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The predictive utility of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in screening of coronary heart disease in end-stage renal disease patients undergoing dialysis: A cross-sectional study

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ABSTRACT

End-stage renal disease (ESRD) patients undergoing dialysis are at increased risk for developing coronary heart disease (CHD). Recent studies have shown that neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) may be used to determine individuals at high risk of CHD. This study aims to examine whether NLR and PLR could predict the risk of CHD characterized by elevated carotid intima-media thickness (CIMT) in ESRD patients. Our cross-sectional study includes patients with ESRD on hemodialysis (HD)- or continuous ambulatory peritoneal dialysis (CAPD)-based renal replacement therapy (RRT) at Moewardi General Hospital in Surakarta, Indonesia, from January to July 2022. The primary outcome in this study is the presence of a high risk of CHD characterized by CIMT ≥1 mm, and the main predictors used in this study are NLR and PLR. Among the patients (n = 72), the analysis showed that NLR [OR 1.474 (95% CI: 1.031–2.106); p = 0.033] had a statistically significant association with the CIMT status. Group analysis showed NLR association with CIMT on CAPD patients [OR 5.957 (95% CI: 1.189–29.847); p = 0.030]. The association was not significant with PLR (p > 0.05). Optimal cut-offs were established in NLR ≥2.72 area under the curve (AUC: −0.909; p = 0.001; sensitivity = 95.45%, specificity = 83.33%) and PLR ≥93.09 (AUC: −0.969; p = 0.001; sensitivity = 90.91%, specificity = 83.33%) in CAPD patients, with lower AUC and specificity values in the analysis of both RRTs and HD patients. NLR and PLR are excellent yet simple predictors of CHD risk in ESRD patients undergoing dialysis.

INTRODUCTION

Chronic kidney disease (CKD) is highly prevalent globally, with consistent global prevalence estimates ranging from 11% to 13% (Hill *et al*., 2016). The progression of CKD to its terminal form, which prompts renal replacement therapy (RRT), also known as end-stage renal disease (ESRD), continues to be a significant cause of diminished quality of life and premature mortality. In several nations, continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD) are the most prevalent RRT. In Hong Kong, 80% of patients with ESRD undergo CAPD; many patients also undergo CAPD in New Zealand, Korea, and Singapore. Meanwhile, HD was utilized by 90% of dialysis patients in China, Japan, and Taiwan. In Indonesia, the estimated incidence was 251 per million individuals, and the prevalence was 499 per million healthy individuals (Indonesian Association of Nephrology, 2018). In the past 12 years, the number of peritoneal kidney patients in developing nations reached 24.9 per million compared to 21.8 per million in developed nations (Yulianti *et al*., 2015).

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CKD is an independent risk factor for coronary heart disease (CHD) and CHD complications cause the majority of CKD-related deaths (Hill *et al*., 2016). CKD patients have 1.5 to 3 times the general population's CHD incidence. More than 50% of CKD deaths are associated with CHD. Atherosclerosis and chronic inflammation are components of the malnutrition-inflammatory-atherosclerosis syndrome, which underlies the pathogenesis of CHD in patients with ESRD. As kidney function declines, the risk of cardiovascular disease rises (Dastani *et al*., 2015; Gansevoort *et al*., 2013; Kasliwal *et al*., 2014; Kaya *et al*., 2019).

The carotid intima-media thickness (CIMT) examination is a noninvasive diagnostic tool widely used to determine the presence of carotid plaque in CHD. In healthy middle-aged adults, a CIMT value between 0.6 and 0.7 mm is considered normal. In contrast, a CIMT value of 1 mm or greater is associated with a significantly increased absolute risk of CHD. CIMT has been the subject of extensive research and is linked to cardiovascular events and subclinical atherosclerotic disease (Gary *et al*., 2013; Kaligis *et al*., 2016; Muljadi *et al*., 2014; Sharma *et al*., 2017).

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are commonly used as markers of systemic inflammation in a variety of disease states, including limb ischemic and arterial stiffness (Taymez *et al*., 2016; Yu *et al*., 2015). NLR and PLR are also associated with chronic inflammation, mortality risk, and erythropoietin resistance in CKD (Guasti *et al*., 2011). These findings suggest that NLR and PLR may be used to determine individuals at high risk for CHD characterized by elevated CIMT. This study will investigate whether NLR and PLR can predict CIMT in ESRD patients undergoing dialysis.

MATERIAL AND METHODS

Setting

Moewardi General Hospital was founded in 1977 due to the merging of three separate general hospitals in the city of Surakarta. Besides its mission to improve the quality of healthcare in surrounding cities, it also operates as a university hospital to accommodate the education of medical doctors at Sebelas Maret University. Since its founding, the Department of Nephrology and Hypertension has become responsible for managing patients with various types of kidney disease. Currently, the Moewardi General Hospital is the only tertiary hospital located in the city of Surakarta. Patients with renal disease receive outpatient service and inpatient services if necessary. HD and CAPD are performed as indicated. Most patients receive healthcare coverage from a national health insurance legal entity.

Study design and population

This observational analytic study uses a cross-sectional approach conducted at the Department of Renal-Hypertension and Hemodialysis Unit in Moewardi General Hospital in Surakarta, Indonesia, from January 1 to July 1, 2022. All patients aged 18 years or older with a diagnosis of ESRD and on at least 3-month HD or CAPD-based RRTs were included in the study. The presence of cardiovascular, neoplastic, chronic inflammatory, or infectious disease and the usage of immunosuppressants or antiplatelet drugs preclude the patient from participating in the study.

Outcomes and predictors

The main outcome of this study is the presence of a high risk of CHD characterized by CIMT ≥1 mm (Kaligis *et al*., 2016; Muljadi *et al*., 2014). The risk of CHD will be operated as a categorical variable: CIMT <1 mm and CIMT ≥1 mm. The main predictors used in this study are NLR and PLR. The absolute values of neutrophils and platelets were divided by the absolute values of lymphocytes to get the NLR and PLR values, respectively. Several confounding variables were also considered, including age, gender, nutrition status, CKD duration, presence of diabetes mellitus, and other hematologic parameters. These hematologic parameters include hemoglobin, leukocyte count, platelet count, neutrophils, and lymphocytes. These predictors will be operated as numerical or categorical variables, accordingly.

Measurement

Patients who met the inclusion and exclusion criteria will be asked to sign informed consent followed by history-taking and blood sampling. The blood samples were then ordered for a routine hematology examination using a hematology analyzer in the clinical pathology department. The measurement of CIMT will be carried out by a cardiologist in the cardiovascular department using B-mode ultrasound. The cardiologist will measure both carotid arteries and a higher measurement of CIMT will be recorded (Fig. 1).

Data extraction and statistical analysis

The data were first exported to Microsoft Excel and then imported into Statistical Package for the Social Sciences (version 22) for quantitative statistical analysis software. All variables were subjected to descriptive statistics to describe the characteristics of the subject's frequency, percentage, means, and SDs before analysis. A comparative analysis was also performed to identify the factor of the confounding variable that affected the primary outcome. Separate logistic regression models were performed to analyze the relationship between the significant and the main outcome. The predictive values of the main predictors were also evaluated by constructing receiver operating characteristics (ROCs) curves and identifying the most discriminatory cutoff values. A level of significance was accepted when the two-tailed p-value was less than or equal to 0.05.

Ethical clearance and clinical registry

The study was conducted in accordance with the Declaration of Helsinki. Before the commencement of the study, a proposal was submitted to the local ethics committee. This study was approved by the Health Research Ethics Committee at Moewardi General Hospital with the number 1.338/I/HREC/2021. We also obtained informed consent from all the eligible patients. The study protocol was registered on ClinicalTrials.gov with ID NCT05472805.

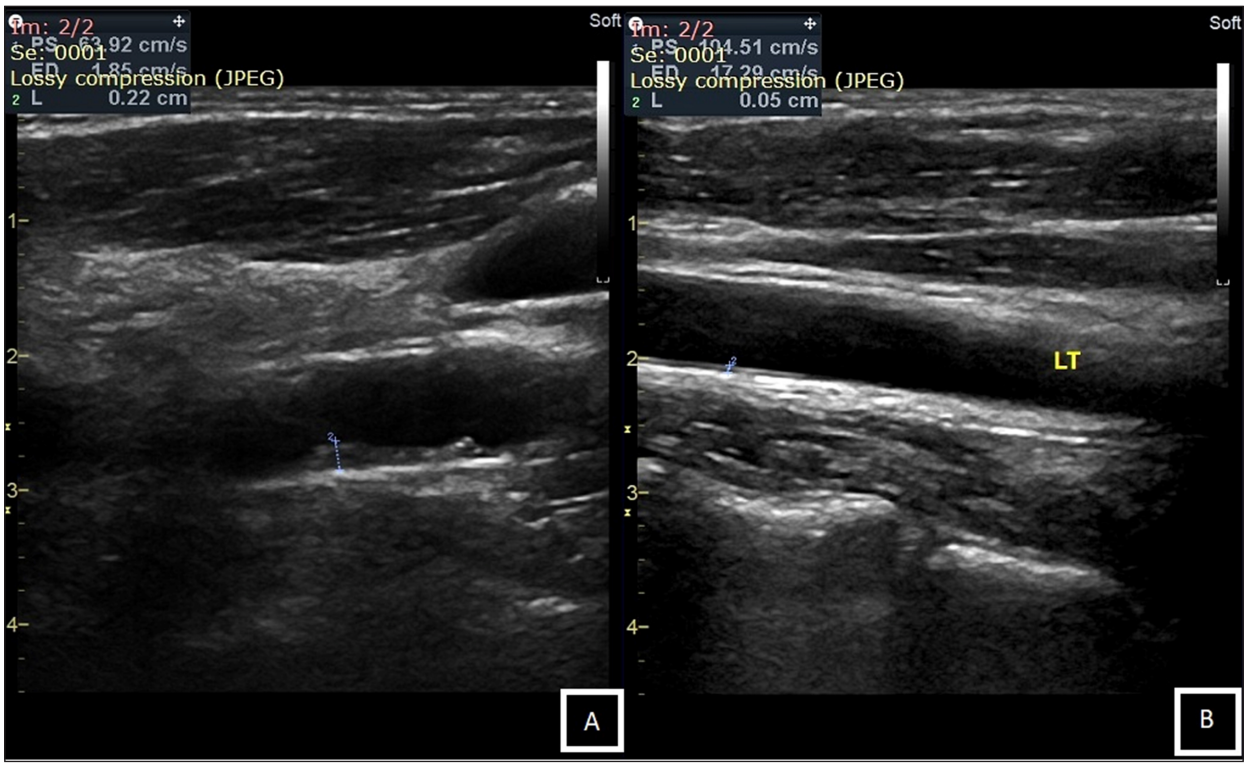

Figure 1. CIMT measurement using B-mode ultrasound; (A). Example of an individual with increased thickness of CIMT (CIMT = 2.2 mm). (B). Another example of an individual with a normal thickness of CIMT (CIMT = 0.5 mm).

RESULTS

The present study includes 72 patients with ESRD in the Department of Renal-Hypertension and Hemodialysis Unit at Moewardi General Hospital. Most of the patients were males (68.1%), with a mean age of 45.06 ± 11.30, with a mean CKD duration of 4 years. Most ESRD patients were on HD-based RRT (HD, $n = 44$ *vs*. CAPD, $n = 28$). Table 1 shows that most of these individuals (78.6%) had CIMT ≥1 mm and were subjected to a higher risk of CHD.

The comparison analysis of the effect of confounding variables, namely, age, gender, nutrition status, CKD duration, RRT method, and other routine hematologic parameters, was carried out and is shown in Table 2. The analysis showed that the effect of confounding variables was insignificant ($p > 0.05$), excluding neutrophils and lymphocytes, which also influence the NLR and PLR.

Using logistic regression analysis, the strength of the predictive utility of NLR and PLR in determining CIMT status was determined and is presented in Table 3. The analysis showed that only NLR has a significant predictive utility in determining CIMT status, collectively [OR 1.474 (95% CI: 1.031–2.106); $p = 0.033$] and on CAPD group only [OR 5.957 (95% CI: 1.189–29.847); $p = 0.030$].

Further ROC analysis was also performed to determine the area under the curve (AUC) and the predictors' cutoff value with the best sensitivity and specificity values. Previous analysis (Table 2) that showed the significance of the RRT method used prompted the ROC analysis to be performed separately according to the method used. As shown in Table 4, NLR (AUC: −0.909; $p = <0.001$; 95% CI: 0.567–0.983) and PLR (AUC-0.969; $p = < 0.001$; 95% CI; 0.757–0.996) in CAPD patients showed the highest AUC, and lower NLR and PLR value of AUC was observed in HD patients. Taking these RRTs together, only NLR was found to have a significant (AUC-0.663; $p = 0.010$; 95% CI; 0.501–0.781), albeit lower than in the CAPD group.

Based on the ROC curve, an optimal cutoff with high sensitivity and specificity for the risk of CHD was established for the CAPD patients (Table 5), with NLR ≥2.72 (sensitivity = 95.45%; specificity = 83.33%) and PLR ≥93.09 (sensitivity = 90.91%; specificity = 83.33%). Our ROC analysis also determined the cutoff of NLR and PLR on both RRT and HD-only patients, as shown in Table 5, albeit with a lower specificity value.

DISCUSSION

To the best of our knowledge, this is the first study to propose the utility of NLR and PLR, as well as their clinical cutoff point, for determining the risk of CHD in ESRD patients, with respect to the RRT method used, with significant high sensitivity and specificity. It was hypothesized that NLR and PLR, identified as inflammatory biomarkers, would be significantly related to increased CIMT in CKD patients undergoing dialysis. We present evidence that ESRD patients with CIMT ≥1 at risk for CHD had significantly greater NLR and PLR than patients with lower values of these markers.

Our analysis showed that the NLR and PLR cutoff points of 2.72 and 93.09 on CAPD patients, respectively, had

Table 1. Clinical and laboratory parameters characteristic of the subjects.

Variable	Frequency	Mean ± SD
Age (years)		45.06 ± 11.30
Gender		
Male	49 (68.1%)	
Female	23 (31.9%)	
Nutrition status		
Underweight	7 (9.7%)	
Normoweight	54 (75%)	
Overweight	9 (12.5%)	
Obese	2 (2.8%)	
ESRD duration (years)		4.70 + 2.66
DM		
Yes	4 (5.6%)	
No	68 (94.4%)	
Hematology		
Hemoglobin (g/dl)		9.10 ± 1.53
Leukocyte (10^3/µl)		7.58 ± 2.66
Platelet (10^3/µl)		201.80 ± 67.42
Neutrophil (%)		70.76 ± 10.51
Lymphocyte (%)		20.09 ± 6.78
NLR		4.15 ± 2.12
PLR		140.65 ± 64.31
RRT method		
HD	44 (61,1%)	
CAPD	28 (38,9%)	
CIMT		1.14 ± 0.33
≥1 mm	52 (72.2%)	
<1 mm	20 (27.8%)	

NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; RRT, renal replacement therapy; HD, hemodialysis; CAPD, continuous ambulatory peritoneal dialysis; CIMT, carotid intima-media thickness.

Table 2. Comparison of the effect of confounding variables on the status of CIMT.

Variable	CIMT thickness		*p*-value
	≥1 mm	<1 mm	
Age (years)[a]	45.15 ± 11.67	44.85 ± 10.56	0.774
Gender[b]			0.052
Male	39 (79.6%)	10 (20.4%)	
Female	13 (56.5%)	10 (43.5%)	
Nutrition status[b]			0.232
Underweight	3 (42.9%)	4 (57.1%)	
Normoweight	41 (75.9%)	13 (24.1%)	
Overweight	6 (66.7%)	3 (33.3%)	
Obese	2 (100%)	0 (0.0%)	
CKD duration (years)[a]	4.83 ± 2.54	4.38 ± 2.99	0.830
DM[b]			0.202
Yes	4 (100%)	0 (0.0%)	
No	48 (70.6%)	20 (29.4%)	
RRT method[b]			
HD	30 (68.2%)	14 (31.8%)	0.337
CAPD	22 (78.6%)	6 (21.4%)	
Hematology[a]			
Hemoglobin (g/dl)	9.08 ± 1.39	9.16 ± 1.87	0.848
Leukocyte (10^3/ul)	7.64 ± 2.28	7.42 ± 3.53	0.746
Platelet (10^3/ul)	206.11 ± 66.85	190.60 ± 69.33	0.381
Neutrophil (%)	72.46 ± 9.88	66.32 ± 11.07	0.031[c]
Lymphocyte (%)	18.97 ± 6.39	23.00 ± 7.07	0.029[c]

[a]analysis used chi-square; [b]analysis used logistic regression; [c]significance at $p < 0.05$.
NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; RRT, renal replacement therapy; HD, hemodialysis; CAPD, continuous ambulatory peritoneal dialysis.

Table 3. Association between NLR and PLR to the status of CIMT between RRT methods and collectively.

Variable	CIMT (Mean ± SD)		OR	*p*-value	95% CI of OR	
	≥1 mm	<1 mm			Lower	Upper
CAPD						
NLR	4.82 ± 2.26	2.28 ± 1.07	5.957	0.030*	1.189	29.847
PLR	147.75 ± 62.92	70.00 ± 23.53	1.258	0.092	0.963	1.643
HD						
NLR	4.25 ± 2.27	3.68 ± 1.31	1.169	0.389	0.820	1.667
PLR	144.72 ± 57.58	151.03 ± 77.72	0.998	0.757	0.989	1.008
Both						
NLR	4.49 ± 2.26	3.26 ± 1.38	1.474	0.033*	1.031	2.106
PLR	146.00 ± 59.31	126.72 ± 75.69	1.005	0.257	0.996	1.014

*$p < 0.05$ = significant (logistic regression).
NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CIMT, carotid intima-media thickness.

an optimal sensitivity and specificity in determining the risk of CHD, as assessed by another noninvasive measurement of CHD risk, namely, CIMT. Previous studies have consistently shown that higher NLR and PLR were associated with worse cardiovascular outcomes (Demir *et al*., 2014; Li *et al*., 2020; Yüksel *et al*., 2016; Yulianti *et al*., 2015). These studies showed that both of these easily available markers always had prognostic utility in managing cardiovascular disease. Despite that, evidence regarding the utility of these biomarkers as CHD risk assessment on individuals at risk, especially in the ESRD population, was lacking and therefore was urgently needed. Regarding NLR, available evidence shows that even at a low level of 1.53, it was significantly associated with coronary microvascular dysfunction (Chen *et al*., 2021). Our NLR cutoff point of 2.72 was a bit higher than other studies on non-ESRD patients, which invariably set the cutoff at 1.96–2.26, albeit ours had higher sensitivity and specificity (Fernando *et al*., 2015; Kizilarslanoğlu *et al*., 2017). Our PLR cutoff point of 93.09 was considerably lower than any available evidence of cutoff point in other studies of non-ESRD patients, which was invariably determined at 137–150, although these studies ultimately observe the prognostic implication of the cutoff point (Lee *et al*., 2018; Li *et al*., 2017). Our high sensitivity and specificity of these cutoff values in CAPD patients should be noted with caution because these values were determined based on CIMT status, which did not conclude the presence of CHD but rather determined the higher risk of CHD. This should also apply to the cutoff in our HD groups and collectively, albeit our results showed lower specificity in these groups.

Table 4. Receiver operative curve analysis between NLR and PLR to the status of CIMT between RRT methods and collectively.

Variable	AUC	Std. Error	*p*-value	95% CI of AUC	
				Lower	Upper
CAPD					
NLR	0.9091	0.0778	<0.001[a]	0.567	0.9837
PLR	0.9697	0.0334	<0.001[a]	0.7577	0.9966
HD					
NLR	0.5333	0.0916	0.358	0.3309	0.6889
PLR	0.4738	0.1027	0.600	0.2501	0.6495
Both					
NLR	0.6639	0.071	0.010[a]	0.5011	0.7814
PLR	0.6115	0.086	0.097	0.4154	0.7533

[a]$p < 0.05$ = significant, null hypothesis: true area = 0.5.
NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; HD, hemodialysis; CAPD, continuous ambulatory peritoneal dialysis.

The underlying role of neutrophils, platelets, and lymphocytess in the pathophysiology of CHD and related disorders has been extensively researched worldwide. It was thought to be related to their nature in immune-inflammatory activity. These laboratory tests provide a low-cost and broadly accessible screening technique for at-risk groups, particularly CKD patients. Increased inflammatory activity in CKD patients was mainly attributed to elevated systemic concentrations of proinflammatory cytokines due to impaired renal clearance and increased synthesis (Uysal *et al*., 2022). These conditions will further increase the process of atherosclerosis, increasing the risk of an injury to the tunica intima of arteries and the blood vessels' endothelium, which causes neutrophil adhesion, aggregation, and platelet activation. Neutrophil extracellular traps (NETs) are the most well-known initiation mechanism for thrombus formation in individuals at risk. DNA and histones constitute the matrix of active NETs (Kapoor *et al*., 2018). This matrix serves as a scaffold and binds erythrocytes and platelets (Fuchs *et al*., 2007, 2010). Through platelet binding to DNA and subsequent activation by histones, they increase platelet activation, platelet aggregation, and thrombosis (Fuchs *et al*., 2010, 2011). Activated platelets resulting from the interaction between NETs and platelets connect to neutrophils via glycoprotein Ib and stimulate further NET recruitment; this vicious cycle propagates thrombus development (Kapoor *et al*., 2018; von Brühl *et al*., 2012). This platelet activation will further propagate atherosclerosis formation (Yulianti *et al*., 2015).

Table 5. Receiver operative curve analysis of sensitivity and specificity of NLR and PLR cutoff to the status of CIMT between RRT methods and collectively.

Variable	Cut-off[a]	Sensitivity	95% CI of Sensitivity		Specificity	95% CI of Specificity	
			Lower	Upper		Lower	Upper
CAPD							
NLR	≥2.72	95.45%	77.16%	99.88%	83.33%	35.88%	99.58%
PLR	≥93.09	90.91%	70.84%	98.88%	83.33%	35.88%	99.58%
HD							
NLR	≥2.40	83.33%	65.28%	94.36%	21.43%	4.66%	50.80%
PLR	≥82.46	90.00%	73.47%	97.89%	21.43%	4.66%	50.80%
Both							
NLR	≥2.50	86.54%	74.21%	94.41%	40.00%	19.12%	63.95%
PLR	≥85.62	90.38%	78.97%	96.80%	40.00%	19.12%	63.95%

[a]Determined by best sensitivity and Youden Index.
NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; HD, hemodialysis; CAPD, continuous ambulatory peritoneal dialysis.

The role of lymphocytes in the development of atherosclerosis remained contentious. The T-helper (Th1), a subpopulation of CD4+ T cells, which generates IFN-γ and TNF-α preferentially (Frostegård *et al*., 1999), possesses strong proatherogenic activity (Hedrick, 2015; Li and Ley, 2015). Th2 cells, in contrast to Th1 cells, are antiatherogenic because switching the T-cell response from Th1 to Th2 is related to a reduction in atherogenicity, although this remains controversial (Huber *et al*., 2001; Schulte *et al*., 2008). Regulatory T cells (Tregs) and B cells have been proposed as antiatherogenic, despite the small number of studies in this area (Hedrick, 2015; Li and Ley, 2015). Furthermore, in acute coronary syndrome (ACS) patients, NLR and PLR have also been established to be related to the severity of the ACS (Goutham *et al*., 2015). The increase in NLR will increase the risk of death by 2.1 times (Tatar *et al*., 2016), and especially in CAPD patients, poses a higher risk of arterial stiffness and a greater risk of cardiovascular death (Lu *et al*., 2018).

Dialysis-related cardiac complications in CKD patients were not uncommon. It was long debated whether CAPD or HD patients had a higher risk of cardiovascular disease or mortality. Among these, HD was associated with a higher prevalence of de novo congestive heart failure (Wang *et al*., 2016) and more cardiovascular events, including atrial fibrillation and peripheral artery disease, compared to CAPD patients, despite considerably lower cardiovascular mortality (Ng *et al*., 2020). This is in favors of our study result, which showed that all patients in HD groups are at risk of CHD, marked by elevated CIMT. Evidence of aberrant metabolic marker alterations, mainly albumin, apolipoprotein-B, homocysteine, and C-reactive protein, between HD and CAPD was available, yet unremarkable, rendering the pathophysiology behind this trend mostly unclear (Helal *et al*., 2010). It was long believed that the dialysis procedure in CAPD and HD produces inflammation and oxidative stress related to its dialysate, regardless of the technique. Bioincompatibility and other dialysis-related factors can result in the release of proinflammatory cytokines and endothelial dysfunction. These elevated proinflammatory cytokines will increase the number of circulating neutrophils, which will, in turn, promote platelet activation in impaired endothelium locations and initiate the vicious cycle of neutrophil-platelet activation previously described (Kapoor *et al*., 2018; von Brühl *et al*., 2012). These will increase the neutrophil and platelet, thus relatively increasing NLR and PLR, consecutively. These vicious cycles of recruitment of neutrophils and platelet would increase inflammatory markers, such as TNF-α and CRP, thereby accelerating atherosclerosis as renal function decreases. Several other factors, including oxidative stress and chronic infection, may also be involved in the inflammatory process (Mehrotra *et al*., 2016; Nurhayatun, 2017).

The chronic inflammatory conditions experienced by CKD patients undergoing dialysis contribute to the incidence of atherosclerosis and its complications (Nusair *et al*., 2012). Cardiovascular mortality is two times higher in stage III CKD patients and three times higher in stage IV CKD patients compared to individuals with normal kidney function (Kasliwal *et al*., 2014). Other studies support the relationship between kidney damage and cardiac cell death by reporting that in CAPD patients, CIMT showed an association with cardiac troponin T levels and concentric left ventricular hypertrophy (Asicioglu *et al*., 2021; Benedetto *et al*., 2001).

In this study, the results of the CIMT measurement obtained a mean value of 1.14 ± 0.33 mm and more subjects in CIMT ≥1 mm groups. CIMT in this study was measured in both the right and left carotid. Then the maximum CIMT value is used in the statistical analysis. The maximal CIMT has been shown as an independent predictor of CHD and has a positive relationship with anterior and posterior coronary wall thickness (Ruscica *et al*., 2019). Across several studies, the cutoff ≥1 mm gave 31%–66% sensitivity and 79%–90% specificity in the prediction of CHD (Lu *et al*., 2018; Zhang *et al*., 2014).

As a cross-sectional study, the primary limitation of the current investigation is that its nature cannot establish a causal relationship between exposure and disease. In determining the risk of cardiovascular disease, the study also did not compare NLR and PLR with other established inflammatory biomarkers, such as TNF-α, IL-1, IL-6, and CRP. This is justified in our study because we aim to determine alternative cost-effective, and widely available CHD markers, especially in lower setting centers, wherein those biomarkers are typically unaffordable.

The primary diagnosis of CHD by coronary arteriography and other noninvasive cardiovascular imaging modalities, including CIMT, is expensive and time-consuming and exposes the patient to radiation. On the other hand, we showed that more affordable and widely available hematology analysis parameters, namely, NLR and PLR, could also be used as an initial screening to determine the risk of CHD. These parameters could be developed further as a preliminary CHD risk assessment or routine examination of individuals with ESRD, particularly in lower setting centers, before referral to advanced imaging modalities available in more advanced centers.

CONCLUSION

The present study demonstrated a new option in assessing, predicting, and evaluating the occurrence of atherosclerosis in ESRD, both HD or CAPD, by using one of the most commonly available and simple laboratory analyses, the NLR and PLR. We advocate the use of these laboratory data in a novel strategy for early diagnosis, prediction, and assessment of atherosclerosis that is less expensive and less complicated, especially in limited-resource settings. Furthermore, these findings could promote several similar studies to further develop better choices in the early detection of cardiovascular complications to better minimize the already heavy burden of ESRD patients needing RRTs.

AUTHORS' CONTRIBUTIONS

WP, DNB, and AW were involved in planning and supervising the work; AS, HP, NAP, and YSP performed the measurements; WP, DNB, AW, AS, HP, NAP, and YSP processed the experimental data, performed the analysis, and designed the figures. WP, DNB, AW, AS, HP, NAP, and YSP performed the data calculation and statistical analysis. All authors equally contributed to interpreting the results and worked on the draft of

the manuscript. All authors discussed the results and approved the manuscript.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the international committee of medical journal editors (ICMJE) requirements/guidelines.

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CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

ETHICAL APPROVALS

This study was approved by the Health Research Ethics Committee at Moewardi General Hospital with the number 1.338/I/HREC/2021. We also obtained informed consent from all the eligible patients. The study protocol was registered on ClinicalTrials.gov with ID NCT05472805.

DATA AVAILABILITY

All data generated and analyzed are included in this research article.

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