stage was the key cause of sepsis associated significantly with the non-survivors (60 %).

The present study parameters were compared based on the RDW levels which was observed at the time of admission. The RDW levels were divided in to three groups such as

normal (RDW <14.2), moderate (RDW 14.2-15.2) and high (RDW >15.2). The mortality rate was highly significant in moderate and high RDW groups ($P<0.0001$). While the RDW values increased, the mortality rate was also increased in the present study. The SOFA values were also significantly varied in all the three groups. The severity of sepsis increased, the SOFA did not increased accordingly. Hence, the SOFA could not be a prognostic marker based on this study results. But, it also shown significant difference ($P<0.0001$). When the severity of sepsis increased, obviously the inotrope and mechanical ventilator supports required by the patients. The inotrope support were highly significant in both moderate ($P=0.0009$) and severe stages of sepsis ($P<0.0001$). But, the mechanical ventilator support was significant only with severe sepsis stage ($P=0.0260$). The RDW levels were modulates constantly depends on the sepsis levels. Hence, the RDW levels were directly proportional to the sepsis levels. This association was confirmed with the chi-squared analysis (Table:1)(Fig:1).The chi-squared analysis revealed that there was a significant association between RDW levels and severity of sepsis that leads to mortality.

Table 1 : Chi-squared analysis of RDW with survivors and non-survivors

RDW levels	Survivors	Non-Survivors
RDW<14.2	38	2
RDW14.2-15.2	2	6
RDW >15.2	6	17
Total	46	25
Chi-squared	58.62	
P value	0.0365	

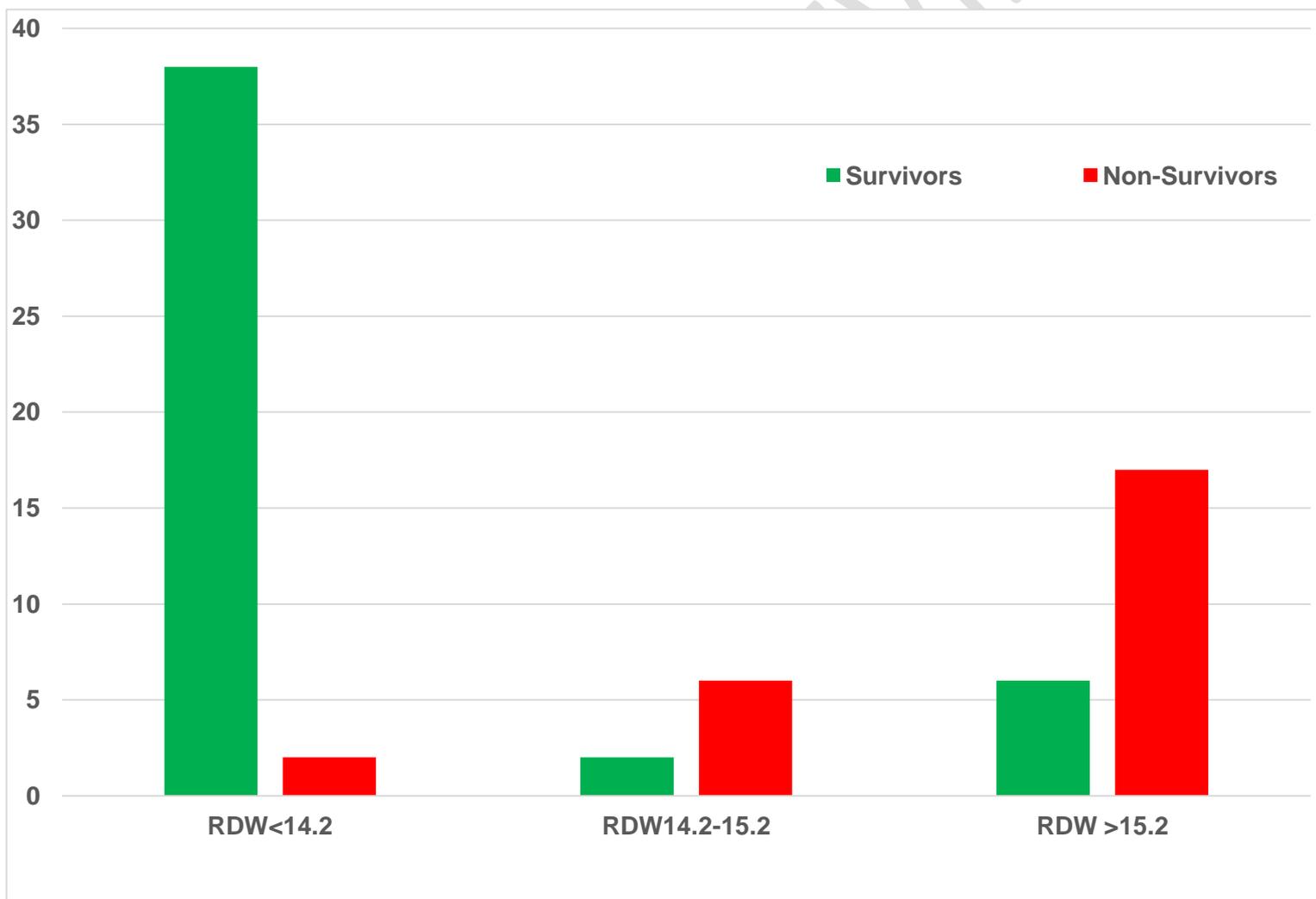


Figure 1 : Chi-squared analysis of RDW with survivors and non-survivors

This analysis described that the sepsis levels increased, the RDW levels were also increased. Therefore, RDW could be a better prognostic marker for sepsis based on the present study results. Further strengthen the present study results, comparison of diagnostic accuracy of both RDW and SOFA at the time of admission showed that RDW had 100 % sensitivity and specificity whereas SOFA showed 100 % and 50 % sensitivity and specificity respectively(Table:2)

Table 2 : At admission time Diagnostic accuracy of RDW and SOFA in non-survivors

Diagnostic accuracy	RDW	SOFA	P Value
Mean± SD	16.16±1.91	5.48±1.82	<0.0001
Sensitivity %	100	100	
Specificity %	100	50	
Accuracy %	100	78.12	

DISCUSSION

The present study was conducted to find the RDW was correlated with SOFA score as a prognostic marker in sepsis patients. When RDW value was increase during on admission, 72 hours and 7th day in sepsis patients there is significant increase in mortality when correlate with SOFA score. In our study SOFA score was not increased in non-survivor so it cannot be used as prognostic marker. Kim J et al (13), Jo YH et al(14), Jo et al studies showed RDW was significantly higher in non-survivors ,30 days following critical care admission. This study have certain limitations , single centred and surgical ward patients was not included other inflammatory cytokines not measured. However , large multicentre study with serial RDW value measurement needed for further clarification. The underlying

mechanism liable for this relationship remains a matter of continued research. Future studies with larger samples are needed to verify these findings. In conclusion, RDW could be a better prognostic marker for sepsis based on the present study results.

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