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Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Evaluation of Inflammation and Nutritional Status in Chronic Kidney Disease Patients

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ABSTRACT

Background: Malnutrition and inflammation have significant roles in chronic kidney disease (CKD), which causes cardiovascular mortality and morbidity.

Objective: To evaluate the value of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as an inflammatory marker among CKD patients and their association with the nutritional status of the patients.

Patients and Methods: A case-control study included 60 adult patients' non-dialysis CKD stage G3-5, from Ain Shams University Hospitals, and 30 healthy volunteers as a control group. Anthropometric measurements include body mass index, mid-arm circumference, triceps skin fold thickness, mid-arm muscle circumference (MAMC), and modified subjective global assessment (m-SGA). Laboratory parameters include complete blood count, NLR and PLR, hs-CRP, routine blood chemistry, and urinary albumin/creatinine ratio. **Results:** The mean of NLR in patients' group was significantly higher compared to healthy subjects. The mean of PLR in patients' group was higher than the control group, but with no statistically significant difference. Both ratios PLR and NLR were positively correlated to high hs-CRP in patients' group. The mean of hs-CRP among CKD patients was significantly higher than that in the control group. There was a significant correlation of NLR with MAMC in patients' group. But there was no statistically significant correlation between m-SGA score and NLR, PLR, or hs-CRP among patients' group.

Conclusions: Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio can be used as inflammatory markers in chronic kidney disease patients with malnutrition.

Keywords: NLR, PLR, Inflammation and Nutritional Status, CKD Patients.

INTRODUCTION

Even in the early stages of chronic kidney disease (CKD), malnutrition is a common problem in patients in pre dialysis stages, and it gets more pronounced as kidney function declines [(1)]. Nutritional status is evaluated using serum proteins. Patients with CKD frequently have hypoalbuminemia, which is linked to a high mortality rate, particularly in those who are receiving dialysis [(2)].

There are many factors related to the development of sustained low-grade inflammation in CKD patients, including increased proinflammatory cytokines production, decreased clearance, metabolic acidosis and oxidative stress, chronic and recurrent infection, altered metabolism of adipose tissue, intestinal dysbiosis, and vitamin D deficiency because of its role in the regulation of immune system, in addition to the effect of genetic and epigenetic conditions [(3)].

Inflammation and malnutrition are considered as a component of CKD that can lead to a poor outcome [(4)]. The relation of inflammation and malnutrition to CVD is mentioned in previous studies, known as malnutrition, inflammation, and atherosclerosis referred to as MIA syndrome, considered as a silent factor for increased cardiovascular mortality rates in CKD patients [(5)].

Neutrophil-to-lymphocyte ratio (NLR) is introduced as an inflammatory marker in many cardiac and noncardiac diseases [(6)]. It was also reported to be significantly elevated under pathological conditions, like systemic inflammation or severe infection, and closely related to severity and clinical outcome of these conditions; it is an easily determined and cost-effective predictor of mortality in patients with heart failure and myocardial infarction (7). In some research, NLR is found to be associated with CKD and its progression (6) and reported to be closely related to inflammation in both hemodialysis (HD) and peritoneal dialysis (PD) with limited data regarding this association in pre-dialysis CKD patients. (6)

Platelet-to-lymphocyte ratio (PLR) is an inflammatory marker that is reported as predictor for morbidity and mortality in various cardiovascular and oncological diseases and associated strongly with inflammation in patients on maintenance HD (4). The role of these ratios in monitoring disease activity is mentioned in previous studies. Although hemodialysis (HD) patients are mostly investigated, the information related to predialysis patients is limited (8).

AIM OF THE STUDY

We aims to investigate the clinical utility of NLR and PLR as inflammatory markers and their association with nutritional status of non-dialysis CKD stage G3-5.

SUBJECTS AND METHODS

This was a pilot case-control study including 60 pre-dialysis CKD patients compared to 30 healthy

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volunteers as a control group matched in age and gender. Patients were recruited from an outpatient clinic of Ain Shams University Hospitals, Cairo, Egypt. Patients with fever, acute infection, advanced liver cell failure, decompensated heart failure, chronic lung disease, malignancy, intestinal malabsorption disease, or major surgery in the past 3 months were excluded. All studied population were subjected to full history taking and full clinical examination.

Nutritional status parameters include the following:

I. Dietary intake: Energy and protein intake have been evaluated during 24-hour recall method (for the last week), including type, amount, and frequency of meals per day; the calories and grams of protein they contain have been calculated according to food chart and estimated as Kcal/Kg/day for energy and gm/Kg/day for protein [(9)].
II. Anthropometric measurements: BMI was calculated by dividing the patient's weight in kilograms by height in meters squared. BMI = body weight (kg)/height (m^2) [(10)]. MAC (mid-arm circumference) in cm: By using a plastic tape, all participants were in standing position with their back to the measurer and their arms hanging by their sides. After asking the subject to flex their arm to 90°, the midway is taken between olecranon and acromion processes, the vertical level at which the circumference will be measured. Then, the subject was asked to relax the arm and horizontal measures across this point were taken by non-tight tape in nondominant arm. Three measurements were taken; the average of 3 results is equal to MAC. MAC adequacy was determined for all patients by using the following formula: MAC adequacy % = obtained MAC/MAC 50 percentile for age and sex × 100. Nutritional status was classified as follows: <70% severe malnutrition, 70–80% moderate malnutrition, 80–90% mild malnutrition, 90–110% eutrophic, 110–120% overweight, and >120% obese [(11)].

TSF (triceps skin fold thickness) in mm was measured by conventional skin fold caliper using standard technique. Subjects stood with their left arm dangling loosely and rolled up their left shirt sleeve. Palpation was used to locate the left acromion's posterolateral boundary, after which the upper end of a fabric measuring tape was placed against it and ran down to contact the upper border of the olecranon. An ink mark was placed halfway between these two points after the distance between them was measured to the nearest inch (3-2 mm). This ink mark is described as being in the typical middle position. The left thumb and fingers were used to pull out a skinfold in the vertical plane about 1 inch (2–5 cm) above the typical midpoint. 3 measurements were taken, and the average of these readings was considered as a final measurement. TSF adequacy (%) was determined by using this formula: obtained TSF/TSF 50 percentile for age and sex 100%. Nutritional status was classified as severe malnutrition for < 70%, moderate for 70–80%, mild for 80–90%, eutrophic for 90–110%, overweight for 110–120%, and obese for >120% [(11)].

MAMC (mid-arm muscle circumference) in cm is calculated by the following formula: MAMC (cm) = MAC – [0.314 ×TSF (mm)] (24). MAMC adequacy% was calculated by the following formula: MAMC adequacy% = MAMC/MAMC 50th percentile for sex and age × 100, and nutritional status according to it is classified to severe malnutrition for less than 70%, moderate malnutrition for 70–80%, mild malnutrition for 80–90%, and eutrophic for more than 90% [(11)].

Modified SGA of PhilSPEN—The Philippine Society of Parenteral and Enteral Nutrition form, which consists of seven parts and assigns SGA grades (A, B, and C) modified for BMI, albumin level, and TLC, was completed. This form's total score, which divides nutritional status into normal, moderate, and severe categories, is based on the total score. SGA grading is A = 0, B = 1, and C = 3. Total score is obtained after modification to BMI (18–24.9 = 0, 25–29.9 = 1, and less than 18.5 or more than 30 = 2), TLC (more than or equal to 1500 = 0, 900 but less than 1500 = 1, and less than 900 = 2), and albumin g/dl (more than 3.4 = 0, 2.5–3.4 = 1, and less than 2.5 = 2). Total score is as follows: 0 = normal, 1-2 = moderate malnutrition, and 3 or more = severe malnutrition [(12)].

Laboratory parameters include the following:

Venous blood samples were drawn from all subjects after an overnight fasting period for 12–14 hours and the following laboratory tests were done: automated complete blood count (CBC), including differential leucocyte count, HB, and platelet. Biochemistry analysis (blood urea nitrogen (BUN), serum creatinine, total calcium (Ca), phosphorus (po4), parathyroid hormone (PTH), serum sodium (Na), serum potassium (K), serum albumin, total cholesterol, triglyceride, serum transferrin, ferritin, total iron-binding capacity (TIBC). Albumin-creatinine ratio (ACR) is measured by collection of 5–10 mL first urine in the morning (first-void urine). Samples are delivered to the laboratory within 2–6 hours [(13)]. e-GFR was calculated according to MDRD equation (mL/min/1.73 m^2) = 30.849 × (Scr 1.154 × (age) − 0.203 × (0.742 if female) × (1.212 if black) [(14)]. Patients are classified as G1-G5, based on e-GFR, and A1-A3 based on the ACR (albumin-creatinine ratio).

Absolute neutrophil count was divided by absolute lymphocyte count to create the NLR [(7)]. PLR was calculated by dividing absolute platelet count by absolute lymphocyte count [(15)]. C-reactive protein (CRP) was measured by a high-sensitivity enzyme immunoassay for quantitative determination of CRP concentration in human serum assay **(**hs-CRP ELISA) test, using kits supplied by Immunospec Corporation (Immunospec, Los Angeles, CA, USA) (Ca # E29-058). The obtained values of hs-CRP are determined according to the corresponding standard curve in ng/ml for both patients and controls and then multiplied by

dilution factor 100. The expected range of the kit for a healthy adult is from 68 to 8200 ng/ml [16].

Ethical consent:

The Academic and Ethical Committee at Ain Shams University approved the study. Each patient signed a written informed consent form to agree to participate in the study. The Declaration of Helsinki, the World Medical Association's code of ethics for studies involving humans, guided the conduct of this work.

Statistical Analysis

With the aid of the IBM SPSS software package version 20.0, data were fed into the computer and evaluated. (IBM Corp; Armonk, New York) Number and percentage were used to describe qualitative data. The normality of the distribution was examined using the Kolmogorov-Smirnov test. The range (minimum and maximum), mean, standard deviation, and median were used to characterise quantitative data. At the 5% level, significance of the results was determined. The tests that are used are the Chi-squared test for categorical variables to compare between different groups, Fisher's exact or Monte Carlo correction for Chi-squared when more than 20% of the cells have expected counts lower than 5, Student's t-test for quantitative variables with normally distributed distributions to compare between two studied groups, and Mann-Whitney test for quantitative variables with abnormally distributed distributions to compare between two studied groups. Spearman's coefficient was employed to determine the correlation between two normally distributed quantitative variables. The significance of a P value of 0.05 or less was determined.

RESULTS

This study encompassed 60 non-dialysis CKD patients and 30 controls. Patients were 43 males (71.7 %) and 17 females (28.3%), with mean of age of 64.23 ± 7.99. The mean of BMI is 30.48 ± 5.78 and was higher in CKD patients than in control. CKD duration mean is 2.80 ± 0.63 and e-GFR mean 28.29 ± 6.39. Studied m-SGA mean is 3.60 ± 0.86; according to it, 71.7% of patients have severe malnutrition and 28.3% of patients have moderate malnutrition. The mean of protein intake in patients was 0.78 ± 0.17 and mean of energy intake is 23.43 ± 3.67, mean of systolic BP is 136.3 ± 16.07, and mean of diastolic BP is 83.50 ± 7.94, which was higher in patients than in control. Etiology of CKD is as follows: DM 16.7%, HTN 25%, obstructive uropathy 8.3%, APKD 3.3%, and gout 1.7%; common comorbidities included HTN 76.7%, CVD 60%, and HCV 15% of cases. Medications taken were L-carnitine in 36 cases, erythropoietin in 18 cases, and ferrous sulfate in 14 cases. Distribution of patients CKD stages is as follows: G3, 31 cases; G4, 22 cases; and G5, 7 cases. Demographic data are shown in detail in Table **1**.

Table (1): Comparison between patients and control groups according to demographic data:

	CKD patients (n = 60)		**Control (n = 30)**		**Test of Sig.**	**P**
	No.	**%**	**No.**	**%**		
Gender						
Male	43	71.7	16	53.3	χ^2= 2.977	0.084
Female	17	28.3	14	46.7		
Age (years)						
Mean ± SD.	64.23 ± 7.99		61.53 ± 7.27		t=1.556	0.123
Weight (kg)						
Mean ± SD.	85.55 ± 14.32		71.43 ± 4.38		t=7.007*	<0.001*
Height (cm)						
Mean ± SD.	169.0 ± 8.13		167.37 ± 4.77		t=1.198	0.234
BMI (kg/m^2) Mean± SD	30.48 ± 5.78		25.71 ± 0.90		t=6.238	<0.001*
	No	%	No	%		
Normal	7	11.66	30	100		
Overweight	24	40.00	0	0		
Obese	29	48.33	0	0		
Systolic blood pressure mmHg Mean±SD	136.3 ± 16.07		118.67 ± 9.55		T=6.517*	<0.001*
Diastolic mmHg (Mean ±SD)	83.50 ± 7.94		75.83 ± 4.75		T=5.712*	<0.001*
Energy intake (Kcal/kg/day), /Mean±SD	23.43±3.67		24.60±2.05		t=1.945	0.055
Protein intake (G/kg/day), Mean±SD	0.78±0.17		1.55±0.26		U=114.5	<0.001*
m-SGA, Mean±SD	3.60±0.86		0.0±0.0		U=0.0	<0.001*
Normal	0	0.0	30	100.0		
Moderate	17	28.3	0	0.0	X²=90.0	<0.001*
Sever	43	71.7	0	0.0		
Duration of CKD (years), Mean±SD	2.80±0.63		0.0±0.0			
e-GFR(ml/min)	28.29±6.39		0.0±0.0			

*:Statistically significant at p ≤ 0.001.

NLR mean was 2.83 ± 0.61 and hs-CRP (ng/ml) mean is 8195.0 ± 2014.8; both were statistically significant higher in patients' group than in control, while PLR mean was 144.6 ± 33.42 higher in cases than control group but with no statistical significance. Laboratory data like creatinine, BUN, albumin-creatinine ratio in urine, K, phosphorus, PTH, total cholesterol, and TG are significantly higher; with significantly lower HB and albumin in patients, the protein intake is found to be lower significantly in patients' group and there is no significant difference regarding energy intake, as shown in Table **2**.

Table (2): Comparison between patients and control groups according to laboratory data.

	Cases (n = 60)	**Control (n = 30)**	**Test of sig**	**P**
s.Cr (mg/dl)				
Mean ± SD.	2.71 ± 0.35	0.79 ± 0.14	U=0.0	<0.001*
BUN (mg/dl)				
Mean ± SD.	37.01 ± 3.42	11.43 ± 2.52	U=3.50*	<0.001*
s.Na (meq/l)				
Mean ± SD.	139.03 ± 4.19	138.13 ± 3.71	t=1.038	0.303
s.k (mmol/l)				
Mean ± SD.	4.74 ± 0.61	4.19 ± 0.41	t=5.047	<0.001*
P (mg/dl)				
Mean ± SD.	4.44 ± 1.07	3.64 ± 0.52	t=4.790*	<0.001*
T.Ca (mg/dl)				
Mean ± SD.	9.20 ± 0.76	9.46 ± 0.45	t= 2.064	0.042
PTH (pg/ml)				
Mean ± SD.	169.5 ± 39.9	27.83 ± 4.61	U= 111.0*	<0.001*
T. cholesterol (mg/dl)				
Mean ± SD.	160.7 ±38.7	105.2 ±21.05	t= 615.50	0.015*
TG(mg/dl)				
Mean ± SD.	160.7 ±37.9	105.2 ±21.05	U= 615.50	0.015*
ACR(mg/g)				
Mean ± SD.	490.5 ± 17.9	1.02 ± 0.21	U= 0.0	<0.001*
HB (g/dl)				
Mean ± SD.	11.67 ±1.91	13.28 ±1.19	t= 0.4920*	<0.001*
s. albumin (g/dl) Mean±SD	3.71±0.56	4.21±0.39	t=4.998*	<0.001*
WBC (×10^3/mm				
Mean ± SD.	7.18 ±1.32	7.72 ±1.36	t= 1.102	0.276
Platelets(×10^3/cm)				
Mean ± SD.	253.9 ±62.02	264.0 ±64.05	t= 0.587	0.559
Ferritin (ng/ml)				
Mean ± SD.	152.2 ±36.3	102.4 ±18.71	U= 872.0	0.811
TIBC (ug/dl)				
Mean ± SD.	292.2 ±69.67	295.3 ±33.10	t= 0.292	0.771
Transferrin (mg/dl)				
Mean ± SD.	248.7 ±8.8	236.3 ±5.32	U= 797.50	0.380
hs-CRP(ng/ml) Mean ± SD.	8195.0±214.8	456.7±16.5	0.000*	0.001*
PLR				
Mean ± SD.	144.6 ± 33.42	130.2 ± 30.11	U=771.0	0.269
NLR				
Mean ± SD.	2.83 ± 0.41	1.64 ± 0.23	U=509.50*	0.001*

*: Statistically significant at p≤0.05.

Anthropometric measures: TSF mean is 15.16 ± 3.12, mean of TSF% is 102 ± 24.56, MAC mean is 31.61 ± 7.22, MAC% mean is 101.1 ± 23.59, MAMC mean is 26.84 ± 6.05, and MAMC% mean is 102.7 ± 23.89. MAC, MAC%, MAMC, and MAMC% are found to be significantly higher in patients' group than in control, as shown in Table **3**.

Table (3): Comparison between the two studied groups according to TSF, MAC & MAMC

Anthropometric parameters	Cases (n = 60)		Control (n = 30)		Test of Sig.	P
	No.	%	No.	%		
TSF (mm) Mean ±SD	15.16±3.12		17.63±4.12		t= 1.520	0.132
TSF (%) Mean ± SD	102.0±24.56		99.04±7.15		t=0.741	0.461
Nutritional status by TSF						
Euotrophic	0	0.00	30	100		
mild	15	25.0	0	0.0		
Moderate	9	15.0	0	0.0	χ^2=97.384*	MC P <0.001 *
Severe	7	11.7	0	0.0		
Obese	23	38.3	0	0.0		
Overweight	6	10.0	0	0.0		
MAC (cm) Mean±SD	31.61±7.22		28.43±0.94		t=3.350	0.001*
MAC% (Mean ± SD)	101.1±23.59		91.18 ± 0.85		t=3.261	<0.002*
Nutritional status by MAC						
Eutrophic	0	0.0	30	100		
Mild	22	36.7	0	0.0		
Moderate	2	3.3	0	0.0	χ^2=98.505	MC p 0.055
Obese	23	38.3	0	0.0		
Overweight	6	10.0	0	0.0		
Severe	7	.11.7	0	0.0		
MAMC (cm) Mean±SD	26.84±6.05		23.13±2.40		t=4.152	<0.001*
MAMC % Mean±SD	102.7±23.89		94.19±6.83		t=2.564	0.0012*
Nutritional status by MAMC						
Eutrophic	31	51.7	30	100.0		
Mild	19	31.7	0	0.0	χ^2= 32.020	MC P = <0.001*
Moderate	6	10.0	0	0.0		
Severe	4	6.7	0	0.0		

*: Statistically significant at p≤0.05.

Correlations between NLR and PLR and anthropometric measures showed significant positive correlation between PLR and hs-CRP in patients' group (r = 0.278, P = 0.031) and significant positive correlation between NLR and (BMI, hs-CRP, and MAMC) in patients' group (r = 0.266, P = 0.011; r = 0.358, P = 0.001; and r = 0.232, P = 0.027, resp.) (Tables **4** and **5** and Figures **1** and **2**).

Table (4): Correlation of PLR with demographic data, anthropometric measurements in patients' group.

	PLR	
	r_s	P
Age (years)	-0.080	0.541
Weight (kg)	0.082	0.532
Height (cm)	-0.135	0.302
BMI (kg/m²)	0.059	0.656
TSF (mm)	0.181	0.692
MAC (cm)	0.052	0.692
MAMC(cm)	0.029	0.824
m-SGA	0.126	0.337
e-GFR (ml/min)	-0.055	-0.055
s.Cr (mg/dl)	-0.041	0.757
BUN (mg/dl)	0.057	0.665
s.K (meq/l)	0.056	0.655
P (mg/dl)	0.064	0.626
T.Ca (mg/dl)	-0.083	-0.155
PTH (pg/ml)	0.059	0.765
ACR (mg/g)	0.148	0.260
S.Albumin (g/dl)	-0.037	0.778
T. cholesterol (mg/dl)	0.073	0.581
TG (mg/dl)	-0.036	0.782
HB (g/dl)	-0.158	0.229
Ferritin (ng/ml)	-0.101	0.442
TIBC (ug/dl)	0.018	0.889
Transferrin (mg/dl)	-0.036	0.783
hs- CRP (ng/ml)	0.278	0.031*

rs ; Spearman coefficient, *statistically significant at p≤0.005.

Table (5): Correlation of NLR with demographic data, anthropometric measurements and laboratory data in patients' group.

	NLR	
	r_s	**P**
Age (years)	-0.069	0.197
Weight (kg)	0.244	0.060
Height (cm)	0.244	0.107
BMI (kg/m²)	0.266	0.011*
TSF (mm)	-0.115	0.218
MAC (cm)	0.202	0.057
MAMC(cm)	0.232	0.027*
m-SGA	0.138	0.295
e-GFR (ml/min)	-0.039	0.765
s.Cr (mg/dl)	0.126	0.337
BUN (mg/dl)	0. 40	0.759
s.K (meq/l)	0.046	0.455
P (mg/dl)	0.057	0.700
T.Ca (mg/dl)	-0.090	-0.123
PTH (pg/ml)	0.070	0.865
ACR (mg/g)	0.150	0.254
S.Albumin (g/dl)	-0.075	0.570
T. cholesterol (mg/dl)	0.032	0.859
TG (mg/dl)	0.048	0.781
HB (g/dl)	-0.215	0.053
Ferritin (ng/ml)	-0.004	0.976
TIBC (ug/dl)	0.208	0.111
Transferrin (mg/dl)	-0.060	0.651
hs- CRP (ng/ml)	0.358	0.001*

rs ; Spearman coefficient, *satatistically significant at p≤0.005.

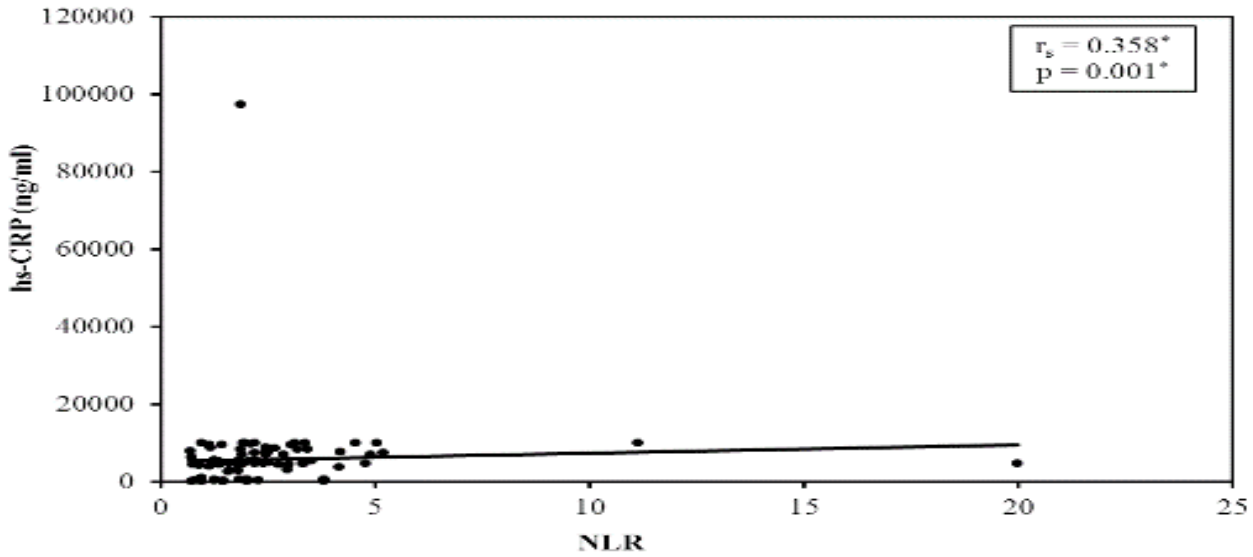

Figure (1): Significant Correlation between NLR and hs-CRP among CKD patients , P≤0.005

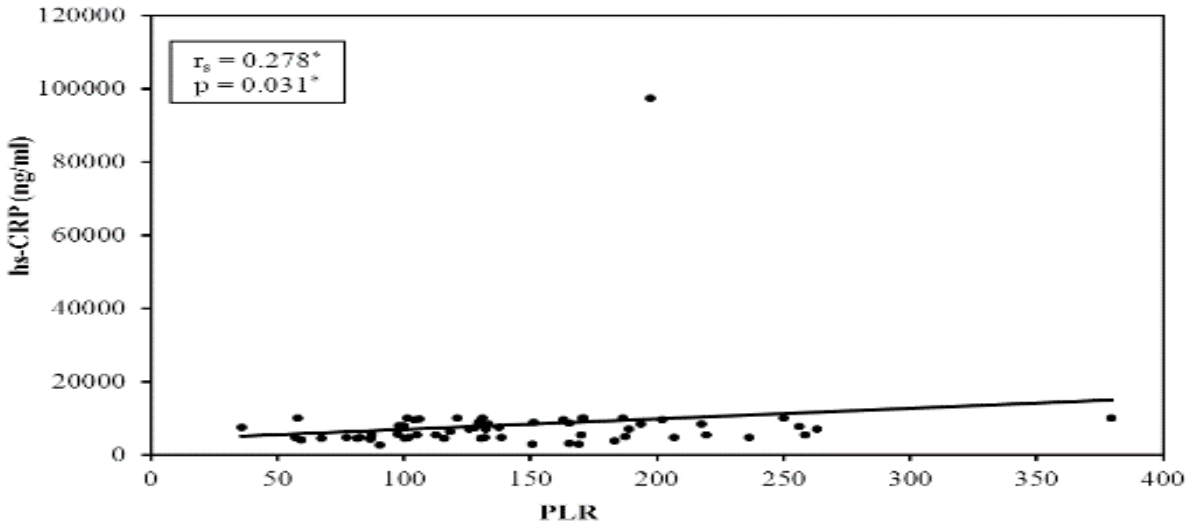

Figure (2): Significant correlation between PLR and hs-CRP among CKD patients , P≤0.005

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m-SGA was positively significantly correlated to BUN (r = 0.502, P <0.001), creat (r = 0.551, P <0.001), ACR (r = 0.685, P <0.001), and Po4 (r = 0.285, P = 0.027) and negatively significantly correlated to albumin (r = −0.338, P = 0.008), HB (r = − 0.433, P = 0.001), and total calcium (r = –0.335, P = 0.005) with no significant correlation between m-SGA and PLR (r = 0.126, P = 0.337) and NLR (r = 0.138, P = 0.295) in patients' group, as described in Table **6**.

Table (6): Correlation between m-SGA and different parameter

	SGA	
	r_s	P
Age (years)	0.064	0.626
Weight (kg)	0.118	0.368
Height (cm)	-0.153	0.243
BMI (kg/m2)	0.220	0.091
e-GFR (ml/min)	0.331	0.088
S.CR (mg/dl)	0.551	<0.001*
BUN (mg/dl)	0.502	<0.001*
s.K (meq/l)	0.153	0.243
P (mg/dl)	0.285	0.027*
T.Ca (mg/dl	-0.355	0.005*
PTH (pg/ml)	0.290	0.500
ACR (mg /gm)	0.685	<0.001*
Serum Albumin (g/dl)	-0.338	0.008*
T cholesterol (mg/dl)	-0.098	0.445
TG (mg/dl)	-0.145	0.269
HB (g/dl)	-0.433	0.001*
Ferritin (ng/ml)	0.136	0.301
TIBC (ug/dl)	-0.167	0.201
Transferrin (mg/dl)	-0.183	0.162
PLR	0.126	0.337
NLR	0.138	0.295
hs-CRP (ng/ml)	0.019	0.886

rs ; Spearman coefficient, *satatistically significant at p≤0.005 .

DISCUSSION

The blood levels' NLR was significantly higher in studied CKD patients with malnutrition compared to healthy subjects. The blood levels' PLR was higher in patients than in healthy subjects but without statistical significance. The elevation of NLR and PLR in CKD patients can be explained by the presence of chronic inflammatory status with activated immune system that leads to high levels of neutrophils, platelets, and low lymphocytes. Presence of inflammation in our patients can be reflected by the presence of significantly higher hs-CRP in patients than in healthy subjects. The inflammatory markers NLR and PLR are used in the present study. hs-CRP is positively correlated to both NLR and PLR; this correlation can reflect the ability of these ratios to express the inflammatory status among our pre-dialysis patients.

Okyay *et al.* [7] agreed with our result regarding NLR, which revealed the presence of significantly higher NLR in CKD patients than that of healthy subjects. Also manifested the presence of higher NLR ratio in both pre-dialysis and dialysis patients, and A significantly higher NLR was manifested along with higher PLR among CKD patients, which is not consistent with our result regarding the non-significantly elevated PLR[18].

Generally, the use of PLR is more recent and investigated mainly for its relation to CVD and malignancies. PLR was found to be better than NLR as an indicator of inflammation in ESRD as mentioned by **Turkmen *et al.*** [19] demonstrating the presence of higher PLR along with NLR in pre-dialysis CKD patients with polycystic kidney disease compared to healthy subjects and increased levels of both ratios with progression of disease toward HD.

hs-CRP is observed in previous studies to be elevated among CKD patients. **Li *et al.*** [20] revealed significantly higher levels of hs-CRP in CKD patients than healthy subjects which can indicate the presence of inflammatory activity in different stages of CKD. And mentioned the correlation of inflammatory markers to PLR and NLR. Study revealed the positive significant

correlation between PLR, NLR, and hs-CRP, and who described a higher NLR ratio in both pre-dialysis and dialysis CKD patients in relation to other inflammatory markers when compared to healthy subjects [7]. These results are consistent with our results, which indicate the same association.

In the present study, malnutrition is manifested in patients' group when compared to healthy subject and we used different tools in the assessment of nutritional status and m-SGA along with anthropometric measurements (BMI, MAC, MAMC, and TSF) in association with laboratory parameters. **Oluseyi and Enajite** [1] also revealed that malnutrition is common in pre-dialysis CKD patients. Also studied pre-dialysis patients in India and found a high prevalence of malnutrition (65%). Most of previous studies concentrate on nutritional status among HD patients where the manifestations of malnutrition are becoming more obvious [21].

In the current study, we found a higher BMI in patients than in healthy subjects. Our patients are then classified according to BMI to obese, overweight, and normal. There are no underweight patients. Higher MAC and MAC adequacy are noted in our patients along with increasing MAMC and MAMC adequacy compared to healthy subjects, and there is no significant difference regarding TSF or TSF adequacy in our patients.

The previous studies mentioned the prevalence of increased BMI in CKD patients as well as the obesity prevalence in general populations revealed increased BMI to be a promotor for kidney disease not only by indirect effect of comorbidities but also by direct renal disease[22], as well as study that considered obesity as a potent risk factor for development of CKD and revealed DM with obesity accelerates the occurrence of CKD and all overweight and obese individuals should be screened periodically for renal function abnormalities[23].

It was found that MAC, MAMC, and TSF significantly reduced in severely malnourished CKD patients [24]. This result is against our mentioned results in which higher MAC and MAMC were found in patients' group. These increased measurements can be explained by the presence of obesity, where increased adipose tissue in the arm causing increased MAC and increased MAMC can be explained by the hypothesis presented earlier regarding elevated adiposity causing additional overloading of the antigravity muscles (e.g., quadriceps and triceps) during routine daily activities (e.g., walking and climbing steps).

NLR mean values but not PLR were positively correlated to BMI and MAMC in CKD patients' group with poor correlation between NLR and other anthropometric measurements, non-significantly elevated PLR and significantly elevated hs-CRP founded with poor correlation to BMI. Agreed with our results in association between NLR and BMI that revealed the presence of significant higher NLR in higher BMI patients and inconsistency with our notes regarding poorly correlated hs-CRP to BMI in our patients [25].

On the other hand, there were no relation between NLR and BMI [26], and also study noted the presence of positive correlation between BMI and neutrophils, lymphocytes, total leucocytic count, and all platelets' indices with the presence of higher NLR level among normal BMI [27].

Campbell *et al.* [9] revealed low reproducibility and reliability on an individual basis, making the anthropometric measurements less important than other measurements requiring more sophisticated techniques. They have limitation in reflecting defects in body components with low differentiation between fat, muscle, bone, and water and can be affected by different mechanisms that cause muscle wasting in CKD patients, which cause variation in hydration status.

NLR and PLR in the present study were found with no statistically significant correlation to m-SGA scores. There was no significant correlation between NLR, PLR and malnutrition score [17], which was consistent with our finding. Previous studies reveal the validity of SGA and modified forms of it as a nutritional assessment tool in CKD patients. **Cuppari *et al.*** [28] revealing 7-point SGA to be a valid tool to assess malnutrition in non-dialysis CKD patients. It was concluded that SGA is a valid assessor of nutritional status and an independent predictor of all-cause mortality both in CKD non-dialysis and dialysis patients [29]. The reliability of SGA in the diagnosis of malnutrition in adults on HD [30]. These studies showed significant correlation between SGA and other nutritional parameters, and according to this correlation, SGA is considered an accepted tool for nutritional status assessment.

In the present study, m-SGA has variable results regarding correlation with other nutritional parameters; poor correlation was found between SGA and BMI, MAC and MAMC, with significant correlation between SGA and TSF, positive correlation of SGA to serum creatinine, BUN, ACR, and phosphorus, negative correlation regarding serum albumin, HB, and serum calcium. A poor correlation was found between m-SGA and hs-CRP. Despite the presence of many studies contrary to our findings that revealed the presence of significance correlation between nutritional status and MAC, like that of **Marr *et al.*** [31], there are also results inconsistent with our notes. That revealed no significant correlation between BMI and nutritional status [32]. The presence of variable hydration status, like edema, in patients can affect BMI, and this agrees with our results, where poor correlation between SGA and BMI was found in patients' group. It was noted that there was no correlation between MAC and nutritional status[33]. An Australian study by revealed no correlation between MAMC, TSF, and nutritional status in HD patients and according to the presence of variation in body component regarding CKD patients[30]. SGA may not be a valid nutritional assessment tool among obese HD patients[34].

Erb *et al.* [34], in contrast to our findings, found no statistically significant association between nutritional status and lipid levels with lower total cholesterol and triglyceride observed in mild to moderately malnourished patients, which may be related to poor dietary intake, despite the higher risk of occurrence of dyslipidemia in ESRD and a few studies demonstrating its relationship with poor nutritional status.

In our patients, NLR and PLR also don't correlate with e-GFR. According to the research by **Sevencan and Ozkan[35]** the NLR and PLR were not independent risk variables that affected eGFR.

CONCLUSIONS

Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio can be used as inflammatory markers in chronic kidney disease patients with malnutrition.

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