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Effect of Parathormone and Phosphate Level on Platelet Indices and Platelet Lymphocyte Ratio in End Stage Renal Disease Patients on Hemodialysis

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ABSTRACT

Background: A higher risk of death is linked to elevated levels of parathyroid hormone (PTH). Chronic kidney disease (CKD) is one of numerous inflammatory diseases that has recently developed neutrophil lymphocyte ratio and platelet lymphocyte ratio (PLR) as prognostic indicators. **Objective:** To determine how hemodialysis-dependent end-stage renal disease (ESRD) patients' parathormone and phosphate levels affected platelet indices and PLR.

Subjects and Methods: Analytical cross-sectional trial was conducted on 140 subjects aged ≥ 18 years old of both sexes. They were separated into three groups: Group I (n=100): ESRD on HD, group II (n=20): CKD patients not on HD and group III (n=20): healthy subjects as a control group.

Results: Mean platelet volume (MPV) was positively correlated with CRP, total calcium, and ionized calcium. Plateletcrit (PCT) was positively correlated with sex, total leukocytic count (TLC), absolute lymphocytes, platelets, PLR and estimated glomerular filtration rate (eGFR). Platelet distribution width (PDW) was positively correlated with serum creatinine. PLR was positively correlated with platelets, PCT, and CRP. PCT was significantly lower in ESRD than in controls, while PDW was significantly higher in the same comparison. PDW had the largest area under the curve of ROC curve and can discriminate ESRD from CKD and CKD from controls.

Conclusions: Hyperphosphatemia could lower MPV and vice versa but has no effect on other platelet indices or PLR. There was no effect of parathormone level variation on any of platelet indices or PLR. CKD can be strongly suspected from PDW variation and fairly suspected from MPV.

Keywords: End-Stage Renal Disease, Chronic Kidney Disease, Hemodialysis, Parathormone, Renal Replacement Therapy, Phosphate Level.

INTRODUCTION

The demand for renal replacement therapies like hemodialysis (HD) is increasing as the occurrence of end-stage renal disease (ESRD) rises due to global aging [1]. Platelet parameters, like plateletcrit (PCT), mean platelet volume (MPV), platelet distribution width (PDW), and platelet count, evaluate size, shape, and anisocytosis of circulating platelets and can also portray platelet activity [2].

A new prognostic indicator linked to inflammation in numerous diseases, including chronic kidney disease (CKD), is the platelet lymphocyte ratio (PLR) [3].

This investigation evaluated the impact of parathyroid hormone (PTH) and phosphate levels on platelet indices and PLR in ESRD on HD.

SUBJECTS AND METHODS

A cross-sectional trial was directed on 140 subjects aged ≥ 18 years old of both sexes, with ESRD on regular HD, CKD patients not on HD (stages 3, 4, 5ND) and healthy control subjects, from January 2023 to June 2023.

Individuals with a history of parathyroidectomy, a serious infection, cancer, or an unstable medical condition within the past 30 days were excluded.

Participants were separated into 3 groups: group I (n=100): ESRD on HD (CKD stage 5D), group II (n=20): CKD patients not on HD (stages 3, 4, 5ND) [4] and group III (n=20): healthy participants as a control group.

Detailed medical history taking, physical examination, and diagnostic testing were administered to each patient [complete blood count (CBC), CRP, kidney function tests (serum creatinine and blood urea), eGFR to estimate CKD stage was calculated by CKD-EPI creatinine equation 2021 [5], serum calcium (total and ionized), phosphorus and PTH].

Measurement of platelet count (normal range: 150,000-450,000), PCT (normal range: 0.22–0.24%), MPV (normal range: 7.5:12 fL) and PDW (normal range: 8.3:56.6%) and calculation of PLR was done.

Ethical considerations:

The study was done after being accepted by the Research Ethics Committee, Tanta University (approval code: 36181/12/22). All patients provided written informed consents prior to their enrolment. The consent form explicitly outlined their agreement to participate in the study and for the publication of data, ensuring protection of their confidentiality and privacy. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

We used SPSS Inc.'s (Chicago, IL, USA) version 23 to analyze the data. For the purpose of describing qualitative data, percentages and numbers were utilized. For numerical variables, we used standard deviation and mean. A p-value of 0.05 or less was considered statistically significant.

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RESULTS

No significant differences in age, sex distribution, total leukocyte count (TLC), absolute lymphocytes, MPV, and PLR across the studied groups. Hemoglobin levels were significantly lower in both the ESRD and CKD groups than controls. Procalcitonin (PCT) and eGFR were notably reduced in the ESRD group than CKD and controls. In contrast, PDW, PTH, phosphorus, CRP, and serum creatinine were elevated in ESRD. Total and ionized calcium were lower, and blood urea was higher in CKD than other groups **(Table 1)**.

Table 1: Comparison among all the studied groups as regards demographic data and laboratory investigations

		ESRD group (n=100)	CKD group (n=20)	Control group (n=20)	P
Age (Years)		60.40±7.82	58.2±8.54	45.45±10.45	**<0.001*** (a)
Sex	**Male**	61 (61%)	11 (55%)	10 (50%)	0.621 (b)
	Female	39 (39%)	9 (45%)	10 (50%)	
Laboratory investigations					
Hemoglobin (g/dL)		10.27±1.69	10.27±1.43	12.39±1.27	**<0.001*** (a)
		P1 = 0.984, **P2 < 0.001*, P3 < 0.001***			
TLC (×10³ Cells/mm³)		6.4258±1.3992	7.623±1.4992	7.0231±1.9799	0.129 (a)
Absolute lymphocytes (Cell/mm³)		1939.63±78.35	1917.85±94.8	2136±51.5	0.523 (a)
Platelets (×10³ cell/mm³)		206.935±8.7293	245.35±8.1063	222.6±27.6584	0.059 (a)
MPV (fl)		9.78±1.29	9.37±0.45	10.0±0.82	1.625 (a)
PCT (%)		0.198±0.059	0.225±0.078	0.234±0.023	**0.017*** (a)
		P1 = 0.064, **P2 = 0.014*,** P3 = 0.623			
PDW (fl)		14.18±3.32	11.59±2.98	12.5±1.47	**<0.001***
		P1 < 0.001*, P2 = 0.028*, P3 = 0.346			
PLR		119.62±7.96	135.89±7.53	110.65±8.54	0.321 (a)
Phosphorus (mg/dL)		5.26 ± 1.06	4.85±0.79	4.06±0.30	**0.021*** (a)
		P1 = 0.346, **P2 = 0.006*, P3** = 0.159			
Total calcium (mg/dL)		9.84±1.23	8.89±0.44	9.56±0.41	**0.002*** (a)
		P1 < 0.001*, P2 = 0.287, **P3** = 0.053			
Ionized calcium (mg/dl)		1.088±0.16	0.98±0.07	1.086±0.093	**0.009*** (a)
		P1 = 0.003*, P2 = 0.967, **P3 = 0.02***			
PTH (pg/mL)		463.98±87.07	305.46±51.85	38.9±6.75	**<0.001*** (a)
		P1 = 0.011*, P2 < 0.001*, P3 < 0.001*			
CRP (mg/L)		10.15 ± 2.18	6.3 ± 1.3	6.1 ± 0.97	**<0.001*** (a)
		P1 < 0.001*, P2 < 0.001*, P3 = 0.887			
Blood urea (mg/dL)		83.49±7.19	110.85±28.42	29.8±5.16	**<0.001*** (a)
		P1 < 0.001*, P2 < 0.001*, P3 < 0.001*			
Serum creatinine (mg/dl)		7.62±1.67	3.13±0.63	0.69±0.13	**<0.001*** (a)
		P1 < 0.001*, P2 < 0.001*, P3 < 0.001*			
eGFR (ml/min/1.73m²)		7.17±1.24	21.12±3.19	117.55±11.42	**<0.001*** (a)
		P1 < 0.001*, P2 < 0.001*, P3 < 0.001*			

Data are presented as mean ± SD or frequency (%). *: Significant p value <0.05, (a): one-way ANOVA test, (b): Chi² test, P: P-value between groups. P1: p-value for comparing between group I and group II. P2: p-value for comparing between group I and group III. P3: p-value for comparing between group II and group III.

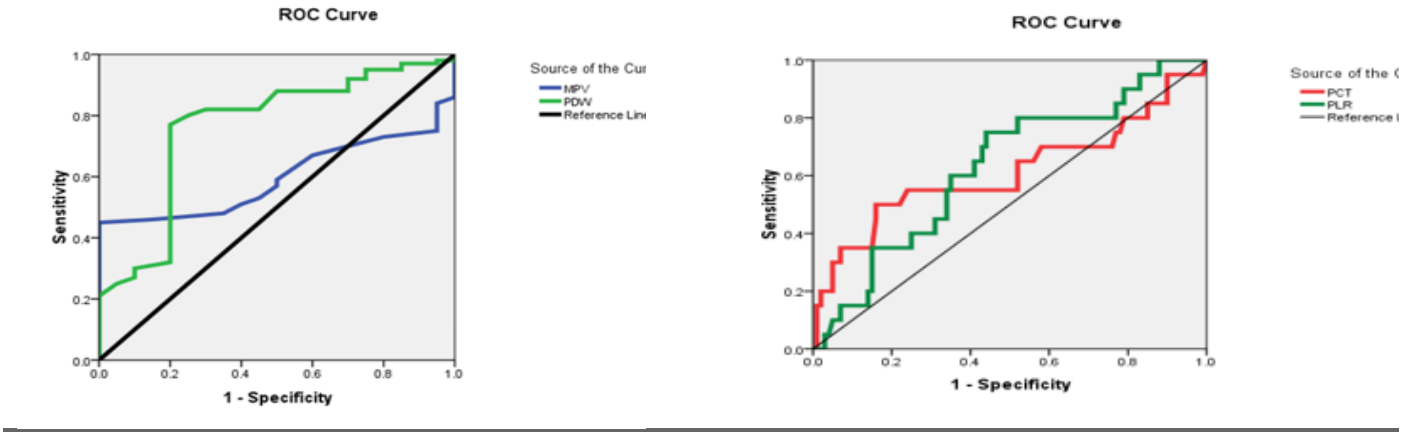
MPV negatively correlated with TLC, platelets, PLR, and phosphorus, while positively correlating with CRP, total calcium, and ionized calcium. PCT was negatively correlated with age and serum creatinine but positively associated with sex, TLC, lymphocytes, platelets, PLR, and eGFR. PDW positively correlated with serum creatinine and negatively with eGFR. PLR showed negative correlations with absolute lymphocytes, MPV, and calcium, but positive correlations with platelets, PCT, and CRP. Phosphorus and PTH exhibited various correlations with other parameters **(Table 2)**.

Table 2: Correlations between platelet indices, PLR, phosphorus, PTH and other parameters

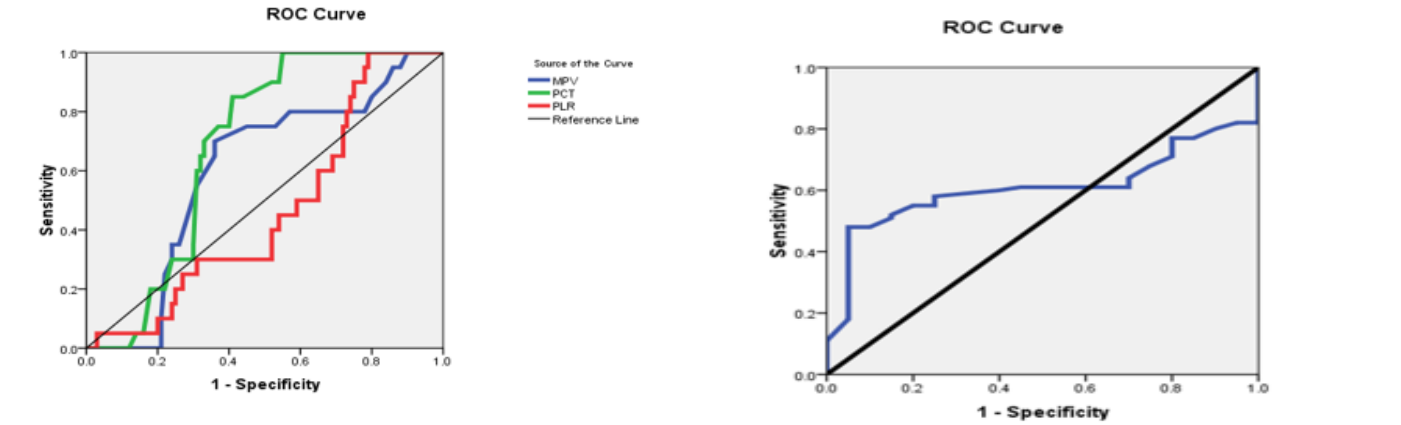
	MPV		PCT		PDW		PLR		Phosphorus		PTH	
	r	p	r	P	r	p	r	p	r	p	r	p
Age	-0.116	0.172	**-0.242**	**0.004***	0.103	0.227	0.066	0.440	**0.250**	**0.003***	**0.297**	**<0.001***
Sex	-0.091	0.284	**0.198**	**0.019***	-0.104	0.220	1.00	0.239	**-0.206**	**0.014***	-0.001	0.987
Hb	0.016	0.853	0.09	0.288	0.032	0.711	-0.044	0.605	**-0.212**	**0.012***	**-0.195**	**0.021***
TLC	**-0.246**	**0.003***	**0.436**	**<0.001***	-0.023	0.785	-0.117	0.167	-0.065	0.442	-0.056	0.511
Absolute lympho-cytes	-0.112	0.188	**0.429**	**<0.001***	0.115	0.177	**-0.570**	**<0.001***	-0.049	0.567	-0.02	0.812
Platelets	**-0.338**	**<0.001***	**0.915**	**<0.001***	-0.01	0.905	**0.313**	**<0.001***	-0.031	0.715	-0.05	0.554
MPV	-------	---------	0.001	0.995	0.083	0.328	**-0.197**	**0.02***	**-0.223**	**0.008***	-0.059	0.489
PCT	0.001	0.995	--------	---------	-0.007	0.935	**0.254**	**0.003***	-0.115	0.175	-0.124	0.143
PDW	0.083	0.328	-0.007	0.935	-------	----------	-0.067	0.435	0.073	0.394	0.011	0.895
PLR	**-0.197**	**0.02***	**0.254**	**0.003***	-0.067	0.435	-------	-------	0.12	0.156	-0.014	0.871
CRP	**0.197**	**0.019***	0.063	0.461	0.059	0.492	**0.275**	**<0.001***	0.165	0.065	**0.247**	**0.003***
Blood urea	0.086	0.310	-0.107	0.207	-0.049	0.565	0.052	0.540	**0.211**	**0.012***	**0.209**	**0.013***
Serum creatinine	-0.082	0.337	**-0.180**	**0.033***	**0.403**	**<0.001***	-0.001	0.990	**0.244**	**0.004***	**0.382**	**<0.001***
eGFR	0.081	0.338	**0.191**	**0.024***	**-0.174**	**0.039***	-0.056	0.514	**-0.224**	**0.008***	**-0.492**	**<0.001***
Total calcium	**0.198**	**0.019***	-0.158	0.063	-0.049	0.564	**-0.226**	**0.007***	**-0.183**	**0.03***	0.06	0.484
Ionized calcium	**0.178**	**0.035***	-0.123	0.148	-0.05	0.561	**-0.185**	**0.028***	**-0.334**	**<0.001***	0.044	0.607
Phosphorus	**-0.223**	**0.008***	-0.115	0.175	0.073	0.394	0.120	0.156	-------	--------	0.282	**<0.001***
PTH	-0.059	0.489	-0.124	0.143	0.011	0.895	-0.014	0.871	**0.282**	**<0.001***	-------	---------

r: Pearson coefficients, *: Statistically significant at $p \leq 0.05$, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet distribution width, TLC: Total leucocytic count, PLR: Platelet to lymphocyte ratio, PTH: Parathormone, CRP: C-reactive protein, eGFR: estimated glomerular filtration rate, Hb: hemoglobin.

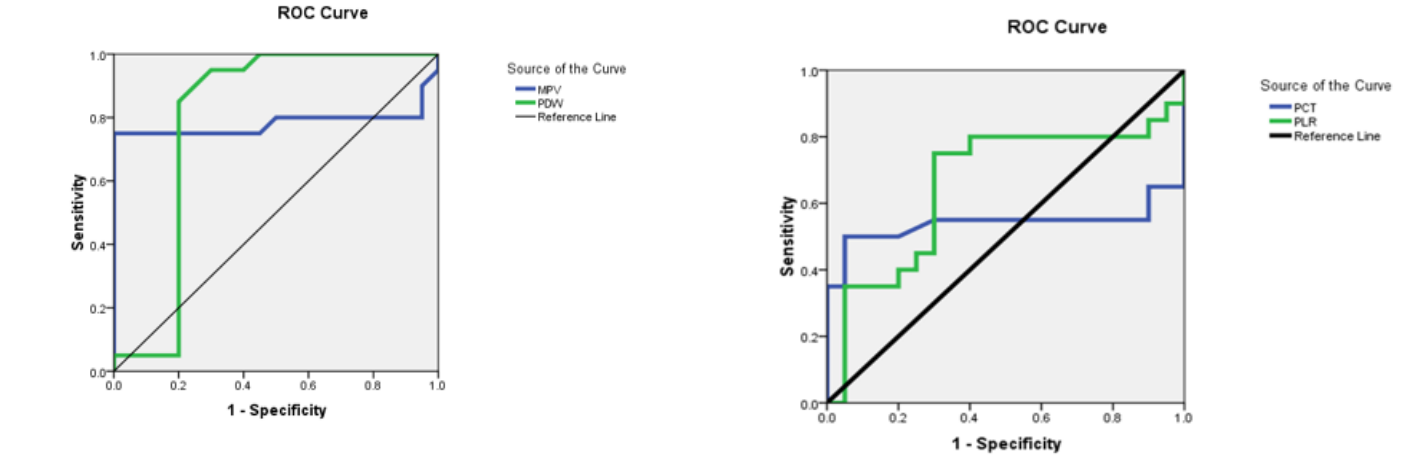
Regarding the ability of PDW to discriminate ESRD from CKD at a cut-off value of 9.45; the AUC was 0.764, the sensitivity was 95.0%, the specificity was 85.0%, PPV was 96.94%, and NPV was 77.2%, while regarding ROC curve analysis for PCT to discriminate ESRD from control at a cut-off value of 0.129; the AUC was 0.685, the sensitivity was 100.0%, the specificity was 88.0%, PPV was 62.5%, and NPV was 100.0%, and regarding ROC curve analysis for MPV and PDW to discriminate CKD from control respectively at a cut-off value of 8.95 and 9.05; the AUC was 0.782 and 0.794, the sensitivity was 80.0% and 100.0%, the specificity was 80.0% and 90.0%, PPV was 80.0% and 90.9%, and NPV was 80.0% and 100.0% **(Figure 1)**.



(A)



(B) **(C)**



(D)

Figure 1: ROC curve to discriminate end-stage renal disease from (A) chronic kidney disease, (B) control. group, (C) platelet distribution width of end-stage renal disease from control, and (D) chronic kidney disease from control.

DISCUSSION

Renal replacement therapy (RRT) is required when ESRD develops, which impacts an estimated 11% to 13% of the world's population and leads to a diminished quality of life and early death [6].

In agreement with this study results about CBC, **Aziz *et al.*** [7] demonstrated that mean Hb was 12.90 ±1.70 g/dl in healthy individuals, 10.41 ± 2.03 g/dl in CKD and 10.54 ±1.31 g/dl in ESRD. The platelet count ($x10^3/mm^3$) was significantly higher in healthy group (295.3 ± 70.30) in comparison to CKD (138.43 ± 85.19) and ESRD (112.7 ± 53.46). **Li *et al.*** [8] showed that in non-dialysis ESRD patients, platelet counts were (170.18 ± 74.10) × 10^9/L, which were lower than those observed in our patients, while the PLR was 154.80 (109.98–235.47), higher than that seen in our patient group. **Aziz *et al.*** [7] found no statistically significant variation among the groups with due regard to MPV with p-value = 0.187. In the CKD group, PDW was substantially greater (12.81 ± 1.49 fl) in comparison with the healthy group (11.85 ± 0.98 fl). **Li *et al.*** [8] noted that phosphorus was (5.86 ± 2.36 mg/dL) and calcium was (7.80 ± 1.32 mg/dL) in non-dialysis ESRD patients. **Toraman *et al.*** [9] noted higher PTH with a mean of (617.46±501.93 pg/mL) in the CKD group. **Jairam *et al.*** [10] showed that the ESRD group had much higher CRP levels than the control group with a mean of 35.8 ± 3.4 mg/L in the ESRD group and 1.01 ± 0.06 mg/L in the control group.

In this investigation, MPV was negatively correlated with TLC, platelets, PLR, and phosphorus, but positively correlated with CRP, total calcium, and ionized calcium, with no correlation to other studied parameters. Age and serum creatinine were found to have a negative correlation with PCT, while being positively correlated with gender, TLC, absolute lymphocytes, platelets, PLR, and eGFR. Serum creatinine and eGFR were positively and negatively correlated with PDW, respectively. **Erken *et al.*** [11] documented that reduced MPV was linked to impaired renal function.

In this investigation, PLR was negatively correlated with absolute lymphocytes, MPV, total calcium, and ionized calcium. Also, it was positively correlated with platelets, PCT, and CRP, while it did not correlate with phosphorus and PTH. In the same way, **Yaprak *et al.*** [12] found a positive correlation between CRP and PLR. Similarly, **Li *et al.*** [13] informed that the correlation between PLR and platelet count was positive, while the correlation between PLR and lymphocyte count was negative.

Phosphorus negatively correlated with sex, hemoglobin, mean platelet volume, total calcium, and ionized calcium, while positively correlating with age, PTH, blood urea, and serum creatinine. PTH was negatively correlated with hemoglobin and positively with age, phosphorus, CRP, blood urea, and creatinine. Hyperphosphatemia decreased MPV and vice versa.

As well, **Arora *et al.*** [14] demonstrated a statistically significant positive correlation was found between PTH and serum creatinine, with no significant correlation between PTH and blood urea. Additionally, there was a positive correlation between PTH and phosphorus, and a negative correlation between PTH and serum calcium.

In the current trial, MPV could fairly discriminate CKD patient from a healthy individual, i.e. at a cut-off value of 8.95; the accuracy was 78%, the sensitivity was 80%, the specificity was 80.0%. PCT could discriminate ESRD from healthy individual with accuracy 68.5%, 100% sensitivity and 88% specificity.

In the present study, PDW could discriminate CKD patients from normal subjects; at a cut-off value of 9.05; the area under the curve was 0.794, the sensitivity was 100.0%, the specificity was 90.0%. Moreover, PDW could fairly discriminate ESRD from CKD i.e. could predict the progression of CKD to ESRD requiring RRT: at a cut-off value of 9.45; the area under the curve was 0.764, the sensitivity was 95.0%, the specificity was 85.0%. Thus, PDW had the largest area under the curve among all of platelet's indices, with 95% sensitivity and 85% specificity in discriminating ESRD from CKD, followed by PCT, which could discriminate between ESRD and controls. Furthermore, PDW had 100% sensitivity and 90.9% specificity in discriminating CKD from normal controls.

Conversely, **Aneez *et al.*** [15] reported that the PLR demonstrated over 80% sensitivity and specificity, suggesting its potential as a novel predictive marker for assessing the severity of CKD.

A small sample size and the study's focus on a single location were two of the study's limitations.

CONCLUSION

Hyperphosphatemia could lower MPV and vice versa but has no effect on other platelet indices or PLR. There was no effect of parathormone level variation on any of platelet indices or PLR. CKD can be strongly suspected from PDW variation and fairly suspected from MPV. ESRD could be suspected of PCT. PDW was found to have an acceptable prognostic value. This suggests that monitoring PDW could be useful for the early diagnosis of CKD and ESRD, since it is simple, inexpensive, and widely available.

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Conflict of Interest: Nil.

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