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Original Article

Red Blood Cell Distribution Width to Platelet Count Ratio as a Marker of Cardiovascular Complications in CKD Patients

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Abstract

Background: Chronic Kidney Disease (CKD) significantly increases the risk of cardiovascular complications, the leading cause of morbidity and mortality in this population. Identifying reliable markers, such as the Red Blood Cell Distribution Width (RDW) to Platelet Count Ratio (RPR), could improve early intervention and management.

Aim: to determine Red blood cell distribution width to platelet ratio as a marker of cardiovascular complications in CKD patients.

Methods: This observational study involved 100 CKD patients receiving dialysis. Data collection included medical history, clinical evaluations, and laboratory investigations. Cardiovascular assessments were conducted using electrocardiography and echocardiography. The RPR was calculated and analyzed for its correlation with cardiovascula complications.

Results: The study included 52 males and 48 females, with a mean age of 66.79 ± 9.38 years. Hematological parameters included a mean hemoglobin level of 10.88 ± 2.47 g/dL, WBC count of 9.813 ± 3.988 x10⁹/L, platelet count of 201.17 ± 64.84 x10^9/L, and RDW of 14.54 ± 1.59. The mean RDW to platelet ratio was 0.07 ± 0.02. Significant correlations were observed between higher RPR and the presence of diabetes mellitus, ischemic heart disease, diastolic dysfunction, and segmental wall motion abnormalities (SWMA). Lower RPR was associated with left ventricular hypertrophy (LVH) and reduced ejection fraction (EF). ROC-curve analysis demonstrated that RPR could predict major adverse cardiac events with high specificity and positive predictive value.

Conclusion: The RDW to Platelet Count Ratio (RPR) is a significant marker of cardiovascular complications in CKD patients. This non-invasive and cost-effective parameter could enhance clinical risk stratification and guide therapeutic interventions

Keywords: Chronic Kidney Disease, Cardiovascular Complications, Red Blood Cell Distribution Width, Platelet Count, Biomarkers, Predictive Value

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Introduction

Chronic Kidney Disease (CKD) is a major global public health issue, marked by the progressive decline of kidney function over time. Individuals with CKD face a heightened risk of cardiovascular complications, which are the primary cause of illness and death in this group. [1] Identifying reliable biomarkers for predicting cardiovascular events in CKD patients is essential for early intervention and the development of better management strategies.

Recent research has investigated the potential of the Red Blood Cell Distribution Width (RDW) to Platelet Count Ratio (RPR) as an indicator of cardiovascular complications across different clinical contexts. RDW, which measures the variability in red blood cell size, is linked to inflammation and oxidative stress, both of which play roles in cardiovascular disease (CVD). Platelet count, on the other hand, plays a critical role in thrombosis and hemostasis, which are key processes in the pathogenesis of cardiovascular events. [3]

The RDW to Platelet Count Ratio (RPR) integrates these two parameters and has been proposed as a novel inflammatory indicator with prognostic value in critically ill patients. [3] Studies have shown that an elevated RPR is associated with increased mortality in sepsis patients and adverse outcomes in heart failure. [4]

This suggests that RPR could potentially serve as a valuable marker of cardiovascular complications in CKD patients.

This study seeks to examine the correlation between RPR and cardiovascular complications in CKD patients, offering insights that could improve clinical risk assessment and inform therapeutic strategies.

Patients and methods

This observational study was conducted at our Hospital, specifically within the Department of Internal Medicine and the Coronary Care Unit during the period from May 2023 to June 2024.

Ethical Approval: The Institutional Review Board, Faculty of Medicine permitted this work [8 /2 /2023] (Approval no. NCT05754827), and all participants provided a well- informed consent to join the work.

The study included 100 patients who met specific inclusion criteria: they had to be diagnosed with CKD with and without dialysis, and they had to be over the age of 18. Several exclusion criteria were applied to refine the study population. Patients were excluded if they had serious complications in other organs, had undergone kidney transplantation, had infections, received blood transfusions, or were on immunosuppressive drugs within the past three months. Pregnant women, individuals with chronic hematological diseases, and those under 18 were also excluded from the study.

Data Collection and Measurements

Each patient underwent a thorough medical evaluation that began with the collection of personal and family medical histories. This included information on age, sex, smoking status, history of hypertension (HTN), diabetes mellitus (DM), ischemic heart disease, and any family history of chronic kidney diseases. Following this, a detailed clinical examination was conducted for each participant.

Peripheral venous blood samples were collected using appropriate vacutainers, and a series of laboratory investigations were performed. These included a complete blood count (CBC) to measure hemoglobin (HB), mean corpuscular volume (MCV), platelet count (PLT), and white blood cell count (WBCs). The RDW levels were also deterined, with normal ranges defined by the laboratory machine Sysmex XL 1000 (11.5 to 14.5). Additional tests included serum creatinine and blood urea levels to assess kidney function, and a full lipid profile to evaluate cardiovascular risk factors.

Cardiovascular assessments were conducted using electrocardiography (ECG) to detect ischemic changes and echocardiography to identify segmental wall motion abnormalities (SWMA) and structural heart diseases. These assessments were crucial in evaluating the cardiovascular health of the participants and identifying any complications associated with CKD.

The RDW to platelet ratio (RPR) was calculated for each patient using the formula: RPR = (RDW × 100) / PLT (10^9/L). This ratio was analyzed to determine its potential correlation with cardiovascular complications in CKD patients. Through these comprehensive evaluations and measurements, the

study aimed to provide insights into the significance of RPR in predicting cardiovascular outcomes in this patient population.

Statistical analysis

Data analysis was performed using IBM SPSS software version 25.00 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Qualitative data were presented as numbers and percentages, while quantitative data were described using range, mean, standard deviation, median, and interquartile range (IQR). The Shapiro-Wilk test assessed the normality of distribution. Statistical significance was set at the 5% level. The following tests were employed: Chi-square test, Mann Whitney test and Kruskal-Wallis test.

Results

This study enrolled 100 patients with CKD who were receiving dialysis treatment. Their ages ranged from 46 to 85 years, with a mean age of 66.79 ± 9.38 years. Gender distribution was almost even, with 52% males and 48% females, resulting in a male-to-female ratio of 1.08:1. Regarding comorbidities, 28% of the patients had diabetes mellitus (DM), 48% were hypertensive, 88% had ischemic heart disease, and 40% were smokers. Additionally, 28% of the patients had a positive family history of CKD **(Table 1).**

Table 1: Demographic data and comorbidity of the studied cases.

		Studied patients (N= 100)	
		N	**%**
Age (years)	**Mean± SD**	66.79± 9.38	
	Median	68.0	
	Range	46.0 – 85.0	
Gender	**Male**	52	52.0%
	Female	48	48.0%
Comorbidities	DM	28	28.0%
	HTN	48	48.0%
	IHD	88	88.0%
	Smoking	40	40.0%
Family history of CKD		28	28.0%

Vital signs and hemodynamic assessments showed that the mean systolic blood pressure was 133.96 ± 22.87 mm/Hg, and the mean diastolic blood pressure was 78.96 ± 10.82 mm/Hg. The mean heart rate was 97.58 ± 19.45 beats/min, and pallor was observed in 40% of the cases.

The CKD staging among the patients revealed that 48% were in stage 5, 16% were in stage 4, and 36% were undergoing regular dialysis. The mean estimated glomerular filtration rate (eGFR) was 13.5 ± 9.15 ml/min/1.73m².

Hematological parameters indicated that the mean hemoglobin level was 10.88 ± 2.47 g/dL. The mean WBC count was 9.813 ± 3.988 $x10^9$/L, and the mean platelet count was 201.17 ± 64.84 $x10^9$/L. The mean RDW was 14.54 ± 1.59, and the MCV was 83.68 ± 7.80. The mean RDW to platelet ratio was 0.07 ± 0.02 **(Table 2).**

Table 2: Distribution of patients as regard laboratory data.

	Studied patients (N= 100)						
	Mean	**±SD**	**Median**	**IQR**		Range	
Hb (g/dl)	10.88	±2.47	10.5	9.50	12.2	6.9	**15.50**
WBCs (×10^9/L)	9.813	±3.988	8.8	7.5	11.9	3.5	**20.0**
Platelets count (×10^9/L)	201.17	±64.84	193.0	158.0	233.0	96.0	**404.0**
RDW	14.54	±1.59	13.9	13.5	15.4	12.0	**19.3**
MCV	83.68	±7.80	85.0	81.0	89.0	66.0	**99.0**
RDW: PLT ratio	0.07	±0.02	0.07	0.06	0.09	0.04	**0.1**
S. Creatinine (mg/dL)	5.13	±2.03	5.0	4.3	5.80	1.7	**9.5**
Blood urea (mg/dL)	120.29	±35.29	110.0	100.0	140.0	60.0	**193.0**
CRP (mg/dL)	**0.46**	±**0.49**	**0.0**	**0.0**	**1.0**	**0.0**	**1.0**

Renal function tests showed a mean creatinine level of 5.13 ± 2.03 mg/dL and a mean blood urea level of 120.29 ± 35.29 mg/dL. The mean C-reactive protein (CRP) level was 0.46 ± 0.49 mg/dL. The lipid profile of the patients indicated that the mean triglycerides level was 115.21 ± 42.21 mg/dL. The mean low-density lipoprotein (LDL) level was 71.33 ± 15.33 mg/dL, and the mean high-density lipoprotein (HDL) level was 26.29 ± 4.88 mg/dL.

Electrocardiography (ECG) findings showed that 16% of the patients had a normal sinus rhythm. Inverted T waves were present in 32% of the cases, left bundle branch block (LBBB) in 28%, atrial fibrillation (AF) in 16%, pathological Q waves in 4%, and raised ST segments in 4% **(Table 3).**

Table 3: ECG findings among the studied cases.

		Studied patients (N= 100)	
		N	**%**
ECG	**Normal**	16	16.0%
	Inverted T wave	32	32.0%
	LBBB	28	28.0%
	AF	16	16.0%
	RBBB	8	8.0%
	Pathological Q wave	4	4.0%
	Rising ST segment	4	4.0%

Echocardiography findings revealed that diastolic dysfunction was reported in 76% of the cases, with 56% having grade I and 20% having grade III diastolic dysfunction. Left ventricular hypertrophy (LVH) was observed in 32% of the cases, with 28% having a mild degree and 4% having a mild to moderate degree. The most frequent valvular lesion was mitral regurgitation (56%), followed by tricuspid regurgitation (32%). The mean ejection fraction (EF) was 47.04 ± 12.43%, ranging from 23% to 67%, with 36% having an EF less than 40% **(Table 4).**

Table 4: Echocardiography findings among the studied cases.

		Studied patients (N= 100)	
		N	%
Diastolic dysfunction	**No**	24	24.0%
	Grade 1	56	56.0%
	Grade 3	20	20.0%
Left ventricular hypertrophy	**No**	68	68.0%
	Yes	32	32.0%
	• **Mild**	28	28.0%
	• **Mild to moderate**	4	4.0%
Valvular Lesion	**No**	32	32.0%
	Mild AR	4	4.0%
	Trace MR	4	4.0%
	Mild MR	16	16.0%
	Moderate MR	20	200%
	Severe MR	16	16.0%
	Mild TR	12	12.0%
	Moderate TR	12	12.0%
	Sever TR	12	12.0%
	Aortic sclerosis	4	4.0%
	Sclerotic AV	4	4.0%
SWMA	**No**	8	8.0%
	Yes	92	92.0%
EF (%)	**Mean± SD**	47.04± 12.43	
	Median (IQR)	50 (35- 55)	
	Range	23 – 67	
EF	**EF >40%**	64	64.0%
	EF <40%	36	36.0%

Analysis of the RDW to platelet ratio indicated that patients with DM, ischemic heart disease, and a family history of CKD had significantly elevated RDW to platelet ratios compared to those without these factors ($p = 0.046$, $p = 0.039$, and $p = 0.003$, respectively). No significant relationship was found between the RDW to platelet ratio and CKD stage ($p > 0.05$). Patients with diastolic dysfunction and segmental wall motion abnormalities (SWMA) had significantly higher RDW to platelet ratios compared to those without these factors ($p = 0.013$ for both). Conversely, patients with left ventricular hypertrophy and EF less than 40% had significantly lower RDW to platelet ratios compared to those without LVH ($p < 0.001$) **(Table 5 & 6).**

Table 5: Relation between RDW: PLT ratio and CKD

		RDW: PLT ratio							Kruskal Wallis test	
		Mean	SD	Median	IQR		Range		Kw	P-value
CKD	On Regular dialysis	.071	.018	.070	0.06	0.08	0.04	0.1	0.603	0.740
	Stage 4	.070	.019	.065	0.06	0.09	0.05	0.1		
	Stage 5	.074	.019	.070	0.06	0.1	0.05	0.1		

p>0.05 is not significant, p≤0.05 is significant, p≤0.01 is highly significant, IQR: Interquartile range, Kw: Kruskal Wallis test

Table 6: Relation between RDW: PLT ratio and Echo findings

		RDW: PLT ratio							ZMWU/Kw	P-value
		Mean	SD	Median	IQR		Range			
Diastolic dysfunction	No	0.065	0.017	0.06	0.05	0.07	0.05	0.1	2.490	**0.013**
	Yes	0.074	0.018	0.07	0.06	0.09	0.04	0.1		
Left ventricular hypertrophy	No	0.077	0.019	0.07	0.07	0.1	0.04	0.1	3.90	**<0.001**
	Yes	0.062	0.014	0.06	0.05	0.07	0.05	0.09		
SWMA	No	0.055	0.016	0.055	0.04	0.07	0.04	0.07	2.476	**0.013**
	Yes	0.074	0.018	0.07	0.06	0.09	0.05	0.1		
EF	EF >40%	0.078	0.016	0.071	0.06	0.1	0.06	0.1	4.14	**<0.001**
	EF <40%	0.062	0.018	0.05	0.05	0.07	0.04	0.1		

P value< 0.05 is significant, P value< 0.01 is highly significant, SD: Standard deviation, ZMWU: Mann-Whitney U Test

There was a significant positive correlation between the RDW to platelet ratio and EF (r = 0.306, p = 0.002), and significant negative correlations between the RDW to platelet ratio and both systolic blood pressure (r = -0.244, p = 0.014) and triglyceride levels (r = -0.263, p = 0.008).

Using ROC-curve analysis, the RDW to platelet ratio was found to detect major adverse cardiac events with a sensitivity of 55.6%, specificity of 100%, positive predictive value (PPV) of 100%, and negative predictive value (NPV) of 69.3% (p < 0.001) (Figure 1)

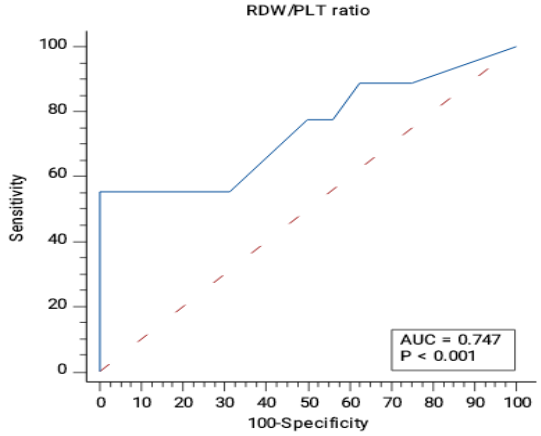

Figure 1: ROC curve of RDW: PLT ratio in prediction of cardiovascular complications in CKD patients.

Discussion

The RDW to Platelet Count Ratio (RPR) has emerged as a key marker of cardiovascular complications in patients with CKD. Research reveals that those with CKD and end-stage renal disease (ESRD) have a heightened risk of cardiovascular events, which are a leading cause of morbidity and mortality in this demographic .[5]Numerous studies have demonstrated that an elevated RPR is a

reliable marker for forecasting cardiovascular events in hemodialysis patients. [6]

This study seeks to evaluate the predictive utility of RPR as a marker for cardiovascular complications in CKD patients. By analyzing the relationship between RPR and the incidence of cardiovascular events, such as myocardial infarction and stroke, in CKD patients, the study aims to determine the efficacy of RPR as a prognostic tool. Ultimately, the goal is to improve early diagnosis, enhance risk stratification, and inform therapeutic interventions to decrease cardiovascular morbidity and mortality in this high-risk group.

Our study provides a comprehensive analysis of the demographic characteristics, clinical profiles, and laboratory parameters of CKD patients. The mean age of our participants was 66.79 ± 9.38 years, with a slight male predominance (52% males, 48% females), mirroring the demographics observed in studies by **Hsieh et al.** [7] and **Roumeliotis et al**,**[8]** where the mean ages were 64.2 ± 12.35 years and 68.5 years (range: 25–89), respectively.

Our assessment of vital signs and hemodynamic parameters revealed mean systolic and diastolic blood pressures, heart rate, and the prevalence of pallor among CKD patients, which were similar to those reported by **Roumeliotis et al. [8]**, establishing a commonality in hemodynamic profiles across studies with a mean systolic pressure of 134.1 ± 22.1 mm Hg and a mean diastolic pressure of 82.1 ± 13.1 mm Hg, comparable to our findings.

The distribution of CKD stages in our cohort showed that nearly half were classified as stage 5, 16% as stage 4, and 36% were undergoing regular dialysis. These distributions were consistent with those observed by **Hsieh et al.** [7]) who reported 28.28% of patients in stage 3, 37.49% in stage 4, and 34.23% in stage 5, while **Deng et al.** [9] found 56.02% in stage 3 and 33.27% in stage 4. The mean eGFR in our study was 13.5 ± 9.15 ml/min/1.73 m², **Wang et al.** [10] observed a mean eGFR of 14.2 ± 8.7 ml/min/1.73 m² in their CKD cohort, further supporting our results.

Our study also examined various laboratory parameters, revealing a mean hemoglobin level of 10.88 ± 2.47 g/dl, a mean WBCs of 9.813 ± 3.988 $x10^9$/L, a mean platelet count of 201.17 ± 64.84 $x10^9$/L, a mean RDW of 14.54 ± 1.59, and a mean MCV of 83.68 ± 7.80. Our results are consistent with study of **Hsieh et al.** [7] who reported a mean hemoglobin level of 10.64 ± 2.14 g/dL, a mean WBC count of 7.49 ± 2.50 x10^3µL, and a mean platelet count of 227.27 ± 75.81 x10^3/µL.

Echocardiographic assessments revealed significant cardiac abnormalities, including diastolic dysfunction in 76% of cases (56% grade I, 20% grade III) and left ventricular hypertrophy (LVH) in 32% (28% mild, 4% mild to moderate). The most common valvular lesion was mitral regurgitation (56%), followed by tricuspid regurgitation (32%). The mean ejection fraction (EF) was 47.04 ± 12.43%, with 36% of patients having EF < 40%. These findings align with those reported by **Jameel et al**,[11] who found similar prevalence rates for LV dysfunction, LV diastolic dysfunction, and LVH in CKD patients.

Our result regarding the RDW: PLT ratio and its correlation with clinical factors showed significant associations with diabetes mellitus, ischemic heart disease, and a family history of CKD. No significant association was found between RDW: PLT ratio and CKD stage. These results are consistent with **Elkhashab et al**,[12] who reported correlations between RDW and various cardiovascular risk factors

Our study identified significant associations between RDW: PLT ratio and various echocardiographic findings, emphasizing its potential as a prognostic indicator in CKD-associated cardiac pathology. Specifically, we found correlations between RDW: PLT ratio and diastolic dysfunction, SWMA, and LVH.

Patients with LVH and an EF less than 40% exhibited a notable decline in RDW: PLT ratio, which suggests that a higher RDW: PLT ratio may be indicative of more severe cardiac dysfunction. This finding is particularly significant as it underscores the potential utility of RDW: PLT ratio in predicting adverse cardiac outcomes in CKD patients.

Our results are in line with those reported by **Elkhashab et al**,[12] who also found significant correlations between RDW and various cardiac parameters, including left atrial size, end-diastolic volume, end-systolic volume, and ejection fraction.

Elkhashab et al. highlighted that elevated RDW levels were associated with worsened cardiac function, which aligns with our observations that a higher RDW: PLT ratio correlates with reduced EF and increased prevalence of diastolic dysfunction and LVH.

Similarly, **Zhu et al.** [6] demonstrated that RDW: PLT ratio is a valuable marker for assessing cardiovascular risk in hemodialysis patients. Their study found that higher RDW: PLT ratios were associated with increased incidence of cardiovascular events, supporting the prognostic value of this ratio in CKD populations. Zhu et al. also noted that RDW: PLT ratio could effectively predict major adverse cardiac events (MACE), with their findings showing a high sensitivity and specificity for this marker, consistent with our ROC-curve analysis.

Kim et al. [13] further validated these findings by identifying a significant association between elevated RDW and increased cardiovascular risk in CKD patients. Their research demonstrated that patients with higher RDW levels were more likely to experience adverse cardiac outcomes, reinforcing the potential of RDW as a non-invasive biomarker for cardiovascular risk stratification in CKD.

Our ROC-curve analysis demonstrated the utility of RDW: PLT ratio in detecting major adverse cardiac events (MACE), revealing a high sensitivity of 55.6% and perfect specificity of 100%. These metrics highlight the RDW: PLT ratio as a robust marker for identifying CKD patients at high risk for severe cardiovascular outcomes.

Our findings are consistent with those of **Zhu et al** ,[6] who evaluated the RDW: PLT ratio in a cohort of hemodialysis patients and found it to be a strong marker of cardiovascular events. Zhu et al. reported an area under the curve (AUC) of 0.88 for the RDW: PLT ratio, with high sensitivity and specificity, underscoring its effectiveness in risk stratification for cardiovascular complications. Their study's results align closely with our findings, suggesting that the RDW: PLT ratio is a reliable indicator across different CKD subgroups.

Similarly, **Wu et al.** [14] investigated the prognostic value of RDW: PLT ratio in hemodialysis patients and reported significant predictive accuracy. They identified an optimal cut-off value for the RDW: PLT ratio that maximized both sensitivity and specificity, supporting the ratio's clinical utility in predicting adverse cardiac events. This further validates our results and emphasizes the importance of incorporating RDW: PLT ratio into routine clinical assessments for CKD patients.

Additionally, **Zhang et al.** [15] conducted a comprehensive study on the predictive power of RDW: PLT ratio for cardiovascular events in CKD patients, reporting an AUC of 0.89. Their analysis demonstrated high sensitivity and specificity, reinforcing the robustness of our findings. Zhang et al. highlighted the RDW: PLT ratio as a non-invasive, easily obtainable marker that could significantly enhance the early detection and management of cardiovascular risks in CKD populations.

Conclusion

In the current study, our aim is to determine Red blood cell distribution width to platelet ratio as a marker of cardiovascular complications in CKD patients. In the current study the RDW to platelet ratio was demonstrated to be an effective marker for the cardiovascular complications in CKD patients. with the area under the curve 0.747 with sensitivity and specificity was 55.6%% and 100% respectively. The present findings suggest that these easily accessible parameters, which can be obtained in a non-invasive and cost-efficient manner, have the potential to be utilized as new diagnostic markers for cardiovascular events in patients with CKD. Further prospective randomized multicenter studies with larger sample size is needed.

Limitation:

- Our study has some limitations, small sample size also differences in participants characteristics may have influenced the results.
- Further prospective randomized multicenter studies with larger sample size is needed.

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