

COMPARISON OF RED CELL DISTRIBUTION WIDTH WITH SOFA SCORE AS A PROGNOSTIC MARKER OF SEPSIS IN ELDERLY PATIENTS

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ABSTRACT

BACKGROUND

Severe sepsis and septic shock are increasing in incidence and contributing significantly to mortality. The prediction of outcome for elderly patients with sepsis may facilitate more aggressive interventions. The SOFA score is a scoring system used to quantify the severity of the patient's illness based on the degree of organ dysfunction.

Various biomarkers are being evaluated for early diagnosis of sepsis. RDW is one of them, which have been shown to predict mortality and morbidity of sepsis. Hence, this study is being done to compare RDW with SOFA score as prognostic marker of sepsis in elderly patients.

AIM

To compare red cell distribution width with SOFA score as a prognostic marker of sepsis in elderly patients.

METHODS

A total of 93 elderly patients in sepsis who were admitted to Intensive Care Unit of M. S. Ramaiah Hospitals between October 2013 and September 2015 were included in the study. ROC (Receiver Operating Curve) was used to determine the optimal cut-off point for RDW for predicting mortality. ROC of RDW was compared with ROC of SOFA score.

RESULTS

Mean age of the patients was 70.72±8.02 and most of the patients were in the age group of 61–70yrs. (53.8%). 52(55.9%) patients were males and 41(44.1%) patients were females. Bronchopneumonia (34.4%) and urosepsis (30.1%) were the most common causes of sepsis; 61.3% of the patients had SOFA score in the range of 5–10. Mean SOFA score was 7.87097±3.22769. Mean RDW was 14.247±2.1151.

CONCLUSION

RDW had a sensitivity of 81.6%, specificity of 77.3%, positive predictive value of 80%, and negative predictive value of 79.1% with a cut-off value of 13.75% in predicting mortality in elderly patients in sepsis.

KEYWORDS

Sepsis, Septic Shock, SOFA Score, Red Cell Distribution Width.

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INTRODUCTION

Worsening sepsis is associated with increased mortality as multiple organ systems fail. Prediction of outcome for patients with sepsis may facilitate more aggressive interventions. 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. It would be advantageous to identify a biomarker that would be associated with the degree of severity in patients with 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.¹ RDW is elevated by increased red cell destruction, nutritional deficiencies and blood transfusions.² Biomarkers of chronic inflammation like erythrocyte sedimentation rate and C-reactive protein, have been associated with elevated RDW.^{3,4} Recent studies have reported that Red Cell Distribution Width (RDW) is associated with prognosis in Critical Illness, Heart Failure, Acute Myocardial Infarction, Pulmonary Embolism, Pneumonia and Cardiac Arrest.⁵⁻¹⁰

In patients with severe sepsis, early diagnosis and treatment with antibiotics is crucial for survival of patients. Various markers are being tested for early diagnosis of Sepsis. Recent studies have shown that elevated RDW levels are associated with sepsis. RDW as a part of Complete Blood Count (CBC) is tested in all patients in sepsis. Hence, this study was done to see the correlation between RDW and sepsis.

AIMS AND OBJECTIVES OF THE STUDY

To compare red cell distribution width with SOFA score as a prognostic marker of sepsis in elderly patients.

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METHODOLOGY

Study was a hospital based prospective observational study conducted over a period of two years from October 2013 to September 2015; 93 elderly patients admitted with sepsis to Intensive Care Units of M.S. Ramaiah Hospitals, Bangalore, were studied.

Inclusion Criteria

Patients aged >60 years admitted to Intensive Care Units (ICU), who met the criteria of sepsis (According to Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012) were included in the study.¹¹

Exclusion Criteria:

- Blood loss >10% blood volume.
- Blood product transfusion in the previous week of admission.
- Recent chemotherapy.
- Previous history of diseases primarily affecting red blood cells.
- Use of drugs known to change morphology and rheology of red blood cells.

METHODS OF DATA COLLECTION

Ninety three elderly patients in sepsis were included in the study. Purpose of study was explained to the patients and their relatives and informed consent was obtained. Thereafter, the patients were assessed and blood samples for complete blood count including RDW and serum procalcitonin were sent on admission. Other tests such as arterial blood gas, liver function tests, renal function tests, prothrombin time, activated partial thromboplastin time, international normalized ratio, chest x-ray, serum electrolytes, blood culture and urine culture were sent in all the patients.

RDW was measured as a part of Automated Complete Blood Count using SYSMEX XE 2100 and XT 2000i.

STATISTICAL ANALYSIS

Data was entered in MS Excel and analyzed using SPSS version 17. All the continuous variables like age, pulse rate, platelet counts, etc. were described using mean and standard deviation. All the qualitative variables were expressed as percentage. ROC (Receiver Operating Curve) was used to determine the optimal cut-off point for RDW for predicting mortality. ROC of RDW was compared with ROC of SOFA score.

RESULTS

Most of the patients were in the age group of 61–70yrs. (53.8%); 52(55.9%) patients were males and 41(44.1%) patients were females. (Table 1) Fever (89.2%) was the most common presenting symptom followed by breathlessness (37.6%) and cough (32.3%). (Table 2) Diabetes Mellitus (51.6%) and Hypertension (46.2%) were most common comorbid conditions. (Table 3) Bronchopneumonia (34.4%) and urosepsis (30.1%) were the predominant causes of sepsis. (Table 4) Mean age of the patients was 70.72±8.02 (Table 5), mean total count was 13075.38±7339.968 (cells/mm³), mean platelet count was 167353.01±120988.964 (cells/mm³), and mean procalcitonin

was 16.526±23.9572 (Table 6). Most of the patients (61.3%) had SOFA score in the range of 5–10. Mean SOFA score was 7.87097±3.22769. (Table 7).

RDW had a sensitivity of 81.6%, specificity of 77.3%, positive predictive value of 80%, and negative predictive value of 79.1% with a cut-off value of 13.75% in predicting mortality in elderly patients in sepsis. (Graph 1 and Table 8) SOFA score had sensitivity of 95.9% and specificity of 77.3% in predicting mortality in elderly patients in sepsis. (Graph 2).

DISCUSSION

Sepsis is the leading cause of death in non-coronary ICU patients, and the tenth most common cause of death overall according to data from the Centers for Disease Control and Prevention (The first being heart disease).¹² Sepsis-related incidence and mortality rates increase with age and pre-existing comorbidity. Various scoring systems have been developed to predict the outcome in sepsis. Among them one of the widely used scoring systems is SOFA Score.

Sequential Organ Failure Assessment (SOFA) score was constructed using physiological measures of dysfunction in six organ systems (Respiratory, cardiovascular, liver, coagulation, renal and central nervous systems) each of which is graded from 0 to 4 with increasing severity of dysfunction.¹³ The first sepsis-related Organ Failure Assessment score, later called the Sequential Organ Failure Assessment (SOFA) score, was introduced in 1994 in a consensus meeting of European society of intensive care medicine and further revised in 1996. The aim was to quantify the severity of the patient's illness based on the degree of organ dysfunction, serially over time.

The Red Blood Cell Distribution Width (RDW), as part of an automated Complete Blood Count (CBC) is a routinely available parameter on hematology analyzers. This parameter is the most commonly reported index of the variation in red cell volume and can be used to detect subtle degrees of anisocytosis. RDW is a numerical measure of anisocytosis. It may be useful in distinguishing certain causes of anemia, in particular in distinguishing Iron Deficiency (RDW raised) from thalassemia (RDW usually normal).

The role of leucocytes in the inflammatory response is well known; nevertheless the rheological changes of Red Blood Cells (RBC) and their physiopathological role during inflammation are not completely understood. Studies by electronic microscopy have founded important alterations in RBC shape during the refractory phase of shock.^{14,15} They also showed morphologic and functional changes during sepsis regarding RBC population. This has brought to discussion the hypothesis that RBC alterations during shock and sepsis may contribute to Multiple Organ Dysfunction Syndrome (MODS). It has been reported previously that the flexibility of RBC may be dysfunctional due to the endotoxins of bacteria in septic shock. The RBC exposed to endotoxin decreased their deformability and showed increased hydroxymyristic acid content which is a component of bacterial endotoxins, suggesting a relationship.¹⁶⁻¹⁷ As sepsis is an inflammatory state, there will be release of various inflammatory mediators like Interleukin-6, Tumor Necrosis Factor. These pro-inflammatory cytokines suppress the maturation of red blood cells and decrease the half-life of red blood cells, which in turn results in elevated RDW.

Recently, highly significant associations have been described between RDW value and all cause, non-cardiac and cardiac mortality in patients with coronary artery disease, acute and chronic heart failure, peripheral artery disease, stroke, pulmonary embolism, and pulmonary artery hypertension.¹⁸⁻²³ High RDW has been associated with increased mortality in patients with stroke, liver disease, peripheral arterial disease and organophosphorous compound poisoning.²⁴⁻²⁸ Moreover, several studies have reported that RDW shows the predictive value of all-cause mortality in critically ill or ICU patients, patients with community acquired pneumonia, gram-negative bacteremia and severe sepsis.²⁹⁻³²

Sepsis and septic shock are one of the leading causes of death worldwide. Early detection and prompt administration of antibiotics has been shown to reduce mortality and morbidity in patients with sepsis. Hence, various markers have been evaluated for earlier diagnosis of sepsis.

Serum procalcitonin as a diagnostic marker of sepsis has been largely studied in adult population and is an established marker of sepsis, but it is expensive. There are many other markers of sepsis which are being evaluated for its diagnosis among which RDW is emerging as a promising marker. It is a part of Complete Blood Count which is a cheap, easily available test. Hence, we have conducted this study to assess the role of RDW as a prognostic marker of sepsis and septic shock.

In our study, the mean age of the patients was 70.72±8.02 and most of the patients were in the age group of 61-70yrs. (53.8%), which is in accordance with the study done by You Hwan Jo, et al. where the median age group was 75 years in nonsurvivors and 70.5 years in survivors. In our study, 55.9% of the patients were males. This is in concordance with the studies done by You Hwan Jo, et al. and Zhongheng Zhang et al. where 57.5% and 65.4% of the patients respectively were males.^{32,33} In our study, Diabetes Mellitus (51.6%) and Hypertension (46.2%) were most common comorbid conditions. This is in concordance with study done by You Hwan Jo, et al. and Sabina Hunziker, et al. where diabetes mellitus and hypertension were the most common comorbid conditions.^{32,34} In the present study, bronchopneumonia (34.4%) was the most common causes of sepsis. This is in concordance with studies done by You Hwan Jo, et al. (50.2%) and Leonardo Lorente, et al. (56.6%), where pneumonia was the most common cause of sepsis.³²

A 61.3% of the patients had SOFA score in the range of 5-10. Mean SOFA score was 7.87097±3.22769. This was similar to the results observed in studies done by Leonardo Lorente, et al. where median SOFA Score was 6 in survivors and 8 in nonsurvivors.

CONCLUSION

Established prognostic markers of sepsis like SOFA score requires various parameters to be measured and calculated, which can be cumbersome. RDW as a part of Complete Blood Count is tested in all patients in sepsis. Hence, in elderly patients in sepsis, RDW can be used as a biomarker which is associated with the degree of severity of sepsis.

Age in Years	Males		Females		Total
	No.	% Within Age Category	No.	% Within Age Category	No.
61-70	25	50	25	50	50
71 - 80	19	63.3	11	36.7	30
81 - 90	8	61.5	5	38.5	13
Total	52	55.9	41	44.1	93

Table 1: Age and Sex Distribution of Patients Studied

Clinical Symptoms	Total Patients (93)	
	No.	%
Fever	83	89.2
Breathlessness	35	37.6
Cough	30	32.3
Gastrointestinal symptoms	24	25.8
Burning micturition	23	24.7
Others	37	39.8

Table 2: Clinical Symptoms

Comorbid Conditions	Number (n=93)	%
Diabetes mellitus	48	51.6
Hypertension	43	46.2
Ischemic Heart Disease	29	31.2
Chronic Kidney Disease	15	16.1
Chronic Obstructive Pulmonary Disease	10	10.8
Chronic Liver Disease	4	4.3

Table 3: Comorbid Conditions

Cause of Sepsis	Number (n=93)	%
Bronchopneumonia	32	34.4
Urosepsis	28	30.1
Soft tissue	11	11.8
Gastrointestinal sepsis	8	8.6
Hepatobiliary	6	6.5
Miscellaneous	8	8.6

Table 4: Cause of Sepsis

Variables	Mean±SD
Age in years	70.72±8.02
Temperature (° fahrenheit)	100.353±1.245
Heart rate (per minute)	102.39±10.817
SBP(mm Hg)	102.39±15.529
DBP(mm Hg)	63.29±13.213
Respiratory rate (per minute)	24.01±5.097
SpO2(%)	93.33±3.454

Table 5: Comparison of Baseline Variables

Laboratory Parameters	Mean±SD
Hemoglobin % (gm/dl)	11.558710±2.6233298
Total count (cells/mm ³)	13075.38±7339.968
Platelet count (cells/mm ³)	167353.01±120988.964
ESR (mm/hour)	43.194±33.0304
Serum Creatinine (mg/dl)	3.054±2.6354
Total Bilirubin (mg/dl)	2.206±4.1525
Albumin (mg/dl)	2.613±1.5070
Aspartate transaminase (IU/L)	189.33±789.599
Alanine transaminase (IU/L)	131.59±503.096
Procalcitonin	16.526±23.9572
RDW	14.247±2.1151

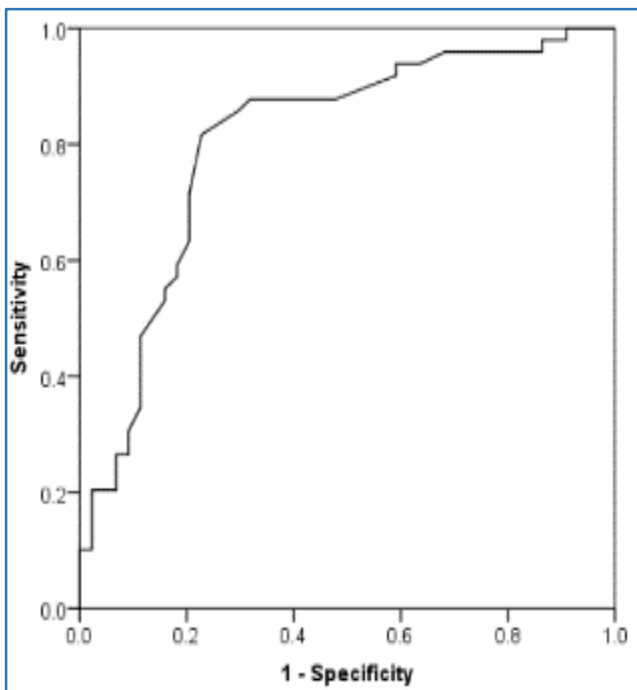
Table 6: Laboratory Parameters

SOFA Score	Number (n=93)	%
<5	17	18.3
5-10	57	61.3
11-15	18	19.4
>15	1	1
Total	93	100

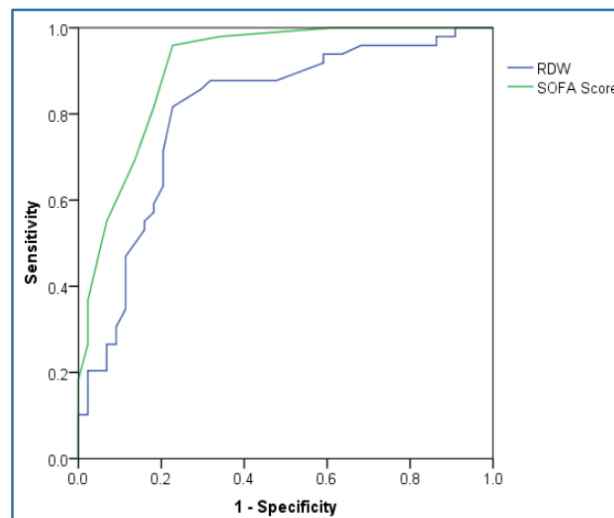
Table 7: SOFA Score

RDW	Death	Survived	Total
>13.75	40	10	50
≤13.75	9	34	43
Total	49	44	93
%	52.7%	47.3%	100.0%

Table 8: RDW Sensitivity, Specificity, PPV, NPV



Graph 1: Area under the ROC to determine the cut-off point for RDW



Graph 2: Comparison of area under the ROC between RDW and SOFA Score

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