NEUTROPHIL TO LYMPHOCYTE RATIO AND ACUTE KIDNEY INJURY IN CRITICALLY ILL PATIENTS.

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ABSTRACT:

Background: *ICU-acquired acute kidney injury (AKI) is a common complication with numerous risk factors. Inflammatory mediators play a major role in the development of AKI. Several studies suggested a link between the neutrophil to lymphocyte ratio (NLR) and the platelet to lymphocyte ratio (PLR) and the occurrence of AKI.*

Objectives: *Study a possible relationship between NLR and PLR and AKI prognosis and see if they could predict more adverse outcomes including renal replacement therapy (RRT) and mortality.*

Methods: *102 ICU patients with AKI were enrolled. Both CBC (to calculate NLR and PLR) and kidney function tests were performed at days 0,3,7 to study the relationship between NLR, PLR and eGFR and their correlation with the overall course of hospital stay and recovery.*

Results: *Regarding the ability to predict mechanical ventilation, NLR had a 96% sensitivity and 81% specificity while PLR had a 92% sensitivity and 89% specificity. Both ratios had similar sensitivity in predicting shock (98%), however NLR had lower specificity. Both NLR and PLR had similar sensitivity (96.2%) and specificity (73%,71.6% respectively) in predicting the need for dialysis during hospital stay. NLR had a 50% sensitivity and 25% specificity in prediction of mortality in comparison to 50% sensitivity and 39% specificity in PLR.*

Conclusion: *Both ratios had sufficient efficacy to predict need for mechanical ventilation, vasopressors, or dialysis. Both ratios had average accuracy in prediction of mortality.*

Keywords: *Acute kidney injury, Neutrophil to lymphocyte ratio, Platelet to Lymphocyte ratio.*

INTRODUCTION:

Acute kidney injury (AKI) is a rising and challenging problem for healthcare systems and that is frequently associated with more adverse outcomes [(1)].

Targeting the risk factors of AKI can improve the outcome greatly. Many factors such as severe sepsis, reduced renal blood flow, multi-system failure, nephrotoxic agents and cardiac surgery are associated with the occurrence of AKI [(2)].

Since AKI has a complex etiology, an optimum biomarker for early diagnosis of AKI has yet to be established. Many underlying pathological mechanisms have been established such as tubulointerstitial injury, glomerular injury and mixed injury [(3)].

Although massive efforts have been targeting the pathogenesis of AKI, there are yet many obstacles and the mortality of AKI patients remains high [(4)].

Neutrophil lymphocyte ratio and platelet lymphocyte ratio are common and easily obtained clinical indices that have the potential to be relatively good indicators for predicting bacteremia and are indicators of inflammatory response, particularly in intensive care units (ICU). Since inflammation plays a rather complicated role in the pathogenesis of AKI, both the NLR and PLR, both as inflammatory markers, have been targeted to detect their ability in predicting AKI(5).

AIM OF THE STUDY:

The aim of the study was to evaluate the ability of the Neutrophil to Lymphocyte ratio (NLR) and Platelet to Lymphocyte ratio (PLR)to relate to the prognosis of in acute kidney injury in adult patients with various etiologies and to evaluate their role in the prediction of both morbidity and mortality over a period of three months.

PATIENTS AND METHODS:

This study was a prospective study performed on 102 adult patients recently hospitalized in the ICU of Ain Shams University Hospitals and diagnosed with acute kidney injury due to different etiologies including sepsis, postoperative complications and drug nephrotoxicity.

AKI was defined according to KDIGO 2012 classification as an increase in serum creatinine by 0.3mg/dL or more within 48 hours or increase in serum creatinine up to 1.5 times baseline or more within the last 7 days or urine output less than 0.5 mL/kg/h for 6 hours.

Exclusion Criteria included the following:

1. Patients with CKD and defined as the following:

a. Patients with abnormalities in kidney structure or function for more than 3 months.

b. Presence of markers of kidney damage (one or more) such as albuminuria (albumin excretion rate {AER} >30 mg/24 hours; albumin creatinine ratio {ACR} >30 mg/g [>3 mg/mmol]), urine sediment abnormallities, electrolyte and other abnormalities due to tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging, history of kidney transplantation and decreased GFR <60 ml/min/1.73 m2 (GFR categories G3a–G5) (**KDIGO CKD,2012**)

2. Any causes of lymphopenia such as viral infections, autoimmune disease and drugs.

All involved subjects underwent:

1. Full history taking and complete physical examination
2. Laboratories investigations in the form of:

- Complete blood picture on days 0, 3,7 using a Coulter Counter (T660; Beckman Coulter, Brea, CA); where Neutrophil to lymphocyte ratio was equal to the absolute neutrophil count divided by the absolute lymphocyte count and Platelet to lymphocyte ratio was equal to the platelet count divided by the absolute lymphocyte count(6).
- BUN and Creatinine on days 0,3,7 assayed with a Synchron CX 9 autoanalyzer (Beckman Coulter, USA); while estimated glomerular filtration rate (eGFR) was calculated by using the 2021 CKD-EPI -Creatinine equation:

  $GFR = 141 * \min(Scr/\kappa,1)^{\alpha} * \max(Scr/\kappa, 1)^{-1.209} * 0.993^{Age} * 1.018$ [if female] * 1.159 [if black]Sodium, Potassium, Calcium, Phosphorous assayed using Beckman Coulter AU480 chemistry analyzer (Beckman Coulter, USA)
- CRP and PTH measured on a chemo luminescence analyzer (Cobas e411, Roche diagnostics, Switzerland)

- Urinalysis and urinary protein/Creatinine ratio

3. Pelvi-abdominal ultrasound was performed using the LOGIQ TM P9 ultrasound system by using convex arrays ultrasound probe, frequency 3-3.5 MHz to exclude any obstruction and with emphasis on kidney size, echogenicity and parenchymal thickness.

Ethical Considerations:

All participants signed an informed consent. This study was granted ethical approval by the Ain Shams University committee.

Statistical Analysis:

SPSS 22.0 was used for the statistical analysis of all data. Independent sample t-test was used to assess the statistically significant difference between two independent means of two study group, Pearson correlation coefficient(r) was used to measure the strength of a linear association between two quantitative variables and Chi square test was used to examine the relationship between two qualitative variables.

RESULTS:

This study included 102 ICU participants with AKI with mean age 50.1 ± 13.7 years. Most of the included patients were males. Seventy-four patients were hemodynamically unstable and mechanical ventilation was required for 28 patients ***(table 1).*** In our study, the majority of cases were admitted in the ICU due to major neurological insults (32%) followed by sepsis (26%) ***(figure 1).*** Prerenal AKI was diagnosed in 74 patients while 28 patients had renal causes of AKI. The commonest cause of reported AKI was sepsis and infection (63.7%) followed by drug nephrotoxicity (10.8%) and glomerulonephritis (10.8%) ***(figure 2)***. Mean value of serum creatinine was 2.5 ± 1.8 mg/ dL and eGFR was 48.3 ± 25.1 ml/ min/ 1.73m^2. Urinalysis was bland in 25.5% of patients. According to KDIGO classification of AKI, 66 patients had stage 1 AKI, 13 patients were stage 2 and 23 patients had stage 3 ***(table 2).*** As regards the outcome of AKI, 51% of the patients showed complete recovery while 45% showed partial recovery only 2% were maintained on regular hemodialysis ***(figure 3)***

Both NLR and PLR were higher among male patients ***(p< 0.001)***. NLR was higher among chronic liver disease patients ***(p< 0.001)***. Both ratios showed significant elevation among patients with shock ***(p< 0.001)***. Both ratios had the lowest values among patients who were admitted for renal causes and highest values in patients with hepatic affection ***(table 3).*** NLR varied greatly among the study population and was associated with different outcomes ***(figure 4).***There were also significant effects of hypertension, diabetes, and chronic liver disease on PLR. No significant correlation could be established between mechanical ventilation and PLR.

Both NLR and PLR were significantly higher in renal AKI in comparison to prerenal AKI. There was a statistically significant difference between different causes of AKI regarding NLR. The difference mainly was detected among sepsis related AKI patients ***(p= 0.006) (table 4)***. On discharge, there was statistically significant positive correlation between serum creatinine and PLR ***(p< 0.001) (table 5)***. Only NLR could correlate significantly with hemodialysis during hospital stay and the outcome of the patient ***(table 6).***

At a cutoff value of 2.9, NLR had a 96% sensitivity and 81% specificity in the prediction of mechanical ventilation while at cutoff value equal of 17.3, PLR had a 92% sensitivity and 89% specificity in the prediction of mechanical ventilation. At cutoff value equal to 1.2, PLR had a 98% sensitivity and 88% specificity in the prediction of shock ***(table 7).***

At a cutoff value of 1.2, NLR had a 96.2% sensitivity and 73% specificity in the prediction for the need of dialysis during hospital stay. At cutoff value of 11.3, PLR had a 96.2% sensitivity and 71.6% specificity in the prediction for the need of dialysis during hospital stay ***(table 7) (figure 5).***

At a cutoff value of 0.6, NLR had a 50% sensitivity and 68% specificity in prediction of full recovery. At cutoff value equal to 1.5, PLR had a 73% sensitivity and 84% specificity in prediction of full recovery ***(table 7).***

At a cutoff value equal to 0.44, NLR had a 50% sensitivity and 25% specificity in prediction of mortality while at cutoff value equal to 3.3, PLR had a 50% sensitivity and 39% specificity in prediction of mortality ***(table 7) (figure 6).***

Table (1): Demographics and baseline characteristics:

	Total cohort (n= 102)
Age (years)	50.1 ± 13.7
Sex No. (%)	
- Male	70 (68.6%)
- Female	32 (32.4%)
Associated medical disorders No. (%)	
- Hypertension	61 (59.8%)
- Diabetes	50 (49%)
- Chronic liver disease	28 (27.5%)
- Cardiac disease	44 (43.1%)
Causes of hospital admission No. (%)	
- Cardiovascular	27 (26.5%)
- Neurological	33 (32.4%)
- Nephrological	14 (13.7%)
- Hepatic	17 (16.7%)
- -Infection and Sepsis	11 (10.8%)
Critical condition No. (%)	
- Ventilation	28 (27.5%)
- Shock	74 (72.5%)

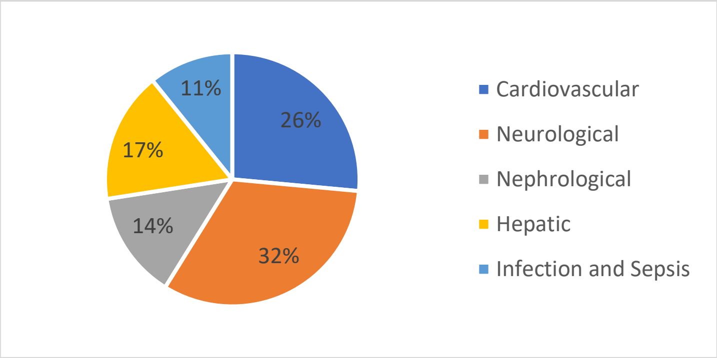

Figure (1): Causes of ICU admission

Table (2): Data related to diagnosis of acute kidney injury:

	Total cohort (n= 102)
Type of acute kidney injury No. (%)	
- Prerenal	74 (72.5%)
- Renal	28 (27.5%)
Cause of acute kidney injury No. (%)	
- Drug related	11 (10.8%)
- Sepsis	65 (63.7%)
- Rhabdomyolysis	7 (6.9%)
- Glomerulonephritis	11 (10.8%)
- Hemolytic uremic syndrome	6 (5.9%)
- Hepatorenal syndrome	2 (2%)
Urine output (mL/ 24 hours)	995.5 ± 383.4
S. creatinine (mg/dL)	2.5 ± 1.8
Urea (mg/dL)	169.2 ± 97.4
Urinary protein/ creatinine ratio (g/mg)	1.3 ± 0.12
eGRF (ml/min/1.73m^2)	48.3 ± 25.1
Urine analysis:	
- Bland	26 (25.5%)
- Pus	36 (35.3%)
- Albumin	8 (7.8%)
- RBCs	4 (3.9%)
- Albumin + pus	21 (20.6%)
- Albumin+ Pus + RBCs	7 (6.9%)
Abdominal ultrasonography	
- Normal	95 (93.1%)
- Grade 1 echogenicity	5 (4.9%)
- Nephrolithiasis	2 (1.9%)
Acute kidney injury stage	
- AKI stage1	66 (64.7%)
- AKI stage2	13 (12.7%)
- AKI stage3	23 (22.5%)

eGRF: estimated glomerular filtration rate, AKI: acute kidney injury

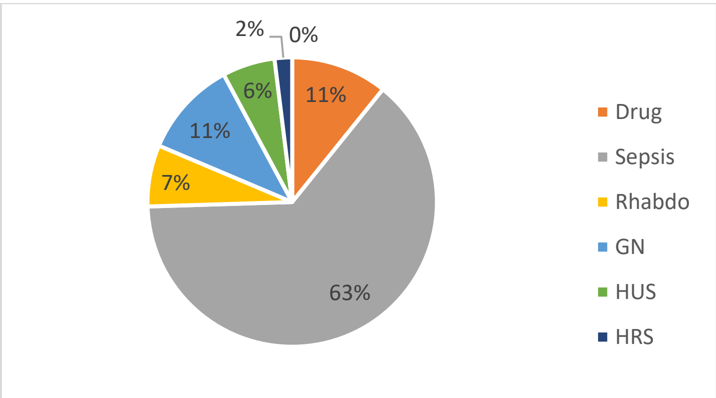

Figure (2): Causes of AKI

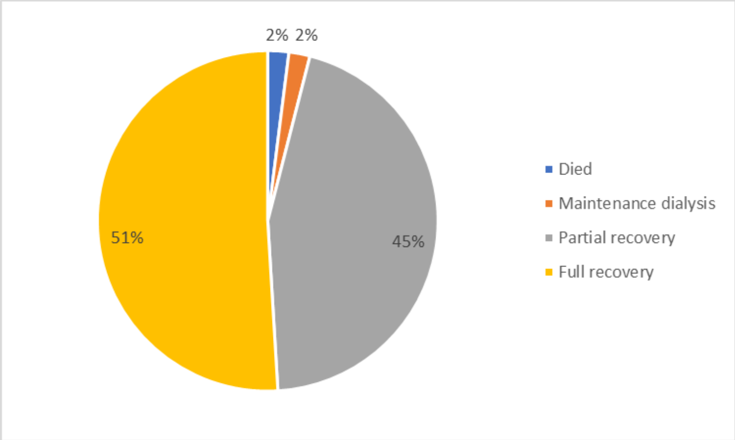

Figure (3): Final outcomes of ICU patients

Table (3): Neutrophil/ lymphocyte ratio, Platelet/ lymphocyte ratio and baseline data:

		NLR		PLR	
		Mean ± SD	p-value (t)	Mean ± SD	p-value (t)
Sex	Male	1.3 ± 0.3	***<0.001****	19.6 ± 7.6	***<0.001***
	Female	0.7 ± 0.35		5.8 ± 2.7	
Hypertension	No	1.1 ± 0.3	0.44*	24.4 ± 11.1	0.24
	Yes	1.1 ± 0.1		9.5 ± 1.2	
Diabetes	No	1.1 ± 0.2	0.49*	7.5 ± 3.5	0.54
	Yes	1.1 ± 0.15		23.6 ± 11.9	
Liver disease	No	0.9 ± 0.4	***<0.001****	33.2 ± 12.7	***<0.001***
	Yes	1.7 ± 0.8		8.5 ± 1.1	
Cardiac disease	No	0.9 ± 0.4	0.34*	17.7 ± 8.4	0.9
	Yes	1.3 ± 0.7		12.3 ± 3.9	
Mechanical ventilation	No	1.2 ± 0.6	***<0.001****	18.5 ± 7.4	0.07
	Yes	0.8 ± 0.3		7 ± 3.5	
Shock	No	0.6 ± 0.3	***<0.001****	17.3 ± 8.9	***<0.001***
	Yes	1.6 ± 0.7		13.4 ± 1.3	
Cause of admission	Cardiovascular	0.9 ± 0.4	***<0.001 *****	5.8 ± 2.6	0.75 **
	Neurological	1.5 ± 0.6		4.1 ± 2.1	
	Hepatic	2.8 ± 1.8		3.9 ± 1.7	
	Renal	0.2 ± 0.1		0.4 ± 0.03	
	Infection & sepsis	0.6 ± 0.3		0.6 ± 0.3	

*: Paired r- test; **: analysis of variance (ANOVA) test; level of significance < 0.05
NLR: Neutrophil /Lymphocyte ratio , PLR: Platelet /Lymphocyte ratio

Table (4): Relationship between both ratios and acute kidney injury parameters:

		NLR		PLR	
		Mean ± SD	p-value	Mean ± SD	p-value
Type of acute kidney injury	Prerenal	1.4 ± 0.3	***<0.001 ****	19.8 ± 7.4	***0.014 ****
	Renal	0.5 ± 0.2		3.76 ± 1.8	
Causes of acute kidney injury	Drug related	0.8 ± 0.07	***0.006 *****	3.3 ± 0.6	0.86 **
	Sepsis	1.4 ± 0.7		2.2 ± 0.7	
	Rhabdomyolysis	0.5 ± 0.03 a, b		3.1 ± 0.2	
	Glomerulonephritis	0.27 ± 0.1a, b		2.1 ± 0.5	
	Hemolytic uremic syndrome	0.6 ± 0.09 b		3.1 ± 1.1	
	Hepatorenal syndrome	0.3 ± 0.1		2.7 ± 1.3	
Acute kidney injury at day 0	AKI stage1	1.3 ± 0.2	***<0.001 *****	10.9 ± 5.2	0.63**
	AKI stage 2	1.18 ± 0.3		8.68 ± 4.1	
	AKI stage 3	0.4 ± 0.2 a		10.3 ± 3.1	
Acute kidney injury at day 3	AKI stage 1	0.7 ± 0.1	0.08 **	15.3 ± 5.3	0.89 **
	AKI stage 2	1.6 ± 1.1		20.8 ± 2.3	
	AKI stage 3	0.9 ± 0.4		14.3 ± 6.3	

*: Paired t- test; **: analysis of variance (ANOVA) test, AKI: acute kidney injury

Table (5): Correlation analysis of renal function at different time points to neutrophil/ lymphocyte ratio and platelet/lymphocyte ratio:

	NLR		PLR	
	R	P value	R	P value
Day 0				
S. creatinine	-0.23	*0.018*	-0.007	0.94
Urea	-0.25	*0.011*	0.035	0.73
Urinary protein/ creatinine ratio	-0.23	*0.02*	-0.043	0.67
eGRF	0.63	*<0.001*	-0.025	0.8
Sodium	0.14	0.16	0.09	0.37
Potassium	0.12	0.25	-0.19	0.05
Albumin	-0.1	0.3	-0.009	0.93
Calcium	-0.5	*<0.001*	-0.13	0.2
Phosphorus	-0.082	0.4	-0.014	0.9
intact PTH	-0.35	*<0.001*	-0.04	0.6
ESR	0.18	0.06	-0.029	0.77
Platelets/ lymphocyte ratio	0.06	0.53	0.063	0.53
Neutrophil/platelet/lymphocyte ratio	0.75	*<0.001*	-0.009	0.93
Day 3				
S. creatinine	0.01	0.9	0.11	0.3
eGRF	0.035	0.7	-0.043	0.67
Platelets/ lymphocyte ratio	-0.11	0.25	-0.13	0.2
Neutrophil/platelet/lymphocyte ratio	-0.04	0.7	-0.02	0.8
Day of discharge				
S. creatinine (discharge)	-0.1	0.2	0.33	*<0.001*
eGRF (discharge)	0.075	0.4	-0.13	0.2
Platelets/ lymphocyte ratio	0.15	0.13	-0.093	0.35

*Pearson Correlation; r: Correlation coefficient; Level of significance< 0.05
NLR: Neutrophil /Lymphocyte ratio, PLR: Platelet /Lymphocyte ratio
PTH: Parathyroid hormone, ESR: Erythrocyte Sedimentation Rate

Table (6): Relationship between neutrophil/ lymphocyte and platelet/ lymphocyte ratio to dialysis and outcome of patients:

		NLR		PLR	
		Mean ± SD	P value	Mean ± SD	P value
Dialysis during stay	No	1.3 ± 0.3	***<0.001 ****	19.33 ± 7.4	0.19
	Yes	0.5 ± 0.3		5.1 ± 2.4	
Outcome	Died	0.3 ± 0.1	***0.04 *****	2.3 ± 1.1	0.74
	Maintenance dialysis	0.5 ± 0.2		2.7 ± 0.15	
	Partial recovery	0.8 ± 0.3a, b		2.3 ± 0.9	
	Full recovery	0.9 ± 0.4a, b, c		2.4 ± 1.2	

*: Paired t -test; **: analysis of variance (ANOVA) test; Level of significance < 0.05

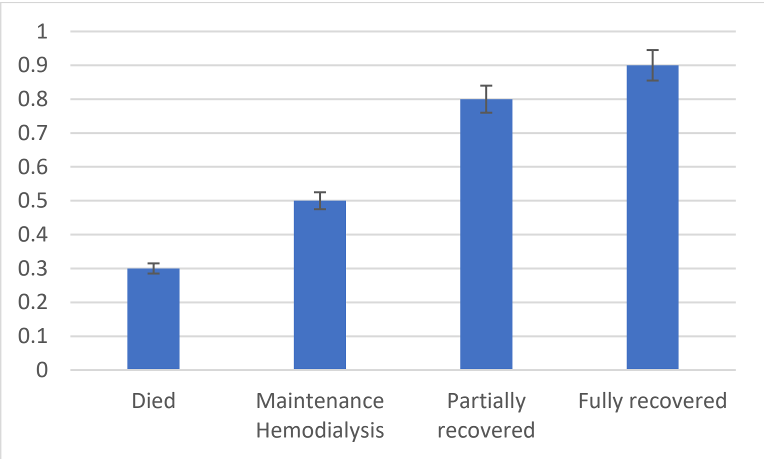

Figure (4): NLR between the different outcomes

Table (7): Accuracy of studied ratios in the prediction of mechanical ventilation, shock, need for hemodialysis and full recovery of AKI patients:

Accuracy of different ratios in the prediction of mechanical ventilation for acute kidney injury among hospitalized AKI patients							
	Cut off	Sensitivity	Specificity	95% confidence interval		Area under curve	P value
				Lower	Upper		
Neutrophil/ lymphocyte ratio	2.9	96%	81%	0.377	0.609	0.49	0.9
Platelet/ lymphocyte ratio	17.3	92%	89%	0.429	0.671	0.55	0.4
Accuracy of different ratios in the prediction of shock for acute kidney injury among hospitalized AKI patients:							
	Cutoff	Sensitivity	Specificity	95% confidence interval		Area under curve	P value
				Lower	Upper		
Neutrophil/ lymphocyte ratio	0.21	98%	76.5%	0.694	0.869	0.78	<0.001
Platelet/ lymphocyte ratio	1.2	98%	88%	0.674	0.86	0.76	<0.001
Accuracy of different ratio in the prediction of the need for hemodialysis during hospital stay among hospitalized AKI patients							

	Cutoff	Sensitivity	Specificity	95% confidence interval		Area under curve	P value
				Lower	Upper		
Neutrophil/ lymphocyte ratio	1.2	96.2%	73%	0.604	0.83	0.714	*<0.001*
Platelet/ lymphocyte ratio	11.3	96.2%	71.6%	0.526	0.77	0.653	*0.018*
Accuracy of different ratios in the prediction of full recovery among hospitalized AKI patients							
	Cutoff	Sensitivity	Specificity	95% confidence interval		Area under curve	P value
				Lower	Upper		
Neutrophil/ lymphocyte ratio	0.62	50%	68%	0.275	0.493	0.384	0.037
Platelet/ lymphocyte ratio	1.5	73%	84%	0.266	0.486	0.376	0.028
Accuracy of different ratios in the prediction of mortality among hospitalized AKI patients							
	Cutoff	Sensitivity	Specificity	95% confidence interval		Area under curve	P value
				Lower	Upper		
Neutrophil/ lymphocyte ratio	0.44	50%	25%	0.69	0.97	0.83	*<0.001*
Platelet/ lymphocyte ratio	3.3	50%	39%	0.54	0.91	0.73	*<0.017*

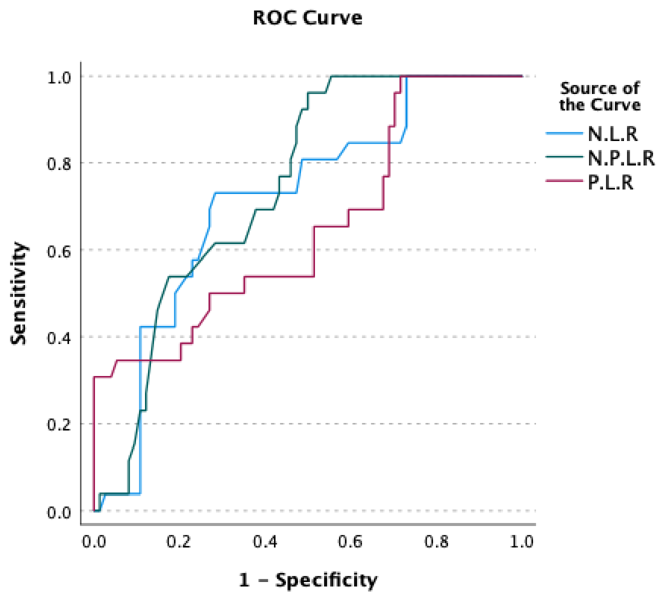

Figure (5): Analysis of the accuracy of both parameters in predicting the need for hemodialysis during hospital stay among hospitalized AKI patients

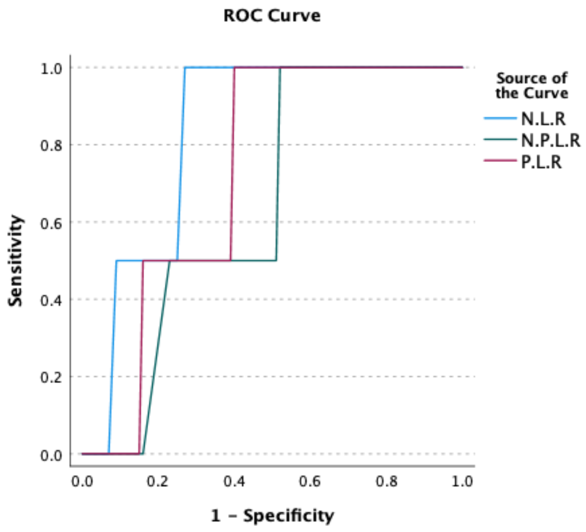

Figure (6): Analysis of the accuracy of both parameters in predicting mortality among hospitalized AKI patients

DISCUSSION:

AKI complicating ICU admission is considered a major player that can have a detrimental effect on mortality and morbidity. AKI unfortunately has a complex etiology that is diverse and multifactorial with many risk factors such as renal hypoperfusion, sepsis, nephrotoxicity drugs and urinary obstruction. These factors often result in tissue hypoxia, oxidative stress, triggering and activating the immune system and lastly often resulting cell death [(7)].

NLR as an inflammatory mediator that might affect the progression of diseases with an inflammatory background. Many studies proved a link between NLR and the outcome of sepsis, cancer and cardiac surgery [(8)].

Since many inflammatory mediators are incriminated in the development of AKI several authors studied neutrophil to lymphocyte ratio (NLR) to detect its ability to predict rather worse outcomes such as the need for RRT or even a more complicated hospital course in hospitalized AKI patients. Their results support the idea that NLR has the potential to play a diagnostic and prognostic role in inflammation-mediated conditions. However, till now, the validity and reliability of the results that imply the association between an elevated NLR and a rather adverse outcome remains contra-dictory [(9)].

Platelet-to-lymphocyte ratio (PLR) was assessed in several studies as a prognostic marker in a variety of clinical situations such as sepsis, myocardial ischemia, heart failure, gastrointestinal bleeding, pancreatitis, Chronic Obstructive Pulmonary Disease (COPD) exacerbation and diabetic ketoacidosis. However, fewer studies assessed the role of PLR in ICU patients and in AKI [(5)].

The study included 102 adult patients with mean age 50.1 ± 13.7 years. Most of the population were males (68.6%). 60% of AKI patients were hypertensive. Diabetes was reported in 49% of patients. About 43.1% of AKI patients had cardiac disease. Most of AKI patients in the present study were shocked (72.5%). About 27.5% of AKI patients were mechanically ventilated. A high percent of mechanically ventilated patients was reported among AKI patients in a study by Aylward [(10)]. Magboul et al., similarly stated that most of AKI patients were mechanically ventilated (75.6%) [(3)].

Sepsis was by far the most reported cause of AKI in our study (63.7%). Similarly, many studies reported sepsis as a main cause of AKI in hospitalized patients (6,7,1). About 10.8% of AKI cases in the current study were exposed to nephrotoxic medications. Similarly, Arogundade et al., also reported similar frequencies of drug related AKI [12].

Other reported causes of AKI, in the present study, were rhabdomyolysis (6.9%), GN 10.8%, HUS (5.9%) and hepatorenal syndrome (2%). Other previous studies also reported lower frequencies of rhabdomyolysis and GN among AKI hospitalized patients [13,14].

Mean values of estimated GFR at the time of diagnosis were 48.3 ± 25.1 ml/min/1.73m^2. In a study by Kim et al., proteinuria was present in 42.3% of AKI patients [11]. Among AKI patients 72.5% of the patients were due to a prerenal cause of AKI while 27.5% of patients were due to renal causes. Similar precents were obtained in a study by Aylward et al. [10]. KDIGO AKI stage 3 was reported in 22.5% of our patients, stage 2 in 12.7% of patients and stage 1 in 64.7% of patients at baseline. This changed after 3 days as most of the patients became stage 3 (78.4%).

In the present study, neutrophil/ lymphocyte ratio (NLR) did not differ significantly from day 0 (1.2 ± 0.19) to day 3 (0.88 ± 0.4) or the day of discharge (1.1 ± 0.6). In a study by Kim et al., NLR mean values among AKI patients after burn were 1.9 ± 1.2 with significant difference when compared to the non- AKI group. He reported NLR as a significant predictor for AKI [15]. Alfeilat et al., found higher NLR among AKI patients (11.7 ± 1.5) without significant difference when compared to the non- AKI group and NLR did not show dynamic changes from time of admission to time of AKI and then discharge [16]. Another study by Kim et al., reported a NLR value of 2.5 among AKI patients [15]. Parlar et al., showed that NLR among AKI patients was 3.3 ± 2.1 [17].

Bu et al., reported higher mean values of NLR among AKI patients (2.04 ± 1.16) yet with no significant dynamic changes between day of admission and day of maximum rise of serum creatinine [18]. Sun et al., also reported much higher NLR levels (4.2 ± 1.2) among AKI patients after PCI(percutaneous coronary intervention) for cardiac patients. He reported NLR as a significant predictor for AKI among cardiac patients [19]. Yaun et al., found higher NLR among AKI patients (8.08) with statistically significant difference when compared to non- AKI patients and significant dynamic changes from admission to peak serum creatinine and discharge. He reported that NLR is a significant predictor for AKI among cardiac patients [20]. Kurtul et al., delivered similar findings where NLR was above 3.46 and had a 73% specificity and 70% sensitivity for developing AKI among cardiac patients [21]. Also, Yilmaz et al., using a cut-off point of 10.15 for NLR, reported a sensitivity of 90.2% and a specificity 92.9% for predicting AKI in sepsis patients [22].

The current results showed that platelets/ lymphocyte ratio among AKI patients was 15.6 ± 6.4 and increased significantly at different time points reaching peak at discharge. Similar results by Sun et al., showed that among AKI patients, PLR mean values were 17.3 ± 6.2 [19]. Chen et al., found that PLR mean values were 11.5 ± 1.4 in sepsis induced AKI patients[23]. Also, Parlar et al., reported that PLR among AKI patients was 15.4 ± 3.1. He reported PLR as a significant predictor for AKI among cardiac patients with higher sensitivity and specificity than NLR. Zheng et al., reported higher PLR among AKI patients in the ICU (28.5 ± 2.56) [24]. Akin et al. established that patients with higher PLR values prior to contrast administration developed CIN (contrast-induced nephropathy) [25].

26 patients (25.5%) required renal replacement therapy while only 2 patients

continued hemodialysis. In the current study, we reported low mortality rate among hospitalized AKI patients (2%). In contrary, Aylward et al., reported about 31.8% mortality rate in his study [10]. Halle et al., also reported high mortality rates (36.9%) [1]. About 96.1% of patients in the present study were discharged with either partially or full recovery of renal function with mean serum creatinine 1.5 mg/ dL. Similar recovery rates were reported by Halle et al., (84.2% showed full recovery and 14.7% showed partial recovery) [1]. Lower frequency of recovery (86.7%) was reported in a study by Aylward et al., with mean serum creatinine 2.1 mg/dL[10].

Male patients had higher NLR at time of AKI with significant difference. Unlikely, Bu et al., did not find significant differences as regards NLR and gender [18].

The current results showed significant differences between patients who needed hemodialysis and those who did not as regards the NLR. In concordance to the current study, Kim et al., also found significant differences between patients who received dialysis and who did not[15]). Unlikely, Abu Alfeilat et al., did not find significant correlation between NLR and need for hemodialysis[16].

In our study, NLR showed significant differences between variable outcomes and had the ability to predict mortality and recovery. On the other hand, Bu et al., did not report NLR as significant predictor for mortality or recovery [18]. In addition, Abu Alfeilat et al., could not find significant correlation between NLR and the outcome of the patients [16].

In the present study, the accuracy of NLR was evaluated for the prediction of different outcomes. At a cutoff value 2.9, NLR had high sensitivity and specificity to predict need for mechanical ventilation. However, at best cutoff value, NLR had low sensitivity (50%) and specificity (68%; 25%) in prediction recovery or mortality. Better sensitivity (62.1%) and specificity (68.9%) of NLR at cutoff value 1.71 to predict the outcome was reported by Bu et al. [18]. Also, Sun et al., reported that a NLR cutoff of 2.9 or higher for the outcomes of AKI among cardiac patients with a sensitivity of 73.5% and a specificity of 70.4% [19].

Also, PLR correlation to different clinical and laboratory parameters was evaluated. Males had higher PLR with statistically significant difference. Similarly, Zheng et al., reported that male patients had higher PLR among males than females [24]. On the contrary, Jeon et al., could not find significant differences between males and females regarding PLR [5].

PLR correlated significantly to hypertension, diabetes, and liver diseases in the present study. Zheng et al., also reported significant differences between patients that had any of these diseases and patients who had not regarding PLR ratio [24].

There were no statistically significant differences between different AKI stages regarding PLR. This is against what was reported by Jeon et al., in Brazil who found higher ratios among sepsis induced AKI patients than other causes [5].

In our study PLR did not show significant difference between patients who received hemodialysis and who did not. On the other hand, Zheng et al., reported significant difference between patients who received hemodialysis and who did not regarding PLR [24]. Jeon et al., confirmed this finding and reported higher PLR among patients who received hemodialysis [5].

PLR did not have significant ability to predict the outcome of hospital- acquired AKI in the current study with no significant difference between mortality cases and patients who recovered. On the other hand, Chen et al., reported that PLR is a significant predictor for mortality among sepsis induced AKI patients [23]. Also, Zheng et al., found significant association between PLR and mortality among AKI cases in the ICU (24). Temiz et al., also claimed associated PLR with mortality in patients with AKI after myocardial infarction [26].

We evaluated the accuracy of PLR in the prediction of different outcomes. PLR had around 73% sensitivity and 84% specificity in prediction of recovery. Chen et al., reported similar sensitivity (70.7%) and specificity (65.4%) PLR values to predict AKI prognosis (24). Zheng et al., reported significant correlation between PLR and the need for vasopressors or mechanical ventilators [24]. Also, Jeon et al., found significant association between PLR and both the need for vasopressors and the need for mechanical ventilation [5].

The study had the advantages of being conducted on a relatively large sample size and included patients of variable causes of admission. The included patients had also variable causes of AKI and were of different AKI stages.

Some limitations included in the study were the absence of non- AKI control group and the effect of certain treatment modalities as some antibiotics or interventions on the studied markers was not investigated. Therefore, we recommend more studies involving a more diverse group of patients including non-AKI groups and with longer periods of follow up.

Conclusion

Both ratios had sufficient efficacy to predict need for mechanical ventilation, vasopressors, or dialysis. Both ratios had average accuracy in prediction of mortality. Platelet/ lymphocyte ratio had higher ability to predict recovery with higher sensitivity and specificity.

Authors' contributions

- Dr.Ashraf Okba and Dr Rasha Youssef designed and coordinated the roles of the participants and revised the manuscript.
- Dr. Eman Abdelsalam and Dr.Norhan Nagdi collected and analyzed the data and wrote the manuscript.
- All authors have read and approve the final manuscript. Funding and Conflict of interests.

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Conflict of interest

All authors declare that there is no conflict of interest.

List of Abbreviations:

ICU: Intensive care unit, AKI: Acute kidney injury, CBC: Complete Blood Count, NLR: Neutrophil m, /Lymphocyte ratio, PLR: Platelet /Lymphocyte ratio, RRT: Renal Replacement Therapy

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نسبه النيوتروفيل الى نسبه كرات الدم الليمفاويه واصابه الكلى الحاده في مرضى الحالات الحرجه

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الخلفيه:تعد إصابة الكلى الحادة المكتسبة من وحدة العناية المركزة من المضاعفات الشائعة مع وجود العديد من عوامل الخطروتلعب عوامل الالتهاب دورقوي كمسببات لاصابه الكلى الحاده. اقترحت العديد من الدراسات وجود علاقة بين نسبة النيوتروفيل إلى الخلايا الليمفاوية ونسبة الصفائح الدموية إلى الخلايا الليمفاوية وحدوث اصابه الكلى الحاده.

الأهداف: دراسه العلاقه المحتمله مابين نسبه النيوتروفيل الى الخلايا الليمفاويه ونسبه الصفائح الدمويه الى نسبه الخلايا الليمفاويه وحدوث الاصابه الكلويه ومعرفة اذا ما كان بإمكانهم التنبؤ بنتائج أكثر سلبية بما في ذلك العلاج التعويضي للفشل الكلوي.

الطرق: تم ادراج ١٠٢ مريض بالرعايه المركزه مصابين بقصور كلوي حاد وتم عمل صوره دم كامله وذلك لقياس نسبه النيوتروفيل الى الخلايا الليمفاويه ونسبه الصفائح الدمويه الى نسبه الخلايا الليمفاويه كما تمت متابعه وظائف الكلى في الأيام ٠، ١، ٣ وذلك لدراسه العلاقه بينهم وبين معدل الترشيح الكبيبي التقديري وارتباطهم بمسار الاقامه داخل المستشفى وبالشفاء.

النتائج: بخصوص القدره على التنبؤ بالتنفس الاصطناعي كانت الحساسيه والدقه لنسبه النيوتروفيل الى الخلايا الليمفاويه هي ٩٦ %و ٨١ % بالترتيب بينما كانت نسبه الحساسيه والدقه لنسبه الصفائح الدمويه الى نسبه الخلايا الليمفاويه هي ٩٢ % و ٨٩ % بالترتيب.

كان للنسبتين؛ نسبه النيوتروفيل الى الخلايا الليمفاويه و لنسبه الصفائح الدمويه الى نسبه الخلايا الليمفاويه قدره جيده على التنبؤ بهبوط الدوره الدمويه (٩٨ %) ولكن بدقه أقل لنسبه النيوتروفيل الى الخلايا الليمفاويه كماكان للمعدلين حساسيه جيده على التنبؤ بالاحتياج لجلسات الغسيل الكلوي خلال الاقامه بالمستشفى (٩٢ %) ودقه ٧٣ و ٧١.٦ % بالترتيب.

كان نسبه النيوتروفيل الى الخلايا الليمفاويه حساسيه ٥٠٪ ودقه ٢٥٪ بالنسبه للقدره على التنبؤ بالوفيات مقارنه ب ٥٠ % و ٣٩ % لنسبه الصفائح الدمويه الى نسبه الخلايا الليمفاويه.

الاستنتاج: كان للنسبتين قدره كافيه على التنبؤ بالاحتياج للتنفس صناعي أو للأدويه داعمه للضغط أو للغسيل كلوي بينما كانت لهما قدره متوسطه على التنبؤ بالوفاه.