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Original Research Article

EVALUATION OF THE EFFECT OF RED CELL DISTRIBUTION WIDTH ON THE DEVELOPMENT OF ACUTE RENAL FAILURE IN PATIENTS WITH SEPSIS

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Abstract

Background: Sepsis is the primary cause of Acute Kidney Infection (AKI) in ICU, affecting 15%-20% of patients requiring renal replacement therapy. AKI has a mixed aetiology, with sepsis, ischaemia, and nephrotoxicity co-existing. This study aimed to assess and validate the predictive factor of RDW for sepsis-induced acute kidney injury in the emergency unit. **Materials and Methods:** This prospective, observational study was conducted in the Emergency Department of a tertiary-care hospital, for one year, from January 2022 to December 2022. One hundred and fifty-nine adult SA-AKI patients admitted to the ICU were assessed. Their demographics, RDW, serum creatinine, creatinine clearance, and severity of AKI were assessed and recorded in a pre-structured proforma. Serum creatinine and creatinine clearance were assessed at admission and after 48 hrs. **Results:** Female (67%) preponderance was observed, and normal level (12-15%) RDW was observed among 38.4% of the study population mean, while abnormality (>15%) was seen among 61.6%, with a mean RDW of 16.06±2.663 mL/min. Elevated serum creatinine level was seen among 64.2% on admission and 59.7% after 48hrs. Creatinine clearance abnormal level was seen among 99.5% of the population on admission and after 48hrs. While correlating the serum creatinine with RDW, we observed patients with abnormal levels of RDW showed significantly (p=0.015 & p=0.013) higher serum creatinine levels among 52.5% on admission and 47.5% after 48 hrs screening. A statistically significant association was noted between abnormal RDW and serum creatinine and creatinine clearance. **Conclusion:** RDW predicts sepsis-induced acute renal disease in patients admitted to the intensive care unit.

INTRODUCTION

The term sepsis refers to a dysregulated host response to an infection that causes life-threatening tissue damage and organ failure. These lethal infections can result in hemodynamic alterations, multiple organ dysfunction, and shock. Each organ system may experience changes ranging from minor malfunction to total organ failure. Sepsis is a potentially dangerous illness with a 15-20% death rate and significant long- and short-term morbidity. An unexplained organ failure in an acutely unwell patient should raise suspicion of the potential presence of sepsis and stimulate an adequate diagnostic assessment.[1,2]

One of the main factors affecting morbidity and mortality in sepsis is Acute Renal Failure (ARF).

Vis-a-vis, the most significant factor causing ARF in critically ill patients in the intensive care unit is sepsis. Endothelial and tubule alterations, inflammatory cell infiltration, and intrarenal hemodynamic abnormalities with intraglomerular thrombosis are all part of sepsis-associated ARF (SA-ARF).[2,3]

Early detection of SA-ARF patients with a high mortality risk can give and empower clinicians with necessary diagnostic and therapeutic information. Along with traditional complete blood count values, red blood cell distribution width (RDW), a measure of the degree of circulating erythrocyte size heterogeneity, is typically used to estimate the prevalence of haematological system illnesses such as anaemia. RDW has been proposed over time as a potent, independent prognostic marker for many

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associated diseases, with a link between elevated RDW and illness severity and death established in a wide range of inflammatory diseases, including sepsis. According to recent research, increased RDW may be linked to the emergence of AKI in patients with acute medical problems. Patients with higher RDW at the time of admission to the coronary care unit were significantly more likely to develop AKI, according to Hu et al.

Similarly, a study by Wang et al. adopting a cut-off of 14.25% revealed high RDW levels to be an independent predictor for the frequency of AKI and mortality in patients with traumatic brain injuries. However, little information is available regarding the connection between RDW and SA-AKI, especially in the Indian population.[4-7] Therefore, this study aimed to investigate the effect of red cell distribution width on the development of acute renal failure in sepsis and further validate RDW as a prognostic marker for this condition.

MATERIALS AND METHODS

This single-centre prospective, observational study was conducted from January 2022 to December 2022 in the Division of Emergency Care of the urban, academic, and tertiary care Kovai Medical Center and Hospital, Coimbatore, India. The study group included 159 adult patients (18 years or older) hospitalised in the emergency department and diagnosed with sepsis and acute renal failure/acute kidney injury (AKI). Kidney Disease: Improving Global Outcomes criteria based on serum creatinine and urine output was used to define AKI.8 Sepsis 3.0 criterion, sepsis was diagnosed, or infection was suspected in patients with a sequential organ failure assessment (SOFA) score ≥2. 9 The Institutional Ethical Board approved the study protocol, and informed consent was obtained from all the study cohorts.

Inclusion criteria: All adult patients (≥ 18 years) with a diagnosis of sepsis and those who satisfied the diagnostic criteria for AKI and for whom complete clinical data were available were included.

Exclusion criteria: Those who were younger than 18 years, had a history of chronic dialysis, haematological disease, those who had had a transfusion of blood products within one week, patients with conditions like a history of chemotherapy, cardiogenic shock, hepatic cirrhosis, pregnancy where changes in red blood cell morphology can occur were excluded.

The variables recorded included age, gender, temperature, heart rate, oxygen saturation, blood pressure, complete blood count, Glasgow coma scale, urinary output, RDW serum creatinine and creatinine clearance. Standard protocols were followed during phlebotomy and biochemical analysis. Sysmex XE_5000 analyser (Sysmex Canada, Inc., Canada, USA) was used for blood tests, and RDW were determined from whole blood. Red Cell Distribution Width (RDW) between 12 – 15 % was considered normal, while values above 15 % were considered abnormal. Serum creatinine and creatinine clearance were assessed at admission and 48 hrs after hospitalisation. Serum creatinine <1.2 mg/dl was considered normal. Renal disease severity was graded based on creatinine clearance. Based on creatinine clearance, renal disease severity was graded. When creatinine clearance was < 15 mL/min, it was labelled End stage renal disease. It was called severe impairment between 15-29 mL/min, <30 to 59 mL/min moderate impairment, and values between <60 to 89 mL/min were considered a mild impairment. The data was collected using the pre-structured observation checklist.

Statistical analysis: Data were analysed using SPSS version 24 (IBM, Armonk, New York, USA) and Excel TM 16.0 (Microsoft, Redmond, Washington, USA). Categorical data were analysed as frequencies and percentages, while continuous data were analysed using standard deviation and mean. A chi-square test for association was conducted to determine the association between patient characteristics and outcomes. The statistical level $p < 0.05$ at the 95% confidence interval was considered significant.

RESULTS

A total of 159 adult patients with S-ARF were included in the study based on inclusion and exclusion criteria. Females (67.3%) predominated over males (32.7%) in the study population. The age of the patients ranged from 18 – 90 years, with a mean of 57.57±14.264. The age group >60 years was observed more frequently in this study (47.2%), followed by 40-59 years (40.9%), while only 12 % were less than 40 years.

Table 1: Distribution of gender, age, RDW, and severity

		Frequency	Percentage
Gender	Female	52	32.7%
	Male	107	67.3%
Age	< 20	3	1.9%
	20 - 39	16	10.1%
	40 - 59	65	40.9%
	60 - 79	69	43.4%
Red cell distribution width	Normal (12% -15%)	61	38.4%
	Abnormal (> 15%)	98	61.6%

Renal disease severity	End-stage renal disease (<15 mL/min)	24	15%
	Severe impairment (<15 - 29 mL/min)	25	16%
	Moderate impairment (<30-59 mL/min)	45	28%
	Mild impairment (<60-89 mL/min)	65	41%

Normal levels of red cell distribution width (12–15%) were seen in 38.4% of the study population on average, whereas abnormal levels (>15%) were seen in 61.6% of the study population. The mean value of RDW observed in this study was 16.06±2.663 mL/min. Fifteen percent of the cases were in end-stage renal disease, 16 % severe, 28 % moderate, and 41% mild impairment (Table 1).

We found that 64.2% of the population on admission and 59.7% of the population after 48 hours had increased serum creatinine levels. On admission, the mean Sr. creatinine value was 2.021 mg/dL; after 48 hours, it was 2.198 mg/dL.

Table 2: Serum creatinine level and creatinine clearance

		On admission	At 48 hrs
Sr creatinine level	<1.2 mg/dL	57 (35.8%)	64 (40.3%)
	>1.2 mg/dL	102 (64.2%)	95 (59.7%)
Creatinine clearance	Abnormal <90 mL/min	158 (99.5%)	158 (99.5%)
	Normal > 90 mL/min	1 (0.5%)	1 (0.5%)

We observed abnormal creatinine clearance levels (<90 mL/min) among 99.5% of the population at the time of hospitalisation and after 48hrs. The mean creatinine clearance value was 41.17 mg/dL on admission and 43.75 mg/dL after 48 hrs (Table 2).

Table 3: Correlation of serum creatinine with red cell distribution width

Red Cell Distribution Width	On admission		At 48 hrs	
Sr. Creatinine	Normal	Abnormal	Normal	Abnormal
<1.2	29 (47.5%)	28 (28.6%)	32 (52.5%)	32 (32.7%)
>1.2	32 (52.5%)	70 (71.4%)	29 (47.5%)	66 (67.3%)
P value	0.015		0.013	

We observed that patients with aberrant levels of red cell distribution width had significantly higher serum creatinine levels than 52.5% of other patients upon admission and 47.5% of other patients after 48 hours of screening (p=0.015, χ^2 = 5.883 & p=0.013, χ^2 = 6.133 respectively) (Table 3).

Table 4: Correlation of creatinine clearance with red cell distribution width

Creatinine clearance	On admission		at 48hrs	
	RCDW (12-15%)	RCDW (>15%)	RCDW (12-15%)	RCDW (>15%)
End-stage renal disease (<15 mL/min)	2	22	3	18
Severe impairment (<15 - 29 mL/min)	8	17	5	19
Moderate impairment (<30-59 mL/min)	14	31	11	24
Mild impairment (<60-89 mL/min)	37	28	42	37
P value	<0.0001		<0.0001	

In this study, out of 24 patients admitted with end-stage renal illness, 22 had abnormal levels of RDW distributions, and significant renal impairment was seen in 17 cases out of 25 individuals (Table 4).

Table 5: Correlation of serum creatinine and creatinine clearance with RCDW

Red cell distribution width		Mean	Std. Deviation	P value
Serum creatinine on admission	Normal	1.5508	1.12393	0.005
	Abnormal	2.3133	1.89136	
Creatinine clearance on admission	Normal	48.118	16.54357	0.002
	Abnormal	36.2714	19.69508	
Serum creatinine	Normal	1.4984	1.48789	0.046
	Abnormal	2.6337	2.1022	
Creatinine clearance	Normal	50.459	15.73168	0.000
	Abnormal	39.7959	19.45492	

The variables serum creatinine and creatinine clearance were correlated with RCDW on admission and at 48 hrs. This investigation found that the cohort's serum creatinine level was significantly higher upon admission and 48 hours later. Also, creatinine clearance was significantly higher upon admission and 48 hours after screening. A statistically significant correlation was noted between serum creatinine and creatinine clearance with RDW on admission, with a P value of 0.005 and 0.002, respectively. Also, a significant correlation (P=0.000) was noted between creatinine clearance and RDW at 48 hours. We observed no significant correlation between serum creatinine and RDW at 48 hrs (P=0.046) (Table 5).

DISCUSSION

A variety of factors causes sepsis, a potentially fatal condition characterised by multiple organ failure, and it is monitored and treated in the intensive care unit. In sepsis, the kidney is one of the most commonly attacked organs.[2] Acute Renal failure/Acute kidney injury is a common medical problem associated with higher mortality, extended hospital stays, and the possibility of developing chronic kidney disease.[10] It is a syndrome of several clinical symptoms brought on by abrupt renal malfunction and is associated with an underlying illness. Sepsis and septic shock, which account for more than 50% of AKI cases in the ICU, are the most frequent causes of AKI in patients with critical illnesses. In various epidemiological studies, AKI occurs in 11–60% of sepsis patients, 23% of severe sepsis patients, and 51–64% of septic shock patients. Sepsis-Associated AKI (SA-AKI) is AKI occurring in critically ill sepsis patients in the intensive care unit. Sepsis accounts for 45%–70% of all AKI cases in the ICU. Despite the advancement of supportive care technologies, the morbidity and death rate of SA-AKI is still extremely high. An improved understanding of prognostic biomarkers will enhance the disease outcomes for patients with SA-AKI in the ICU.[11-13]

Investigations correlating serum creatinine, creatinine clearance and red cell distribution width in sepsis-associated acute renal failure in the ICU setting in the Indian population are sparse. Hence, this study intended to test the prognostic value of the above biomarkers as independent predictors of AKI associated with sepsis. In our study, red cell distribution width was observed normal level (12-15%) among 38.4% of the study population mean, while abnormality (>15%) was seen among 61.6% of the study population, and the mean RDW was 16.06 mL/min.

Many observational studies have found a link between increased RDW and changes in inflammatory biomarkers. As a result, the systemic inflammatory response most likely contributes to the putative association between RDW and mortality in critically ill patients with AKI; however, the precise mechanisms underlying these relationships are unknown.[14,15] A prospective, single-centre investigation examined the ability of RDW and five different prognostic scoring models to predict 30-day death in adult patients admitted to ICUs with AKI requiring dialysis. Thirty consecutive AKI patients were studied. RDW (%) amongst non-survivors was 15.58, while its mean value was 14.26 amongst survivors. In an adult AKI patient admitted to ICU with a requirement for renal replacement therapy (RRT), red blood cell distribution width predicts death better than other disease severity rating methods.[16] Wang et al., in a multivariate analysis, investigated the impact of RDW on prognosis for 14,078 critically ill patients with AKI.

A high RDW is linked to increased mortality (RDW 15.7-21.2% versus 11.1-13.4%).[17]

Kara et al. retrospectively investigated the records of 120 patients for the effect of RDW on AKI in sepsis patients admitted to the ICU. The cohorts were divided into two groups based on RDW group 1 (RDW≥16.8) and group 2 (RDW<16.8). 57.5% were male, and 42.5% were female. The mean age of the patients was 50.18 ±14.36 years. In contrast, we noted female predominance and a mean age of 57.57±14.264 years. A statistically significant relationship between AKI and RDW (p<0.001) follows the results of the present study. The study concluded that elevation in RDW is associated with the increased risk of developing AKI.[2]

In their investigation of the association of RDW with kidney function tests, Lippi reported a mean age of 61±13 years (range 35–95 years) and a mean RDW of 13.4±1.3 % (range 11.2–28%). Our study found a mean age of 57.57±14.264 years and a mean RDW of 16.06±2.663 (range 12.60 – 29.60). They found a strong correlation between increased RDW and a decline in kidney function. In our study, we found a similar association. Increased RDW (>15 %) was noted in higher serum creatinine at admission and after 48 hrs. Also, abnormal RDW was associated with varying degrees of creatinine clearance impairment.[15]

Rameries et al. conducted a retrospective analysis of 849 critically sick sepsis patients in the intensive care unit to assess the relationship between red blood cell distribution width and acute renal disease in sepsis. A male preponderance, higher mean age, and higher levels of creatinine and RDW were noted in the AKI group. In their investigation, RDW was found to be independently associated with sepsis-induced acute renal disease, similar to our findings.[3]

Zhang et al. 2018 published a study on the clinical utility of RDW in the early prediction of acute kidney damage in children with sepsis. According to the presence or lack of AKI, 126 children with sepsis were separated into two groups: AKI (n=66) and non-AKI (n=60). According to the mean RDW, these patients were divided into high-RDW and low-RDW groups. The AKI group had significantly higher creatinine and RDW levels than the non-AKI group. High-RDW group had significantly higher creatinine. Parallel to our findings, these researchers discovered that RDW had clinical utility in the early prediction of AKI in children with sepsis.[18]

From January 2011 to December 2016, Gong et al. studied 196 sepsis patients admitted to the intensive care unit (ICU). They observed that the change in RDW values during hospitalisation was linked to worse outcomes in sepsis patients. Elevated RDW predicts the progression of sepsis and a poor prognosis.[19]

Magal et al., in their investigation, observed varied results in their analysis of RDW with outcomes among AKI patients in critical care settings. Their prospective observational cohort study included 207

adult AKI patients between May 2021 and May 2022 in the various ICUs in a tertiary care hospital in India. Although RDW was high in the mortality group, the researchers opined that its predictive value was inferior to the often-used SOFA score in ICU. So, the researchers concluded that Although RDW cannot be used as an independent variable to predict mortality, they do have the potential to be part of a bigger score to predict death among AKI patients in ICU.[20]

There were some potential limitations to our investigation. The sample size of 159 people may not be large enough to validate the findings. Additional biomarkers might have improved our understanding of RDW behaviour in AKI in critical conditions. Further, it being a single-centre trial with no researcher intervention or sequential RDW analysis limits its potential applicability to clinical settings.

CONCLUSION

According to the clinical findings, this study observed a strong and independent association of red cell distribution width with sepsis-associated acute renal disease. One of the study's unique advantages is that it is relatively cheap and based on routine blood tests for critically ill patients admitted to the emergency room. Red cell distribution width can be employed as a low-cost diagnostic for sepsis-related acute renal disease in the emergency department, and large-scale research should be done to determine the true predictive value of red blood cell distribution width.

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