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Platelet- Lymphocyte Ratio as a Predictor of Major Adverse Cardiac Events in Patients with St-Elevation Myocardial Infarction

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Abstract

Background: Inflammation and thrombosis play an important interaction in the pathophysiological process of ST-segment elevation myocardial infarction (STEMI). It occurs due to atherosclerotic plaque rupture, superimposed thrombus formation, and coronary occlusion. As a reflection of excess inflammatory status and thrombotic activity, elevated blood platelet count is considered a valuable predictor of adverse cardiovascular outcomes. Decreased lymphocyte count is also related to worse cardiovascular prognosis, which may be explained by the role of lymphocyte in plaque stability. Thus, platelet to lymphocyte ratio (PLR) can be used as a potential marker to identify patients who are at high risk of developing major adverse cardiac events (MACE) after acute STEMI. **Materials and Methods:** This was a prospective observational study conducted in the Departments of Emergency Medicine and Cardiology, of a tertiary care hospital. The aim of the study was to demonstrate the use of PLR in predicting MACE following an episode of STEMI. Adults ≥ 18 years presenting to Emergency Department and diagnosed with STEMI between October 2020 to August 2021 were included. Patients with platelet disorders, liver dysfunction, chronic kidney disease, sepsis and hematological malignancies were excluded. The MACE was studied at 7 days and 30 days following STEMI and were correlated with PLR. **Results:** Among total 130 patients, 51 patients developed MACE within 7 days and 52 within 30 days. PLR ≥ 105 predicts MACE at 7 days with a sensitivity of 86.27%, 95% CI (73.7 – 94.3) and specificity of 86.08%, 95% CI (76.5 – 92.8). PLR ≥105 predicts MACE at 30 days with a sensitivity of 86.54%, 95% CI (74.2 – 94.4) and specificity of 87.18, 95% CI (77.7 – 93.7). PLR ≥ 105 was an independent predictor of MACE at 7 days with an odds ratio of 107.743 with 95% CI: 16.729- 693.933 and p value of 0, according to multivariate logistic regression. PLR ≥ 105 was an independent predictor of MACE at 30 days with an odds ratio of 107.74 with 95% CI: 16.724- 693.937 and p value of 0.002, according to multivariate logistic regression. **Conclusion**: High PLR is a significant and independent prognostic factor in predicting MACE in patients with STEMI.

Keywords: ST elevation myocardial infarction; Platelet to lymphocyte ratio (PLR); Major Adverse Cardiac Events (MACE); Global Registry of Acute Coronary Events (GRACE) score; Stroke; Re-infarction; Acute decompensated heart failure; Arrhythmia.

Abbreviations

ACS: Acute coronary syndrome; AMI: Acute myocardial infarction; ACS: Acute coronary syndrome; ADHF: Acute decompensated heart failure; AMI: Acute myocardial infarction; AWMI: Anterior wall myocardial infarction; CAD: Coronary artery disease; CI: Confidence interval; CKD: Chronic kidney disease; CNS: Central nervous system; CVD: Cardiovascular death; DM: Diabetes mellitus; GRACE score: Global registry of acute coronary events; LWMI: Lateral wall myocardial infarction; ICU: Intensive care unit; IWMI: Inferior wall myocardial infarction; MACE : Major adverse cardiac events; MI: Myocardial infarction; NLR: Neutrophil to lymphocyte ratio; OR: Odds ratio; PLR: Platelet to lymphocyte ratio; PPCI: Primary percutaneous intervention; PWMI: Posterior wall myocardial infarction; ROC: Receiver operating characteristic; SBP: Systolic blood pressure; SD: Standard deviation; SOB: Shortness of breath; STEMI: ST segment elevation myocardial infarction; SX score: SYNTAX score; TIMI: Thrombolysis in myocardial infarction; WHO: World health organization; STEMI: ST elevation myocardial infarction

Introduction

ST-segment elevation myocardial infarction (STEMI) is a result of atherosclerotic plaque rupture, superimposed thrombus formation, and coronary occlusion. Inflammation and thrombosis interact during this pathophysiological process. Besides, lymphocyte count is inversely correlated with inflammation and lower lymphocyte count causes increased cardiovascular risk and mortality [1]. Because "time is muscle", early reperfusion is associated with an improved prognosis in patients with STEMI. Nevertheless, impaired angiographic reflow remains a challenging major issue within the management of the patients with STEMI undergoing primary percutaneous coronary intervention (PPCI). Impaired coronary reflow is associated with larger infarct size, poor functional recovery, higher incidence of major adverse cardiac events (MACE), and short and long-term morbidity and mortality in acute STEMI. The mechanisms responsible for impaired coronary reflow include extravascular compression, microvascular vasoconstriction, and a platelet/leukocyte capillary plugging [2]. Platelets play a key role in atherothrombosis and increased platelet count is significantly

associated with increased risk of mortality after myocardial infarction (MI) [4,5].

Major adverse cardiovascular events (MACE) following ACS, like re-infarction and recurrent ischemia, also pose heavy burden on health-care resources. Even with the arrival of coronary intervention techniques and progress in medication, the prognosis of ACS remains unsatisfactory. Thus, it is of great significance to identify high-risk ACS patients who require intensive control of risk factors, more aggressive therapy, proper monitoring and a close follow-up. As a mirrored image of excess inflammatory status and thrombotic activity, elevated blood platelet count is taken into account as a valuable predictor of adverse cardiovascular outcomes. Also, decreased lymphocyte count is additionally associated with worse cardiovascular prognosis, which can be partly explained by the role of lymphocyte in protection of plaque stability. In this context, a novel marker, platelet to lymphocyte ratio (PLR), seems to be a potential indicator in of predicting MACE in patients with ACS [3]. The aim of our study was to find the usefulness of platelet to lymphocyte ratio (PLR) in predicting major adverse cardiac events in STEMI patients.

Materials and Methods

Design and Setting

The study was conducted in the Departments of Emergency Medicine and Cardiology of a tertiary care hospital.

A total of 130 patients with STEMI who presented to the emergency department from October 2020 – August 2021 was included in the study. This was a prospective, single-centered observational study.

Participants

Adults ≥ 18 years presenting to Emergency Department, and diagnosed with STEMI during the study period were included in the study. Patients aged less than 18 years, those known to have platelet disorders, hematological malignancies, liver diseases, sepsis, chronic kidney diseases, alcoholism, known case of CAD and patients or legally authorized representative not willing to give consent were excluded from the study.

Data Collection

Patients were recruited according to the inclusion and exclusion criteria.

A detailed clinical history including history of hypertension, diabetes mellitus, hyperlipidemia and smoking was obtained. A detailed physical examination was performed. Blood samples were taken for various investigations including for complete blood count (CBC) analysis. HORIBA Medical Pentra XLR was used for CBC analysis. Troponin I levels were measured by Radiometer AQT 90 Flex analyzer.

From the CBC report, platelet and absolute lymphocyte count were obtained. The ratio of platelet to absolute lymphocyte count was then calculated as platelet-lymphocyte ratio (PLR).

Seven-day and thirty-day follow up were ascertained by clinical visit and / or telephonic contact to find if any MACE occurred during that time. MACE is defined differently in various clinical trials and researches [6]. “classical 3-point MACE" is defined as a composite of nonfatal stroke, nonfatal myocardial infarction, and cardiovascular death [7,8]. But another study defines MACE as "CVD events, admission for HF (Heart Failure), ischemic cardiovascular [CV] events, cardiac death, or MACE" [9]. Yet another study defined MACE as "CV death, hospitalization for HF, or myocardial infarction (MI) [10]. Hence in our study we defined MACE as Major Adverse Cardiac Events –re-infarction, cardiogenic shock, stroke, heart failure, arrhythmias, bleeding and death due to cardiovascular causes that occur within 7 days and 30 days.

All variables were transferred to standardized case report forms and then statistically analyzed.

Statistical analysis

All data were analysed using SPSS Statistical Software. Descriptive statistics of baseline characteristics were presented as mean ± standard deviation (continuous variables) and number (%) (categorical variables). ROC analysis was done to find out cut-off of PLR to predict MACE at 7 days and 30 days. It was compared with GRACE score predicting MACE. Variables that were significant at 5% level of significance in the univariate analysis were included in the multivariate logistic regression analysis. The p-value <0.05 was considered statistically significant.

Results

Out of 130 patients, majority of the patients, 89 (68%) belonged to the age group 45-65 years. Mean age of the study population was 54.12 ± 11.63. Majority of the patients (80%) were males.

The baseline demographic and clinical characteristics of the study population are summarized in Tables 1 and 2.

Sixty patients (46%) had anterior wall STEMI while the second most common type of STEMI was inferior wall MI (22%). Seventy eight percent of patients were treated successfully with thrombolysis, 6% were treated with PPCI while 16% patients presented out of window period phase and received no thrombolysis or PPCI.

A significant finding was that 51 (39%) of the study patients developed MACE within 7 days of STEMI. Of all the MACE that happened within 7 days, acute heart failure was the most prevalent one, occurring in 16 patients, followed by arrhythmia. Nine patients had cardiovascular death. 52 (40%) of the study population developed MACE within 30 days. Again, acute heart failure and arrhythmias were the most prevalent MACE within 30 days of STEMI in our study population and 9 patients had cardiovascular death.

ROC curve of platelet to lymphocyte ratio for predicting major adverse cardiac events at 7 days showed an AUC of 0.865, with 95% CI of 0.795-0.919, P<0.0001. The ROC curve could assess platelet to lymphocyte ratio as a satisfying marker

of predicting MACE at 7 days, yielding a cutoff of ≥ 105, with a sensitivity of 86.27, 95% CI (73.7-94.3) and specificity of 86.08%, 95% CI (76.5-92.8).

ROC curve of platelet to lymphocyte ratio for predicting major adverse cardiac events at 30 days had an AUC of 0.870, 95% CI of 0.800-0.923, P<0.0001. The ROC curve could assess platelet to lymphocyte ratio as a satisfying marker of predicting MACE at 30 days, yielding a cutoff of ≥ 105, with a sensitivity of 86.54, 95% CI (74.2-94.4) and specificity of 87.18%, 95% CI (77.7-93.7).

The comparison of ROC curves of platelet to lymphocyte ratio and GRACE score for predicting major adverse cardiac events at 7 days showed a difference between areas as 0.0329 with 95% CI: -0.0757- 0.142, p=0.55.

The comparison of ROC curves of platelet to lymphocyte ratio and GRACE score for predicting major adverse cardiac events at 30 days showed a difference between areas as 0.0497 with 95% CI: -0.0602- 0.160, p=0.37.

Both PLR and GRACE score are independent predictors of MACE, but there is no statistically significant difference in both PLR and GRACE score in predicting MACE.

ROC curve of PLR predicting MACE at 7 days in patients with Killip class 1 and 2 had an AUC of 0.904. The curve yielded a PLR cut off of 106.5 with a sensitivity of 92% and specificity of 86.1% for predicting MACE at 7 days in patients with Killip class 1 and 2.

ROC curve of PLR predicting MACE at 30 days in patients with Killip class 1 & 2 has an AUC of 0.911. The curve yielded a PLR cut off of 106.5 with a sensitivity of 92.3% and specificity of 87.2% for predicting MACE at 30 days in patients with Killip class 1 and 2.

All patients in Killip class 3 and 4 had MACE at 7 days and 30 days.

ROC curve of neutrophil to lymphocyte ratio for predicting major adverse cardiac events at 7 days. AUC is 0.731, 95% CI: 0.646-0.805, P<0.0001. The ROC curve could assess neutrophil to lymphocyte ratio as a satisfying marker of predicting MACEs at 7 days, yielding a cutoff of ≥ 2.9, with a sensitivity of 76.47, 95% CI (62.5-87.2) and specificity of 62.03%, 95% CI (50.4-72.7).

ROC curve of neutrophil to lymphocyte ratio for predicting major adverse cardiac events at 30 days. AUC is 0.731, 95% CI: 0.646-0.805, P<0.0001. The ROC curve could assess neutrophil to lymphocyte ratio as a satisfying marker of predicting MACEs at 30 days, yielding a cutoff of ≥ 2.9, with a sensitivity of 76.92, 95% CI (63.2-87.5) and specificity of 62.82%, 95% CI (51.1-73.5).

PLR ≥ 105 was an independent predictor of MACE at 7 days with an odds ratio of 38.857 with 95% CI: 14.002-107.832 and p value of 0, according to univariate logistic regression.

PLR ≥ 105 was an independent predictor of MACE at 7 days with an odds ratio of 107.743 with 95% CI: 16.729-693.933 and p value of 0, according to multivariate logistic regression.

PLR ≥ 105 was an independent predictor of MACE at 30 days with an odds ratio of 38.859 with 95% CI: 14.004-107.840 and p value of 0.001, according to univariate logistic regression.

PLR ≥ 105 was an independent predictor of MACE at 30 days with an odds ratio of 107.74 with 95% CI: 16.724-693.937 and p value of 0.002, according to multivariate logistic regression.

Other independent predictors were clinical presentation of shortness of breath, and diaphoresis. In comorbidities, diabetes mellitus was an independent predictor.

A systolic BP ≤ 90 mmHg was an independent predictor of MACE.

GRACE score, lactate ≥ 2mmol/L, creatinine ≥ 1.5 mg/dl were also independent predictors of MACE at 7 days and 30 days according to univariate and multivariate logistic regression.

	NO MACE (n= 79)		**MACE PRESENT (n=51)**	
AGE </= 50	37 (46.8%)		16 (31.4%)	
AGE > 50	42 (53.2%)		35 (68.6%)	
Gender	FEMALES 17 (21.5%)	MALES 62 (78.5%)	FEMALES 9 (17.6%)	MALES 42 (82.4%)
Chest pain	79 (100%)		51 (100%)	
SOB	9 (11.4%)		25 (49.0%)	
Diaphoresis	74 (93.7%)		40 (78.4 %)	
Palpitations	0		5 (9.8%)	
Syncope	2 (2.5%)		6 (11.8%)	
Nausea	24 (30.4%)		19 (37.3%)	
Vomiting	12 (15.2%)		10 (19.6%)	
T2DM	31 (39.2%)		33 (64.7%)	
HTN	31 (39.2%)		28 (54.9%)	
DLP	4 (5.1%)		4 (7.8%)	
Smoking	41 (51.9%)		30 (58.8%)	
Tobacco	3 (3.8%)		5 (9.8%)	
Family H/O CAD	6 (7.6%)		2 (3.9%)	
HR </= 100	60 (75.9%)		31 (60.8%)	
HR > 100	19 (24.1%)		20 (39.2%)	
SBP >90	77 (97.5%)		41 (80.4%)	
SBP </=90	2 (2.5%)		10 (19.6%)	

TROP > 0.02	77 (97.5%)	51 (100%)
TROP </= 0.02	2 (2.5%)	0
CREAT > 1.5	4 (5.1%)	12 (23.5%)
CREAT </= 1.5	75 (94.9%)	39 (76.5%)
LACTATE >/= 2	31 (39.2%)	42 (82.4%)
LACTATE < 2	48 (60.8%)	9 (17.6%)
PLR </= 105	68 (86.1%)	7 (13.7%)
PLR > 105	11 (13.9%)	44 (86.3%)

Table 1: Baseline demography, clinical and laboratory details in mace and no mace groups.

	N	MEAN ± SD or MEDIAN (Minimum – Maximum)
Vital Signs		
HR	130	88.32 ± 22.41
SBP	130	128.51 ± 27.88
DBP	130	78.93 ± 17.31
Laboratory Parameters		
RBS	130	176.01 ± 70.83
TROP I	130	11 (0 – 11)
Creatinine	130	1.16 ± 0.48
Lactate	130	10 (1 – 10)
HB	130	14.19 ± 2.04
HCT	130	43.05 ± 5.80
MCV	130	92.62 ± 9.32
MCH	130	30.78 ± 3.52
MCHC	130	32.85 ± 2.78
PLT	130	215316.15 ± 54086.28
MPV	130	103 (7 – 110)
WBC	130	9520.07 ± 1368.20
NEU	130	6741.97 ± 1388.80
LYM	130	2175.98 ± 639.15
PLR	130	106.42 ± 30.49
NLR	130	3.35 ± 1.44

Table 2: Baseline data parameters.

MACE- 7	Unadjusted		Adjusted	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Age >50 years	1.93 (0.92-4.03)	0.082		
Sex	0.78 (0.32-1.92)	0.590		
Shortness of breath	7.48 (3.09- 18.12)	0.000	2.10 (0.33- 13.36)	0.434
Diaphoresis	0.25 (0.08 – 0.76)	0.014	0.09 (0.01- 0.91)	0.041
Palpitations	1.02 (0.10-5.32)	0.999		
Syncope	5.13 (0.99- 26.52)	0.051		
Nausea	1.36 (0.65- 2.86)	0.417		
DM	2.84 (1.37- 5.89)	0.005	0.49 (0.09- 2.59)	0.397
HTN	1.89 (0.92- 3.85)	0.081		
DLP	1.60 (0.38- 6.69)	0.523		
smoking	1.32 (0.65- 2.70)	0.439		
Family h/o CAD	0.50 (0.10- 2.56)	0.403		
GRACE score	1.06 (1.034- 1.08)	0.000	1.08 (1.03- 1.12)	0.001
Heart rate >100	2.04 (0.95- 4.37)	0.068		
Systolic blood pressure </=90 mmHg	9.39 (1.96- 44.90)	0.005	0.35 (0.01- 12.88)	0.566
Troponin > 0.02	1.08 (0.99- 1.18)	0.075		
Lactate >/=2	7.23 (3.09- 16.90)	0.000	1.95 (0.42- 9.07)	0.396

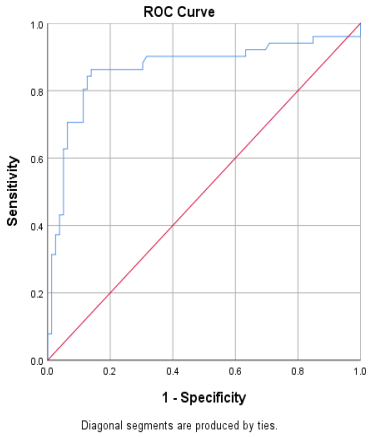
Creatinine >1.5	5.77 (1.75- 19.08)	0.004	0.62 (0.05- 8.31)	0.720
PLR >105	38.86 (14.00- 107.83)	0.000	107.74 (16.73- 693.93)	0.000

Table 3: Logistic regression.

MACE 30	**Unadjusted**		**Adjusted**	
	Odds ratio (95% CI)	**p-value**	**Odds ratio (95% CI)**	**p-value**
Age >50 years	1.94 (0.92-4.07)	0.085		
Sex	0.79 (0.32-2.01)	0.620		
Shortness of breath	7.47 (3.07- 18.00)	0.000	2.10 (0.33- 13.45)	0.451
Diaphoresis	0.24 (0.08 – 0.74)	0.013	0.09 (0.01- 0.91)	0.042
Palpitations	1.02 (0.20-5.46)	0.995		
Syncope	5.13 (0.99- 26.51)	0.052		
Nausea	1.36 (0.65- 2.87)	0.420		
DM	2.83 (1.36- 5.89)	0.005	0.48 (0.09- 2.58)	0.399
HTN	1.89 (0.93- 3.85)	0.090		
DLP	1.60 (0.38- 6.69)	0.527		
Smoking	1.33 (0.65- 2.70)	0.441		
Family h/o CAD	0.50 (0.10- 2.57)	0.410		
GRACE score	1.06 (1.03- 1.07)	0.001	1.07 (1.03- 1.12)	0.002
Heart rate>100	2.04 (0.95- 4.37)	0.070		
Systolic blood pressure </=90 mmHg	9.39 (1.96- 44.90)	0.005	0.35 (0.01- 12.88)	0.568
Troponin>5	1.08 (0.99- 1.18)	0.072		
Lactate >/= 2	7.22 (3.08- 16.90)	0.001	1.95 (0.42- 9.07)	0.390
Creatinine >1.5	5.77 (1.74- 19.07)	0.005	0.62 (0.05- 8.31)	0.724
PLR>105	38.86 (14.00- 107.84)	0.001	107.74 (16.72- 693.94)	0.002

Table 4: MACE.

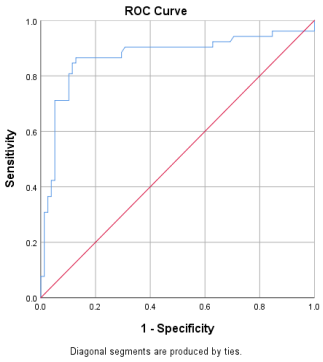
ROC Curve of plr predicting MACE at 7 days



Receiver-operating characteristic (ROC) curve of platelet to lymphocyte ratio for predicting major adverse cardiac events at 7 days. AUC is 0.865, 95% CI: 0.795-0.919, P<0.0001. The ROC curve could assess platelet to lymphocyte ratio as a satisfying marker of predicting MACEs at 7 days, yielding a cutoff of ≥ 105, with a sensitivity of 86.27, 95% CI (73.7-94.3) and specificity of 86.08%, 95% CI (76.5-92.8).

ROC Curve of plr predicting MACE at 30 days

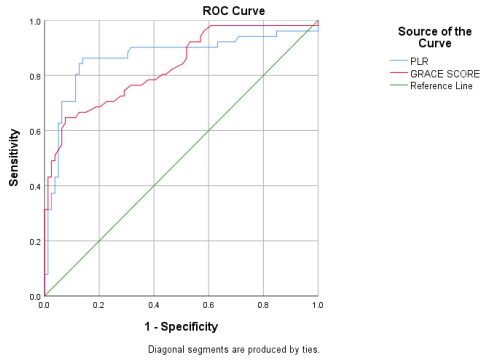
Receiver-operating characteristic (ROC) curve of platelet to lymphocyte ratio for predicting major adverse cardiac events at 30 days. AUC is 0.870, 95% CI: 0.800-0.923, P< 0.0001. The ROC curve could assess platelet to lymphocyte ratio as a satisfying marker of predicting MACEs at 30 days, yielding a cutoff of ≥ 105, with a sensitivity of 86.54, 95% CI (74.2-94.4) and specificity of 87.18%, 95% CI (77.7-93.7).



GRACE score is a scoring system to predict in hospital mortality in ACS especially in STEMI patients. It consists of eight parameters and is difficult to calculate in a cumbersome ED. GRACE score is occasionally used to determine the prognosis is NSTEMI patients as well to determine early intervention versus normal delayed intervention. GRACE score predicts 30-day mortality post discharge, MACE and re-admission [11]. In a study done by Sergio Raposeiras-Roubín et al. the sensitivity and specificity of GRACE score predicting MACE at 30 days were adequate (78.1% and 63.3%,

respectively [11]. Hence here in our study, we compared the simple bedside tool PLR with GRACE score to see how both the elements predicted MACE at the end of 7 days and 30 days.

ROC curve of PLR and GRACE score in predicting MACE at 7 days

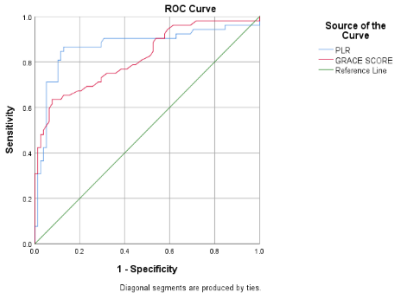


Receiver-operating characteristic (ROC) curve of platelet to lymphocyte ratio and GRACE score for predicting major adverse cardiac events at 7 days. AUC for PLR is 0.865, 95% CI: 0.795-0.919. AUC for GRACE score is 0.833, 95% CI: 0.757- 0.892.

Comparison of the ROC curves

The difference between areas is 0.0329 with 95% CI: -0.0757- 0.142, p=0.55.

ROC curve of PLR and GRACE score in predicting MACE at 30 days



Receiver-operating characteristic (ROC) curve of platelet to lymphocyte ratio and GRACE score for predicting major adverse cardiac events at 30 days. AUC for PLR is 0.870, 95% CI: 0.800-0.923. AUC for GRACE score is 0.820, 95% CI: 0.743- 0.882.

Comparison of the ROC curves

The difference between areas is 0.0497 with 95% CI: -0.0602-0.160, p=0.37.

MACE 7

	MACE 7- YES	MACE 7 – NO
PLR > 105	44	11
PLR ≤ 105	7	68

Sensitivity (95% CI)- 86.27 % (73.70 – 94.30)
Specificity (95% CI)- 86.08% (76.50 – 92.80)
Positive likelihood ratio (95% CI)- 6.20 (3.50 – 10.80)
Negative likelihood ratio (95% CI)- 0.16 (0.08- 0.30)
Area under curve (95% CI)- 0.865 (0.795- 0.919)

MACE 30

	MACE 30 - YES	MACE 30 – N0
PLR > 105	45	10
PLR ≤ 105	7	68

Sensitivity (95% CI)- 86.54 % (74.20– 94.40)
Specificity (95% CI)- 87.18% (77.70 – 93.70)
Positive likelihood ratio (95% CI)- 6.75 (3.70 – 12.20)
Negative likelihood ratio (95% CI)- 0.15 (0.08- 0.30)
Area under curve (95% CI)- 0.870 (0.800- 0.923).

Figure 1: Age distribution

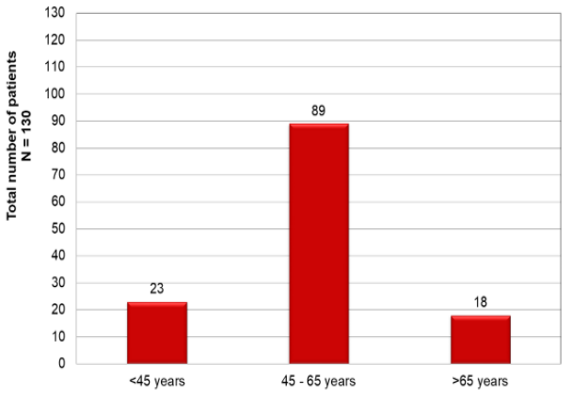
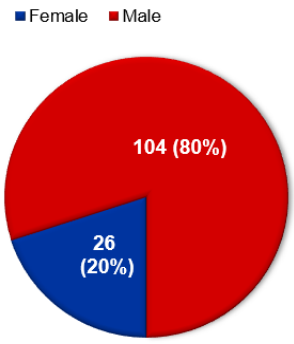


Figure 2: Gender Distribution



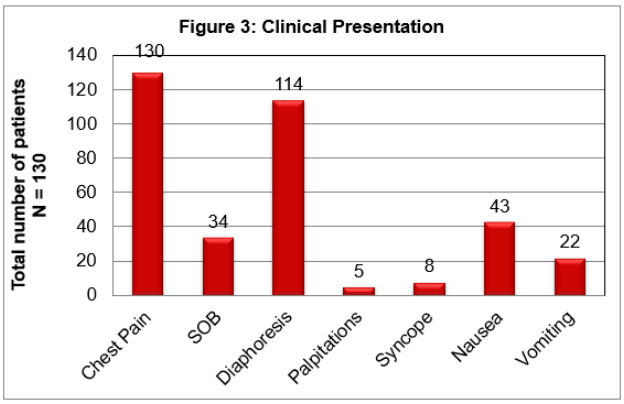


Figure 3: Clinical Presentation
Total number of patients N = 130
130
34
114
5
8
43
22
Chest Pain
SOB
Diaphoresis
Palpitations
Syncope
Nausea
Vomiting

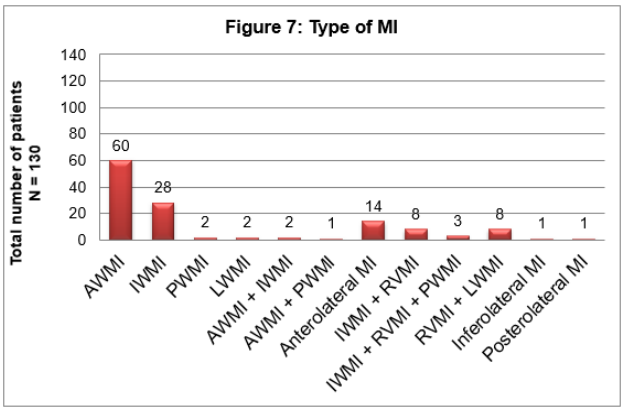


Figure 7: Type of MI
Total number of patients N = 130
60
28
2
2
2
1
14
8
3
8
1
1
AWMI
IWMI
PWMI
LWMI
AWMI + IWMI
AWMI + PWMI
Anterolateral MI
IWMI + RVMI
IWMI + RVMI + PWMI
RVMI + LWMI
Inferolateral MI
Posterolateral MI

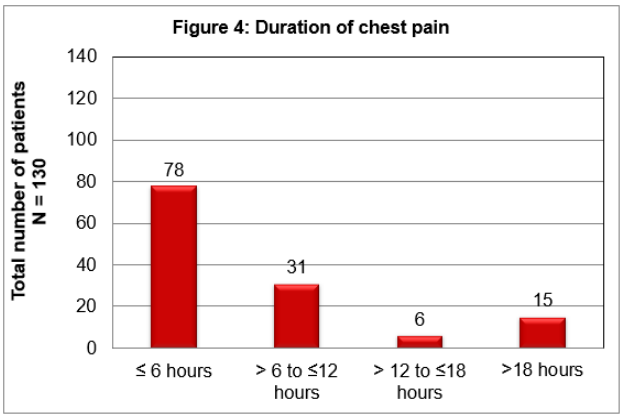


Figure 4: Duration of chest pain
Total number of patients N = 130
78
31
6
15
≤ 6 hours
> 6 to ≤12 hours
> 12 to ≤18 hours
>18 hours

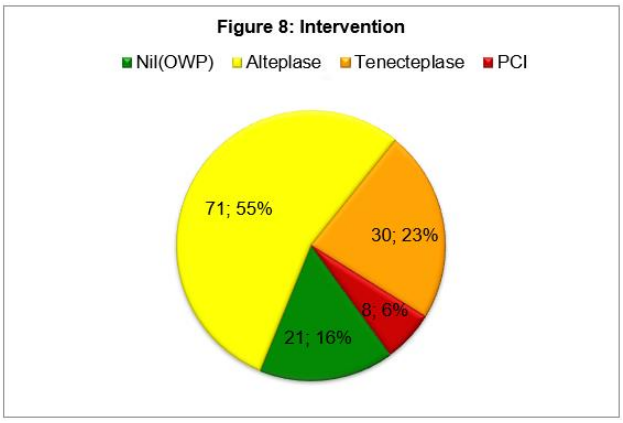


Figure 8: Intervention
Nil(OWP)
Alteplase
Tenecteplase
PCI
71; 55%
30; 23%
8; 6%
21; 16%

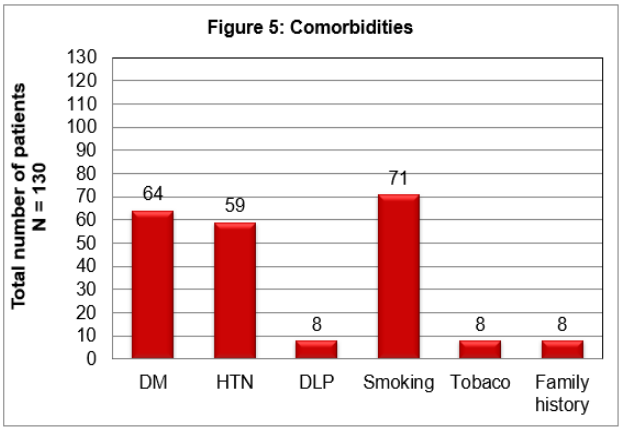


Figure 5: Comorbidities
Total number of patients N = 130
64
59
8
71
8
8
DM
HTN
DLP
Smoking
Tobaco
Family history

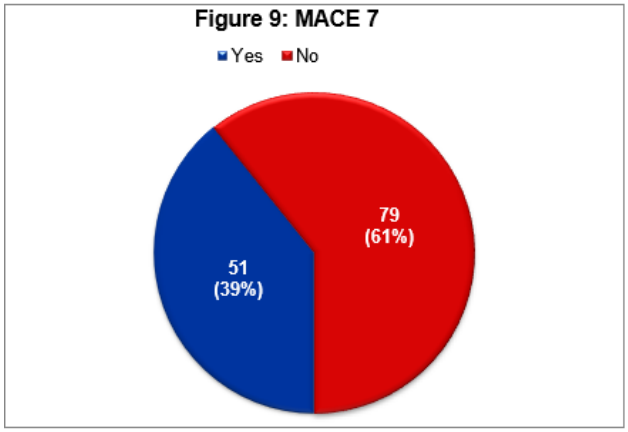


Figure 9: MACE 7
Yes
No
79 (61%)
51 (39%)

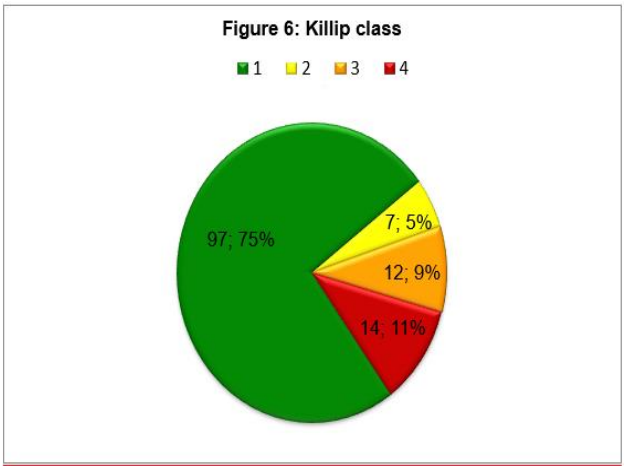


Figure 6: Killip class
1
2
3
4
97; 75%
7; 5%
12; 9%
14; 11%

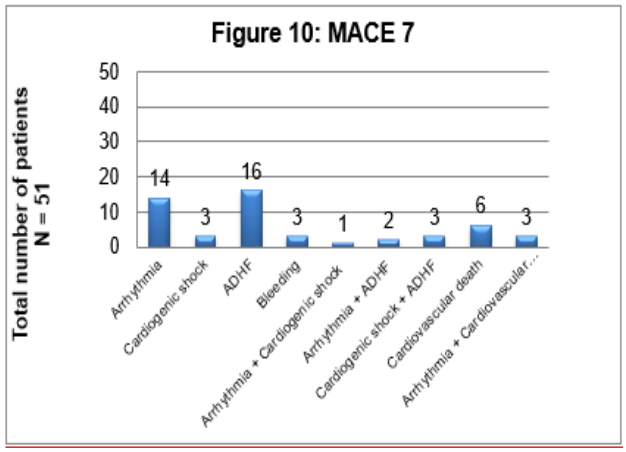
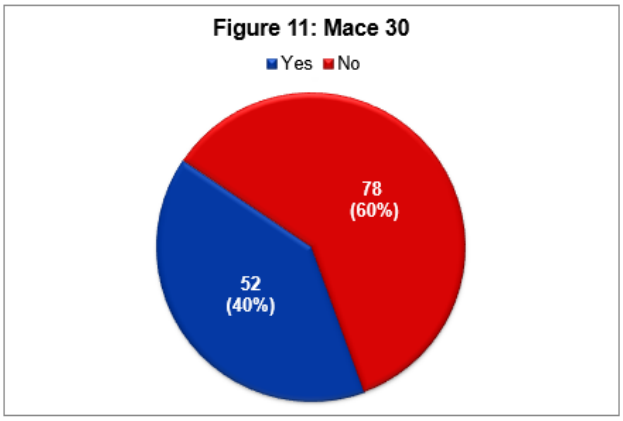
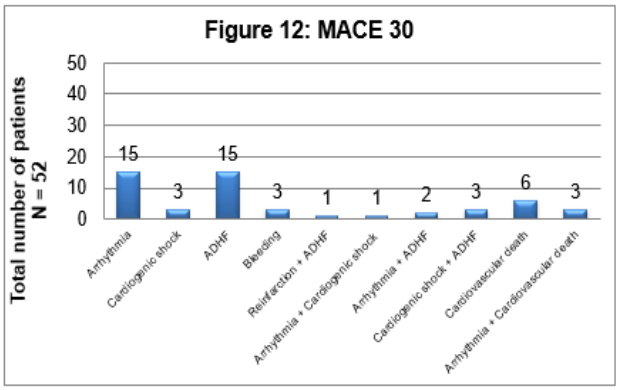


Figure 10: MACE 7
Total number of patients N = 51
14
3
16
3
1
2
3
6
3
Arrhythmia
Cardiogenic shock
ADHF
Bleeding
Arrhythmia + Cardiogenic shock
Arrhythmia + ADHF
Cardiogenic shock + ADHF
Cardiovascular death
Arrhythmia + Cardiovascular...





Discussion

This is a prospective observational study, conducted in the Department of Emergency Medicine, AIIMS, New Delhi. 130 STEMI patients who presented to the Emergency Department were included in the study. The aim of the study was to demonstrate the use of PLR in predicting MACE.

ACS is the leading cause of morbidity and mortality from coronary heart diseases [12]. MACE following ACS pose a huge burden on the health care system. Even with the advent of coronary intervention techniques and progress in medication, the prognosis of ACS is still not satisfactory. Thus, it is of great significance to identify high-risk ACS patients who require more intensive control of risk factors, more aggressive therapy and more close follow-up.

As the pathogenesis of ACS is explained by the interaction of thrombosis and inflammation, elevated peripheral blood platelet count reflects excess inflammatory status and thrombotic tendency. On the other hand, lymphocytes which play a role in plaque stability is reduced in ACS [13]. Thus together increased platelet and decreased lymphocyte count as platelet to lymphocyte ratio can be used as a potential marker to identify patients who are at high risk of developing adverse effects after an event of ACS.

Demographic profile

The study revealed majority of the patients who presented with STEMI were in the age group 45-65 years and there was a male preponderance, which has been the pattern observed in all previous studies [14,15]. All patients presented with chief complaint of chest pain. Other chief presenting complaints were diaphoresis, nausea, shortness of breath in descending order. Most of the patients presented within 6 hours of chest pain. Among comorbidities and addictions, smoking was most prevalent among the study population followed by diabetes mellitus and systemic hypertension. Anterior wall myocardial infarction was the most common type, constituting 46% which was in agreement with the available literature [16].

As the study was conducted during covid pandemic, thrombolysis was the preferred mode of intervention over PPCI.

78% underwent thrombolysis out of which 55% was done with alteplase and 23% with tenecteplase. 6% underwent PPCI. 16% presented out of window period, therefore no acute intervention was done. On further analysis there was no statistically significant difference among the thrombolysis and PPCI groups and their subsequent clinical outcomes.

Platelet to lymphocyte ratio

From the haemogram report, platelet and absolute lymphocyte count were obtained. The ratio of platelet to absolute lymphocyte count was then calculated as platelet-lymphocyte ratio (PLR).

Using receiver operator characteristic curve, a cut off value of PLR>105 was a predictor of MACE at 7 days and 30 days.

Major adverse cardiac events

According to our study, there were 51 patients, that is 39% of the study population who developed MACE within 7 days of STEMI and 52 patients that is 40% who developed MACE within 30 days.

Overall ADHF and arrhythmia were the leading causes and 9 patients had cardiovascular death.

In a retrospective study on 'Platelet-to-lymphocyte ratio is a predictor of in-hospital mortality in patients with acute coronary syndrome' conducted by Mustafa Oylumlu et al., it was demonstrated that a PLR>142 predicted in-hospital mortality with a sensitivity of 69% and specificity of 63% [17].

In a cohort study on the prognostic role of platelet-to-lymphocyte ratio in patients with acute heart failure conducted by Gui-lian Ye et al. identified high PLR (>110.63) as poor prognostic factors for survival [18].

Burak Ayca et al. found out PLR>137 was associated with high morality as per the study Platelet to lymphocyte ratio as a prognostic marker in primary percutaneous coronary intervention [19].

Association of platelet-to-lymphocyte ratio with severity and complexity of coronary artery disease in patients with acute coronary syndromes was a study conducted by Alparslan Kurtul and colleagues. A PLR ≥ 116 had 71% sensitivity and 66% specificity in predicting intermediate to high SXscore. The SYNTAX score (SXscore) is an anatomic scoring system based on coronary angiography (CA) that not only quantifies lesion severity and complexity but also

predicts poor cardiovascular outcomes, including mortality, in patients with acute coronary syndromes (ACS) [2].

Bartosz Hudzik and colleagues conducted a study on Platelet-to-lymphocyte ratio is a marker of poor prognosis in patients with diabetes mellitus and ST-elevation myocardial infarction. In this study, PLR has emerged as a strong marker of worse outcomes. 523 patients were enrolled. Low PLR (group 1, n=349) was defined as ≤ 124 and high PLR (group 2, n=174) as >124. In-hospital and 1-year mortality was higher in group 2.PLR remained an independent risk factor early and late mortality [20].

In a retrospective two centre cohort study conducted by Maimaiti et al. to find association of platelet-to-lymphocyte count ratio with myocardial reperfusion and major adverse events in patients with acute myocardial infarction, 43% developed MACE in the high PLR group, out of which 28% had ventricular arrhythmias, 7% had stroke and 4 patients (3%) had cardiovascular death. 32% patients in the low PLR group developed MACE [15]. In our study, among the MACE group, 86.3% had PLR>105 and in the 13.7% had PLR ≤ 105. ADHF and arrhythmia were the chief MACE observed in our population and 9 patients had cardiovascular death.

Neutrophil to Lymphocyte Ratio

Neutrophil to lymphocyte ratio predict mortality and major adverse cardiac events in acute coronary syndrome: A systematic review and meta-analysis conducted by Chao-Hui Dong et al. concluded that higher pretreatment NLR value was associated with higher in-hospital mortality in ACS patients. The NLR value of 5.0 maybe a cut-off value for ACS risk as per the study. We got a cut off of > 2.9 with a sensitivity of 76.47% and specificity of 62.03%.

PLR and GRACE score

Both PLR and GRACE score are independent predictors of MACE. As per our study, they do not have any statistically significant difference in predicting MACE at 7 days and 30 days. Platelet-to-lymphocyte ratio improves the predictive power of grace risk score for long-term cardiovascular events in patients with acute coronary syndrome was a study done by Dong Zhou and colleagues. This study evaluated the relationship between PLR and GRACE risk score. Spearman's rank correlation demonstrated that GRACE risk score was positively correlated with PLR (r=0.190, p<0.001) [21].

PLR as a predictor of MACE in KILLIP CLASS 1 & 2 patients

ROC curve of PLR predicting MACE at 7 days in patients with killip class 1 & 2 has an AUC is 0.904.

The curve yields a PLR cut off of 106.5 with a sensitivity of 92% and specificity of 86.1% for predicting MACE at 7 days in patients with killip class 1 & 2.

ROC curve of PLR predicting MACE at 30 days in patients with killip class 1 & 2 has an AUC is 0.911.

The curve yields a PLR cut off of 106.5 with a sensitivity of 92.3% and specificity of 87.2% for predicting MACE at 30 days in patients with killip class 1 & 2.

All patients in killip class 3 & 4 had MACE at 7 days and 30 days.

Independent predictors of MACE

PLR>105 is an independent predictor of MACE at 7 days with an odds ratio of 38.857 with 95% CI: 14.002-107.832 and p value of 0, according to univariate logistic regression.

PLR>105 is an independent predictor of MACE at 7 days with an odds ratio of 107.743 with 95% CI: 16.729-693.933 and p value of 0, according to multivariate logistic regression.

PLR>105 is an independent predictor of MACE at 30 days with an odds ratio of 38.859 with 95% CI: 14.004-107.840 and p value of 0.001, according to univariate logistic regression.

PLR>105 is an independent predictor of MACE at 7 days with an odds ratio of 107.74 with 95% CI: 16.724-693.937 and p value of 0.002, according to multivariate logistic regression.

Other independent predictors are clinical presentation of shortness of breath, and diaphoresis. In comorbidities, diabetes mellitus is an independent predictor.

A systolic BP ≤ 90 mmHg is an independent predictor of MACE.

GRACE score, lactate ≥ 2mmol/L, creatinine ≥ 1.5 mg/dl are also independent predictors of MACE at 7 days and 30 days according to univariate and multivariate logistic regression.

Conclusion

According to our study:

- Platelet to lymphocyte ratio is a good predictor of MACE at 7 days and 30 days of occurrence of STEMI.
- PLR is an independent predictor of MACE.
- However there is no significant difference between PLR and GRACE score in predicting mortality.
- PLR can even predict development of MACE in patients who are in Killip class 1 & 2, which are the relatively stable patients

Emergency physicians being the first contact portal in most STEMI cases, have a vivid responsibility in timely management as well as risk stratification to the patient and his family members. In ED setting simple and quickly available parameters such as serum lactate and shock index could prove to be a boon in early adverse outcome prediction and hence vigilant monitoring in high-risk population. Validation of above results in larger study population would be beneficial.

Limitations of the Study

1) Relatively small sample size of the study population makes external validation of results difficult.

2) Not all consecutive STEMI patients were included in the study.
3) Stringent exclusion criteria such as excluding patients with liver diseases, chronic kidney disease, sepsis, alcoholism etc led to elimination of a vast portion of STEMI patients presenting to the ED. This questions the utility of the variables under study on a bigger picture where a large strata of STEMI patients would be presenting with underlying comorbidities and hence on multidrug therapies.
4) The 30-day follow up of patients was telephonic which might have caused a bias in interpretation of information or concealment / missing of vital information in a few cases.

Disclosures

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author Contributions

AN: protocol preparation, data collection, writing manuscript
PA: writing supervision and editing
SB: writing supervision
NJ: literature review, writing supervision

Declaration of Interest Statement

1) **Conflict of Interest**

No conflict of interest exists.
We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

2) Funding

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