General Medicine

The Association of Platelet Count, Lymphocyte Count and Platelet/Lymphocyte Ratio with the Severity of Coronary Artery Disease

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| **Abstract** | **Original Research Article** |

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in most industrialized societies. Inflammation plays a substantial role in the initiation and propagation of the complex atherosclerotic process that lies beneath the cardiovascular diseases. High platelet and low lymphocyte counts have been suggested to be indicators of worse cardiovascular outcomes. Platelet to lymphocyte ratio is a new prognostic marker that integrates the risk prediction of these two parameters into one. We aimed to explore the association of platelet count, lymphocyte count and platelet to lymphocyte ratio (PLR) with the severity of atherosclerosis in coronary artery disease. Clinical and laboratory data of 100 patients who underwent coronary angiography were evaluated retrospectively. Gensini score, which indicates the severity of atherosclerosis, was calculated for all the patients. Patients with CAD were categorized as mild and severe atherosclerosis, according to their Gensini score. Twenty three patients with normal coronary arteries formed the control group. Platelet count, Lymphocyte count and mean PLR values of the three study groups were compared. The platelet count correlated positively with the severity of atherosclerosis, while the lymphocyte count correlated inversely with the severity of atherosclerosis. The mean PLR of the severe atherosclerosis group was significantly higher (223.89 ± 41.56) than that of the mild atherosclerosis group (176 ± 45.82) and control groups (104.17 ± 22.47) (p=0.001). Also, PLR correlated positively with Gensini score in CAD patients. A cut-off value of 176.5 for PLR predicted severe atherosclerosis with 94.1 % sensitivity and 77.6% specificity. Our study suggests that high PLR appears to be additive to the conventional risk factors and the commonly used biomarkers in predicting severe atherosclerosis.

Keywords: Cad, platelet, lymphocyte, atherosclerosis, gensini scoring.

INTRODUCTION

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in most industrialized societies [1]. Epicardial coronary arteries are the major site of atherosclerotic disease, with risk factors being high LDL, low HDL, cigarette smoking, hypertension and diabetes mellitus [2]. It is known that inflammation plays a substantial role in the initiation and propagation of the complex atherosclerotic process that lies beneath cardiovascular disease [3]. It is found that a low blood lymphocyte count is related with worse cardiovascular consequences in patients with CAD [4-6]. Also, ongoing inflammatory conditions lead to increased proliferation in megakaryocytic series and relative thrombocytosis [7].

Increased platelet activation plays an important role in initiation and progression of atherosclerosis [8]. High platelet and low lymphocyte counts in the circulation have been suggested to be indicators of worse cardiovascular outcomes [7]. Platelet to lymphocyte ratio is a new prognostic marker that integrates these two parameters into one. It gives an idea about both the aggregation and inflammation pathways, and it may be more valuable than either platelet or lymphocyte count alone in the prediction of coronary atherosclerotic burden [7].

This ratio of these two simple, cheap and readily available biomarkers could help identify individuals at risk for an advanced CAD, who might be candidates for an aggressive therapeutic approach. There is need for more evidence, and additional studies are still necessary to demonstrate the association of these findings with clinical outcome.

Aim and objectives
- To estimate the platelet count, lymphocyte count, and platelet-to-lymphocyte ratio (PLR).

- To calculate the Gensini Score based on Coronary angiogram.
- To compare the platelet-to-lymphocyte ratio and Gensini Score in patients with coronary artery disease.

MATERIALS AND METHODS

Our study is an observational cross sectional study done on patients admitted in the hospitals attached to Bangalore Medical College And Research Institute, Bangalore during the period of November 2016- May 2018. 100 patients admitted in the department of medicine fulfilling the inclusion and exclusion criteria were enrolled in the study. Demographic data, history was collected and detailed cardiovascular system examination was performed. Steps were taken to send for all the necessary investigations like complete blood profile and Platelet to lymphocyte ratio was determined. ECG, 2D echocardiography and Coronary angiograms were obtained and Gensini Score was calculated.

Inclusion criteria
Patients with angiographically established CAD diagnosis

Exclusion criteria
Patients with active infection, haematological disorders, systemic inflammatory conditions

Assessment of coronary atherosclerosis severity
CAD was defined as the presence of stenosis of at least 50% of the vessel diameter in any of the main coronary arteries, according to the American College of Cardiology/American Heart Association (ACC/AHA) lesion classification [9]. The Gensini scoring system was used to identify the severity of CAD [10]. This method classifies and scores the degree and extent of the stenosis of the coronary arteries. This system scores 1 point for 1% to 25% stenosis, 2 points for 26% to 50%, 4 points for 51% to 75%, 8 points for 76% to 90%, 16 points for 91% to 99% stenosis, and 32 points for total occlusion. The score is then multiplied by a factor representing the importance of the lesion's location in the coronary arterial system. For the location, scores are multiplied by 5 for a left main lesion; 2.5 for the proximal left anterior descending (LAD) or left circumflex (LCX) artery; 1.5 for the mid-segment LAD and LCX; 1 for the distal segment of the LAD and LCX, first diagonal branch, first obtuse marginal branch, right coronary artery, posterior descending artery, and intermediate artery; and 0.5 for the second diagonal and second obtuse marginal branches.

According to their coronary angiograms, patients were categorized into three groups. The first group consisted of patients with normal coronary arteries (control group). The rest of the patients with coronary artery disease were divided into two according to their Gensini score: [11,15] those with mild atherosclerosis (Gensini score <25 points) and severe atherosclerosis (Gensini score ≥25 points).

Statistical analysis
The data was entered in Microsoft excel sheet and was analyzed using SPSS version 22 software. The categorical data was represented in the form of frequency and percentage. Chi square/Fisher's exact test was used to test the significance for qualitative data. Continuous data was represented as mean and standard deviation. One-way analysis of variance (anova) was used to compare 3 groups. Multivariate linear regression analysis was applied to determine independent variables significantly associated with gensini score. p value <0.05 was considered as significant. ROC curve was drawn to assess the validity of the platelet lymphocyte ratio with area under curve. Cut off value, sensitivity and specificity was also calculated for the ratio.

RESULTS
A total of 100 patients were enrolled in our study. 77 patients had established coronary artery disease and 23 patients had normal coronary arteries proven angiographically. According to Gensini scoring, of the 77 cases, 25 had mild atherosclerosis and 52 had severe atherosclerosis. Baseline demographic, biochemical, and haematological characteristics of the groups are outlined in the table 1.

Table-1

	Normal (n - 23	Mild atherosclerosis (n- 25)	Severe atherosclerosis (n – 52)		F value	p value
Age	51.22 ± 7.25	55.80 ± 10.43	57.77 ± 11.51		3.16	0.05*
BMI	27.09 ± 6.08	28.86 ± 4.51	27.81 ± 4.87		0.75	0.48
Biochemical parameters						
Total cholesterol	175.52 ± 42.91	195.96 ± 65.70	163.92 ± 51.86		2.99	0.05*
HDL	40.04 ± 11.08	36.74 ± 7.91	33 ± 9.89		4.43	0.01*
LDL	87.78 ± 31.16	103.24 ± 56.14	90.03 ± 30.82		1.23	0.30
TGL	150.35 ± 68.72	196.50 ± 152.86	157.69 ± 74.76		1.66	0.20
Blood Sugar	153.22 ± 60.49	158.40 ± 70.10	202.27 ± 98.31		3.78	0.03*
Creatinine	0.74 ± 0.45	0.91 ± 0.29	0.88 ± 0.27		1.97	0.15
Hemotological parameters						
Hb	12.83 ± 1.59	14.18 ± 2.81	12.85 ± 1.66		4.23	0.02*
WBC	8.48 ± 1.65	9.76 ± 2.30	9.19 ± 2.13		2.30	0.11
absolute lymphocyte count	2208 ± 666.31	1929.68 ± 558.97	1719.96 ± 424.16		7.091	0.001*
Platelet	2.33 ± 0.93	3.26 ± 0.47	3.92± 0.35		64.841	0.001*
P/L ratio	104.17 ± 22.47	176 ± 45.82	223.89 ± 41.56		74.866	0.001*

*Significant at p < 0.05 level

The study groups were compared. Patients in severe atherosclerosis group were older compared to the mild atherosclerosis group and controls.

Fasting serum glucose was significantly higher in the severe atherosclerosis group (202.27 ± 98.31) than the mild atherosclerosis group (158.40 ± 70.10) and control group (153.22 ± 60.49).

The severe atherosclerosis group had significantly lower HDL (33 ± 9.89) levels as compared to mild atherosclerosis group (36.74 ± 7.91) and control group (40.04 ± 11.08).

When the haematological parameters were considered, the severe atherosclerosis group had significantly higher platelet count of 3.92± 0.35 compared to the mild atherosclerosis group (3.26 ± 0.47) and control group (2.33 ± 0.93).

Lymphocyte count was comparable between the all the three groups. In the control group it was 2208 ± 666.31, in mild and severe it was 1929.68 ± 558.97 and 1719.96 ± 424.16 respectively which was statistically significant. PLR was significantly higher in the severe atherosclerosis group 223.89 ± 41.56 when compared to the mild atherosclerosis group (176 ± 45.82) and the control group (104.17 ± 22.47). PLR values of patients with CAD correlated significantly with their Gensini scores as shown in figure 1.
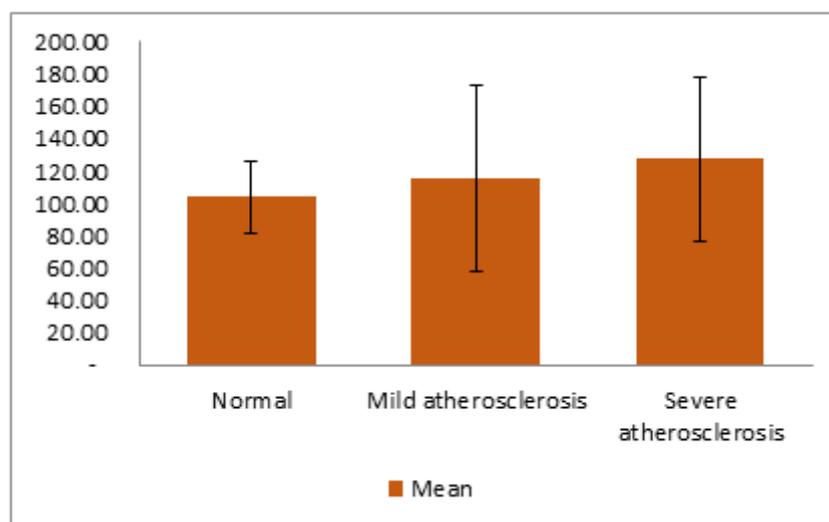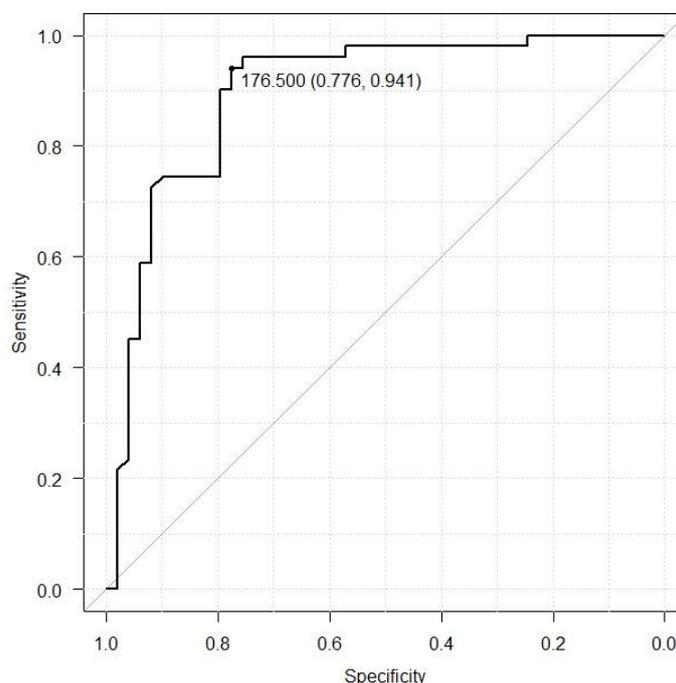

Fig-1: Mean platelet –to- lymphocyte ratio of controls, mild and severe atherosclerosis groups

Using a cut off level of 176.5, PLR predicted severe atherosclerosis with a sensitivity of 94.1% and a specificity of 77.6%, with area under the curve =0.896, 95 % CI: 0.8295 - 0.9625; P =0.000 (Figure 2).

Fig-2: The receiver operating characteristic (ROC) curve analysis of platelet-to-lymphocyte ratio for predicting severe atherosclerosis.

DISCUSSION

Inflammation plays a crucial role at all stages of atherosclerosis [3,15-17]. It is found that in chronic inflammation, lymphocytopenia occurs, either due to decreased production from bone marrow or increased apoptosis. In our study, we found that lymphocyte count correlated inversely with the severity of coronary artery disease. In the study by Ommen at al [5], low lymphocyte count was suggested to have an independent prognostic value. Multiple other studies have also demonstrated the diagnostic and prognostic usefulness of a low lymphocyte count in patients with acute coronary syndrome and stable CAD [5, 18].

The ongoing inflammatory state in the body results in a prothrombotic condition due to increased proliferation in megakaryocytic series and relative thrombocytosis. The circulating platelets contribute to the initiation of atheromatous plaque formation and triggers its complications [14].

Our study showed that platelet values were positively correlated with the severity of CAD. Studies done previously had also suggested that high platelet and low lymphocyte counts in circulation to be risk indicators of worse cardiovascular outcomes [5,6,8,12,13].

The relationship between systemic inflammation and coronary atherosclerosis is demonstrated by many studies, but in our study, we aimed to correlate the PLR with the severity of coronary atherosclerosis and therefore with the severity of coronary artery disease and the Gensini score.

Hence, in our study we combined both the parameters to obtain a PLR. We observed that high PLR was independently associated with the severity of coronary atherosclerosis. There was a positive correlation between PLR values and Gensini scores of patients with CAD. We further observed that PLR > 176.5 predicted severe atherosclerosis with a sensitivity of 94.1% and a specificity of 77.6%.

A study by Yuksel *et al*. [7], also showed similar results, where PLR > 111 predicted severe atherosclerosis with a sensitivity of 61% and specificity of 59%. In a study by Azab *et al*. [12] have shown that higher PLR values were associated with an increase in long-term all-cause mortality in patients admitted with non-ST-segment elevation myocardial infarction (NSTEMI).

In a study by Acar *et al*. [13], PLR was found to be independently related with coronary collateral development in patients with chronic total occlusions.

In a study by Yildiz *et al*. [14] showed that higher PLR was associated with poor prognosis in patients with CAD. High PLR (> 160) was an independent predictor of no-reflow in patients presenting with STEMI.

Diabetes and low plasma level of HDL are important risk factors for CAD. We also found a positive correlation of fasting blood glucose and a negative corelation of HDL with the severity of coronary atherosclerosis, similar to the study done by Karan *et al*. [20].

CONCLUSION

We conclude that high PLR appears to be additive to conventional risk factors and commonly used biomarkers in predicting severe atherosclerosis as it correlates positively with the Gensini score. This simple, cheap and readily available biomarker could help identify individuals at risk for CAD, who might be candidates for an aggressive therapeutic approach and closer clinical follow up.

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