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Original Research Article

Red cell distribution width as a prognostic marker in severe sepsis and septic shock

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ABSTRACT

Background: The incidence of severe sepsis and septic shock has increased over the past 30 years, and the annual number of cases is now >700,000 (~3 per 1000 population). There are many markers of sepsis which are being evaluated for its diagnosis among which RDW is emerging as a promising marker. Hence this study is being done to see the correlation between RDW and sepsis.
Methods: A total of 162 patients-81 survivors and 81 non-survivors of severe sepsis and septic shock fulfilling inclusion and exclusion criteria who were admitted to intensive care unit between October 2013 and September 2015 were included in the study. Baseline variables, laboratory parameters, complications, and RDW were compared between the two groups.
Results: Majority of patients - 73(45.06%) were in the age group of 61 - 80 years. Mean RDW was 15.20±2.29 in non-survivors and 13.86±2.20 in survivors, which was statistically significant (p<0.001). Mean RDW was higher and statistically significant among non-survivors with respect to duration of stay and requirement of inotropes.
Conclusions: RDW levels measured on admission can be used as a prognostic marker in patients in severe sepsis and septic shock.

Keywords: Red cell distribution width, Sepsis, Septic shock

INTRODUCTION

Sepsis and septic shock are one of the leading causes of death worldwide. According to data from the Centers for Disease Control and Prevention, sepsis is the leading cause of death in non-coronary ICU patients.[1] 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 a numerical measure of RBC variability and heterogeneity. RDW values are used to analyze the type of anaemia.[2] Recent studies have reported that Red Cell Distribution Width is associated with prognosis in critically ill patients, sepsis in elderly, and organophosphorous compound poisoning.[3-5] Aim of the study was to study the role of Red cell distribution width as a prognostic marker in severe sepsis and septic shock.

METHODS

Study was a hospital based prospective observational study conducted from October 2013 to September 2015. 162 Patients admitted with severe sepsis and septic shock to intensive care units of M.S.Ramaiah Hospitals, Bangalore, Karnataka, India were studied.

Inclusion criteria

- Patients admitted to Intensive Care Units who met the criteria of severe sepsis and septic shock

(According to Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock).[6]

Exclusion criteria

- Patients with previous history of diseases primarily affecting RBCs, blood loss >10% of blood volume, blood product transfusion one week prior to admission, use of drugs known to change morphology and rheology of RBCs and pregnant patients were excluded from the study.

Data collection

162 Patients with severe sepsis and septic shock were included. Complete Blood Count including RDW, prothrombin time, activated partial thromboplastin time, international normalized ratio, liver function tests, renal function tests, arterial blood gas, serum Procalcitonin, blood culture, and urine culture were sent on admission. RDW was measured as a part of Automated Complete Blood Count using SYSMEX XE 2100 and XT 2000i. The reference range for RDW in our laboratory is 12-14%. Study subjects were divided into 2 groups of 81 survivors and 81 non-survivors. Clinical parameters, Laboratory investigations, and RDW were compared among the two groups.

Statistical analysis

Data was entered in MS excel and analyzed using SPSS version 17. Descriptive studies of mortality and complications were analyzed and presented in terms of Percentages. Chi-Square Test was used to compare the proportion of death and complications between the groups.

RESULTS

46.9% of the non-survivors and 43.2% of survivors were in the age group of 61-80 years. 60.5% of the patients were males. Fever (86.4%) was the most common presenting symptom and Diabetes Mellitus (39.5%) and Hypertension (34.5%) were most common co- morbid conditions.

Table 1: Cause for sepsis.

Cause	Non -survivors		Survivors		Total	
	No.	%	No.	%	No	%
Bronchopneumonia	32	40	26	32	58	36
Urosepsis	21	26	17	22	38	24
Gastrointestinal sepsis	11	14	8	10	19	12
Hepatobiliary	8	10	5	6	13	8
Soft tissue	11	14	5	6	16	10
Miscellaneous	7	8	12	15	19	12

Bronchopneumonia (36%) was the predominant cause of sepsis, followed by urosepsis (26%) and gastrointestinal sepsis (24%) (Table 1). 64 (79%) patients among non-survivors required ionotropic support when compared to 23 (28.3%) patients among survivors. 26 (32%) patients among non-survivors required ventilator support when compared to 8 (9.9%) patients among survivors.

Mean heart rate, and respiratory rate was higher among non-survivors, Mean systolic blood and diastolic blood pressures were lower among non survivors when compared to survivors (Table 2). In our study anemia was seen in both the groups with mean hemoglobin being 11.47±4.47 in non-survivors and 10.9±2.43 in survivors.

Table 2: Comparison of baseline variables with outcome.

Variables	Outcome		Mean±SD	P Value
	Non-survivors	Survivors		
Age (years)	60.6±17.8	57.78±15.48	59.1±16.7	0.16
Temperature	100.71±1.30	100.23±1.033	100±1.2	0.07
Heart rate	107.33±9.46	98.74±11.03	103±11.1	<0.001*
SBP (mm Hg)	91.20±8.90	113.55±15.02	102±16.7	<0.001*
DBP (mm Hg)	56.19±8.90	73.30±12.29	64.8±13.7	<0.001*
RR	27.32±3.51	20.19±4.13	23.8±5.23	<0.001*
SpO_2 (%)	92.40±3.47	94.40±3.06	93.4±3.42	<0.001*

Leukocytosis was seen in both the groups with mean total count being 13784.29±8231. The mean platelet count was less in non-survivors (1.39±1.02) when compared with survivors (2.06±1.19) with significant p value. The mean total bilirubin value was higher in non-survivors (2.42±3.38) when compared with survivors (1.69±3.69) (Table 3). *E. coli* (5%) was the most common organism isolated in Blood followed by Coagulase negative *Staphylococcus aureus* methicillin resistant - CONS MR (3.7%) and *Pseudomonas* (2.4%).

E. coli (4.9%) and *Pseudomonas* (1.8%) were the most common organisms isolated in urine cultures. *Acinetobacter* (16.7%) and Methicillin resistant *Staphylococcus aureus* - MRSA (16.7%) were the most common organisms isolated in Sputum; and Acinetobacter (15%) and *Klebsiella* (13.8%) were the most common organisms isolated in ET culture.

Most of the patients had SOFA score in the range of 5 - 10. Mean SOFA score was higher among non-survivors (10.39±2.99) when compared with survivors (5.55±2.05).

The mean serum PCT among survivors was 11.98±15.82 and 14.61±23.82 in non-survivors. Mean RDW in non-survivors (15.20±2.29) was higher and statistically significant when compared to survivors (13.86±2.20) (p<0.001) (Figure 1).

Moratlity (%), SOFA score, duration of stay, requirement of ionotropic support was statistically significant between the RDW groups.

Table 3: Laboratory parameters - a comparison in two groups.

Lab parameters	Non-survivors	Survivors	P Value
Hemoglobin (gm%)	11.47±4.47	10.9±2.43	0.37
Total count	13955.92±9129	13612.46±7278	0.69
Platelet count(*100000/mm³)	1.39±1.02	2.06±1.19	<0.001*
ESR	34.59±26.83	44.23±32.35	0.05
Serum Creatinine	3.04±2.79	2.94±2.56	0.98
Total Bilirubin	2.42±3.38	1.69±3.69	0.02*
Albumin	2.58±1.56	2.37±0.73	0.63
Aspartate transaminase	191.77±652.93	190.40±669.60	0.45
Alanine transaminase	155.34±563.65	105.47±253.78	0.18

Table 4: Outcome of patients based on RDW.

	RDW			P Value
	<14.2%	14.2% - 15.2%	>15.2%	
	n =86	n = 38	n = 38	
Mortality (%)	32.60%	32.10%	33.30%	<0.001*
SOFA score, median	6	9	10	<0.001*
PCT, mean	13.2±19.5	13.9±20.2	14.02±16.4	0.181
Duration of stay, median	7	10	11	<0.001*
Mechanical Ventilation, median	13	8	9	0.47
Blood c/s	12	7	8	0.58
Ionotropic support	29	31	28	<0.001*

It was also observed that the complications like requirement of ionotropic support and death, duration of ICU stay and SOFA score were progressively increasing with higher RDW value (Table 4). Higher RDW values were associated with higher SOFA score and presence of complications (Table 5).

DISCUSSION

In present study, Bronchopneumonia (36%) was the most common cause of sepsis. This is in concordance with studies done by Hwan Y Jo et al (50.2%) and Lorente L et al (56.6%), where pneumonia was the most common cause of sepsis.[7,8]

Median SOFA Score was 10 in non-survivors and 5 in survivors and it was statistically significant. This was similar to the results observed in studies done by Lorente L et al, with SOFA Scores of 6 in survivors and 8 in nonsurvivors.[8] Non-survivors had a higher mean Serum Procalcitonin- 15.14±16.78 when compared with 12.96±20.87 in survivors.

This correlates with a study done by Mori K et al, where the infection group had significantly higher procalcitonin

(18.69±2.06) (P<0.01). Similar finding was noted by Rosenthal SH et al (22.58±2.26), and Quiroga B et al (18.6±1.26), where patients with severe infections and sepsis showed significantly higher procalcitonin values.[9-11]

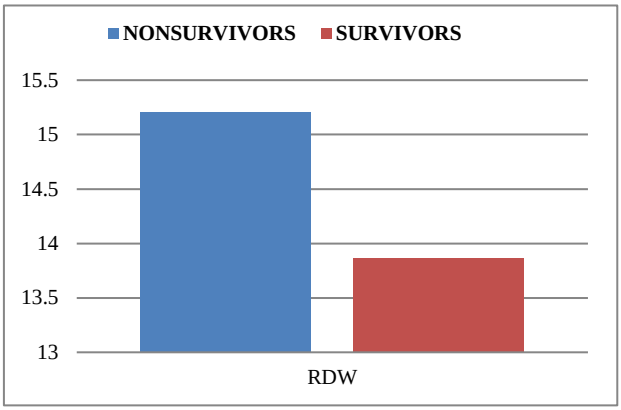

Figure 1: Comparison of serum RDW with outcome.

Table 5: Comparison of RDW with complications, sofa score.

	n	Mean RDW	P value
Duration of stay			
< 7 days	68	13.9±2.18	<0.01*
>7 days	94	14.9±2.23	
Ionotropic support			
No	74	13.76±2.10	<0.001*
Yes	88	15.12±2.18	
Need for mechanical ventilation			
No	132	14.42±2.13	0.43
Yes	30	15.01±2.7	
SOFA score			
<5	28	13.83±2.18	<0.001*
5-10	95	14.23±1.92	
10-15	36	15.61±2.67	
>15	3	17.4±0.81	

Mean RDW among non-survivors was 15.20±2.29 and 13.86±2.20 in survivors which was statistically significant (p <0.001). This result is comparable to the other study done by Jo YH et al, in which median RDW was 15.8 among non-survivors and 14.4 in survivors. In another study by Esper RC et al, mean RDW among non-survivors was 16.82±2.33 and 15.90±1.79 in survivors (p<0.05).[7,12] RDW is a parameter of volumetric variation in erythrocyte.

It is calculated by dividing standard deviation of RBC volume by 100.[13] In conditions where there is accelerated RBC proliferation; larger reticulocytes are released into circulation and cause increase in RDW. Elevated RDW indicates a greater difference in size among RBCs. Any changes influencing the production of RBC causes alteration in RDW. Pro inflammatory states play a crucial role in insufficient erythropoiesis leading to structural and functional alteration of RBC. Cytokines such as tumour necrosis factor alpha, interferon gamma, interleukins 1 beta and 6 have shown to effect RBC production and survival.

The Pro inflammatory state of sepsis can negatively impact RBCs leading to elevated RDW.[3] Acute inflammation and increased oxidative stress seen in sepsis can result in increased RDW values. Hence RDW measured on admission can be used as a prognostic marker in patients with severe sepsis and septic shock.[7]

CONCLUSION

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. Whereas RDW is a simple and inexpensive test, hence RDW levels measured on admission can be used as a prognostic marker in severe sepsis and septic shock.

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