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Original Research Article

Correlation of Serum Calcium and Serum Cholesterol with Platelet Indices in Cardiac Patients: A Prospective Observational Study

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Abstract:

Background: Cardiovascular diseases (CVD) are a leading cause of morbidity and mortality worldwide. Platelet activation and dyslipidemia play a crucial role in the pathogenesis of atherosclerosis and its complications. Serum calcium has also been implicated in cardiovascular risk, though its relationship with lipid profile and platelet indices remains less clearly defined.

Aims and Objectives: To evaluate the correlation between serum calcium and serum cholesterol, and to assess the association of platelet indices with serum cholesterol and various cardiovascular diseases in patients admitted to ICCU.

Material and Methods: This prospective observational study included 153 cardiac patients admitted to the ICCU of R.D. Gardi Medical College, Ujjain. Serum calcium, serum cholesterol, and platelet indices (MPV, PDW, P-LCR, platelet count, PCT) were measured. Correlation analysis was performed using appropriate statistical methods.

Results: Many patients were in the 51–60 years (26.8%) and 61–70 years (26.8%) age groups, with male predominance (68%). The most common diagnosis was coronary artery disease (26.1%), followed by myocardial infarction (20.9%). Serum cholesterol was significantly higher in myocardial infarction patients. A significant positive correlation was observed between serum calcium and serum cholesterol ($p = 0.038$). Serum cholesterol also showed significant positive correlations with PDW ($r = 0.450$, $p = 0.011$), MPV ($r = 0.617$, $p = 0.002$), and P-LCR ($r = 0.537$, $p = 0.023$).

Conclusion: Serum cholesterol is significantly associated with platelet activation indices, indicating increased thrombotic potential in cardiac patients. Platelet indices may serve as simple, cost-effective markers for identifying high-risk individuals.

Keywords: Cardiovascular disease, Serum calcium, Serum cholesterol, Platelet indices, Mean platelet volume, PDW, P-LCR.

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Introduction

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide and continue to impose a major clinical, social, and economic burden, particularly in low- and middle-income countries [1]. According to the World Health Organization, CVDs were responsible for an estimated 19.8 million deaths globally in 2022, accounting for nearly one-third of all deaths [1]. India bears a disproportionately high burden of cardiovascular morbidity and mortality, with epidemiological transitions, urbanization, dietary changes, sedentary behavior, and increasing prevalence of metabolic risk factors contributing substantially to this rise [2,3]. Data from the India State-Level Disease Burden Initiative have shown a marked increase in the contribution of CVDs to total deaths and disability-adjusted life years over the last few decades, emphasizing the need for early identification of simple and accessible biomarkers of cardiovascular risk [2].

Among the modifiable risk factors for cardiovascular disease, dyslipidemia occupies a central role. Elevated total cholesterol and low-density lipoprotein cholesterol (LDL-C), along with reduced high-density lipoprotein cholesterol (HDL-C) and hypertriglyceridemia, are strongly associated with atherosclerotic plaque development and

adverse cardiovascular outcomes [4]. Cholesterol accumulation within the vascular wall promotes endothelial dysfunction, oxidative stress, inflammation, and plaque instability, thereby facilitating progression of coronary artery disease [4]. In addition to its direct vascular effects, altered lipid metabolism has also been shown to influence platelet reactivity and thrombotic potential, which are critical determinants of acute ischemic events [5,6].

Calcium, a ubiquitous divalent cation, is essential for numerous physiological processes including skeletal mineralization, neuromuscular transmission, intracellular signaling, myocardial contraction, and blood coagulation [7]. Serum calcium homeostasis is tightly regulated by parathyroid hormone, calcitonin, and vitamin D. Beyond its classical physiological roles, growing evidence suggests that serum calcium may also have important cardiovascular and metabolic implications. Higher circulating calcium levels have been linked with insulin resistance, metabolic syndrome, hypertension, vascular calcification, and increased cardiovascular risk in several observational studies [7,8]. Some studies have also explored the controversial relationship between calcium supplementation and cardiovascular events, suggesting that calcium metabolism may influence vascular health through complex biological pathways [7]. Since metabolic disturbances often coexist in cardiac patients, evaluation of serum calcium in relation to lipid abnormalities may provide additional insight into cardiometabolic risk.

Platelets play a pivotal role in the pathogenesis of atherothrombosis, which underlies most acute coronary syndromes and ischemic vascular events [9]. Activated platelets contribute not only to thrombus formation but also to endothelial dysfunction, inflammatory signaling, and progression of atherosclerotic plaques [10]. Advances in automated hematology analyzers have enabled routine measurement of platelet indices, including platelet count, plateletcrit (PCT), mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR), as part of the complete blood count. These indices are inexpensive, readily available, and increasingly recognized as potential surrogate markers of platelet activation [9–11].

Among these parameters, MPV, PDW, and P-LCR are considered particularly relevant because larger platelets are metabolically and enzymatically more active, contain denser granules, produce more thromboxane A2, and exhibit greater prothrombotic potential than smaller platelets [11,12]. Elevated MPV has been associated with coronary artery disease, acute coronary syndromes, myocardial infarction, and other cardiovascular risk states [11,13]. Similarly, altered PDW and P-LCR have been reported in patients with ischemic heart disease and metabolic disorders, suggesting a possible association between platelet morphology and cardiovascular risk burden [10,12].

A biologically plausible interaction also exists between lipids and platelets. Hypercholesterolemia has been shown to enhance platelet activation, aggregation, and adhesion through oxidative modification of LDL particles, membrane cholesterol enrichment, and receptor-mediated signaling pathways [5,6]. Platelets themselves may further amplify atherosclerosis by interacting with oxidized lipoproteins and the vascular endothelium [5,6]. Thus, assessment of platelet indices in relation to serum cholesterol may help identify an accessible hematological correlation of lipid-driven vascular risk.

Despite increasing interest in these markers, data regarding the interrelationship between serum calcium, serum cholesterol, and platelet indi**ces** in cardiac patients remain limited, especially in the Indian population. Exploring these associations may help clarify whether routinely available biochemical and hematological parameters can provide additional insight into cardiovascular risk stratification. Therefore, the present study was undertaken to evaluate the correlation between serum calcium and serum cholesterol, and to assess the relationship of serum cholesterol with platelet indices in patients with cardiac disease.

Materials And Methods

This prospective observational study was conducted in the Intensive Cardiac Care Unit (ICCU) of R.D. Gardi Medical College and C.R. Gardi Hospital, Ujjain, Madhya Pradesh, over a period of 20 months from November 2017 to June 2019. A total of 120 consecutive patients admitted with clinical suspicion or confirmed diagnosis of cardiovascular disease were included in the study. The diagnosis of cardiovascular disease was established based on documented medical records, clinical presentation, elevated cardiac biomarkers, and supportive electrocardiographic and echocardiographic findings. The spectrum of cardiovascular conditions included coronary artery disease, acute myocardial infarction, heart failure, arrhythmias, and valvular heart disease.

Patients who were unwilling to provide informed consent or those who refused blood sample collection were excluded from the study. After obtaining written informed consent, detailed demographic data, clinical history, and cardiovascular examination findings were recorded from patient case sheets. Relevant clinical parameters including blood pressure, heart rate, jugular venous pressure, electrocardiography,

echocardiography, and cardiac biomarkers were documented.

Venous blood samples were collected at the time of admission under aseptic precautions. Approximately 2 mL of blood was collected in an EDTA vial for hematological analysis, and 3 mL was collected in a plain tube for biochemical investigations. Platelet indices, including platelet count, mean platelet volume (MPV), platelet distribution width (PDW), platelets (PCT), and platelet large cell ratio (P-LCR), were measured using an automated hematology analyzer (Sysmex XS-800). Serum calcium and serum total cholesterol levels were estimated using a fully automated VITROS-250 chemistry analyzer.

Serum calcium estimation was based on the Arsenio III colorimetric method, in which calcium forms a colored complex with the dye, and the intensity of the color measured spectrophotometrically is directly proportional to the calcium concentration. Serum cholesterol estimation was performed using an enzymatic method involving cholesterol esterase, cholesterol oxidase, and peroxidase reactions, producing a colored product measured photometrically, with intensity proportional to cholesterol concentration.

Quality control procedures were followed throughout the study period using standard calibrators and controls for both hematological and biochemical parameters. All measurements were performed in accordance with manufacturer guidelines to ensure analytical accuracy and precision.

Statistical analysis was carried out using SPSS software version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Pearson correlation analysis was used to assess the relationship between serum calcium, serum cholesterol, and platelet indices. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 153 patients with cardiovascular disease were included in the present study. The demographic, clinical, biochemical, and platelet indices were analyzed to determine their association with various cardiovascular diagnoses.

The age distribution showed that many patients belonged to the 51–60 years and 61–70 years age groups, each accounting for 26.8% of the total sample. This was followed by the 41–50 years age group (20.9%). Only 11.1% of patients were younger than 40 years, while > 80 =3.9% were older than 80 years. These findings indicate that cardiovascular diseases were predominantly observed in the fifth to seventh decades of life.

About gender distribution, there was a clear male preponderance, with 104 males (68.0%) and 49 females (32.0%).

Among the various cardiovascular diagnoses, coronary artery disease (CAD) was the most common diagnosis, observed in 40 patients (26.1%), followed by myocardial infarction (MI) in 32 patients (20.9%). Cardiomyopathy and heart failure were each noted in 24 patients (15.7%), while arrhythmia was present in 19 patients (12.4%) and valvular heart disease (VHD) in 14 patients (9.2%).

On comparing the biochemical and platelet indices across the different diagnostic groups, serum cholesterol showed a statistically significant association with diagnosis ($p = 0.001$). The highest mean cholesterol level was observed in MI patients (197.16 ± 34.91 mg/dL), followed by CAD patients (175.39 ± 47.02 mg/dL). In contrast, the lowest mean cholesterol was observed among heart failure patients (148.50 ± 33.36 mg/dL). Similarly, platelet distribution width (PDW) also differed significantly across the disease categories ($p = 0.018$), with the highest value noted in the MI group (14.53 ± 1.6 FL). Serum calcium demonstrated a borderline statistical significance ($p = 0.050$), whereas platelet count, MPV, P-LCR, and PCT did not show a statistically significant difference among the various diagnoses.

Correlation analysis further revealed that serum calcium had a weak but statistically significant positive correlation with cholesterol ($r = 0.167$, $p = 0.038$), suggesting that higher cholesterol levels were associated with slightly higher calcium values. No significant correlation of calcium was found with platelet count, PDW, MPV, P-LCR, or PCT.

Similarly, serum cholesterol demonstrated significant positive correlations with PDW ($r = 0.450$, $p = 0.011$), MPV ($r = 0.617$, $p = 0.002$), and P-LCR ($r = 0.537$, $p = 0.023$), indicating that increasing cholesterol levels were associated with higher platelet activation indices. However, cholesterol did not show any significant correlation with platelet count or PCT.

When cholesterol levels were categorized as <200 mg/dL and >200 mg/dL, the highest proportion of patients with hypercholesterolemia (>200 mg/dL) was seen in the MI group (46.9%), followed by CAD (29.3%), arrhythmia (21.1%), and cardiomyopathy (20.8%). In contrast, only 8.3% of heart failure patients and 14.3% of VHD patients had cholesterol values above 200 mg/dL. This suggests that elevated cholesterol is more commonly associated with ischemic cardiovascular conditions, particularly myocardial infarction.

Overall, the present study highlights that serum cholesterol and selected platelet indices, particularly PDW, MPV, and P-LCR, are associated with specific cardiovascular diagnoses and may have potential value in disease characterization and risk stratification.

Table 1: Baseline characteristics of the study population (n = 153)

Variable	Category	Frequency (n)	Percentage (%)
Age group (years)	<40	17	11.1
	41–50	32	20.9
	51–60	41	26.8
	61–70	41	26.8
	71–80	16	10.5
	>80	6	3.9
Gender	Male	104	68.0
	Female	49	32.0
Diagnosis	Arrhythmia	19	12.4
	CAD	40	26.1
	Cardiomyopathy	24	15.7
	Heart failure	24	15.7
	MI	32	20.9
	VHD	14	9.2

Table 2: Comparison of biochemical and platelet indices across cardiovascular diagnoses

Diagnosis	Cholesterol (mg/dL)	Calcium (mg/dL)	Platelet count (lakh/cu mm)	PDW (FL)	MPV (FL)	P-LCR (%)	PCT
Arrhythmia	156.47 ± 48.51	9.53 ± 0.90	2.53 ± 1.12	13.53 ± 2.20	11.68 ± 1.49	29.37 ± 8.50	0.05 ± 0.20
CAD	175.39 ± 47.02	9.41 ± 1.02	2.68 ± 0.90	13.85 ± 2.20	11.68 ± 1.20	31.34 ± 8.00	0.07 ± 0.26
Cardiomyopathy	159.25 ± 54.68	9.67 ± 0.96	2.54 ± 0.88	13.00 ± 2.16	15.42 ± 20.40	30.58 ± 7.20	0.00 ± 0.00
Heart failure	148.50 ± 33.36	8.96 ± 0.86	2.25 ± 0.84	13.67 ± 2.20	11.00 ± 2.20	30.54 ± 6.60	0.13 ± 0.30
MI	197.16 ± 34.91	9.56 ± 1.13	2.66 ± 0.65	14.53 ± 1.60	12.03 ± 1.28	33.75 ± 7.90	0.00 ± 0.00
VHD	151.07 ± 56.67	8.86 ± 1.09	2.00 ± 0.55	12.29 ± 2.05	11.36 ± 1.33	29.00 ± 7.60	0.00 ± 0.00
p value	**0.001**	**0.050**	0.084	**0.018**	0.464	0.313	0.183

Table 3: Correlation of calcium and cholesterol with platelet indices

Variable	Parameter	r value	p value
Calcium	Cholesterol	0.167	0.038*
	Platelet count	0.085	0.293
	PDW	-0.016	0.834
	MPV	-0.021	0.795
	P-LCR	0.026	0.748
	PCT	-0.960	0.237
Cholesterol	Calcium	0.167	0.038*
	Platelet count	0.072	0.633
	PDW	0.450	0.011*
	MPV	0.617	0.002*
	P-LCR	0.537	0.023*
	PCT	0.044	0.589

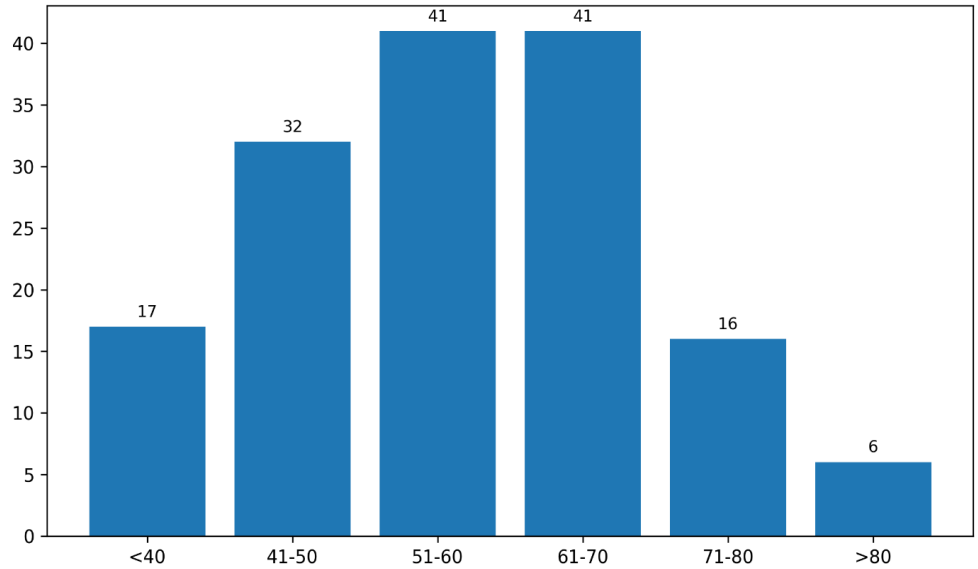

Figure 1: demonstrates the variation in mean cholesterol levels among different cardiovascular diagnoses. The highest mean cholesterol level was observed in patients with myocardial infarction (197.16 ± 34.91 mg/dL), followed by those with coronary artery disease (175.39 ± 47.02 mg/dL). In contrast, relatively lower mean cholesterol values were noted in patients with heart failure (148.50 ± 33.36 mg/dL) and valvular heart disease (151.07 ± 56.67 mg/dL). This intergroup variation was found to be statistically significant (p = 0.001), indicating a meaningful association between serum cholesterol levels and the type of cardiovascular disease.

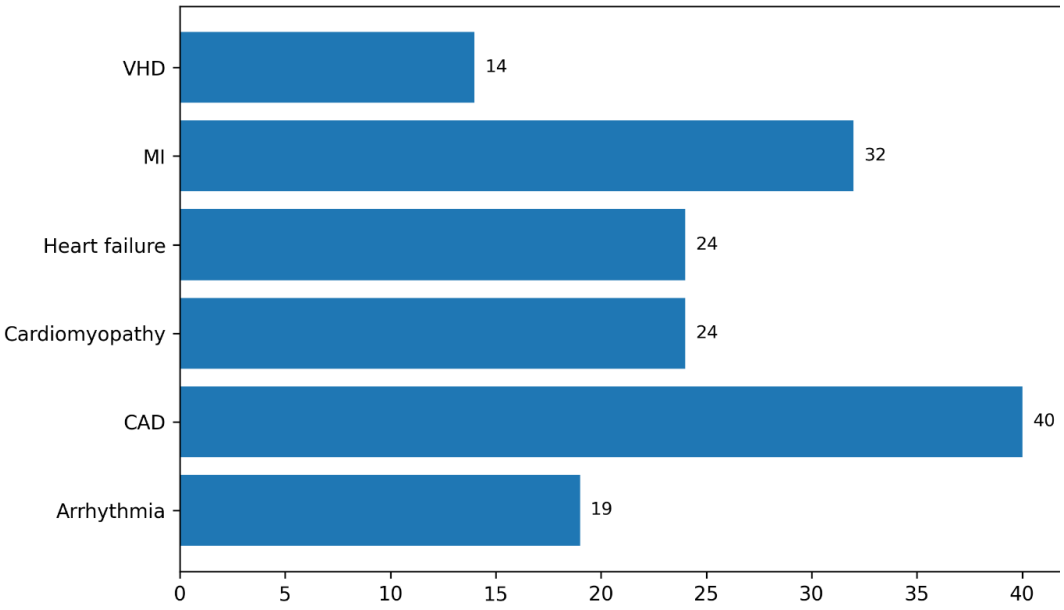

Figure 2: Shows the relationship between serum cholesterol and mean platelet volume (MPV) among the study participants. A positive linear correlation was observed, suggesting that higher serum cholesterol levels were associated with increased MPV values. Statistical analysis revealed this association to be significant (r = 0.617, p = 0.002). This finding suggests that elevated cholesterol may be linked with enhanced platelet activation, thereby potentially contributing to increased thrombotic risk in cardiovascular disease patients.

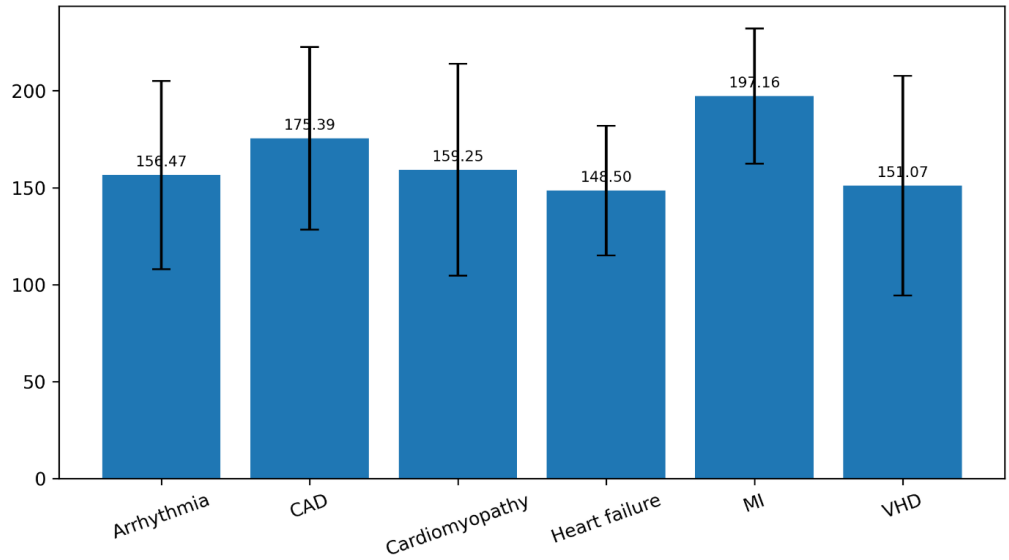

Figure 3: illustrates the correlation between serum cholesterol and platelet distribution width (PDW). A positive association was evident, with increasing cholesterol levels corresponding to higher PDW values. The relationship was found to be statistically significant (r = 0.450, p = 0.011). This suggests that patients with higher cholesterol levels may have greater variability in platelet size, reflecting ongoing platelet activation and heterogeneity, which may have implications in cardiovascular pathology.

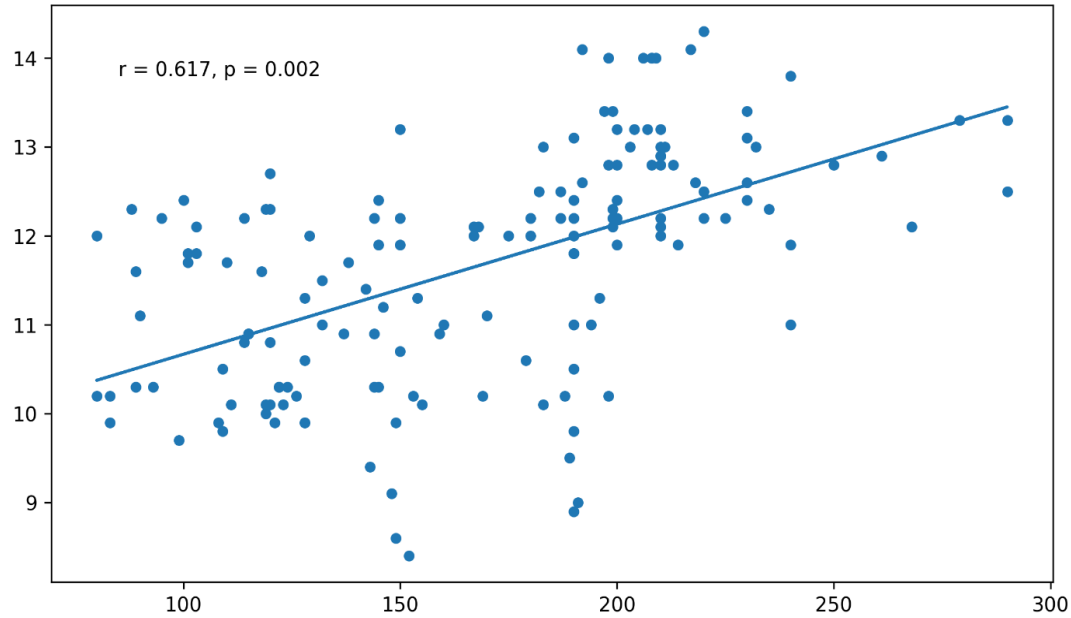

Figure 4: depicts the relationship between serum cholesterol and platelet large cell ratio (P-LCR). A significant positive correlation was noted, with higher cholesterol levels being associated with increased P-LCR values (r = 0.537, p = 0.023). This indicates that elevated cholesterol may be associated with a greater proportion of larger platelets, which are more metabolically and enzymatically active and may contribute to a prothrombotic state in cardiovascular disease.

Discussion

Cardiovascular diseases (CVDs), particularly coronary artery disease (CAD) and myocardial infarction (MI), remain among the leading causes of morbidity and mortality worldwide. Platelet activation is a key event in the progression of atherosclerosis and in the transformation of stable vascular disease into acute thrombotic events such as acute coronary syndrome and ischemic stroke [1].

In addition to conventional risk factors such as dyslipidemia, increasing evidence suggests that serum calcium may also influence cardiovascular risk through metabolic and vascular pathways [5]. The present study was therefore undertaken to evaluate the relationship of serum calcium and serum cholesterol with platelet indices in cardiac patients.

In the present study, most patients belonged to the fifth to seventh decades of life, and there was a clear male predominance. This agrees with the established epidemiology of cardiovascular disease, which shows that ischemic heart disease is more common in middle-aged and elderly men [7]. Similar age and sex patterns have been described in Indian and international studies on cardiovascular disease and platelet indices [15]. The predominance of CAD and MI in our study population is also expected, as these remain the most common causes of ICCU admissions and are closely linked to atherothrombosis.

One of the important findings of the present study was the significant positive correlation between serum cholesterol and platelet indices, particularly MPV, PDW, and P-LCR. This suggests that increasing cholesterol levels are associated with enhanced platelet activation and greater platelet heterogeneity. This relationship is biologically plausible, as dyslipidemia has been shown to alter platelet membrane composition, increase oxidative stress, enhance platelet aggregability, and promote a prothrombotic state [2]. Thus, elevated cholesterol may not only contribute to plaque formation but also increase the thrombotic tendency of circulating platelets.

Among platelet parameters, mean platelet volume (MPV) is the most extensively studied marker of platelet activation. Larger platelets are more metabolically active, contain more dense granules, and have greater thrombogenic potential [3]. In the present study, serum cholesterol demonstrated a significant positive correlation with MPV, indicating that higher cholesterol levels may be associated with the presence of larger and more reactive platelets. These findings are consistent with the meta-analysis by Chu et al., who showed that elevated MPV is associated with acute myocardial infarction, restenosis, and adverse cardiovascular outcomes [16]. Rucinski et al. also demonstrated that higher MPV values in acute MI patients undergoing PCI were associated with increased mortality and poorer long-term prognosis [6].

Similarly, the present study demonstrated a significant positive association between serum cholesterol and PDW. Platelet distribution width reflects variability in platelet size and is considered another marker of platelet activation and anisocytosis [11]. Increased PDW has been associated with acute coronary syndrome, severity of coronary artery disease, and worse cardiovascular outcomes [17]. In the present study, the positive relationship between cholesterol and PDW supports the hypothesis that dyslipidemia contributes to increased platelet turnover and activation. A significant positive association was also found between serum cholesterol and P-LCR, indicating a higher proportion of large circulating platelets in patients with elevated cholesterol levels. This finding is clinically relevant because larger platelets are considered more thrombogenic and have been linked to worse outcomes in ischemic heart disease [18].

The observed relationship between cholesterol and platelet indices in our study is also supported by earlier work in hyperlipidemic populations. Grotto et al. reported that platelet volume indices such as MPV, PDW, and P-LCR were significantly higher in hyperlipidemic patients than in controls [19]. Likewise, Khan et al. found that platelet count and MPV differed significantly across subjects with normal, borderline, and elevated cholesterol levels, suggesting that platelet morphology and function may be influenced by lipid status [20]. Although some studies have reported weaker or inconsistent associations, the overall trend across available literature supports a meaningful link between dyslipidemia and platelet activation.

Another notable finding of the present study was the significant positive correlation between serum calcium and serum cholesterol. This suggests that serum calcium may be linked with metabolic disturbances that contribute to cardiovascular risk. Gallo et al. demonstrated that progressive increases in serum calcium were associated with worsening lipid profiles, including total cholesterol and triglycerides, particularly in men and postmenopausal women [21]. Reid has also highlighted the potential cardiovascular implications of elevated serum calcium and calcium supplementation, suggesting that serum calcium may influence vascular disease through mechanisms such as vascular calcification, endothelial dysfunction, and altered metabolic homeostasis [22]. Thus, the positive relationship between calcium and cholesterol observed in our study is biologically plausible and consistent with prior evidence.

However, in contrast to its association with cholesterol, serum calcium did not show a significant direct correlation with platelet indices in the present study. This suggests that calcium may not directly influence platelet morphology in the same way as cholesterol, or that its effects may be mediated indirectly through vascular and metabolic mechanisms rather than through measurable changes in platelet size indices. This finding is important because it indicates that while serum calcium may reflect a broader cardiometabolic milieu, platelet activation in cardiac patients appears to be more strongly driven by dyslipidemia than by calcium levels alone.

When disease-specific comparisons were made, serum cholesterol levels were relatively higher in myocardial infarction patients than in other cardiac diagnoses. This is clinically understandable, as MI

is strongly associated with plaque rupture, thrombosis, and lipid-rich atherosclerotic lesions [1,2]. Although platelet indices were also relatively higher in MI patients, these differences were not statistically significant across all disease groups. Nevertheless, the trend is in line with previous studies reporting higher MPV and related platelet indices in acute coronary syndromes and myocardial infarction compared with stable coronary artery disease [9–11].

The present study has important clinical implications. Platelet indices such as MPV, PDW, and P-LCR are routinely available as part of automated complete blood counts and do not require additional cost or specialized testing. Their positive association with serum cholesterol suggests that these markers may serve as useful adjuncts in identifying cardiac patients with increased thrombotic and cardiovascular risk. In resource-limited settings, such inexpensive and easily obtainable biomarkers may be particularly valuable for risk stratification and secondary prevention.

However, certain limitations of the study should be acknowledged. The study was conducted at a single tertiary care center, which may limit the generalizability of the findings. The cross-sectional observational design also precludes any inference of causality. In addition, a detailed lipid profile including LDL, HDL, and triglycerides was not uniformly correlated in all analyses, and follow-up data were not available to assess the prognostic value of these parameters over time. Larger prospective studies are therefore needed to validate these observations and determine whether platelet indices can independently predict cardiovascular events in cardiac patients.

Overall, the present study demonstrates that serum cholesterol is significantly associated with platelet activation indices such as MPV, PDW, and P-LCR, while serum calcium shows a modest but significant positive association with serum cholesterol. These findings support the concept that dyslipidemia and platelet activation are closely interlinked in cardiovascular disease and that simple hematological indices may have value in identifying high-risk patients.

Conclusion

The present study highlights the clinical relevance of routinely available biochemical and hematological markers in cardiac patients. Cardiovascular disease was found to be more common in males and in patients belonging to the fifth to seventh decades of life, with coronary artery disease and myocardial infarction being the most frequent diagnoses. A significant positive relationship was observed between serum calcium and serum cholesterol, suggesting an underlying metabolic association in patients with cardiovascular disease. More importantly, serum cholesterol demonstrated a significant positive correlation with platelet activation indices, namely mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR). These findings indicate that rising cholesterol levels may be associated with increased platelet activation and thrombotic tendency. Since platelet indices are inexpensive, easily measurable, and routinely available as part of complete blood counts, they may serve as useful adjunctive markers for early identification of high-risk cardiac patients and may support future cardiovascular risk stratification strategies.

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