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PLR AS A PROGNOSTIC INDICATOR TO ESTIMATE THE RISK OF IN-HOSPITAL MORTALITY AND MAJOR ADVERSE CARDIAC EVENTS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Background: Platelet to lymphocyte ratio (PLR) is a new prognostic value for both inflammatory and thrombotic process which have a vital role in the pathophysiology of myocardial infarction and major adverse myocardial outcomes. **Objective:** To assess the prognostic value of PLR as an indicator of in-hospital complications and mortality in patients with AMI. **Materials and methods**: Study sample included patients with AMI admitted to the CCU at Tishreen University Hospital-Latakia –Syria from April 2020 to April 2021. PLR was calculated from complete blood count for all patients. The study population was divided into tertiles based on their admission PLR. Patients having values in the third tertile was defined as the high PLR group (n=33) and those having values in the lower 2 tertiles were defined as the low PLR group (n=66). **Results**: 99 patients were included, 75 were male (75.8%) and the median age was 59. In-hospital mortality was significantly higher among patients in the upper PLR tertile when compared with the middle and lower PLR tertile groups (p=0.0001). Using a cutoff point of 140.5, the PLR predicted in-hospital mortality with a sensitivity of 83.3% and specificity of 82.8%, and PLR values were positively correlated with GRACE score (P=0.0001). According to multivariant analysis any increase in the value of PLR upon admission is associated with an increase of in-hospital mortality (Or=3.3, P=0.0001), arrhythmias (Or=4.1, P=0.0001) and cardiogenic shock (Or=3.2, P=0.002). **Conclusions**: PLR is an inexpensive and readily available biomarker that may be useful for cardiac risk stratification in patients with acute myocardial infarction.

KEYWORDS: Acute myocardial infarction, PLR, mortality, cardiogenic shock, MACEs.

INTRODUCTION

Ischemic heart disease is the single most common cause of death worldwide and its frequency is increasing. Several recent studies have highlighted a fall in short and long-term mortality following ST segment elevation myocardial infarction (STEMI) (and NSTEMI) in parallel with greater use of reperfusion therapy, primary percutaneous coronary intervention (PCI), modern antithrombotic therapy, and secondary prevention; Nevertheless, mortality remains substantial; in-hospital mortality of unselected patients with STEMI in the national registries of the ESC countries varies between 4 and 12%.[1]

Therefore, it is important to distinguish high-risk MI patients who need more emphasis in controlling risk factors, intensive treatment and close medical follow-up, as the interaction between the thrombotic and inflammatory processes is the decisive factor in the pathogenesis of myocardial infarction. Since the pro-inflammatory state and the activity of the thrombotic process reflect an increase in the number of platelets in the peripheral blood, so they can help predict cardiac complications. On the other hand, lymphocyte deficiency indicates a disturbance in the immune mechanism and thus a poor prognosis from the heart side, as lymphocytes contribute to maintaining the stability of the atheroma.[2]

The inflammatory event that occurs in the context of acute coronary syndrome plays an important role in the development and instability of acute coronary syndrome, and several biomarkers have been identified with independent predictive values for the severity of acute coronary syndrome but are not routinely used for their high cost such as (IL-6 and Matrix metalloproteinase).[2]

It was found that platelets have a role in the development of atheroma and in acute coronary syndrome. In addition, the decrease in lymphocytes indicates an inhibitory immune response that is associated with negative results at the level of the cardiovascular system.[2]

Therefore, the aim of this study is to explore the association between PLR and in-hospital mortality and MACEs in patients with acute myocardial infarction.

MATERIALS AND METHODS

The present analysis was a prospective observational study conducted at Tishreen University Hospital (Latakia, Syria) between April 2020 and April 2021.

Patients with acute myocardial infarction (AMI) (both STEMI and NSTEMI) admitted to the cardiac care unit, Tishreen University Hospital, Latakia, were studied. Exclusion criteria were hypo/hyperthyroidism, significant valvular disease, cardiogenic shock state upon admission, autoimmune diseases, active septic status upon admission, blood diseases (such as inhibiting one of the blood chains), chronic renal or hepatic insufficiency, malignancies, patients on corticosteroids, patients on cytotoxic drugs (tumor drugs), immunosuppressants or patients on Glycoprotein IIb/IIIa inhibitors.

The PLR value was taken from the complete blood count which is routinely performed for all patients admitted with acute myocardial infarction within the first 18 hours of symptoms in addition to the rest of the routine emergency blood test upon admission. The complete blood count was performed on the URIT-3000 Plus device.

A detailed history was taken, the associated risk factors were known, the GRACE score was calculated, a full clinical examination with infarction pattern was determined from initiation, and the patients were managed and followed up accordingly.

All subjects underwent two-dimensional echocardiography to determine left ventricular ejection fraction (LVEF) before discharge (unless needed earlier). All required investigative and therapeutic procedures were done as available.

The study population was divided into tertiles based on admission PLR values. The high PLR group (n=33) was defined as having values in the highest tertile (PLR >132), and the low PLR group (n=66) was defined as having values in the lower 2 tertiles (PLR ≤132).

Acute coronary syndrome was defined as presentation with symptoms of ischemia in association with electrocardiographic changes or positive cardiac enzymes.[1] Arterial hypertension was considered in patients with repeated blood pressure measurements >140/90 mm Hg or active use of antihypertensive drugs. Diabetes mellitus was defined as fasting plasma glucose levels more than 126 mg/dL in multiple measurements or active use of antidiabetic medications. Smoking was defined as current smoking. Patients having fever or symptoms or signs of urinary tract or respiratory system infection (leukocytosis or nitrite positivity in urine, infiltration in chest x-ray) were defined as active infection. PLR was calculated as the ratio of platelet count to lymphocyte count. We defined adverse cardiovascular events during in-hospital period as cardiogenic shock, arrhythmia (ventricular fibrillation and ventricular tachycardia after 24h of symptoms), acute heart failure (with reduced ejection fraction), stroke and re-infarction.

Statistical analysis

The analysis was performed using the Statistical Package for Social Sciences (SPSS) (version 20) (IBM Corporation, Armonk, New York, USA) and Excel 2010 program. A predictive value less than 0.05 was considered statistically significant. Basic Descriptive statistics included means, standard deviations (SD), Frequency and percentages. Statistical analyses were performed using the chi- square test, Student's t-test, Spearman and Pearson correlation and Fischer's exact test. Multivariate logistic regression was used to assess the association of explanatory variables with mortality in the presence of other potential confounders/risk factors.

RESULTS

Our study included 99 patients with acute myocardial infarction, males were 75 patients (75,8%) and females were 24 patients (24,2%). The median age of patients was 59 years in a range of 22-82 years.

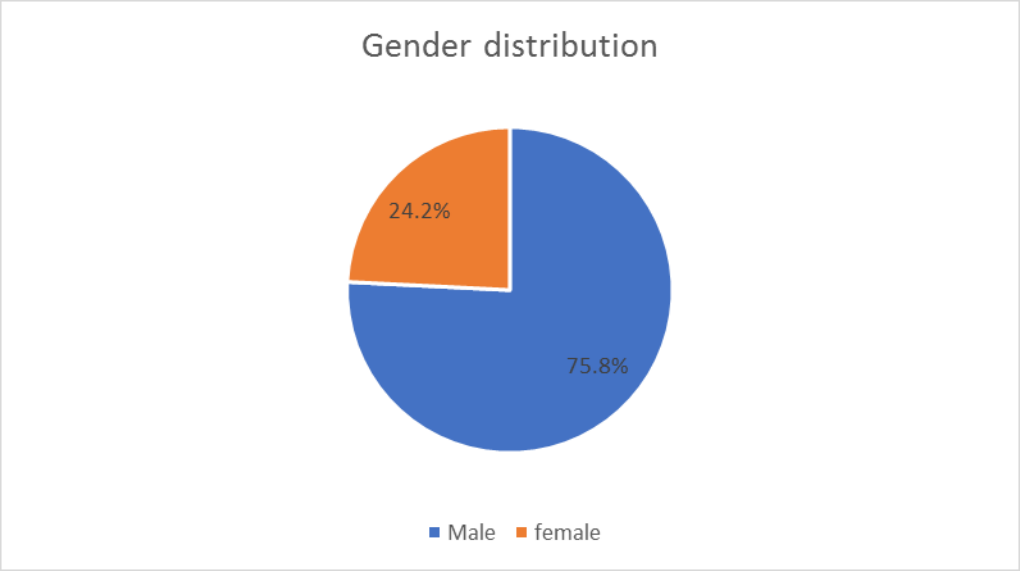

Figure 1: Distribution of a sample of 99 patients with acute myocardial infarction by gender with sex Ratio (M:F) = 3.1:1.

Table (1): Distribution of a sample of 99 patients with acute myocardial infarction according to the type of infarction.

Infarction Pattern	The number	Percentage
STEMI	86	86.9%
NSTEMI	13	13.1%
The total	99	100%

We notice that 86.9% of the sample of patients with myocardial infarction had a STEMI.

Table (2): Differences of demographic distribution upon admission among groups of acute myocardial infarction patients according to the value of the PLR.

Differences of demographic distribution	PLR<94 71.16±14.7	94≤PLR≤132 114.67±11.7	PLR>132 190.86±76.8	p-value
Gender Male Female	 20(60.6%) 13(39.4%)	 26(78.8%) 7(21.2%)	 29(87.9%) 4(12.1%)	0.03
Age(years)	58.4±9.3	55.7±11.3	61.6±10.1	0.01

We notice that men were more in the high PLR group (P= 0.03) and also ages were greater in the high PLR group (P= 0.01)

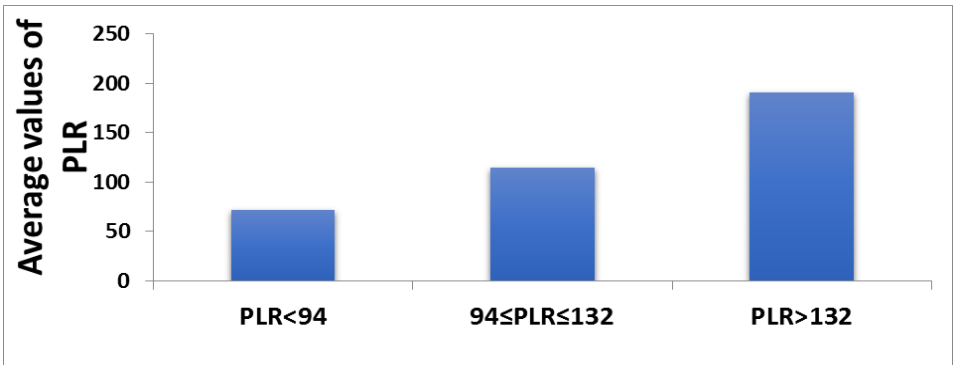

Figure 2: Mean values of platelet to lymphocyte ratio in a sample of 99 acute myocardial infarction patients.

Table (3): Distribution differences according to risk factors among groups of patients with acute myocardial infarction according to the value of the PLR.

Risk factors	PLR<94	94≤PLR≤132	PLR>132	p-value
Diabetes mellitus	14(42.4%)	6(18.2%)	10(30.3%)	0.03
Hypertension	16(48.5%)	10(30.3%)	12(36.4%)	0.3
dyslipidemia	6(18.2%)	5(15.2%)	6(18.2%)	0.9
obesity	5(15.2%)	4(12.1%)	1(3%)	0.2
smoking	28(84.8%)	28(84.8%)	24(72.7%)	0.3
CVA	0(0%)	5(15.2%)	3(9.1%)	0.02
Coronary or peripheral artery disease	4(12.1%)	8(24.2%)	7(21.2%)	0.4
Family history of cardiovascular disease	24(72.7%)	17(51.5%)	13(39.4%)	0.02

We note from the previous table that there are statistically significant differences with regard to the presence of diabetes and cerebrovascular accidents, as well as in the case of a family history of cardiovascular disease, as with the value of PLR > 132 there were 30.2% had diabetes, 9.1% had cerebrovascular accidents, and 39.4 % having a family history of CVD.

Table (4): Differences of mean values of laboratory parameters among groups of acute myocardial infarction patients according to the value of the PLR.

Laboratory parameters	PLR<94	94≤PLR≤132	PLR>132	p-value
Creatinine	1.65±3.6	1.13±0.4	1.20±0.3	0.5
Urea	30.79±11.6	36.15±14.3	39.17±13.7	0.03
CRP	12.05±22.4	11.16±19.5	7.87±12.2	0.7
GLU	180.8±102.4	169.4±76.1	191±92.9	0.6
NLR	2.69±1.4	3.96±1.6	5.62±1.6	0.0001
MPV	9.31±1.3	8.72±1.1	8.87±1.6	0.2

In the previous table there are statistically significant differences with regard to urea, as it increases with the increase in the value of the PLR(P=0.03), as well as the ratio of neutrophils to lymphocytes (P=0.0001).

Table (5): Distribution differences according to the type of infarction and echogenic findings among groups of infarct patients according to the value of the PLR.

	PLR<94	94≤PLR≤132	PLR>132	p-value
Infarction type STEMI NSTEMI	 29(87.9%) 4(12.1%)	 26(78.8%) 7(21.2%)	 31(93.9%) 2(6.1%)	0.1
EF	46.86±9.1	44.37±7.1	40.44±9.2	0.02

From the previous table, there were statistically significant differences with regard to ejection fraction (EF), which decreased with higher PLR values(P=0.02).

Table (6): Differences according to clinical status and GRACE score among infarction patient groups according to PLR value.

	PLR<94	94≤PLR≤132	PLR>132	p-value
Blood pressure Systolic Diastolic	 130.03±24.8 79.56±14.3	 136.30±19.5 81.72±11.7	 137.03±30.1 82.22±15.7	 0.4 0.7
Pulse	82.28±14.4	76.90±20.6	90.81±17.7	0.008
Cardiac arrest	0(0%)	1(3%)	1(3%)	0.6
GRACE score	105.66±21.1	109.1±23.9	134±30.3	0.0001

From the previous table, there are statistically significant differences with regard to the mean values of the pulse upon admission, as well as the GRACE score, as with the increase in the values of the PLR, there was a rise in the mean values of each.

Table (7): The differences according to the procedures taken among the groups of patients with infarction according to the value of the PLR

Procedure	PLR<94	94≤PLR≤132	PLR>132	p-value
Conservative treatment	12(36.4%)	16(48.5%)	8(24.2%)	0.1
fibrinolytic therapy (streptokinase) Success Failure	21(63.6%) 19 2	17(51.5%) 17 0	24(72.7%) 15 10	 0.2 0.002
Primary PCI	———	———	———	———

There are statistically significant differences regarding the result of streptokinase infusion, in which the failure cases were high with the high values of the PLR(P=0.002), and we did not notice any cases of emergency catheterization because catheter lab was out of service.

Table (8): Differences according to length of stay in hospital, complications and deaths among groups of patients with infarction according to the value of the PLR

	PLR<94	94≤PLR≤132	PLR>132	p-value
Length of stay in hospital	3.2±1.5	3.9±1.7	5.2±10.1	0.4
Complication Cardiogenic shock Arrhythmia CVA	 2(6.1%) 3(9.1%) 0(0%)	 0(0%) 2(6.1%) 0(0%)	 12(36.4%) 11(33.3%) 1(3%)	 0.0001 0.004 0.1
mortality	1(3%)	0(0%)	11(33.3%)	0.0001

From the previous table, there are statistically significant differences with regard to complications occurring within the hospital (cardiogenic shock[P=0.0001] and arrhythmias[P=0.004]), as well as in-hospital mortality [P=0.0001], which were higher with the high PLR values.

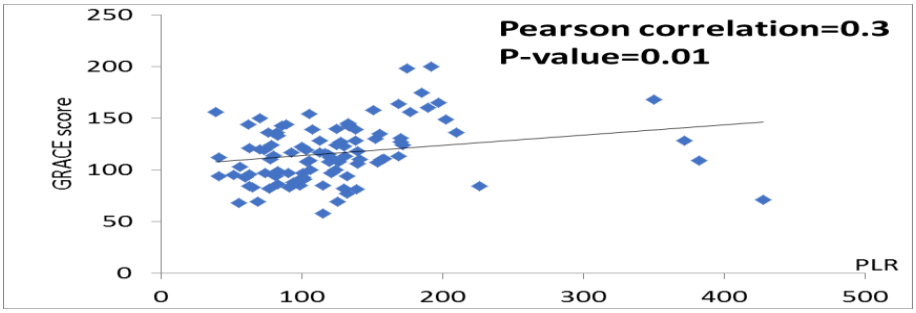

Figure 3: The relationship between the platelet-to-lymphocyte ratio and the GRACE score in patients with myocardial infarction.

Positive correlation, that is, with higher values of PLR, the value of GRACE score rises, in the presence of statistically significant differences.

Table (9): Risk factors associated with in-hospital death for a group of myocardial infarction patients.

Variables	OR a	Confidence interval (95%)	p-value
Age	1.9	[1.1 – 3.2]	0.04
PLR	3.3	[2.2 – 5.6]	0.0001
LYM	3.1	[1.9 – 5.7]	0.001
EF↓	1.6	[1.1 – 3.9]	0.03
GRACE score	2.6	[1.3 – 4.2]	0.002

The statistically significant variables were entered into the logistic regression equation to identify the independent indicators of in-hospital mortality. We found that the high level of the PLR ratio is an independent indicator of in-hospital mortality in association with age, lymphocyte count and GRACE score.

High PLR value upon admission is associated with a risk of in-hospital mortality 3.3 times, as well as advanced age 1.9 times and a high GRACE score 2.6 times and with a decrease in the value of EF there is a risk of death 1.6 times.

Table (10): Platelets to lymphocytes ratio and in-hospital complications occurring for myocardial infarction patients.

Variables	OR a	Confidence interval (95%)	p-value
Arrhythmia	4.1	[1.9 – 7.3]	0.0001
Cardiogenic shock	3.2	[1.5 – 5.9]	0.002

The high level of platelets to lymphocytes ratio PLR upon admission is a risk factor for the occurrence of arrhythmias, as it is associated with a 4-fold risk, as well as a 3-fold risk of cardiogenic shock.

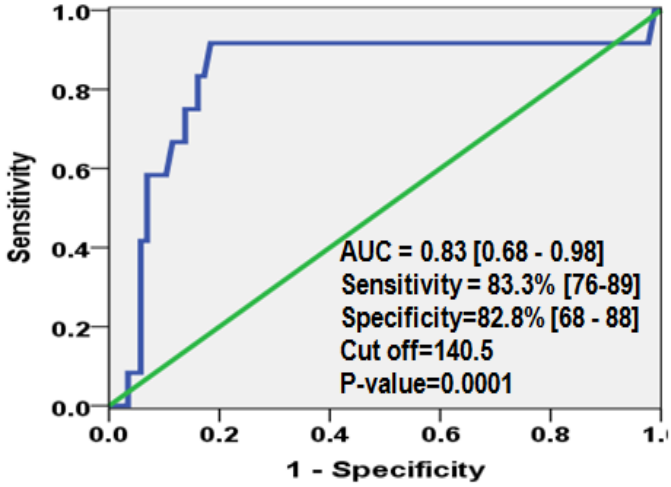

Figure (4) A chart representing the ROC curve between the values of the ratio of platelet to lymphocyte and the risk of death in patients with acute myocardial infarction.

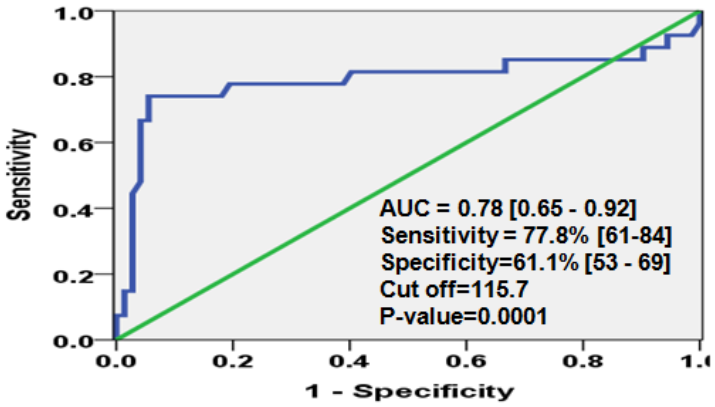

Figure (5): A chart representing the ROC curve between the values of platelet to lymphocyte ratio and the risk of complications in patients with acute myocardial infarction.

DISCUSSION

This study showed that high PLR values in patients with myocardial infarction at admission give an independent prognostic value for in-hospital mortality and major cardiac complications.

Our study demonstrated that PLR≥140.5 is an independent predictive factor for in-hospital mortality.

It also showed that a PLR value < 115.7 is a predictive factor for major cardiac complications (arrhythmias and cardiogenic shock).

It is well recognized that platelets play a key role in thrombotic vascular occlusion at the ruptured coronary atherosclerotic plaque, leading to acute ischemic episodes(ACSs). In addition, both embolization of platelet aggregates and direct, receptor-mediated platelet adhesion to the postischemic microvascular surface result in obstruction and impairment of coronary microcirculation. Such microvascular disturbance may lead to significant additional tissue injury and aggravate myocardial contractile dysfunction. [3]

Platelets play an essential and pivotal role in the pathophysiology of ACS. Besides formation of the thrombotic vascular occlusion, blood platelets participate in microembolization and vasoconstriction, plaque progression, and both local and systemic inflammatory reactions, mechanisms that appear to influence decisively the prognosis of ACS. [3]

Fissuring or rupture of the advanced atherosclerotic lesion leads to endothelial denudation and exposure of the thrombogenic subendothelial matrix to circulating platelets, initiating platelet recruitment to the injured vessel wall in a process that closely resembles primary hemostasis.[3]

Moreover, higher platelet counts may reflect underlying inflammation as several inflammatory mediators stimulate megakaryocytic proliferation and produce relative thrombocytosis.[4] The elevated platelet count had a close correlation with the acute-phase reactants and proinflammatory substances including high sensitivity C-reactive protein (hsCRP), tumor necrosis factor a, interleukin 1, and interleukin 6.[5] Higher platelet counts may reflect aggravated release of inflammatory mediators, increased thrombocyte activation leading destructive inflammatory response, and a prothrombotic status. In addition, high platelet counts may represent greater propensity to form platelet-rich thrombi on atherosclerotic plaques, leading to worse outcomes.[6,7]

Increased lymphocytes in the ischemic zone and in myocardial tissue after perfusion may regulate the immune response and morphology of mononuclear cells and lead to histological inhibition of metalloproteinase-1 production, which increases atheroma stability in patients with acute coronary syndrome.[8]

In acute myocardial infarction, lymphocytes infiltrate to the ischemic and reperfused myocardium and express interleukin-10, which may play a significant role in transmigration of mononuclear cells, and induce the expression of tissue inhibitor of metalloproteinase-1.[9]

The stress condition (hypercortisolism) that occurs in the infarction leads to a low lymphocyte count.[8] Low lymphocyte counts have been associated with increased cardiovascular risk and increased mortality in patients with acute myocardial infarction.[9]

Therefore, the PLR values express two main axes in myocardial infarction: the thrombotic and the inflammatory axis.

CONCLUSION

This study showed that high PLR is an independent predictor of in-hospital mortality and adverse cardiac outcomes in patients with AMI. Complete blood count analysis is a routine and inexpensive method that may be useful for the identification of high-risk patients.

PLR and other inflammatory markers and clinical findings might be helpful in identifying high-risk patients and treatment strategies.

List of abbreviations
AMI: Acute myocardial infarction.
PLR: Platelet lymphocyte ratio.
LVEF: left ventricular ejection fraction..
AHF: acute heart failure.
CS: cardiogenic shock.
MACE: Major adverse cardiovascular events.

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