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RESEARCH ARTICLE
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STUDY OF RED BLOOD CELL DISTRIBUTION WIDTH AND NEUTROPHIL-TO- LYMPHOCYTE RATIO IN PREDICTING ADVERSE OUTCOMES OF ACUTE KIDNEY INJURY IN HOSPITALISED PATIENTS

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INTRODUCTION

Acute kidney injury (AKI), formerly referred to as acute renal failure (ARF), signifies a rapid and frequently reversible decline in renal function, as assessed by glomerular filtration rate (GFR).(1,2) KIDGO defines acute kidney injury (AKI) as a rise in serum creatinine of 0.3 mg/dl or more (26.5 micromoles/L or more) within 48 hours, an increase in serum creatinine to 1.5 times or more of baseline within the preceding seven days, or urine output of less than
0.5 mL/kg/h for at least six hours. The predominant causes of acute kidney injury (AKI) are acute tubular necrosis (ATN) at 45%, prerenal disease at 21%, urinary tract obstruction at 10%, glomerulonephritis or vasculitis at 4%, acute interstitial nephritis (AIN) at 2%, and atheroemboli at 1%.

The clinical manifestations of acute kidney injury (AKI) include azotemia, anuria, oliguria, tachycardia, orthostatic hypotension, and diminished jugular venous pressure (JVP). The consequences of acute kidney injury (AKI) include hyperkalemia, pulmonary edema, and metabolic acidosis. The risk factors for acute kidney injury (AKI) encompass diabetes mellitus, hypertension, chronic liver disease, chronic obstructive pulmonary disease (COPD), shock, and sepsis.

The present diagnostic method for AKI relies on a sudden reduction in GFR, shown by an abrupt elevation in sCr levels and/or a decrease in urine production within a certain time frame. Regrettably, the clinical forecasting of AKI progression continues to provide a problem. Recently identified serum and urinary biomarkers for kidney injury, including neutrophil gelatinase-associated lipoprotein, angiotensinogen, and liver-type fatty acid-binding protein, can facilitate the early diagnosis of acute kidney injury (AKI). Nonetheless, the majority of these biomarkers necessitate

well-controlled conditions and are limited to specific populations. Consequently, they are not extensively utilized at present. Inflammation and immunological response significantly contribute to the pathogenesis and development of acute kidney injury (AKI).(3) Inflammatory markers such as white blood cell count, red blood cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) are significant in forecasting the onset of acute kidney injury (AKI).

Red cell distribution width (RDW) is a metric that assesses variations in circulating red blood cell volume; historically, its therapeutic application was confined to the differential diagnosis of anaemia.(4–6) An elevated RDW was deemed strongly correlated with the probability of unfavourable outcomes in patients with cardiovascular illnesses and multiple myeloma.The neutrophil lymphocyte ratio (NLR), an indicator of host inflammation obtained by dividing neutrophil counts by lymphocyte counts, may have the capacity to predict survival across various human malignancies.(7) RDW has been observed to correlate with deteriorating renal function and negative outcomes in CKD patients. No research has examined routine blood measures in patients with acute kidney injury (AKI). Consequently, our study aimed to investigate the link between RDW and the incidence of AKI in hospitalized patients. Furthermore, we investigated the correlation between RDW and NLR in hospitalized patients with AKI.

MATERIALS AND METHODS

This was a cross-sectional study conducted in a tertiary level hospital in South India among 92 patients with AKI. The study was initiated following the approval from the institutional ethical committee and after obtaining informed written consent from the study participants. All AKI patients between the age of 18 to 89 years with decreased urine output and serum creatinine more than 0.3mg/dl were included in the study. The exclusion criteria included patients who had maintenance renal replacement therapy, patient with CKD stage 5, history of nephrectomy or solitary kidney, kidney transplantation, baseline serum creatinine levels less than 40 µmol/l and haematological malignancy.

The data was collected using Microsoft 365 Excel and analyzed using SPSS v27.0. The normality test (Shapiro-Wilk Test) was performed to analyze the data, and the results were expressed as frequency with percentage and mean with standard deviation or median with interquartile range. Association between categorical variables was assessed using Chi-square test or Fisher's exact test. All the statistical analyses were carried out at a 5% level of significance, and results with the P value < 0.05 were considered statistically significant.

RESULTS

In this study majority of the subjects were males (59.8%). Females constituted 40.2% of the study subjects. In this study majority of the subjects belonged to stage 1 (62.0%), followed by stage 2 (28.3%) and stage 3 (9.8%) (Table 1).

Table 1: Distribution of AKI staging of the study population

Stages of AKI	Frequency	Percentage
Stage 1	57	62.0
Stage 2	26	28.3
Stage 3	9	9.8
Total	92	100.0

In this study there was significant association between mean ALC and AEC and various stages of AKI. It was found that ALC and AEC decreased with an increase in stages of AKI and this

difference in the mean values were statistically significant. In this study there was no significant association between total WBC, mean ANC, mean AMC, mean ABC and various stages of AKI even though these values showed a diminishing pattern with increase in stages of AKI (Table 2).

Table 2: Association between stages of AKI and mean hematological parameters in the study population.

	AKI Stage	N	Mean	Std. Deviation	95% Confidence Interval for Mean		P Value
					Lower Bound	Upper Bound	
TOTAL WBC	1	57	8969.30	2586.99	8282.88	9655.72	0.500
	2	26	8851.54	2538.88	7826.06	9877.02	
	3	9	7897.78	2035.53	6333.13	9462.43	
	Total	92	8831.20	2520.28	8309.26	9353.13	
ANC	1	57	5618.97	1712.78	5164.50	6073.43	0.233
	2	26	6308.82	1956.76	5518.46	7099.17	
	3	9	5490.94	1744.29	4150.16	6831.72	
	Total	92	5801.40	1796.83	5429.28	6173.51	
ALC	1	57	2811.02	974.50	2552.45	3069.59	<0.001*
	2	26	2046.77	935.49	1668.91	2424.62	
	3	9	1756.82	543.38	1339.14	2174.50	
	Total	92	2491.90	1012.23	2282.28	2701.53	
AEC	1	57	354.62	334.05	265.98	443.25	0.016*
	2	26	181.06	119.86	132.65	229.48	
	3	9	178.55	113.36	91.41	265.69	
	Total	92	288.35	284.57	229.41	347.28	
AMC	1	57	329.16	152.74	288.63	369.69	0.067
	2	26	276.92	202.02	195.32	358.52	
	3	9	435.18	223.67	263.25	607.11	
	Total	92	324.77	178.43	287.81	361.72	
ABC	1	57	50.90	56.06	36.02	65.77	0.405
	2	26	35.10	50.37	14.75	55.44	
	3	9	36.26	42.66	3.47	69.05	
	Total	92	45.00	53.37	33.95	56.05	

*p value <0.05; Hence statistically significant

.In this study there was significant association between NLR and various stages of AKI. It was realized that NLR increased with increasing stages of AKI, and this was statistically significant (p <0.001). Similarly, RDW also showed a similar pattern with an increase in stages of AKI. This difference was also statistically significant (p = 0.022) (Table 3).

Table 3: Association between stages of AKI and mean NLR and RDW

	Stage	N	Mean	Std. Deviation	95% Confidence Interval for Mean		P value
					Lower Bound	Upper Bound	
NLR	Stage 1	57	2.12	.67	1.94	2.30	<0.001*
	Stage 2	26	3.45	1.80	2.73	4.18	
	Stage 3	9	4.05	1.95	2.55	5.55	
	Total	92	2.69	1.43	2.39	2.98	
RDW	Stage 1	57	13.28	1.87	12.78	13.77	0.022*
	Stage 2	26	13.80	2.25	12.89	14.71	
	Stage 3	9	15.27	2.169	13.60	16.94	
	Total	92	13.62	2.078	13.19	14.05	

*p value <0.05; Hence statistically significant

This study also found significant association between platelet count and various stages of AKI, with platelet count decreasing with increase in the various stages of AKI. Similar findings were obtained for mean platelet volume in which MPV increased with increase in stages of AKI. This difference was statistically significant. In this study, RBC, Hb and PCV didn't show any significant association with increase in stages of AKI.

Table 4: Association between stages of AKI and mean blood parameters of the study participants.

		N	Mean	Std. Deviation	95% Confidence Interval for Mean		P value
					Lower Bound	Upper Bound	
PLATELET	Stage 1	57	305052.65	89668.11	281260.50	328844.80	0.004*
	Stage 2	26	252269.23	60722.68	227742.81	276795.65	
	Stage 3	9	227444.44	90323.18	158015.90	296872.99	
	Total	92	282543.49	86934.40	264539.88	300547.09	
MPV	Stage 1	57	9.98	1.82	9.50	10.46	<0.001*
	Stage 2	26	12.02	1.92	11.24	12.79	
	Stage 3	9	12.07	2.07	10.48	13.67	
	Total	92	10.76	2.10	10.32	11.20	
RBC	Stage 1	57	4.59	0.79	4.38	4.80	0.540
	Stage 2	26	4.37	1.09	3.93	4.81	
	Stage 3	9	4.61	0.72	4.06	5.17	
	Total	92	4.53	0.87	4.35	4.71	
Hb	Stage 1	57	12.38	2.75	11.65	13.11	0.738
	Stage 2	26	12.36	2.37	11.40	13.32	
	Stage 3	9	13.07	1.59	11.84	14.30	
	Total	92	12.44	2.54	11.91	12.97	
PCV	Stage 1	57	37.16	7.40	35.20	39.13	0.823
	Stage 2	26	37.74	6.73	35.02	40.46	
	Stage 3	9	38.63	4.77	34.96	42.30	
	Total	92	37.47	6.95	36.03	38.91	

*p value <0.05; Hence statistically significant

Urea and creatinine increased with increased stages of AKI. This is an obvious finding and this increase was statistically significant as well. Considering outcomes of the study, it was found that NLR was significantly elevated in those who had death in this study, compared to those who

got better and discharged. This difference was statistically significant. Similarly RDW was also found to be elevated in individuals who succumbed to death and this difference in RDW was also statistically significant.

Table 5: Association between outcome and mean NLR and RDW

		N	Mean	Std. Deviation	95% Confidence Interval for Mean		P value
					Lower Bound	Upper Bound	
NLR	Death	9	5.36	1.85	3.93	6.79	<0.001*
	Discharged	83	2.40	1.04	2.17	2.62	
	Total	92	2.69	1.43	2.39	2.98	
RDW	Death	9	15.13	1.69	13.83	16.42	0.021*
	Discharged	83	13.46	2.05	13.01	13.91	
	Total	92	13.62	2.07	13.19	14.05	

*p value <0.05; Hence statistically significant

DISCUSSION

Inflammation and immune response play an important role in pathophysiology and progression of AKI. Inflammatory parameters like WBC count, red blood cell distribution width(RDW), neutrophil-to-lymphocyte ratio(NLR), platelet- to lymphocyte ratio(PLR) are important in predicting development of AKI.

Lympopenia occurs when the number of white blood cells (neutrophils) increases due to an increase in endogenous cortical catecholamines, which happens in reaction to physiological stressors such inflammation or infection.(8,9) Thus, NLR may rise in response to physiological stress, suggesting a systemic stress response. NLR shows a reaction before total WBC and a left shift on WBC differential analysis, and it quickly rises within 6 hours following physiological stress.(10,11) In addition to its use as a prognostic indicator, NLR has helped differentiate between moderate and severe diseases. As an example, NLR was found by Hajibandeh et al. to be a useful diagnostic tool for appendicitis in patients presenting with right lower quadrant pain, both for early diagnosis and severity detection.(12) Yazar claims that regular diagnostic methods should be improved to better detect appendicitis in pregnant women by adding NLR and platelet-to-lymphocyte ratio.(13)

The mean age of the study population was 50.90 ± 15.01 years. In the study conducted by Jia et al., the mean age of the study population was 63.4 ± 16.2 years. In the study conducted by Chen et al., the mean age of the study population was 68.1 ± 16.6 years. In this study majority of the subjects were males (59.8%). In the Jia et al., study also majority of the subjects were males (58.3%).

In this study majority of the subjects belonged to stage 1 (62.0%), followed by stage 2 (28.3%) and stage 3 (9.8%). In the Jia et al., study the subjects were almost equally divided with respect to the AKI stages. In their study 30.4% belonged to stage 1, 37.2% belonged to stage 2 and 32.4% belonged to stage 3 of the study population.

In the study death occurred among 9 study subjects (9.8%) and 83 subjects (90.2%) got better and was later discharged from the hospital. In the Jia et al., study almost 43.6% of the patients suffered death due to the complications associated with AKI.

In this study the mean NLR was 2.69 ± 1.43 and the mean RDW was 13.62 ± 2.07%. In the Hu et al., study the mean RDW was found to be 13.7 ± 1.5% and ranged between 11.0% to 25.3%. In the study conducted by Chen et al., the mean NLR was found to be on the higher side in the range of 14.9 ± 17.8

In this study it was found that ALC and AEC decreased with an increase in stages of AKI and also

NLR increased with increasing stages of AKI. In the study conducted by Chen et al., the AKI progression was significantly associated with increased NLR values with an odds ratio of 1.38. Similarly, RDW also showed similar pattern with an increase in stages of AKI. RDW is a common parameter for evaluation of anaemia and inflammation. In recent years, much attention has been paid to the relationship between renal function and RDW. The same relationship was also found in the study conducted by Jia et al., in which they found that at various AKI stages, the RDW also increased, and the increase was statistically significant. After adjusting for comorbidities, Ujszaszi et al. found that a lower eGFR was associated with an increased RDW in a cross-sectional study of 723 kidney transplant recipients.(14)

This study also found significant association between platelet count and various stages of AKI, with platelet count decreasing with increase in the various stages of AKI. Similar findings were obtained for mean platelet volume in which MPV increased with increase in stages of AKI.

It was found that NLR was significantly elevated in those who had death in this study, compared to those who got better and discharged. In the Chen et al., study significant association was found between higher values of NLR and hospital mortality with an odds ratio of 1.18.

Similarly, RDW was also found to be elevated in individuals who succumbed to death and this difference in RDW was also statistically significant. In the Jia et al., study, death rates increased from the low RDW group to the high RDW group for all patients and concluded that RDW predicted long-term prognosis better than conventional severity scales. Patients with AKI who were treated with extracorporeal membrane oxygenation or who had sepsis-induced showed correlation between reduced RDW and good survival rate.(15) The usefulness of RDW in predicting the likelihood of CI-AKI was only examined in limited trials. Based on the results of multivariate logistic regression, Akin et al., indicated that RDW was an independent predictor of CI-AKI in a cross-sectional study of 630 patients who had primary percutaneous coronary intervention after an ST-segment-elevation myocardial infarction.(16) Another research by Mizuno et al., came to a similar result.(17)

CONCLUSION

Red blood cell distribution width and neutrophil-to-lymphocyte ratio are important biomarkers for assessing acute kidney injury severity and prognosis in hospitalized patients. As AKI severity increases, mean RDW and NLR levels rise. This correlation suggests that these hematological parameters may identify high-risk patients. RDW and NLR are practical risk stratification methods for AKI due to their accessibility and ease of measurement. These tests are effective in healthcare settings with limited resources because they can be done in labs with few resources. Elevated RDW and NLR values can predict mortality. Clinicians can improve early detection, therapeutic interventions, and patient outcomes by integrating RDW and NLR assessment into routine AKI management. This study emphasizes the importance of simple but powerful diagnostic markers in clinical decision-making, helping identify high-risk individuals and provide timely, targeted care.

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