Study of the Relationship between the Platelet Parameters and Hyperlipidemia

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ABSTRACT

Background: Platelet volume indices (PVI), encompassing parameters such as platelet distribution width (PDW), mean platelet volume (MPV), and the platelet-large cell ratio (P-LCR), are routinely accessible through standard clinical laboratory assays and serve as valuable biomarkers for predicting the likelihood of thrombotic complications.

Objective: This work aimed to assess and to evaluate the platelet parameters and functions in hyperlipidemic patients.

Subjects and methods: This cross-sectional study was carried out on 50 patients aged ≥ 18 years old, both sexes, diagnosed with hyperlipidemia (Group 1) and 30 healthy individuals as control (Group 2). Adenosine diphosphate (ADP) aggregation test was done for all patients.

Results: Platelet count was positively correlated with body mass index (BMI), triglycerides (TG), low-density lipoprotein (LDL-C), very low-density lipoprotein (VLDL-C), cholesterol, ADP, MPV, PDW, P-LCR, plateletcrit (PCT). PDW was positively correlated with TG, LDL-C, VLDL-C, ADP, cholesterol, BMI, MPV, P-LCR, and PCT. P-LCR was positively correlated with TG, LDL-C, VLDL-C, ADP, cholesterol, BMI, PDW, MPV, and PCT. PCT was positively correlated with TG, LDL-C, VLDL-C, ADP, cholesterol, BMI, MPV, PDW, and P-LCR. Platelet count, MPV, PDW, P-LCR, PCT and ADP were significantly lower in patients in the borderline high TG and cholesterol group than the high TG and cholesterol group ($P<0.05$). MPV, PDW, P-LCR, PCT and ADP were significantly lower in the borderline high LDL-C group than the high LDL-C group and the very high LDL-C group ($P<0.05$).

Conclusions: Total cholesterol, LDL-C, high-density lipoprotein (HLDL-C), and TG influence the values of PVI. Lipids and lipoproteins interact with platelets and affect their structure (Platelet membrane lipid) and function (platelet aggregation).

Keywords: Platelet volume indices, Platelet-large cell ratio, Mean platelet volume, Hyperlipidemia, Platelet distribution width.

INTRODUCTION

Hyperlipidemia represents a pathological condition characterized by an elevation in lipid and cholesterol concentrations within the bloodstream. Frequently referred to as dyslipidemia, this condition arises from disruptions in lipoprotein metabolism, leading to aberrant plasma levels of TC and LDL-C. These metabolic derangements establish hyperlipidemia as a traditional risk factor for the pathogenesis of atherosclerosis and its associated sequelae, including coronary artery disease, cerebrovascular events such as stroke, myocardial infarction, diabetes mellitus, and hypertension [1].

The American Heart Association characterizes hyperlipidemia as a metabolic anomaly marked by elevated concentrations of TC and/or TGs, in conjunction with diminished levels of HDL-C [2-4].

Hyperlipidemia is often overlooked as a clinical entity due to its silent progression, lack of overt symptoms, underappreciation of abnormal lipid profile findings during routine screening, and financial constraints in low-income regions. As a result, its diagnosis frequently occurs only when severe complications arise, including acute coronary syndromes, ischemic strokes, or peripheral arterial atherosclerosis culminating in thrombotic events and acute limb ischemia. Although the primary role of platelets is centered on preserving hemostasis, they achieve this by serving as pivotal initiators of the coagulation cascade. It also shows a role in the thrombus consequence of the atherosclerotic plaques [5]. This occur by binding to the injured vascular endothelial cells and releasing many growth factors including PDGF and TGF, which play a major role in the early stages of atherosclerosis [6].

The functionality of platelets is believed to be influenced by their size. Under baseline conditions, larger platelets exhibit an increased secretion of thromboxane A2 and P-selectin (sP-selectin) relative to typical-sized platelets. These mediators, released from the membranes of activated platelets, play a critical role in the initiation and progression of atherosclerosis [7-10], and demonstrate heightened hemostatic activity, thereby augmenting the propensity for thrombus formation.

So, PVI such as Platelet size or MPV can be used indirectly to quantify the platelet activity [11, 12]. PVIs, including MPV, PDW, and P-LCR, are readily accessible parameters in routine clinical laboratory evaluations, offering valuable insights into the likelihood of thrombotic complications. As ischemic stroke, acute coronary syndrome in the hyperlipidemic patients [13, 14]. Furthermore, the pathophysiology of hyperlipidemia includes insulin resistance, inflammation and platelet hyperactivity [15]. So, platelet parameters can be also used as reliable blood biomarkers for screening and early detection of hyperlipidemia and its complication [16, 17]. The aim of this work was to assess and evaluate the platelet parameters and functions in hyperlipidemic patients.

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PATIENTS AND METHODS

The study was done from April 2023 to December 2023. Patients were divided into two groups: Group 1 (n=50) included patients with hyperlipidemia and group 2 (n=30) involved healthy subjects as a control group.

Exclusion criteria: Individuals with pre-existing cardiovascular disorders, coagulopathy or bleeding diatheses, current use of antiplatelet or anticoagulant medications, lipid-lowering agents, diagnosis of thrombocytopenia, anemia, and malignancy. Also, patients undergoing chemotherapy, pregnant women, those with a recent history of blood transfusion, or those with a recent infectious episode.

All patients were subjected to complete history taking, clinical examinations, laboratory investigations [CBC, lipid profile (serum cholesterol, TGs, LDL-C, HDL-C and VLDL-C), ADP aggregation test, PT, APTT, liver and kidney function tests, lactate dehydrogenase (LDH), fasting blood sugar, 2Hrs. postprandial blood sugar and HbA1c].

Blood sampling and processing: In adherence to established quality control and safety protocols for sample collection, a 10 mL venous blood specimen was obtained from both patients and controls. A 2 mL aliquot of blood was transferred into a vacutainer EDTA tube for the analysis of CBC, RBCs, and PLT parameters. An additional 2 mL of blood was placed in a vacutainer containing citrate for the assessment of PT and activated PTT. 4 ml of the collected blood were put into vacutainer citrated tube for ADP aggregation test. 2 ml of the collected blood were put into serum separator tube for lipid profile. The rest of the collected blood was put into plain tube for serum separation for estimation of liver function tests, renal function test and LDH. Liver, renal function tests and LDH (on fully automated chemistry analyzer Au480 Beckman coulter)
PT and PTT: They were processed by Coatron co-agulometer. CBC by automated by ERMA PCE-210N cell counter. Fasting blood glucose by konelab PRIME 60i. Two hours postprandial blood glucose by konelab PRIME 60i. HbA1c by SIEMENS, Dimension.

The concentrations of TC and TG were measured using validated enzymatic assays conducted on an automated spectrophotometer (Hitachi 705; Boehringer, Mannheim, Germany). HDL-C levels were determined following the precipitation of apolipoprotein B-containing lipoproteins using phosphotungstic acid. Non-HDL-C was calculated by subtracting the HDL-C concentration from the total cholesterol measurement, whereas LDL-C levels were estimated using the Friedewald formula. Quality control measurements were performed by using commercially available standards.

Blood specimens for CBC analysis were collected in 5 mL EDTA-containing anticoagulant tubes and processed within 2 to 4 hours post-collection using the automated hematology analyzer Beckman Coulter LH 780. This analyzer utilizes the impedance principle to quantify RBCs and platelets. Specifically, platelets are detected as electrical pulses corresponding to cell sizes ranging from 2 to 20 femtoliters (fl). The system generates three 64-channel histograms representing platelet size distributions. Data acquisition continued for a minimum of 2 seconds and a maximum of 20 seconds or until at least 1500 cells were recorded per histogram, whichever threshold was met first. Subsequently, the collected data were transmitted to the device workstation, where the platelet count was computed based on the area under the size distribution curve. The count is further adjusted using calibration and predilution factors. Derived parameters such as MPV and PDW were computed directly by the analyzer, whereas PCT was determined via calculation.

ADP aggregation test: ADP aggregation test was done using optical aggregometry technique (Thrombomate XRA Fully automated Aggregometry, Behnk Electronik). The technique employed is turbidometric platelet aggregometry, which evaluates platelet aggregation within PRP. This methodology relies on quantifying variations in light transmittance through PRP following the introduction of a platelet agonist, as detected by a photometric system. The aggregation response is characterized by an aggregation index curve, representing dynamic changes in light transmission intensity within the PRP sample upon stimulation with ADP.

Ethical considerations: The study was done after being accepted by The Research Ethics Committee, Tanta University (approval code: 36264MS123/3/23). 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: The statistical analyses were conducted using SPSS software version 26 (IBM Corporation, Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD) and subjected to comparative analysis across the three groups using the Analysis of Variance (ANOVA) test, supplemented by Tukey's post hoc analysis for pairwise comparisons. Categorical variables were represented as frequencies and percentages, and their associations were assessed using the Chi-square test. Correlations among different variables were examined through the Pearson product-moment correlation coefficient. ROC curve analysis was employed to assess diagnostic performance, evaluating sensitivity, specificity, PPV, and NPV. A p-value ≤ 0.05 (two-tailed) was deemed indicative of statistical significance.

RESULTS

Age and sex were insignificantly different between the two groups. BMI was significantly higher in group I than in group II (Table 1).

Table (1): Comparison between all the studied groups as regards demographic data

		Group I (n=50)	Group II (n=30)	Test of sig.	P
Age (Years)		36.18 ± 9.63	32.3 ± 10.58	t= 1.681	0.097[(a)]
Sex	**Male**	27 (64.3%)	15 (35.7%)	X^2= 0.120	0.729[(b)]
	Female	23 (60.5%)	15 (39.5%)		
BMI (kg/m^2)		33.37 ± 4.14	22.97 ± 0.35	t=17.668	**<0.001*[(a)]**

Data are presented as mean ± SD or frequency (%). * Significant p value <0.05, (a): Independent-Sample T-Test, (b): Chi-Square Test, BMI: Body mass index.

FBG, 2h-PPBG, HbA1C, BUN, PT, INR, AST, ALT, albumin, total bilirubin, Hb, WBCs and LDH were insignificantly different between the two groups. Serum TG, LDL-C, VLDL-C, serum cholesterol, ADP, platelet count, MPV, PDW, P-LCR and PCT were significantly higher in group I than in group II. HDL-C was significantly lower in group I than in group II (Table 2).

Table (2): Comparison between all the studied groups as regards laboratory parameters

		Group I (n=50)	Group II (n=30)	Test of sig.	P
Diabetic profile	**FBG (mg/dL)**	90.54±9.1	86.77±10.57	t=1.689	0.095[(a)]
	2h-PPBG (mg/dL)	118.5±18.86	112.77±9.83	t=1.784	0.127[(a)]
	HBA1c (%)	4.74±0.18	4.68±0.13	t=1.727	0.088[(a)]
BUN (mg/dL)		17.54±5.19	17.83±1.09	t=-0.385	0.701[(a)]
PT (%)		13.21±0.72	13.1±0.55	t=0.767	0.445[(a)]
INR		1.02±0.046	1.0±0.036	t=0.979	0.331[(a)]
Liver function test	**AST (U/L)**	27.42±2.14	26.73±3.94	t=0.369	0.713[(a)]
	ALT (U/L)	25.24±3.52	22.87±3.03	t=1.192	0.238[(a)]
	Albumin (g/dL)	3.51±0.11	3.55±0.06	t=-1.927	0.058[(a)]
	Total bilirubin(mg/dL)	0.72±0.17	0.70±0.12	t=0.632	0.529[(a)]
Lipid profile	**TGs (mg/dL)**	267.06±10.66	123±6.71	t=9.173	**<0.001*[(a)]**
	LDL-C (mg/dL)	196.38±49.12	73.43±8.19	t=17.302	**<0.001*[(a)]**
	HDL-C (mg/dL)	43.84±6.40	48.2±2.55	t=-4.282	**<0.001*[(a)]**
	VLDL-C (mg/dL)	41.92±4.72	23.73±2.85	t=21.483	**<0.001*[(a)]**
	Cholesterol (mg/dL)	318.06±26.91	131.87±10.87	t=10.311	**<0.001*[(a)]**
CBC	**Hb (g/dL)**	12.9±1.49	13.17±0.91	t=-0.989	0.326[(a)]
	WBCs (10^3/µL)	7.08±1.61	6.07±1.42	t=2.242	0.055[(a)]
	LDH (U/L)	200.1±16.67	199.4±5.64	t=0.272	0.786[(a)]
ADP (%) platelet aggregation		82.0±4.30	67.37±1.65	t=21.543	**<0.001*[(a)]**
platelet parameters	**Platelet count (10^3/µL)**	423.78±59.88	317.17±42.15	t=8.554	**<0.001*[(a)]**
	MPV (fl)	15.39±2.29	10.15±1.38	t=12.758	**<0.001*[(a)]**
	PDW (fl)	21.96±3.49	11.08±1.51	t=19.219	**<0.001*[(a)]**
	P-LCR (%)	43.36±6.58	13.22±1.04	t=31.739	**<0.001*[(a)]**
	PCT (%)	0.398±0.02	0.145±0.02	t=14.965	**<0.001*[(a)]**

Data are presented as mean ± SD. (a): Independent-Sample T-Test, *: Statistically significant at $p \leq 0.05$, FBG: Fasting blood glucose, 2h-PPBG: postprandial blood glucose, HBA1C: hemoglobin A1C, PT: prothrombin time, BUN: Blood urea nitrogen, INR: International normalized ratio, HDL-C: high-density lipoprotein, VLDL-C: very low-density lipoprotein, LDL-C: low-density lipoprotein, WBCs: white blood cells, MPV: mean platelet volume, LDH: lactate dehydrogenase, PDW: Platelet distribution width, PCT: Plateletcrit, P-LCR: Platelet-large cell ratio, Hb: hemoglobin, CBC; complete blood count, ADP: adenosine diphosphate, TGs: triglycerides.

Platelet count, MPV, PDW, P-LCR and PCT were negatively correlated with HDL-C. Platelet count was positively correlated with BMI, TGs, LDL-C, VLDL-C, cholesterol, ADP, MPV, PDW, P-LCR and PCT. While, the platelet count was not correlated with age, sex, BUN, hemoglobin, WBCs, PT, INR, AST, ALT, albumin, total bilirubin, LDH, FBS, 2h-PP, and HBA1c. MPV was positively correlated with TGs, LDL-C, VLDL-C, ADP, cholesterol, BMI, PDW, P-LCR, and PCT. MPV, PDW, P-LCR and PCT were not correlated with age, sex, WBCs, FBS, 2h-PP, HBA1C, BUN, platelet count, Hb, PT, INR, AST, ALT, albumin, total bilirubin, and LDH. PDW was positively correlated with TGs, LDL-C, VLDL-C, ADP, cholesterol, BMI, MPV, P-LCR, and PCT. P-LCR was positively correlated with TGs, LDL-C, VLDL-C, ADP, cholesterol, BMI, PDW, MPV, and PCT. PCT was positively correlated with TGs, LDL-C, VLDL-C, ADP, cholesterol, BMI, MPV, PDW, and P-LCR (Table 3).

Table (3): Correlations between (platelet count, MPV, PDW, P-LCR and PCT) and other parameters

	Platelet count		**MPV**		**PDW**		**P-LCR**		**PCT**	
	r	P	r	P	r	P	r	P	r	P
Age	-0.043	0.708	0.203	0.071	0.198	0.078	0.226	0.052	0.191	0.09
Sex	0.208	0.064	0.109	0.334	0.079	0.485	0.001	0.996	0.114	0.314
BMI	**0.237**	**0.034***	**0.595**	**<0.001***	**0.741**	**<0.001***	**0.772**	**<0.001***	**0.868**	**<0.001***
FBG	0.029	0.802	0.205	0.068	0.220	0.052	0.174	0.124	0.220	0.0.051
2h-PPBG	0.096	0.397	0.04	0.724	0.005	0.967	0.04	0.722	0.062	0.586
HBA1C	-0.101	0.374	0.133	0.240	0.105	0.353	0.143	0.207	0.086	0.447
BUN	0.021	0.853	0.058	0.611	0.095	0.400	0.051	0.651	0.079	0.486
Prothrombin time	0.144	0.201	0.071	0.529	0.147	0.193	0.124	0.274	0.122	0.280
INR	0.148	0.190	0.058	0.609	0.141	0.213	0.163	0.149	0.124	0.274
AST	0.07	0.536	0.157	0.163	0.053	0.640	0.069	0.540	0.082	0.468
ALT	0.086	0.446	0.194	0.084	0.109	0.336	0.147	0.193	0.144	0.202
Albumin	-0.017	0.879	-0.102	0.367	-0.167	0.138	-0.209	0.062	-0.183	0.105
Total bilirubin	-0.117	0.303	0.118	0.296	0.135	0.232	0.139	0.219	0.140	0.214
TGs	**0.450**	**<0.001***	**0.824**	**<0.001***	**0.786**	**<0.001***	**0.803**	**<0.001***	**0.813**	**<0.001***
LDL-C	**0.753**	**<0.001***	**0.837**	**<0.001***	**0.834**	**<0.001***	**0.896**	**<0.001***	**0.844**	**<0.001***
HDL-C	**-0.352**	**<0.001***	**-0.408**	**<0.001***	**-0.410**	**<0.001***	**-0.456**	**<0.001***	**-0.506**	**<0.001***
VLDL-C	**0.693**	**<0.001***	**0.898**	**<0.001***	**0.870**	**<0.001***	**0.946**	**<0.001***	**0.866**	**<0.001***
Cholesterol	**0.494**	**<0.001***	**0.656**	**<0.001***	**0.689**	**<0.001***	**0.746**	**<0.001***	**0.744**	**<0.001***
Hb	-0.001	0.993	-0.014	0.905	-0.064	0.575	-0.099	0.383	-0.068	0.548
WBCs	0.159	0.159	0.159	0.168	0.169	0.134	0.154	0.161	0.195	0.083
LDH	-0.012	0.913	-0.093	0.412	-0.089	0.430	-0.071	0.531	-0.085	0.455
ADP	**0.686**	**<0.001***	**0.869**	**<0.001***	**0.924**	**<0.001***	**0.956**	**<0.001***	**0.897**	**<0.001***
Platelet count	--	--	-0.036	0.749	-0.161	0.154	-0.153	0.176	-0.095	0.402
MPV	**0.668**	**<0.001***	**--**	**--**	**0.842**	**<0.001***	**0.883**	**<0.001***	**0.863**	**<0.001***
PDW	**0.612**	**<0.001***	**0.842**	**<0.001***			**0.935**	**<0.001***	**0.909**	**<0.001***
P-LCR	**0.683**	**<0.001***	**0.883**	**<0.001***	**0.935**	**<0.001***	**--**	**--**	**0.912**	**<0.001***
PCT	**0.629**	**<0.001***	**0.863**	**<0.001***	**0.909**	**<0.001***	**0.912**	**<0.001***	**--**	**--**

r: Pearson and Spearman correlation,* significant at $p \leq 0.05$, BMI: body mass index, FBG: fasting blood glucose, 2h-PPBG: postprandial blood glucose, HBA1C: hemoglobin A1C, INR: International normalized ratio, AST: Aspartate transaminase, ALT: Alanine aminotransferase, HDL-C: high-density lipoprotein, LDL-C: low-density lipoprotein, VLDL-C: very low-density lipoprotein, BUN: blood urea nitrogen, WBCs: white blood cells, LDH: lactate dehydrogenase, PDW: Platelet distribution width, MPV: mean platelet volume, P-LCR: Platelet-large cell ratio, PCT: Plateletcrit, Hb: hemoglobin, TGs: triglycerides.

According to platelet count, MPV, PDW, P-LCR, PCT and ADP could discriminate patients with hyperlipidemia from the control group at a cut-off values of ≤ 255, ≤ 8.25, ≤ 8.5, ≤ 12.75, ≤0.145 and ≤65.5, AUC was 0.662, 0.986, 1.00, 0.851, 0.819 and 0.999, the sensitivity was 93.3%, 100%, 100%, 92.0%, 92.0% and 100%, the specificity was 52.0%, 90%,96.6%, 80.0%, 73.3% and 80.0%, PPV was 53.84%, 94.34%, 98.04%, 88.46%, 85.18% and 89.29%, and NPV was 92.86%, 100%, 100%, 85.71%, 84.61% and 100% respectively (Figure 1).

(A) **(B)**

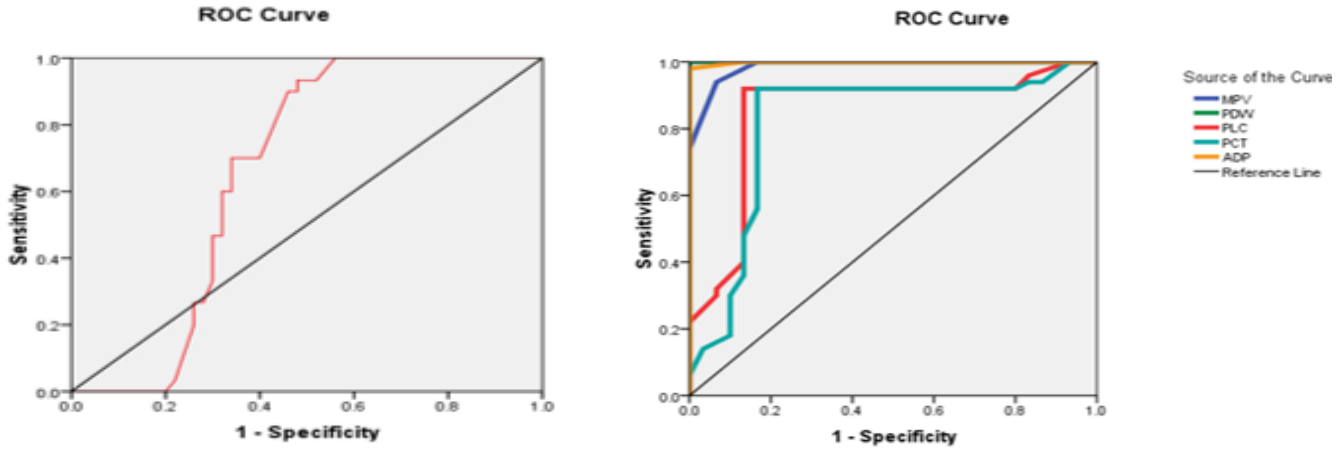

Figure (1): ROC curve for (A) platelet count and (B) mean platelet volume, platelet distribution width, platelet-large cell ratio, plateletcrit, and adenosine diphosphate to discriminate patients with hyperlipidemia (n = 50) from the control group (n = 30).

Regarding comparison between borderline high TGs group and high TGs group, platelet count, MPV, PDW, P-LCR, PCT and ADP were significantly lower in patients in the borderline high TGs group than in the high TGs group (P<0.05). Regarding comparison between borderline high cholesterol group and high cholesterol group, platelet count, MPV, PDW, P-LCR, PCT and ADP were significantly lower in patients in the borderline high cholesterol group than in the high cholesterol group (P<0.05) (Table 4).

Table (4): Comparison between the studied groups as regards platelet parameters

	Group I		**Test of sig.**	**P**
	Borderline high TGs Group (n=25)	**High TGs Group (n=25)**		
Platelet count (10^3/µL)	246.2±9.39	320.52±23.54	t=-2.530	**0.015*(a)**
MPV (fl)	14.86±1.35	16.27 ± 1.4	t=-3.619	**<0.001*(a)**
PDW (fl)	20.22±3.29	23.97 ± 3.51	t=-3.896	**<0.001*(a)**
P-LCR (%)	39.88±6.11	47.4 ± 6.73	t=-4.139	**<0.001*(a)**
PCT (%)	0.342±0.11	0.502 ± 0.08	t=-5.773	**<0.001*(a)**
ADP Platelet aggregation (%)	79.24±3.33	84.68 ± 3.15	t=-5.936	**<0.001*(a)**
	Borderline high Cholesterol Group (n=10)	**High Cholesterol Group (n=40)**		
Platelet count (10^3/µL)	214.8±9.56	293.88±15.52	t=-2.167	**0.035*(a)**
MPV (fl)	13.6±0.84	15.87±2.3	t=-5.038	**<0.001*(a)**
PDW (fl)	19.45±1.21	22.58±3.59	t=-4.566	**<0.001*(a)**
P-LCR (%)	36.9±1.37	45.0±6.34	t=-7.416	**<0.001*(a)**
PCT (%)	0.29±0.05	0.42±0.11	t=-5.132	**<0.001*(a)**
ADP (%) platelet aggregation	79.25±3.02	83.8±3.52	t=-4.125	**<0.001*(a)**

Data are presented as mean ± SD. (a): Independent-Sample T-Test, *: Statistically significant at p ≤ 0.05, Borderline high cholesterol (200 – 239 mg/dL), High cholesterol (≥240 mg/dL), Borderline high triglycerides (150 – 199 mg/dL), High triglycerides (200 - 499 mg/dL), MPV: mean platelet volume, PDW: Platelet distribution width, P-LCR: Platelet-large cell ratio, PCT: Plateletcrit, TGs: triglycerides.

Platelet count showed insignificant difference between the three groups. MPV, PDW, P-LCR, PCT and ADP were significantly lower in the borderline high LDL-C group than in the high LDL-C group and very high LDL-C group (P<0.05) (Table 5).

Table (5): Comparison between the studied groups as regards platelet parameters

	Group I			Test of sig.	P
	Borderline High LDL-C Group (n=11)	**High LDL-C Group (n=8)**	**Very High LDL-C Group (n=31)**		
Platelet count (10^3/µL)	256.18±14.21	266.62±53.29	297.32±17.34	F= 0.676	0.513(c)
MPV (fl)	13.88±1.19	16.75±1.16	17.63±1.6	F= 26.477	**<0.001*(c)**
	P1<0.001*, P2<0.001*, P3=0.139				
PDW (fl)	18.47±0.53	20.5±1.51	22.76±3.16	F= 11.625	**<0.001*(c)**
	P1=0.101, **P2<0.001*, P3=0.034***				
P-LCR (%)	36.63±0.81	40.0±3.54	48.64±5.91	F= 28.263	**<0.001*(c)**
	P1=0.149, **P2<0.001*, P3<0.001***				
PCT (%)	0.255±0.015	0.401±0.116	0.528±0.037	F= 105.77	**<0.001*(c)**
	P1<0.001*, P2<0.001*, P3<0.001*				
ADP (%) Platelet aggregation	76.82±1.83	81.0±4.41	85.23±3.4	F= 27.335	**<0.001*(c)**
	P1=0.009*, P2<0.001*, P3=0.002*				

Data are presented as mean ± SD. *: Statistically significant at $p \leq 0.05$, 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, (c): One-way Anova Test, Borderline high LDL-C (130 – 159 mg/dL), High LDL-C (160 - 189 mg/dL), very high LDL-C (≥190 mg/dL), LDL-C: Low-density lipoprotein, MPV: mean platelet volume, PDW: Platelet distribution width, P-LCR: Platelet-large cell ratio, PCT: Plateletcrit.

DISCUSSION

Hyperlipidemia encompasses a spectrum of hereditary and acquired conditions characterized by disruptions in lipoprotein metabolism. Often interchangeably referred to as dyslipidemia. This term broadly encapsulates various abnormalities in the metabolic pathways regulating lipoprotein synthesis, transport, and clearance [18].

Consistent with our findings regarding laboratory parameters, **Gautam and Khadgi** [19] observed that the PDW was markedly elevated in individuals with high levels of LDL-C and TC compared to those with normal LDL-C and TC levels within their study cohort. Similarly, **Patel *et al.*** [20] demonstrated that PDW and MPV were significantly elevated among patients with metabolic syndrome and dyslipidemia in the case group compared to the control group.

In the current investigation, a positive correlation was observed between platelet count and BMI. This aligns with these findings, **Jamshidi *et al.*** [21] who reported an increase in platelet count with rising BMI across both genders. However, this association reached statistical significance exclusively among females, where platelet counts were markedly elevated in individuals classified as overweight or obese.

Our results revealed that MPV was negatively correlated with HDL-C. Also, the MPV was positively correlated with TGs, LDL-C, VLDL-C, ADP, cholesterol, BMI, PDW, P-LCR and PCT. In the same line **Ding *et al.*** [22] demonstrated that high MPV was positively associated with overweight patients and those with poor glycemic control. Moreover, **Mohammadzad *et al.*** [23] showed that there was significant and positive correlations between MPV and PDW and P-LCR.

In the current study, P-LCR was negatively correlated with HDL-C. Also, the P-LCR was positively correlated with TGs, LDL-C, VLDL-C, ADP, cholesterol, BMI, PDW, MPV and PCT. In the same line, **Çakırca *et al.*** [24] showed that P-LCR, and HDL-C were negatively correlated. Supporting our results, **Mohammadzad *et al.*** [23] demonstrated that there was a significant positive correlation between P-LCR and MPV.

In the present study, PCT was negatively correlated with HDL-C. Also, the PCT was positively correlated with TGs, LDL-C, VLDL-C, ADP, cholesterol, BMI, MPV, PDW and P-LCR. This comes in line with **Patil *et al.*** [25] who reported that PCT had positive correlation with TC and LDL-C. In the same line, **Harsha *et al.*** [26] reported that there was no statistically significant correlation between MPV and HbA1c in controlled diabetic group. Supporting our results, **Yesmin *et al.*** [27] noted that no statistical correlation was seen between MPV, PDW, and P-LCR and diabetes mellites in the diabetic group.

In the present study, PDW was a significant predictor of patients with hyperlipidemia at a cut-off value ≤ 8.5; AUC was 1.00, the sensitivity was 100%, the specificity was 96.6%, PPV was 98.04%, and NPV was 100%. ADP was a significant predictor of patients with hyperlipidemia at a cut-off value ≤ 65.5; AUC was 0.999, the sensitivity was 100%, the specificity was 80.0%, PPV was 89.29%, and NPV was 100%. MPV was a significant predictor of patients with hyperlipidemia at a cut-off value ≤ 8.25; AUC was 0.986, the sensitivity was 100%, the specificity was

90%, PPV was 94.34%, and NPV was 100%. P-LCR was a significant predictor of patients with hyperlipidemia at a cut-off value ≤ 12.75; AUC was 0.851, the sensitivity was 92.0%, the specificity was 80.0%, PPV was 88.46%, and NPV was 85.71%. PCT was a significant predictor of patients with hyperlipidemia at a cut-off value ≤ 0.145; AUC was 0.819, the sensitivity was 92.0%, the specificity was 73.3%, PPV was 85.18%, and NPV was 84.61%. In the same line **Yuan *et al.*** [28] found a significant positive correlation between LDL-C and PDW. Also, **Gang *et al.*** [29] found positive correlations between MPV and the prevalence of hyperlipidemia.

In the present study, the high cholesterol group showed higher platelet count, PDW, MPV, P-LCR, PCT and ADP than patients in the borderline high cholesterol group. Also, the high TGs group showed higher platelet count, P-LCR, MPV, PDW, PCT and ADP than patients in the borderline high TGs group. Supporting our results, Singh ***et al.*** [30] found that PCT and platelet aggregation were insignificantly different between both groups.

In the current study, the high LDL-C group and the very high LDL-C group showed higher MPV, P-LCR, PDW, PCT and ADP than patients in the borderline high LDL-C group. Contrary, **Singh *et al.*** [30] illustrated that MPV, PDW, P-LCR, PCT and platelet aggregation were insignificantly different between borderline high LDL-C group, high LDL-C group and the very high LDL-C group.

The results of our study revealed that there was a significant increase in the platelet count, platelet indices and platelet aggregation in patients with hyperlipidemia, making the platelets more active and more liable to aggregate and form atheroma, atherosclerosis and thrombosis than the non-hyperlipidemic patients.

Limitations: The study's limitations included a relatively modest sample size and its conduct within a single center. Additionally, as a cross-sectional design, it was inherently limited in establishing causal relationships. Furthermore, the analysis did not account for the potential influence of various comorbidities and environmental factors that may have impacted platelet count and functionality.

CONCLUSIONS:

TC, LDL-C, HDL-C and TGs influence the values of PVI. As, Lipids and lipoproteins interact with platelets and affect their structure (Platelet membrane lipid) and function (platelet aggregation). This is supported by the results of our study, which showed that PVI (MPV, PDW, PCT and P-LCR) and ADP aggregation were significantly higher in hyperlipidemic patients than in the non-hyperlipidemic patients. So, PVI can be used as a cheap, easy tool for screening of hyperlipidemia patients, and those with higher PVI are at higher risk of the adverse complications and needs prompt anti-hyperlipidemic measures together with anti-platelets measures.

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