Zagazig University Medical Journal
www.zumj.journals.ekb.eg

https://doi.org/10.21608/zumj.2024.234154.2873 Volume 30, Issue 1.6, September 2024, Supplement Issue
Manuscript ID:ZUMJ-2311-3024 (R2) DOI:10.21608/ZUMJ.2024.251854.3024.

ORIGINAL ARTICLE

Predictive Values of Hematological Indices in Detecting Cardiac Surgery-Associated Acute Kidney Injury

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Submit Date 28-11-2023
Revise Date 06-01-2024
Accept Date 10-01-2024

ABSTRACT

Background: Acute kidney injury (AKI) is a common complication following cardiac surgery. Studying the correlation between hematological indices and the occurrence of postoperative AKI following cardiac surgery seems to be important to predict the incidence of AKI and subsequently improving the outcome. We aimed to evaluate the potential utility of the hematological indices for predicting postoperative AKI in the background of cardiac surgery. **Methods:**This observational, cohort, prospective studywas conducted atCardiothoracic Department and ICU, Zagazig University Hospitals, Egypt, in the period from Jan. to Oct,2023, on 126 patients underwent cardiothoracic surgery. The patients were classified into group 1: (63 patients with no AKI after cardiac surgery) and group 2: (63 patients with AKI after cardiac surgery). The hematological ratios: neutrophil to lymphocyte ratio (NLR) and systemic immune-inflammation (SII) index were calculated. **Results:** In multivariate regression analysis, platelets (OR=0.95, p= 0.014), lymphocytes (OR=10.2, p=0.050), NLR (OR=0.28, p=0.044**)**, SII (OR=1.01, p=0.48), creatinine (OR=364.32, p=0.036), and BUN (OR=1.11, p=0.09) were significant predictors for AKI in patients who underwent valvular replacement. In multivariate regression analysis, BUN (OR=1.13, p=0.003) was a significant predictor for AKI in patients who underwent CABG. There is a correlation between increased NLR in the early postoperative stage and CSA-AKI.**Conclusion:**NLR, as a surrogate of an inflammatory response, could be valuable as a marker for the timely prevention of AKI.

Keywords: Acute kidney injury, Anemia, Neutrophil to lymphocyte ratio, Cardiac surgery, Hematological indices.

INTRODUCTION

The consensus group for Kidney Disease Improving Global Outcomes (KDIGO) defines AKI as an rise in serum creatinine (SCr) of ≥ 0.3 mg/dl or > 50% of the baseline within a 48-hour period or a 7-day time or decrease in urine output <0.5 ml/kg/hour for 6 hours [**1].**

Cardiac surgery-associated acute kidney injury (CSA-AKI) incidence was previously stated at 5–42% [**2].** AKI poses a special risk to patients having cardiac surgery (CS) due to the associated damage from ischemia-reperfusion, inflammation, and oxidative stress. The rate of AKI was greater following aortic surgery than following solo coronary artery bypass surgery (59%)(CABG) (37%), valve surgery (49%) and thoracic surgery (33%) [**3].** Although the precise etiology of CSA-AKI is unknown, systemic inflammatory response was thought to be crucial in the development of CSA-AKI [**4].**

The platelet/lymphocyte ratio (P/LR) can be acquired from a standard blood test and could be used as a stand-alone marker of AKI after

heart surgery [**5].** Easy to compute from a full blood count, the platelet-lymphocyte ratio and the neutrophil/lymphocyte ratio (N/LR) (P/LR) are low-cost indicators of systemic inflammation. Recently, some correlations between elevated N/LR or P/LR and the outcomes of some critical illnesses (such as septic shock) have been reported [**6].**

Deranged N/LR levels have also been described in patients with AKI following major abdominal surgery [**7].** It was demonstrated that preoperatively elevated NLR in patients receiving general anesthesia for non-cardiac surgery (NLR≥3.555) was an independent risk factor linked to postoperative AKI [**8].**

The need to improve diagnostic standards and integrate biomarkers into clinical practice has grown as our understanding of CSA-AKI, a disorder that is time-sensitive, has developed [**9].**This study aims to explore the potential utility of hematological indices for predicting postoperative AKI in the background of cardiac surgery.

METHODS

This prospective, observational, cohort study was carried out in the Cardiothoracic Department and ICU, Zagazig University Hospitals, Egypt on 126 patients undergoing cardiac surgery.

Inclusion criteria:Patients undergoing cardiac surgery who were over the age of eighteen were covered by the study.

Exclusion criteria:Pregnant women andIndividuals suffering from end-stage renal illness, chronic kidney disease, regular hemodialysis, kidney transplantation, obstructive uropathy, nephrectomy, pulmonary embolism, history of organ failure,and individual with active infection such as bone and muscle disease and nephrotic syndrome were excluded from this study.

Sample size:

The patients were classified into group 1: (63 patients with no AKI after cardiac surgery) and group 2: (63 patients with AKI after cardiac surgery). KDIGO criteria for the diagnosis of CSA- AKI was defined as: a 48-hour rise in serum creatinine of at least 0.3 mg/dl; an increase in serum creatinine to at least 1.5–1.9 times baseline levels, presumably within the previous 7 days; and a urine volume increase <0.5 ml/kg/h for 6 h [**4].**

Every patient underwent a thorough medical history, a physical examination, and standard investigations, which included indicators of infection had been done to ensure no infection that can affect results specially procalcitonin, fasting and postprandial blood glucose, whole blood image (basal, 24 and 48 hours after operation) with calculation of hematological ratios; The Neutrophil to lymphocyte ratio (NLR), PLR, blood urea, serum creatinine, and systemic immune-inflammation (SII) index: platelet count × (neutrophil count/lymphocyte count), (basal, 24 and 48 hours after operation), serum uric acid (basal and 48 hours after operation), liver function tests, P.T and PTT, ESR (basal and 48 hours after operation), CRP (basal and 48 hours after operation), lipid profile and urinary album in/creatinine ratio (UACR) and pelvi - abdominal ultrasound with comment on both kidneys.

Ethical and administrative considerations: Patients or their family members gave written informed consent to take part in the study. Additionally, approval from the Zagazig University Institutional Review Board's Faculty of Medicine was acquired (IRB)

(number 9754). The study was conducted according to Declaration of Helsinki.

STATISTICAL ANALYSIS

The statistical analysis of the collected data was performed using the SPSS program (Statistical Package for Social Science), version 23.0. The Kolmogorov-Smirnov test was used to verify the normality of distribution. The Chi- square ($\chi 2$) test was used to compare qualitative data, which were reported as frequencies and relative percentages. Independent Student T (t) test was used to differentiate between two groups' quantitative variables. Mann- Whitney U (MW) test was used to calculate difference between quantitative variables in 2 groups.

RESULTS

Age was significantly increased in AKI group than non-AKI group (P value =0.002)(Table 1).

Albumin (p=0.004), pH (p=0.004) and HCO_3 (p=0.049) was considerably lower in the AKI group compared to the non-AKI group. TG (p<0.001)and cholesterol (p=0.06) were considerably higher in the AKI group compared to the non-AKI group (Table 2).

Troponin -T (p=0.015) and CRP (p<0.001)were considerably higher in the AKI group compared to the non-AKI group (Table 3).

Preoperative investigations showed that neutrophils (p=0.046), NLR (p<0.001), PLR (p=0.002), SII (p<0.001), were considerably higher in the AKI group compared to the non-AKI group. The AKI group had considerably fewer lymphocytes than the non-AKI group (p<0.001).**Postoperative** investigations showed that platelets (p=0.001) and lymphocytes (p=0.029) were considerably lower in the AKI group than in the non-AKI group, and neutrophils (p=0.001), SII (p=0.05) were also considerably higher in the AKI group than in the non-AKI group. Compared to the non-AKI group, the AKI group had a highly significant rise in NLR (p=0.002), creatinine (p<0.001), BUN (p<0.001**)**, and eGFR (p<0.001**)**(Table 4).

Regarding **preoperative** assessment, eGFR was non significantly decreased among individuals who had valve replacement surgery as opposed to CABG patients (P value =0.082). Platelets, neutrophils, lymphocytes, eosinophils, monocytes, NLR, PLR, SII, creatinine, and BUN were insignificantly different between patients who underwent CABG and those who underwent valvular replacement (p> 0.05) (Table 5).Regarding **postoperative** assessment, eGFR showed a high significant decrease compared to individuals who had CABG, those who had valve replacement (P value <0.001). Platelets, neutrophils, lymphocytes, eosinophils, monocytes, NLR, PLR, SII, creatinine, and BUN were insignificantly different between patients who underwent CABG and those who underwent valvular replacement (p> 0.05) (Table 5).

In univariate regression analysis, neutrophils (OR=1.18, p=0.016), lymphocytes (OR=0.33, p=0.001), NLR (OR=1.54, p=0.002), PLR (OR=1.01, p=0.007), SII (OR=1, p=0.005), and BUN (OR=1.11, p<0.001)were significant predictors for AKI in patients who had CABG. In multivariate regression analysis, BUN (OR=1.13, p=0.003) was a significant predictor for AKI in patients who underwent CABG. There is a correlation between increased NLR in the early postoperative stage and CSA-AKI (Table 6).

In univariate regression analysis, BUN (OR=1.08, p=0.002) was a significant predictor for AKI in patients who underwent valvular replacement while platelets, neutrophils, lymphocytes, eosinophils, monocytes, NLR, PLR, SII, creatinine, and eGFR were insignificant predictors for AKI in patients who underwent valvular replacement. In multivariate regression analysis, platelets (OR=0.95, p= 0.014), lymphocytes (OR=10.2, p=0.050), NLR (OR=0.28, p=0.044**)**, SII (OR=1.01, p=0.48), creatinine (OR=364.32,

p=0.036), and BUN (OR=1.11, p=0.09) were significant predictors for AKI in patients who underwent valvular replacement(Table 6).

Table (1): Demographic data of the studied groups.

		Non-AKI group (n=63)	AKI group (n=63)	P value
Age (years)	**Mean ± SD**	56.98 ± 10.83	63.05 ± 10.95	**0.002***
	Range	35 - 81	32 - 86	
Sex	**Male**	43 (68.25%)	44 (69.84%)	0.847
	Female	20 (31.75%)	19 (30.16%)	
Weight (kg)	**Mean ± SD**	68.71 ± 8.76	71.22 ± 9.43	0.125
	Range	55 - 86	55 - 85	
Height (cm)	**Mean ± SD**	165.51 ± 5.54	166.44 ± 5.59	0.347
	Range	155 - 180	155 - 175	
BMI (kg/m^2)	**Mean ± SD**	25.03 ± 2.42	25.67 ± 2.9	0.180
	Range	20.2 - 29.41	21.26 - 31.25	
Type of surgical procedure	**CABG**	39 (61.9%)	36 (57.1%)	0.586
	Valvular replacement	24 (38.1%)	27 (42.9%)	
DM	**Yes**	44 (69.84%)	47 (74.6%)	0.551
	No	19 (30.16%)	16 (25.4%)	
HTN	**Yes**	49 (77.78%)	51 (80.95%)	0.660
	No	14 (22.22%)	12 (19.05%)	

BMI: body mass index, CABG: coronary artery bypass graft, DM: diabetes mellitus, HTN: hypertension, * non-significant P value >0.5, *: significant P value ≤ 0.05,**: highly significant P value <0.001.

Table (2): Routine laboratory data of the studied groups.

		Non-AKI group (n=63)	AKI group (n=63)	P value
ALT (U/L)	**Mean ± SD**	60.18 ± 14.3	72.44 ± 15.35	0.914
	Range	31.5 - 70.6	40.3 - 100.9	
AST (U/L)	**Mean ± SD**	89.3 ± 12.11	116.3 ± 14.28	0.531
	Range	43.9 - 105.7	60 - 120.9	
Albumin (g/dL)	**Mean ± SD**	3.99 ± 0.7	3.65 ± 0.57	**0.004***
	Range	2.05 - 5.36	2.4 - 4.6	
HDL (mg/dL)	**Mean ± SD**	54 ± 22.03	50.14 ± 31.91	0.399
	Range	19.9 - 99.6	17.8 - 150.2	
LDL (mg/dL)	**Mean ± SD**	120.27 ± 38.23	134.61 ± 52.43	0.490
	Range	42.7 - 200	65.6 - 261.7	
Cholesterol (mg/dL)	**Mean ± SD**	169.34 ± 49.28	188.9 ± 48.11	**0.026***
	Range	90.6 - 250.6	97.1 - 263.5	
TG (mg/dL)	**Mean ± SD**	175.47 ± 104.99	258.86 ± 123.05	**<0.001 ****
	Range	100 - 223.2	150 - 423.2	
Uric Acid (mg/dL)	**Mean ± SD**	5.8 ± 1.93	6.21 ± 2.4	0.289
	Range	2 - 11	2.2 - 12.06	

Fasting BG (mg/dL)	**Mean ± SD**	130.27 ± 33.81	150.98 ± 39.47	0.162
	Range	89 - 160	102 - 190	
K (mmol/L)	**Mean ± SD**	4.12 ± 0.44	4.32 ± 0.77	0.091
	Range	3.6 - 5.0	3.64 - 5.5	
Na (mmol/L)	**Mean ± SD**	137.27 ± 22.97	134.82 ± 5.68	0.394
	Range	133 - 145	135 - 144	
Ca (mg/dL)	**Mean ± SD**	8.68 ± 1.31	8.67 ± 0.88	0.948
	Range	8.5 - 9.97	8.7 – 9.8	
Ph (mg/dL)	**Mean ± SD**	4.16 ± 1.28	4.2 ± 1.20	0.85
	Range	2.9 - 5.1	3.5 – 5.4	
pH	**Mean ± SD**	7.38 ± 0.06	7.30 ± 0.05	**0.004***
	Range	7.37 - 7.40	7.28 - 7.34	
PCO_2 (mmHg)	**Mean ± SD**	38.05 ± 7.03	44.28 ± 47.38	0.304
	Range	30.8 - 40	27 - 42	
HCO_3 (mEq/L)	**Mean ± SD**	24.01 ± 3.3	20.83 ± 3.36	**0.049***
	Range	20.9 - 33.2	17.4 - 29.8	

ALT: Alanine transaminase, AST: aspartate transaminase, HDL: high-density lipoprotein, LDL: low-density lipoprotein, TG: triglycerides, BG: blood glucose, ABG: arterial blood gas, non-significant P value >0.5, *significant P value ≤ 0.05, **highly significant P value <0.001.

Table (3): Specific laboratory investigation of the studied groups.

		Non-AKI group (n=63)	AKI group (n=63)	P value
CK-MB (ng/mL)	**Mean ± SD**	35.22 ± 55.27	38 ± 64.77	0.796
	Range	0.87 - 288.2	0.33 - 300	
Troponin -T (ng/ml)	**Mean ± SD**	1199.2 ± 1850.83	2176.31 ± 2552.67	**0.015***
	Range	8.82 - 9309	7.89 - 10000	
CRP (mg/dL)	**Mean ± SD**	28.56 ± 39.95	79.89 ± 106.08	**<0.001****
	Range	0.8 - 141	1.6 - 556.31	
PCT (ng/mL)	**Mean ± SD**	0.4 ± 0.23	0.53 ± 1.15	0.373
	Range	0.09 - 1.1	0.07 - 9	

CK-MB: creatine kinase-myocardial band, CRP: C-reactive protein, PCT: procalcitonin, * non-significant P value >0.5, *: significant P value ≤ 0.05, **highly significant P value <0.001.

Table (4): Preoperative and postoperative laboratory investigation of the studied groups.

		Non-AKI group (n=63)	AKI group (n=63)	P value
Preoperative				
Hb (gm/dl)	**Mean ± SD**	12.2±2.4	11.9±2.2	0.46
	Range	11.5-12.6	11.1-12.3	
RBCs (x10^6/µl)	**Mean ± SD**	4.7±0.7	4.6±0.5	0.35
	Range	4.3-4.9	4.1-4.8	
Platelets (*10^9/L)	**Mean ± SD**	259.33 ± 76.62	242.06 ± 73.29	0.198
	Range	140 - 475	128 - 431	
Neutrophils	**Mean ± SD**	7.72 ± 3.37	9.12 ± 4.35	**0.046***
	Range	2.2 - 16.3	2.6 - 19.7	
Lymphocytes	**Mean ± SD**	2.14 ± 0.95	1.53 ± 0.84	**<0.001****
	Range	0.6 - 4.4	0.2 - 4.3	
Eosinophils	**Mean ± SD**	0.14 ± 0.07	0.16 ± 0.15	0.299
	Range	0.1 - 0.4	0.1 - 0.95	
Monocytes	**Mean ± SD**	0.82 ± 0.34	0.74 ± 0.32	0.157
	Range	0.2 - 1.7	0.3 - 1.5	
NLR	**Mean ± SD**	4.38 ± 2.53	8.46 ± 7.7	**<0.001****
	Range	0.76 - 11.33	1.625 - 32	
PLR	**Mean ± SD**	142.54 ± 63.17	220.69 ± 182.65	**0.002***
	Range	47.73 - 280.77	58.89 - 980	
SII (*10^9cells/L)	**Mean ± SD**	1093.06 ± 585.56	2075.89 ± 2086.73	**<0.001****
	Range	118.34 - 2171.43	312.11 - 9464	
Creatinine (mg/dL)	**Mean ± SD**	0.72 ± 0.22	0.79 ± 0.25	0.14
	Range	0.5 - 1.5	0.5 - 1.5	
BUN (mg/dL)	**Mean ± SD**	18.91 ± 9.28	20.15 ± 26.08	0.30
	Range	10.1 - 25.5	11.5 - 28	
eGFR (mL/min/1.73m^2)	**Mean ± SD**	90.55 ± 12.6	86.72 ± 12.3	0.18
	Range	86.91 - 95.55	75.69 - 89.55	
eGFR stages Stage 1 (90 or above) Stage 2 (60-89) Stage 3a (45-59) Stage 3b (30-44)	**N (%)**	 4 (6.4%) 59 (93.6%) 0 (0%) 0 (0%)	 0 (0%) 63 (100%) 0 (0%) 0 (0%)	 0.2
Postoperative				
Hb (gm/dl)	**Mean ± SD**	11.0±2.2	10.7±2.0	0.43
	Range	11.3-12.4	11.0-12.2	
RBCs (x10^6/µl)	**Mean ± SD**	4.1±0.2	3.9±0.3	0.19
	Range	4.0-4.7	4.0-4.6	
Platelets (*10^9/L)	**Mean ± SD**	284.78 ± 77.79	319.7 ± 72.14	**0.001****
	Range	140 - 475	145 – 495	
Neutrophils	**Mean ± SD**	8.3 ± 3.28	10.61 ± 4.07	**0.001****
	Range	2.2 - 16.3	2.6 - 18.5	
Lymphocytes	**Mean ± SD**	2.15 ± 0.96	1.78 ± 0.92	**0.029***
	Range	0.6 - 4.4	0.6 - 4.3	
Eosinophils	**Mean ± SD**	0.14 ± 0.07	0.13 ± 0.05	0.462

	Range	0.1 - 0.4	0.1 - 0.3	
Monocytes	**Mean ± SD**	0.79 ± 0.32	0.76 ± 0.33	0.644
NLR	**Mean ± SD**	4.16 ± 2.2	6.19 ± 4.73	**0.002***
	Range	0.76 - 9.5	0.9375 - 20.67	
PLR	**Mean ± SD**	144.91 ± 64.49	168.35 ± 85.32	0.021*
	Range	47.73 - 280.77	58.89 - 393.33	
SII (*10^9cells/L)	**Mean ± SD**	1075.76 ± 571.45	1382.12 ± 1114.37	0.05*
	Range	118.34 - 2171.43	281.25 - 4877.33	
Creatinine (mg/dL)	**Mean ± SD**	0.91 ± 0.19	2.81 ± 1.98	**<0.001****
	Range	0.52 - 1.29	1.32 - 10.75	
BUN (mg/dL)	**Mean ± SD**	19.25 ± 7.11	51.78 ± 27.65	**<0.001****
	Range	3.6 - 46.4	21.2 – 136	
eGFR (mL/min/1.73m^2)	**Mean ± SD**	76.04 ± 26.84	56.87 ± 27.02	**<0.001****
	Range	66.19 - 87.55	48.71 - 60.55	
eGFR stages Stage 1 (90 or above) Stage 2 (60-89) Stage 3a (45-59) Stage 3b (30-44)	**N (%)**	 0 (0%) 63 (100%) 0 (0%) 0 (0%)	 0 (0%) 3 (4.8%) 60 (95.2%) 0 (0%)	**<0.001****

NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, SII: systemic immune-inflammation index, BUN: blood urea nitrogen, eGFR: estimated glomerular filtration rate, * non-significant P value >0.5, *significant P value ≤ 0.05,**highly significant P value <0.001.

Table (5): Relationship between type of surgery and different parameters regarding AKI patients (n=63).

		CABG (n=36)	**Valvular replacement (n=27)**	**P value**
Preoperative	**Platelets (*10^9/L)**	248.39 ± 75.25	233.63 ± 71.11	0.433
	Neutrophils	9.21 ± 4.18	9.01 ± 4.65	0.858
	Lymphocytes	1.51 ± 0.81	1.55 ± 0.89	0.841
	Eosinophils	0.18 ± 0.2	0.14 ± 0.06	0.269
	Monocytes	0.74 ± 0.32	0.73 ± 0.33	0.944
	NLR	8.44 ± 7.43	8.48 ± 8.19	0.984
	PLR	224.95 ± 180.59	215.01 ± 188.68	0.833
	SII (*10^9cells/L)	2146.86 ± 2095.15	1981.27 ± 2111.46	0.758
	Creatinine (mg/dL)	0.81 ± 0.26	0.75 ± 0.23	0.324
	BUN (mg/dL)	41.21 ± 30.51	36.4 ± 18.84	0.474
	eGFR (mL/min/1.73m^2)	85.67 ± 3.03	84.7 ± 3.66	0.25
eGFR stages Stage 1 (90 or above) Stage 2 (60-89) Stage 3a (45-59) Stage 3b (30-44)	**N (%)**	 0 (0%) 36 (100%) 0 (0%) 0 (0%)	 0 (0%) 27 (100%) 0 (0%) 0 (0%)	-
Postoperative	**Platelets (*10^9/L)**	230.06 ± 70.12	229.22 ± 76.09	0.964
	Neutrophils	9.11 ± 4.42	7.94 ± 3.51	0.264

	Lymphocytes	1.88 ± 0.99	1.65 ± 0.83	0.337
	Eosinophils	0.14 ± 0.06	0.13 ± 0.05	0.640
	Monocytes	0.76 ± 0.35	0.77 ± 0.32	0.863
	NLR	6.08 ± 4.52	6.34 ± 5.08	0.828
	PLR	151.71 ± 83.37	167.2 ± 88.66	0.480
	SII (*10^{9}cells/L)	1366.45 ± 1075.05	1403.02 ± 1185.18	0.899
	Creatinine (mg/dL)	2.44 ± 1.83	2.96 ± 2.1	0.818
	BUN (mg/dL)	47.96 ± 21.75	54.65 ± 31.36	0.346
	eGFR (mL/min/1.73m^2)	55.99 ± 4.19	51.03 ± 3.1	**<0.001****
eGFR stages Stage 1 (90 or above) Stage 2 (60-89) Stage 3a (45-59) Stage 3b (30-44)	**N (%)**	0 (0%) 3 (8.3%) 33 (91.7%) 0 (0%)	0 (0%) 0 (0%) 27 (100%) 0 (0%)	0.5

Data represented as mean ± SD, NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, SII: systemic immune-inflammation index, BUN: blood urea nitrogen, eGFR: estimated glomerular filtration rate, * non-significant P value >0.5, *significant P value ≤ 0.05, **highly significant P value <0.001.

Table (6): Logistic regression analysis of different preoperative parameters in relationship with AKI in patients who underwent CABG (n=75) and AKI in patients who underwent valvular replacement (n=51).

	Univariate		**Multivariate**	
	OR	**P value**	**OR**	**P value**
AKI in patients who underwent CABG.				
Platelets (*10^9/L)	1	0.708	1	0.678
Neutrophils	1.18	**0.016***	1.34	0.147
Lymphocytes	0.33	**0.001***	0.8	0.797
Eosinophils	8.45	0.280	5.93	0.796
Monocytes	0.37	0.168	0.15	0.116
NLR	1.54	**0.002***	1.16	0.754
PLR	1.01	**0.007***	1.01	0.616
SII (*10^{9}cells/L)	1	**0.005***	1	0.604
Creatinine (mg/dL)	3.46	0.195	1.42	0.809
BUN (mg/dL)	1.11	**<0.001***	1.13	**0.003***
eGFR (mL/min/1.73m^2)	0.97	0.061	0.97	0.222
AKI in patients who underwent valvular replacement				
Platelets (*10^9/L)	0.99	0.141	0.95	**0.014***
Neutrophils	1	0.987	0.65	0.173
Lymphocytes	0.72	0.348	10.2	**0.050***
Eosinophils	0.88	0.978	166.96	0.520
Monocytes	0.65	0.608	1.17	0.919
NLR	1.08	0.171	0.28	**0.044***
PLR	1	0.256	1.01	0.718
SII (*10^{9}cells/L)	1	0.248	1.01	**0.048***
Creatinine (mg/dL)	4.65	0.276	364.32	**0.036***
BUN (mg/dL)	1.08	**0.002***	1.11	**0.009***
eGFR (mL/min/1.73m^2)	1.03	0.262	1.11	0.051

NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, SII: systemic immune-inflammation index, BUN: blood urea nitrogen, eGFR: estimated glomerular filtration rate, OR: odds ratio, CI: confidence interval, * non-significant P value >0.5,*significant P value ≤ 0.05, ** highly significant P value <0.001.

DISCUSSION

Our study revealed that platelets, lymphocytes, NLR, SII, creatinine, and BUN were significant predictors for AKI in patients who underwent valvular replacement while BUN was a significant predictor for AKI in patients who underwent CABG. There is a correlation between increased NLR in the early postoperative stage and CSA-AKI.In the current study, the age of the AKI group was significantly greater than that of the non-AKI group. Sexuality, weight, height, and BMI and type of surgical procedure were insignificantly different between the studied groups. Our study agrees withAlfano *et al*. [10] and Diebold *et al*. [11].This can be explained that aging negatively impacts renal function, resulting in decreased renal response to maximal vasodilation stimulus, renal plasma flow and glomerular filtration rate (GFR). Additionally, aged people are more vulnerable to ischemia and nephrotoxicity, two risk factors for AKI. Additionally, the majority of senior AKI patients had one or more coexisting illnesses[12].

Regarding the liver function tests and lipid profile, Albumin was considerably lower in comparison to the non-AKI group in the AKI group. Compared to the non-AKI group, the AKI group had a highly significant increase in cholesterol and triglycerides. These findings were consistent with Alfano *et al.* [10].The current results revealed that Phosphorus has no significant change both in the AKI and non-AKI groups. Also,Uric acid, FBG, K, Na, and Ca were insignificantly different between the studied groups.This was confirmed by Diebold *et al.* [11]and Alfano*et al.* [10]whoreported that in their study on total of 41 AKI patients, and 147 non-AKI cases. Uric acid, FBG, K, Na, phosphorous and Ca were insignificantly different between the studied groups.

The present study revealed that regarding the acid-base profile the pH and HCO3 were considerably lower in comparison to the non-AKI group in the AKI group. PCO2 was insignificantly different between the studied groups.We were matching with Alfano *et al.* [10]and Trongtrakul*et al*. [13] whoreported in their study the pH was considerably lower in the AKI group compared to the non-AKI group, but PCO2 was barely noticeable different between the studied groups.

The current results showed that Troponin -T and CRP were considerably greater in the group with AKI than in the group without AKI. Procalcitonin (PCT) and cardiac band-derived creatine kinase (CK-MB) were not substantially different between the studied groups. Also, Diebold *et al.* [11]reported that AKI development was linked to increased levels of PCT, creatinine kinase, and C-reactive protein.

The present findings showed that BUN and creatinine were considerably greater in the group with AKI than in the group without AKI. Comparable outcomes were stated byTrongtrakul*et al.* [13] whoreported that regarding AKI group, serum creatinine was 1.02 mg/dl. Serum creatinine for the non-AKI group was 0.81 mg/dl. Significant differences existed between the study groups. Alfano *et al.* [10]reported in their study regarding AKI group the mean serum creatinine was 1.8, and BUN was 46.8. Concerning non-AKI group, serum creatinine was 0.8, and BUN was 26.9. Additionally, there was a substantial difference in bilirubin and ALT between the two groups.Madbouli *et al.* [14] who stated thatthere were high statistical differences

between two groups regarding BUN, creatinine, K, PO4 which was higher among patients with AKI.

In the present study The AKI group had significantly more postoperative neutrophils than the non-AKI group. The AKI group had considerably fewer lymphocytes than the non-AKI group. Hb, Platelets, eosinophils, and monocytes were insignificantly different between the two groups going with Bowe *et al.* [15],Alfano *et al*. [10], Rodrigues*et al*. [16].According to our research, patients having valve replacement surgery have a higher chance of experiencing AKI than people having CABG. These results can be explained by the fact that valve replacements are more involved surgeries that take longer to complete, which may have an immediate impact on renal perfusion and hemodynamic stability [16]. Our data suggests hemodynamic instability as the cause of AKI after valve replacement surgery since dobutamine use was shown to be more common in the postoperative period following valve replacements than in the other surgical procedures studied.

Regarding Postoperative hematological indices of the studied groups NLR, PLR and SII were considerably greater in the group with AKI than in the group without AKI. Because inflammation plays a part in the pathophysiology of AKI, there may be a relationship between the NLR, PLR, SII, and the development of postoperative AKI. given that ischemia/reperfusion damage may be crucial in the emergence of AKI [17]. Adhesion molecules are expressed by endothelial renal cells in response to an acute ischemia insult, which promotes inflammatory blood cell adhesion. Furthermore, systemic inflammatory response syndrome (SIRS) can be brought on by cardiopulmonary bypass (CPB) [17]. Counts of lymphocytes, neutrophils, and total white blood cells (WBCs) may serve as proxy indicators for inflammation. Indeed, it has been discovered that the total WBC count can predict mortality following heart surgery[18].

Although our result showed that postoperative N/L ratio quartile as a categorical variable was a significant predictor of postoperative AKI when analyzed by univariate logistic regression, in univariate regression analysis, neutrophils, lymphocytes, NLR, PLR, SII, and BUN were significant predictors for AKI in patients who underwent CABG while platelets, eosinophils, monocytes, creatinine, and eGFR were insignificant predictors for AKI in patients who underwent CABG .In multivariate regression analysis, BUN was a significant predictor for AKI in patients who underwent CABG while platelets, neutrophils, lymphocytes, eosinophils, monocytes, NLR, PLR, SII, creatinine, and eGFR were insignificant predictors for AKI in patients who underwent CABG.This came in agreement with Shaw *et al.* [19**]** who found that blood urea nitrogen is a significant predictor of acute kidney injury (AKI) that is characterized by a rapid decline in glomerular filtration rate and accumulation of nitrogenous waste products and remains a common, serious complication of cardiac surgery.Kwon *et al*. [20] found that for multivariate analysis of preoperative risk evaluation, logistic regression was repeated with variables that had been significant in previous univariate analysis (age, BSA, sex, pre-proteinuria and emergency operation). The backward stepwise multiple logistic regression model revealed that preoperative proteinuria (OR 2.396; P=0.035) was a risk factor in multivariate analysis.Kocogulları*et al*. [21] reported that in univariate regression analysis, preoperative creatinine (P=0.001), preoperative blood urea nitrogen (BUN) (P=0.0001), and preoperative HbA1c (P=0.0001) levels were found to be associated

with postoperative AKI occurrence. In multivariate regression analysis, HbA1c (OR 11.17, 95% CI:2.21-56.33, P=0.003) was found to be independently associated with an increased risk for AKI.

Our results showed that in multivariate regression analysis, platelets, lymphocytes, NLR, SII, creatinine, and BUN were significant predictors for AKI in patients who underwent valvular replacement while neutrophils, eosinophils, monocytes, PLR, and eGFR were insignificant predictors for AKI in patients who underwent valvular replacement.Numerous clinical contexts have reported on the predictive power of NLR. In many solid tumors (colorectal, gastric, lung, urothelial, and gynecological), elevated NLR is a poor predictive indicator; on the other hand, an NLR that is within the typical range and linked to better survival [22].A reliable indicator of postoperative atrial fibrillation development and long-term mortality following cardiac surgery is elevated perioperative NLR. In critically ill patients, either by itself or in combination with other biomarker parameters like the red cell distribution width and the platelet ratio, an elevated NLR predicts the development of eventual AKI [23].An innovative method for forecasting CSA-AKI is perioperative metabolic panels. A large prospective study with 55,000 patients examined the delta change in albumin, sodium, potassium bicarbonate, urea, creatinine, and urea as tested on a regular basis. Within 72 hours, it was found that this delta change was quite sensitive in predicting AKI [24].The inflammatory process during surgery can be represented by postoperative NLR ratios cardiopulmonary bypass surgery may help to explain the substantial correlation found between postoperative N/L ratios and AKI. Inflammatory responses are brought on by surgery and are more noticeable following heart surgery. CPB in particular raises the inflammatory response by upregulating adhesion molecules and activating neutrophils and endothelial cells [25].

Our results showed that Postoperative creatinine (2.81 ± 1.98 versus 0.91 ± 0.19) and BUN (51.28 ± 27.65 versus 19.25 ±7.11) indicated a significant difference between the AKI and non-AKI groups, respectively. The study groups' eGFRs did not differ statistically from one another, which is in line with earlier research [26, 27]**.** Similar to our findings, prior research indicated that postoperative AKI following heart surgery was independently associated with serum creatinine levels ≥ 1.3 mg/dl [3].

A slight increase in serum creatinine is one of the key markers of renal dysfunction, indicating concurrent renal insufficiency or decreased renal compensatory ability. At that time the patients are more liable to have the intricacy of heart surgery thatmay cause ischemia-reperfusion injury, postoperative hemodynamic fluctuation, and release of inflammatory agents, all of which might worsen renal function. Therefore, closely monitoring renal function following heart surgery willimproveprognosis and it will be greatly aided by correcting factors affecting renal perfusion, ceasing nephrotoxic medicines as soon as possible, implementing renal protection measures, and addressing abnormal serum creatinine [3].

The role of NLR, PLR and SII which are markers of inflammation, has been studied in different cardiovascular conditions. As per well demonstrated, inflammation in the vessel wall plays an important role in the development of atherosclerosis, potentially in process of coronary artery disease and renal injury [28**]**.Our study has the following strength that our findings underscore the importance of identifying hematological indices for detection of AKI after cardiac surgery, which can further the development of effective renoprotective strategies. The

limitations in our study were small sample size and there were no follow up periods.

We recommendusing of elevated neutrophil–lymphocyte ratio for detection of acute kidney injury in cardiac surgery. Further randomized controlled trials in larger multicenter prospective studies are needed to assess whether hematological indices provide added predictive value in detecting cardiothoracic surgery-associated acute kidney injury. This would greatly facilitate studies to establish effective preventive therapies for AKI.

CONCLUSION

Elevated NLR, PLR, and SII during the initial postoperative phase were correlated and CSA-AKI. They can be considered as surrogate markers of a continuing inflammatory reaction, and may serve as a useful marker for the prompt prevention of AKI and early therapeutic interventions.

Authors' Contributions

RA: designed the study, as well as writing this manuscript in a proper scientific manner with assistance from NS & TM. EG and AH: performed the statistical analysis, results' interpretation, patients' clinical assessment. All authors discussed the results and commented on the manuscript and contributed to the writing of the final manuscript.

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Citation:

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