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Study to estimate platelet lymphocyte ratio in acute coronary syndrome as a prognostic marker

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Abstract

Background: Acute Coronary Syndrome is a big burden in India due to urbanization and economic transition. Risk stratification in the emergency room is important for initiating appropriate therapy. Acute Coronary Syndrome has an inflammatory process due to atherosclerosis in which platelets are elevated and lymphocytes are reduced. Earlier studies have tried using Platelet Lymphocyte Ratio in determining the severity of the Acute Coronary event.

Objective: This study aims to use Platelet Lymphocyte Ratio in Acute Coronary Syndrome as a marker of prognosis.

Methods: We conducted a single centre cross-sectional study of 100 random patients with Acute Coronary Syndrome during the study period from November 2019 to October 2021.

Results: There was a statistically significant ($p=0.0001$) correlation between Platelet Lymphocyte Ratio and GRACE score, TIMI score in Acute Coronary Syndrome.

Conclusion: Platelet Lymphocyte Ratio can be used as a prognostic marker in Acute Coronary Syndrome.

Keywords: Platelet Lymphocyte Ratio, Acute Coronary Syndrome, GRACE score, TIMI score

Introduction

In India, Acute Coronary Syndrome is a big burden recently due to rapid urbanization and economic transition ^[1]. As chest pain is the most common reason for Emergency room visits risk stratification is important for initiating appropriate therapy ^[2]. Acute Coronary Syndrome has an underlying inflammatory process due to atherosclerosis in which platelets are elevated and lymphocytes are reduced ^[3]. Many studies have tried using Neutrophil Lymphocyte and Platelet Lymphocyte Ratio in determining the severity and prognosis of an Acute Coronary event ^[4]. But Neutrophil Lymphocyte and Platelet Lymphocyte Ratio vary in different populations based on ethnicity, race, geographical location, age and sex ^[5]. About 40% of patients diagnosed with Acute Coronary Syndrome develop Left Ventricle Systolic Dysfunction having a higher risk for adverse events ^[6]. As there has been an increasing incidence of complex cardiovascular lesions needing early invasive intervention an accurate prognostic tool is essential ^[7].

Materials and Methods

The study was a single centre cross-sectional study conducted at the Emergency room, Department of General medicine, Rajah Muthiah Medical College and Hospital, Chidambaram, Tamilnadu between November 2019 to October 2021. A total of 100 random patients who attended the Emergency room diagnosed with Acute Coronary Syndrome were included in the study after obtaining informed consent based on the inclusion and exclusion criteria. Complete blood count was obtained using an automated analyzer. Platelet Lymphocyte Ratio in different subgroups was observed and used to estimate the prognosis in the patients diagnosed with Acute Coronary Syndrome comparing it with GRACE and TIMI score.

Inclusion criteria: All patients diagnosed with Acute Coronary Syndrome with blood samples collected at the time of presentation and reports obtained using Sysmex automated analyzer.

Exclusion criteria: If there was an error in handling the samples and report collection.

Investigation: Complete blood count, Renal function test, Creatine kinase – MB, Electrocardiogram were done in all patients included in the study.

Statistical Analysis: Regression data analysis was done in LibreCalc. Continuous variables were expressed using mean, standard deviation, range and quartiles. A P-value of less than 0.05 was considered statistically significant. The Correlation test was the test of significance calculated.

Results

Basic observations of the study population are given in Table 1. Many variables were higher in the study population than the general population as shown in Table 2. Platykurtic and Leptokurtic distribution in the study population were

given in Table 3. Platelet Lymphocyte Ratio grading based on 1st and 3rd quartiles is shown in Table 5. Platelet Lymphocyte ratio correlation with other variables in the study population is given in Table 6. The strength of correlation with variables is given in Table 8. Platelet values were higher while lymphocytes values were lower in the study population due to the underlying inflammation in Acute Coronary Syndrome so Platelet to Lymphocyte ratio is increased. But there are no fixed values to that ratio and it's highly variable based on age, ethnicity, geography. Most values ranged from 100 to 300, unlike previous studies where they ranged from 50 to 150. Platelet Lymphocyte Ratio was divided into low, intermediate and high risk based on the 1st and 3rd quartile value in the study population. Platelet Lymphocyte Ratio correlates with TIMI and GRACE score which were statistically significant with a p-value of 0.000.

Table 1: Basic observation of the study population

Variables	Mean SD	SE Variance	Median Mode	Kurtosis Skew	Quartile 1st/3rd
Platelet	3.63 1.01	0.10 1.03	3.56 3.66	-0.75 0.02	2.94 4.29
Lymphocyte	1.97 0.55	0.05 0.30	1.51 1.98	-0.78 -0.11	1.52 2.37
PLR	215.20 127.89	12.78 16391	182.84 194.52	4.00 1.63	124.64 279.97
CKMB	76.13 16.07	1.60 258.31	77.5 59	-0.83 0.077	61.5 89.25
Age	61.16 11.17	1.11 124.96	62 65	-0.99 -0.20	50.75 70
Heart Rate	86.22 22.63	2.26 512.41	90 44	-0.90 -0.19	70 104
Systolic BP	118.42 19.32	1.93 373.33	115 115	1.11 1.19	105.75 124
Creatinine	1.27 0.42	0.04 0.18	1.25 0.9	0.14 0.39	1 1.5
LDL	136.37 33.80	3.38 1142.9	135.5 109	-0.70 0.23	109 161
RBS	299.09 97.18	9.71 9444.5	319 328	-0.98 -0.04	214.75 363.75
Weight	86.8 17.59	1.75 309.61	88 77	-0.82 0.077	73 99

SD – Standard Deviation, SE – Standard Error, PLR – Platelet Lymphocyte Ratio

Table 2: Average mean of variables differing in study population

Higher in study population than general population
Platelets
Platelet Lymphocyte Ratio
Low-Density Lipoprotein
Creatinine
Body Weight
Random Blood Sugar
Lower in study population than general population
Lymphocytes
Same in study population as general population
Heart Rate
Systolic Blood Pressure

Table 3: Outliers of variables in study population

Leptokurtic Peak With Many Outliers
Platelet Lymphocyte Ratio
Platykurtic Belly With Minimal Outliers
Creatine Kinase MB
Low-Density Lipoprotein
Creatinine
Random Blood Sugar
Systolic Blood Pressure
Heart Rate
Body Weight

Table 4: Outcome prediction of variables in study population

Good predictors of every outcome [No Skew]
Platelet Lymphocyte Ratio
Age
Creatinine
Random Blood Sugar
Left Ventricle Ejection Fraction
Body Weight
Good predictors of grave outcomes [Left Skew]
GRACE Score
Creatine Kinase MB
Heart Rate
Low-Density Lipoprotein
Systolic Blood Pressure
Good predictors of safe outcomes [Right Skew]
TIMI Score

Table 5: Platelet lymphocyte ratio grading

Variables	PLR Low <125	PLR Intermediate 125 – 275	PLR High >275
GRACE Score	2.89%	7.92%	12.72%
TIMI Score	9.13%	12.50%	16.44%
CKMB	73.69	73.77	82.92
Age	51.85	62.85	67.35
Heart Rate	79	83	100
Systolic BP	119	121	113
Creatinine	0.96	1.2	1.59
LDL	131	130	153
RBS	196	310	382
Weight	69	86.60	104.96
Ejection Fraction	53.53%	50.6%	43.54%

PLR – Platelet Lymphocyte Ratio

Table 6: Platelet lymphocyte ratio correlation

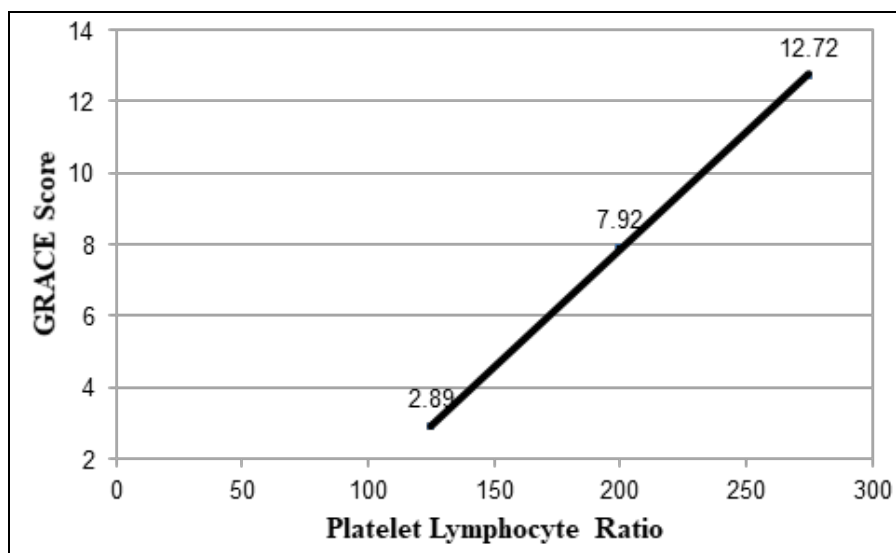
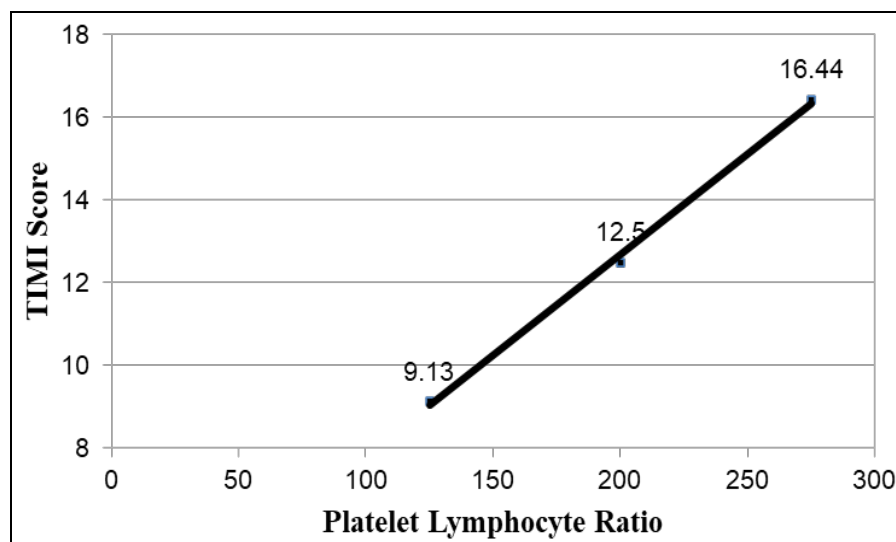
Variables	Platelet Lymphocyte Ratio Correlation	P-value
GRACE Score	0.530	0.000
TIMI Score	0.498	0.000
CKMB	0.211	0.035
Age	0.432	0.000
Heart Rate	0.371	0.000
Systolic BP	-0.187	0.061
Creatinine	0.522	0.000
LDL	0.384	0.000
RBS	0.625	0.000
Weight	0.693	0.000
Ejection Fraction	-0.599	0.001

Table 7: Confounding factors to platelet lymphocyte ratio in study population

Strong Confounders
Age
Body Weight
Creatinine
Random Blood Sugar
Heart Rate
Low-Density Lipoprotein
Poor Confounders
Systolic Blood pressure

Table 8: PLR correlation with other variables in study population

Strong positive correlation
Age
Body Weight
Creatinine
Random Blood Sugar
Strong negative correlation
Left ventricle Ejection Fraction
Weak positive correlation
Heart Rate
Low-Density Lipoprotein
No correlation
Creatine Kinase MB
Systolic Blood Pressure

**Fig 1:** Graded platelet lymphocyte ratio and GRACE score correlation**Fig 2:** Graded platelet lymphocyte ratio and TIMI score correlation**Table 9:** Platelet lymphocyte ratio and GRACE score correlation

Variables	PLR Low <125	PLR Inter 125 – 275	PLR High >275
GRACE	2.89%	7.92%	12.72%
Correlation	0.530		
P Value	< 0.0001		
R ² Value	0.273		

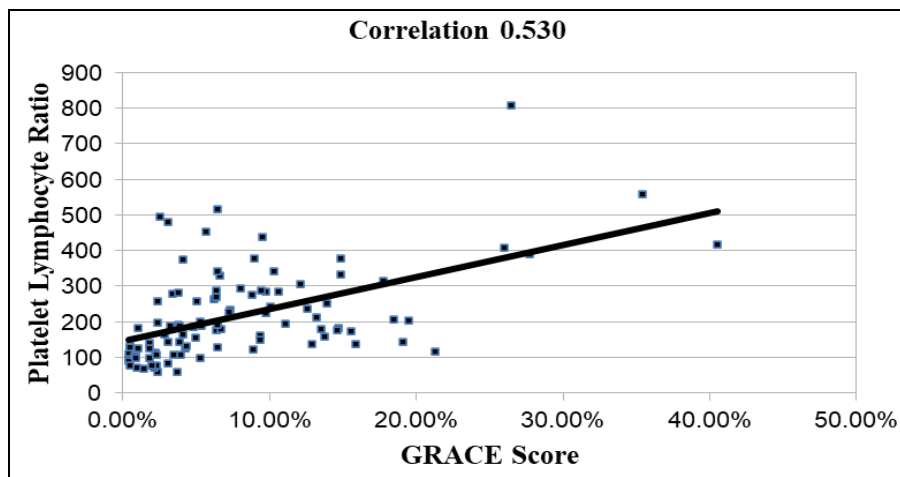


Fig 3: Platelet lymphocyte ratio and GRACE score correlation

Table 10: Platelet lymphocyte ratio and TIMI Score Correlation

Variables	PLR Low <125	PLR Inter 125 – 275	PLR High >275
TIMI	9.13%	12.50%	16.44%
Correlation	0.498		
P Value	< 0.0001		
R ² Value	0.240		

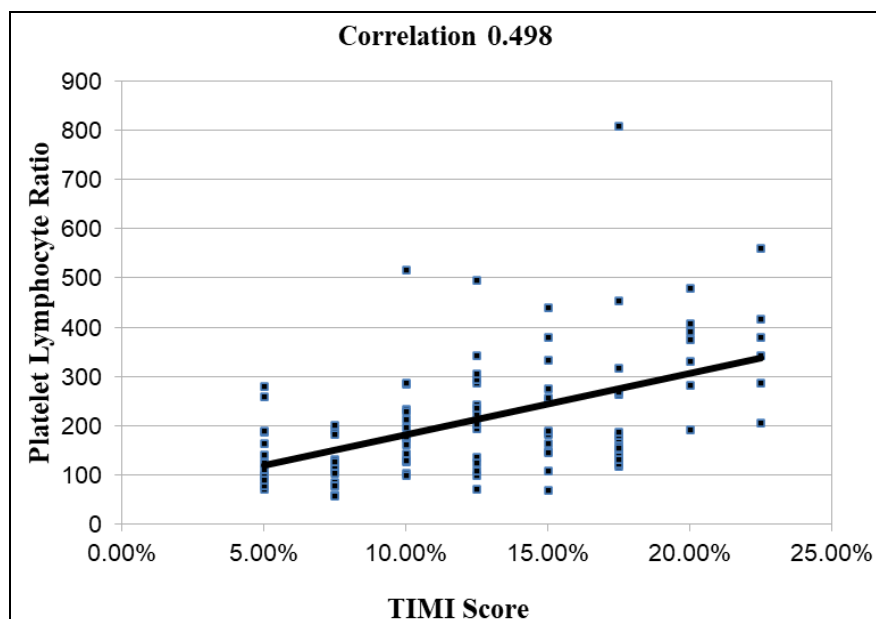


Fig 4: Platelet lymphocyte ratio and TIMI score correlation

Discussion

Atherosclerosis is an active cellular and passive infiltrative inflammatory process in response to endothelial injury leading to narrowing and thickening of arteries involved [8]. This inflammatory process involves the activation of leukocytes like neutrophils and lymphocytes mediated by chemokines and cytokines [9]. Plaque instability is the initial event in Acute Coronary Syndrome (ACS) as this makes leukocytes attracted to the site of injury on tunica intima causing neovascularization [10]. Neutrophils Extracellular Traps (NETs) were increased at the site of occlusion which is highly inflammatory and pro-thrombotic by trapping leukocytes so they are increased in large infarcts and decreased in patients with ST-segment resolution [11]. Follicular B2 and T helper cells slow the inflammatory process thereby reducing atherosclerosis so low lymphocyte count is seen in patients with poor prognosis [12]. Platelets

cause inflammation via CD40L which are not only pro-thrombotic but also pro-atherogenic which causes oxidative modification on endothelial cells by increasing LDL-C resulting in smooth muscle proliferation [13]. Platelets also interact with endothelial cells causing transmigration of monocytes which leads to more inflammation and atherosclerosis [14]. This inflammatory process leads to neovascularization which causes endothelial dysfunction [15]. An increase in stress during an acute coronary event leads to an increase in cortisol which causes a reduction in circulating lymphocytes and CD-4 count [16]. When HDL-C is low there is high CRP and IL-6 levels with severe underlying atherosclerosis [17]. Monocytes interact with tunica intima in the damaged endothelium becoming macrophages eventually forming foam cells by the intake of LDL [18]. Inflammatory cascade activation in any acute coronary event as a result of ischemia leads to an increase in

the levels of superoxide anions, hydrogen peroxide, myeloperoxidase, free oxygen radicals and circulating neutrophils, monocytes and platelets [19]. This Study compared Platelet Lymphocyte Ratio to GRACE and TIMI score in predicting the in-hospital and 6-month mortality of an acute coronary event. Platelet Lymphocyte Ratio could be a simple, cheap, quick tool useful in segregating high-risk patients from low-risk useful in providing appropriate

early invasive interventions like Angioplasty and Bypass Graft. Platelet Lymphocyte Ratio increases as GRACE and TIMI score increase but they also increase as other variables like age, RBS, creatinine and heart rate increase. So it's hard to discern whether Platelet Lymphocyte Ratio can independently predict severity of the underlying inflammatory process or it's altered by other confounding factors like age, RBS, creatinine and heart rate.

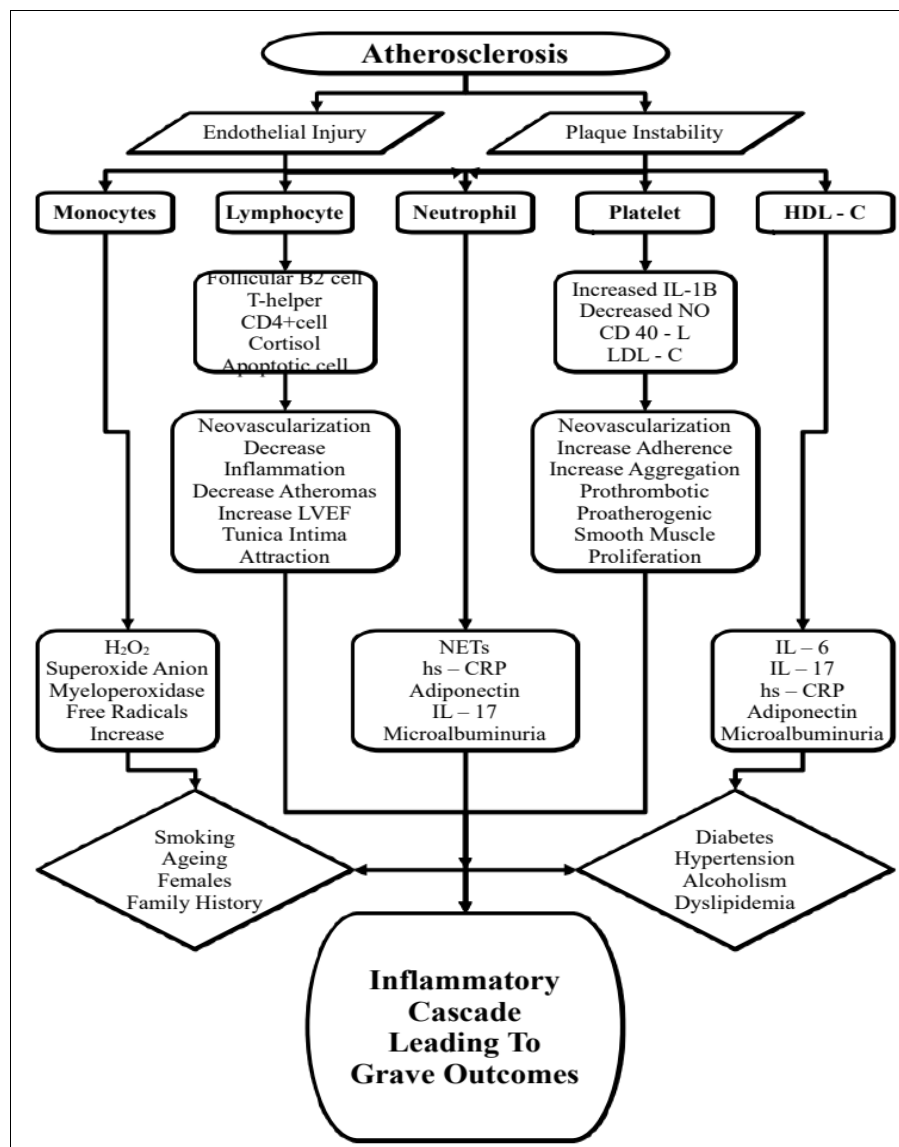


Fig 5: Inflammatory cascade of acute coronary syndrome

Conclusion

The Platelet to Lymphocyte ratio correlates with the prognosis and outcome of an acute coronary event. They could be used as an economic and quick tool to segregate patients into low and high risk so appropriate early intensive therapy could be provided modifying our approach. But the reliability, repeatability and reproducibility of this tool are yet to be tested. But the precision, accuracy and validity in determining the severity look promising. Still, debate exists whether this ratio independently predicts the severity or is influenced by other confounding factors like age, weight, creatinine and random blood sugar which equally alter the Platelet Lymphocyte Ratio.

Limitations of Study

This is a single centre cross-sectional study. Many multi-centre studies, Systemic reviews, Meta-analysis are needed about this subject to validate these results.

Statement of Ethics

This study was approved by the Human Ethics Committee, Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram, Tamilnadu. Informed consent was obtained from every patient.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest to disclose

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