Section: Cardiology

Original Research Article

ASSESSMENT OF THE PROGNOSTIC VALUE OF IMMATURE PLATELET FRACTION IN ST ELEVATION MYOCARDIAL INFARCTION

R.Anto Prabhu[1], C Balachandar[2], A.Arvind[3]

[1]Senior Resident, Department of Cardiology, Tirunelveli Medical College, Tirunelveli, Tamilnadu, India.
[2]Associate Professor, Department of Cardiology, Tirunelveli Medical College, Tirunelveli, Tamilnadu, India.
[3]Assistant Professor, Department of Cardiology, Kilpauk Medical College, Tirunelveli, Tamilnadu, India.

Received : 11/01/2023
Received in revised form : 27/02/2023
Accepted : 11/03/2023

Keywords:
Immature platelet fraction, STEMI, Sysmex XE- 2100, ST Elevation, Myocardial Infarction, TIMI score.

Corresponding Author:
Dr. A.Arvind,
Email: aviasokkumar@gmail.com

DOI: 10.47009/jamp.2023.5.4.102

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (4); 501-506

Abstract

Background: The immature platelet fraction is a valuable indicator for determining the underlying cause of low platelet counts. The study aimed to evaluate the predictive value of immature platelet fraction (IPF) estimation to further stratifies patients with ST Elevation Myocardial Infarction (STEMI) according to their risk for clinical outcomes. **Materials and Methods:** This prospective cohort study was conducted at Govt. Stanley Medical College and Hospital, Chennai, from October 2015 to March 2016, on 100 patients admitted with STEMI in the ICCU. A patient's history includes age, sex, symptoms, risk factors, family history of CAD, and other illnesses. Assessments include vital signs, hemodynamic status, heart failure features, and complications. Blood tests, lipid profiles, and anti-HCV and HIV serology are performed. **Results:** Patients who did not survive had a significantly higher mean immature platelet fraction (IPF) value compared to those who survived (4.8% vs. 2.65%, P<0.0003). Those with failed thrombolysis had a higher mean IPF (4.18%) than those with successful thrombolysis (1.75%). Increasing Killip class was associated with higher mean IPF (1.7%, 3.2%, 4.6%, and 6.1% for classes I to IV). Moderate to severe LV systolic dysfunction was more prevalent in patients with higher IPF values. Major adverse cardiac events (MACE) increased from 5% in the low IPF tertile to 100% in the high IPF tertile. A significant difference in MACE, mortality, ST resolution, Killip, EF, and TIMI scores between IPF. **Conclusion:** Higher immature platelet fraction is closely associated with risk factors like LV systolic dysfunction, TIMI score and Killip class in STEMI patients.

INTRODUCTION

STEMI is a syndrome characterised by symptoms of myocardial ischemia and persistent ST elevation, followed by the release of biomarkers of myocardial necrosis. Coronary artery disease (CAD) has the distinction of being the most common cause of death worldwide. More than seven million people die annually from CAD worldwide, accounting for 12.8% of all deaths.[1] The risk stratification process following STEMI occurs in several steps, based on the initial presenting clinical features, course in the hospital, and patient condition during discharge. Risk stratification is an integrated and dynamic assessment based on the patient's demographic parameters, ECG, cardiac enzymes, and noninvasive and invasive hemodynamic data. When integrated with in-hospital complications, these parameters can provide valuable survival information. Risk stratification aids in estimating the risk of death and MACE events of a patient after MI. This estimate aids in treatment decisions and recommendations and counselling patients and families. The search for newer modalities of risk stratification and prognostic markers in STEMI is a never-ending process driven by the passion for reducing mortality and morbidity.[2]

Platelet activation is the hallmark event in the pathogenesis of intravascular thrombosis, which can lead to Myocardial Infarction and stroke.[3] The entire family of circulating platelets is not uniform but consists of different subcategories, which differ in their response to activation by different agonists.[4] Reticulated platelets (RPs) are the youngest members of the platelet pool, and they are highly thrombogenic.[5] They are also called immature platelets. RPs are larger and contain more cytosolic messenger ribonucleic acid (mRNA) than

normal platelets; this mRNA is highly active in translation.[6-7] RPs are highly reactive compared to mature platelets, which lack RNA.

There is a strong concordant relationship between the levels of immature platelets in the blood pool and refractoriness to antiplatelet drugs, and this indicates the role of immature platelets in antiplatelet drug treatment failure. Persistent refractory platelet activation despite antiplatelet therapy strongly influences mortality and morbidity.[8-10] The study aimed to evaluate the predictive value of immature platelet fraction in ST Elevation Myocardial Infarction (STEMI) and assess whether immature platelet fraction estimation can predict adverse hospital events.

MATERIALS AND METHODS

This prospective cohort study was conducted at Govt. Stanley Medical College and Hospital, Chennai, from October 2015 to March 2016, on 100 patients admitted with STEMI in the ICCU. All the patients and their relatives were explained about the study design at the time of enrollment, and detailed consent regarding their willingness to participate was obtained. Ethical committee approval was obtained before the study started.

Inclusion Criteria

Age > 18 years, male and female sex, patients admitted in ICCU with STEMI diagnosed based on the criteria proposed by ACC/AHA, and patients with STEMI presenting < 72 hours from the symptom onset are included.

Exclusion Criteria

Patients with a previous history of myocardial infarction, patients who received any blood transfusion in the past 30 days, patients with chronic kidney disease, patients with haematological malignancies, and patients with bone marrow diseases were excluded.

A detailed history obtained from the patient and history includes age and sex of the patient, nature and duration of symptoms, risk factor assessment including Diabetes, Hypertension, Smoking and family history of CAD, and history of CAD, other illnesses and surgeries. Performed at the time of admission and periodic assessment of vital signs, hemodynamic status, features of heart failure and complications was performed. Performed at the time of admission and serially if needed. Complete blood count, Blood sugar, Renal function test, Lipid profile, Cardiac enzymes, Liver function test, HBsAg, Anti HCV and HIV serology done for all patients. Immature platelet methods by Sysmex haematology analysers within 48 hours of admission.

Chest X-ray PA view was taken after stabilisation of the patient. Whenever necessary, a 12 lead ECG and right and posterior leads were taken for all patients. Serial ECGs are taken periodically to assess resolution and progress. Area of involvement, presence of conduction disturbances and arrhythmias noted. ST resolution following thrombolysis in ECG assessed by Schroder criteria. Complete echocardiography using Philips machine model No: HD11XE 2011 USA Revision 2.0.5. The entire treatment details, including thrombolysis use of inotropes analysed.

The occurrence of complications such as acute pulmonary edema, cardiogenic shock, arrhythmias and mechanical complications were analysed. In-hospital mortality and MACE, such as reinfarction, unplanned revascularisation, and stroke, were analysed. A coronary angiogram was done with Siemens model 2000-Artis U machine with Axiom Sensis pressure monitoring. Risk stratification was done using ECG ST resolution assessment and applying risk scores such as Killip classification and TIMI score.

Statistical Analysis

Statistical analysis was done using SPSS software version 16.0. Descriptive and inferential statistics were used to analyse the data. The quantitative data were expressed as mean. The qualitative data were expressed as frequency and percentage. A P value of < 0.05 was considered significant. Analysis of two independent variables was done using the student T-test, and analysis of multiple independent variables using the ANOVA test. Statistical analysis of categorical data was done using the Chi-Square test.

RESULTS

Among 100 patients, 73% were males, and 27% were females. The maximum incidence was in the same age group in both males and females. 13.7% of males presented < 40 years of age. The mean age of presentation in males was 53.8 and 55.9 in females (Table 1).

Table 1: Age distribution based on gender

Age group	Male		Female		Total	
	Number	%	Number	%	Number	%
30 - 40	10	13.7	2	7.4	12	12
41 - 50	16	21.9	4	14.8	20	20
51 - 60	27	36.9	15	55.6	42	42
61 - 70	15	20.6	5	18.5	20	20
> 70	5	6.9	1	3.7	6	6
Total	73	100	27	100	100	100

ISSN (O): 2687-5365; ISSN (P): 2753-6556

The maximum incidence of STEMI was in the age group 51-60 years, about 42%. The incidence of AWMI was 61%, and the remaining 39% was IWMI. 78% were thrombolysed, and streptokinase was used for the thrombolysis of all patients. The successfulness of thrombolysis as assessed by 90 min ST resolution based on criteria proposed by Rolf Schroder was 60%, and failed lysis was 40%.

40% of the patients had diabetes, 30% had hypertension, 34% of the patients smoked, 18% had dyslipidemia, and 10% had a family history of coronary artery disease. 49% in Killip Class I, 30% in Killip Class II, 12% in Killip Class III and 9% in Killip Class IV. 37% had a TIMI score of 0-2, 27% had a score of 3/4, 17% had a score of 5/6 and 19% had a score ≥ 7. 61% belonged to low tertiles group, 31% to intermediate tertiles and 8% to high tertiles group (Table 2).

Table 2: Demographic data of the study

		Number	Percentage
STEMI	AWMI	61	61%
	IWMI	39	39%
Thrombolysis	Lysed	78	78%
	Not lysed	22	22%
90 minutes ST resolution	90 min ST resolution	47	60%
	No ST resolution	31	40%
Killip	I	49	49%
	II	30	30%
	III	12	12%
	IV	9	9%
TIMI score	0-2	37	37%
	3/4	27	27%
	5/6	17	17%
	≥7	19	19%
Immature platelet fraction	0-3	61	61%
	3-6	31	31%
	≥6	8	8%

The patients with at least one MACE during in-hospital stay had a higher mean IPF of 5-04% compared to 2.15% in those who did not have a MACE. This association of MACE and IPF was statistically significant at a p-value <0.001. The mean IPF value was higher in patients who died than in those who survived: 4.8% VS 2.65%, and this association had a p-value of <0.0003, which is statistically significant.

The patients with failed thrombolysis had a higher mean IPF of 4.18% compared to 1.75% in those who had successful thrombolysis. Patients in the highest Killip class IV had the highest mean IPF of 6.1%, and those in the least Killip class had the least mean IPF of 1.7%.

Patients with an EF < 45 were found to have a higher mean IPF of 3.44% compared to those with higher EF with a mean value of 2.01%. Patients with a higher TIMI score had a higher mean IPF value than those with lower TIMI scores: 1.7% for TIMI 0-2 versus 5.3% for TIMI > 7 (Table 3).

Table 3: Relationship between various parameters and mean IPF

		Number	Mean IPF	P-value
MACE	MACE	25	5.04%	<0.001
	NO MACE	75	2.15%	
Mortality	Death	9	4.8%	0.0003
	Alive	91	2.65%	
ST resolution	Successful	47	1.75%	<0.0001
	Failed	31	4.18%	
Killip	I	49	1.7%	<0.001
	II	30	3.2%	
	III	12	4.6%	
	IV	9	6.1%	
EF	≥45	42	2.01%	0.0044
	<45	58	3.44%	
TIMI score	0-2	37	1.7%	<0.0001
	3-4	27	2.46%	
	5-6	17	3.43%	
	≥	19	5.3%	

46 out of the 49 (93%) patients in Killip Class I had a mean IPF less than 3 compared to 22.9% (15 out of 51) in patients presenting with Killip Class > I, and none of the Killip Class I patients had mean IPF value > 6. Only 2 out of the 9 (22%) patients in Killip Class IV had a mean IPF < 3, and 5 out of 9 patients (55%) had values > 6. All the patients with mean IPF > 6% presented with Killip Class > I, and a significant difference in Killip between IPF (p<0.0001).

Severe and moderate LV systolic dysfunction was observed in 46% (28 out of 61) patients with IPF 0-

ISSN (O): 2687-5365; ISSN (P): 2753-6556

3%, 74% (23 out of 31) patients with IPF 3-6% and 88% (7 out of 8) patients with IPF > 6%. A significant difference in EF between IPF (p=0.007). In the low tertile IPF group (IPF value < 3%), only 15% had TIMI score ≥5, whereas in the high tertile group (IPF > 6%), 87% had TIMI score ≥5. A significant difference in TIMI score between IPF (p<0.0001).

In the low tertile IPF group (IPF < 3%), 84% had successful 90 min ST resolution as assessed by Schroder criteria. In comparison, none of the patients had successful ST resolution in the high tertile group (IPF > 6%). A significant difference in 90 min ST resolution between IPF (p<0.0001).

In the low tertile IPF group (IPF < 3%), only 5% had any one of the MACE events, while in the high tertile group (IPF > 6%), all the patients had any one of the MACE events. A significant difference in MACE events between IPF (p<0.0001) (Tables 4 and 5).

Table 4: Relationship between various data and IPF

		IPF 0-3%	IPF 3-6%	IPF > 6%	P value
Killip	I	46 (29.89) [8.68]	3 (15.19) [9.78]	0 (3.92) [3.92]	<0.0001
	II	13 (18.30) [1.53]	16 (9.30) [4.83]	1 (2.40) [0.82]	
	III	0 (7.32) [7.32]	10 (3.72) [10.60]	2 (0.96) [1.13]	
	IV	2 (5.49) [2.22]	2 (2.79) [0.22]	5 (0.72) [25.44]	
EF	<45	28 (35.38) [1.54]	23 (17.98) [1.40]	7 (4.64) [1.20]	0.007
	≥45	33 (25.62) [2.13]	8 (13.02) [1.94]	1 (3.36) [1.66]	
TIMI score	0-4	52 (39.04) [4.30]	11 (19.84) [3.94]	1 (5.12) [3.32]	<0.0001
	5-14	9 (21.96) [7.65]	20 (11.16) [7.00]	7 (2.88) [5.89]	
90 min ST resolution	Yes	43 (30.73) [4.90]	4 (13.26) [6.46]	0 (3.01) [3.01]	<0.0001
	No	8 (20.27) [7.43]	18 (8.74) [9.80]	5 (1.99) [4.57]	
MACE	MACE	3 (15.25) [9.84]	14 (7.75) [5.04]	8 (2.00) [18.00]	<0.0001
	NO MACE	58 (45.75) [3.28]	17 (23.25) [1.68]	0 (6.00) [6.00]	

The mortality rate of the low IPF tertiles was 3.4%, the intermediate IPF tertile was 16.1%, and the high IPF tertiles were 25% (Table 5).

Table 5: Distribution of data and IPF

		IPF 0-3%	IPF 3-6%	IPF > 6%
KILLIP	I	46 (93.8%)	3 (7.2%)	0
	II, III, IV	15 (29.4%)	36 (70.6%)	0
EF	<45	54%	26%	12%
	≥45	46%	74%	88%
TIMI score	0-4	85%	35%	13%
	5-14	15%	65%	87%
90 min ST resolution	Yes	84%	18%	0
	No	16%	82%	100%
MACE	MACE	5%	45%	100%
	NO MACE	95%	55%	0
Mortality	Death	2	5	9
	Alive	59	26	91

The highest mean IPF value was found among people with TVD, who had a mean IPF of 4.98%, and people with normal coronaries, recanalised coronaries and minimal CAD had a mean IPF of 1.73%. There was a linear incremental trend in the severity of CAD with increasing values of mean IPF.

DISCUSSION

Coronary artery disease (CAD) has the distinction of being the single most frequent cause of death. Over seven million people die annually from CAD worldwide, accounting for 12.8% of all deaths. STEMI represents 25-40% of the ACS spectrum. In our study, the maximum incidence was in the same age group, 51-60, in both males and females. In individuals under 50 years, males had a higher incidence than females, about 35.6% VS 22.2%. The mean age of presentation in males was 53.8 and 55.9 in females. These observations were on par with the report of higher incidence of premature CAD in India and CAD occurring 10-15 years prior in India compared to their Western counterparts.

In our study, 40% of the patients had diabetes, 30% had hypertension, 34% smoked, 18% had dyslipidemia, and 10% had a family history of coronary artery disease. Diabetes was the dominant risk factor, followed by smoking and hypertension. 49% presented in Killip class I. 41% presented with Killip class > I. This rate was much higher than reported in the Kerala ACS registry, where only 21% presented in Killip class > I. Gusto-1 investigators report a Killip presentation > I of about 15%.[11] This is probably due to the rapid increase in the prevalence of diabetes in India, which is associated with increased severity of CAD. The higher the severity of CAD, the higher the Killip class of presentation. Moreover, the severity of CAD is higher in India compared to Western countries.[12-14]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

In our study, the mean IPF level in our study population was 2.87% which was comparable to the study by Briggs C et al., who reported a mean IPF value of 3.4% (range 1.1%–6.1%) and lower than the mean value reported by Homam Ibrahim et al., of 4.3%.[15,16] In our study, the patients who had at least one of the MACE during in-hospital stay had a higher mean IPF of 5.04% compared to 2.15% in those who did not have a MACE. This association of MACE and IPF was statistically significant at a p-value < 0.001. This association between MACE and mean IPF was also reported by a prior study by Homam Ibrahim et al., who reported a difference of 5.3% VS 3.7%.[16] The in-hospital mortality reported in our study was 9%. The mean IPF value was higher in patients who died than in those who survived: 4.8% VS 2.65%, and this association had a p-value of < 0.0003, which is statistically significant. A similar association had been reported in a prior study by Rosa A. Lopez-Jimenez et al. 6.60% (4.20%-10.80%) VS 4.80% (3.10%-6.95%).[17]

The predictive value of 90 min ST resolution post fibrinolysis was previously reported by Rolf Schroder.[18] The patients who had failed thrombolysis had a higher mean IPF of 4.18% compared to 1.75% in those who had successful thrombolysis. In the low tertile IPF group (IPF < 3%), 84% had successful 90 min ST resolution as assessed by Schroder criteria. In comparison, none of the patients had successful ST resolution in the high tertile group (IPF > 6%). This association between higher IPF values and 90 min ST resolution was statistically significant. Prior studies did not report this association between IPF and 90 min ST resolution.

In our study, the mortality rate of the low tertile IPF group was 3.4%, the intermediate IPF tertile was 16.1%, and the high tertile group was 25%. Similarly, the association between mortality rate and IPF tertiles was reported in a study by Rosa A. Lopez-Jimenez et al.[17], who reported mortality rates of 6% in the low tertile group VS 22% in the higher tertile group. Homam Ibrahim et al.[16] reported mortality rates of 3.3%, 10.3%, and 20% in low, intermediate and higher tertiles, respectively. Our study shows a statistically significant relationship between high IPF value, morality, and MACE rates. Elevated IPF values were significantly correlated with other risk stratification tools such as LV systolic dysfunction, TIMI score, Killip classification and 90 min ST resolution. Hence IPF has prognostic value and gives promise as a risk stratification tool in STEMI.

CONCLUSION

Elevated Immature platelet fraction in a patient presenting with STEMI is associated with higher in-hospital mortality rate and hospital MACE rates. There is a linear relationship between immature platelet fraction, Killip Class, and TIMI scores. Elevated immature platelet fraction is strongly related to other risk stratification tools such as EF, TIMI score, Killip class and 90-minute ST resolution. As elevated immature platelet fraction has predictive value, it can be used as a risk stratification tool.

Limitations

The small sample size limited the number of variables that could be examined to determine the independence of immature platelet fraction as a risk stratification tool. The limited number of MACE events impeded the precise adjustment of all the variables potentially related to mortality.

REFERENCES

1. Gachet C. ADP receptors of platelets and their inhibition. Thromb Haemost 2001;86:222–32.
2. Solet DJ, Zacharski LR, Plehn JF. The role of adenosine 5′-diphosphate receptor blockade in patients with cardiovascular disease. Am J Med 2001;111:45–53.
3. Fager AM, Wood JP, Bouchard BA, Feng P, Tracy PB. Properties of procoagulant platelets: defining and characterising the subpopulation binding functional prothrombinase: Defining and characterising the subpopulation binding a functional prothrombinase. Arterioscler Thromb Vasc Biol 2010;30:2400–7.
4. Denis MM, Tolley ND, Bunting M, Schwertz H, Jiang H, Lindemann S, et al. Escaping the nuclear confines: signal-dependent pre-mRNA splicing in anucleate platelets. Cell 2005;122:379–91.
5. Guthikonda S, Lev EI, Patel R, DeLao T, Bergeron AL, Dong J-F, et al. Reticulated platelets and uninhibited COX-1 and COX-2 decrease the antiplatelet effects of aspirin. J Thromb Haemost 2007;5:490–6.
6. Guthikonda S, Alviar CL, Vaduganathan M, Arikan M, Tellez A, DeLao T, et al. Role of reticulated platelets and platelet size heterogeneity on platelet activity after dual antiplatelet therapy with aspirin and clopidogrel in patients with stable coronary artery disease. J Am Coll Cardiol 2008;52:743–9.
7. Ibrahim H, Nadipalli S, DeLao T, Guthikonda S, Kleiman NS. Immature platelet fraction (IPF) determined with an automated method predicts clopidogrel hyporesponsiveness. J Thromb Thrombolysis 2012;33:137–42.
8. Lopes RD, Siha H, Fu Y, Mehta RH, Patel MR, Armstrong PW, et al. Diagnosing acute myocardial infarction in patients with left bundle branch block. Am J Cardiol 2011;108:782–8.
9. Jain S, Ting HT, Bell M, Bjerke CM, Lennon RJ, Gersh BJ, et al. Utility of left bundle branch block as a diagnostic criterion for acute myocardial infarction. Am J Cardiol 2011;107:1111–6.
10. Jong G-P, Ma T, Chou P, Shyu M-Y, Tseng W-K, Chang T-C. Reciprocal changes in 12-lead electrocardiography can predict left main coronary artery lesion in patients with acute myocardial infarction. Int Heart J 2006;47:13–20.
11. Widera C, Pencina MJ, Meisner A, Kempf T, Bethmann K, Marquardt I, et al. Adjustment of the GRACE score by growth differentiation factor 15 enables a more accurate appreciation of risk in non-ST-elevation acute coronary syndrome. Eur Heart J 2012;33:1095–104.
12. Timmer JR, van der Horst ICC, de Luca G, Ottervanger JP, Hoorntje JCA, de Boer M-J, et al. Comparison of myocardial perfusion after successful primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction with versus without diabetes mellitus. Am J Cardiol 2005;95:1375–7.
13. Shah B, Mathur P. Surveillance of cardiovascular disease risk factors in India: the need & scope. Indian J Med Res 2010;132:634–42.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

14. Gupta R. Recent trends in coronary heart disease epidemiology in India. Indian Heart J 2008;60:B4-18.
15. Briggs C, Kunka S, Hart D, Oguni S, Machin SJ. Assessment of an immature platelet fraction (IPF) in peripheral thrombocytopenia: The IPF in Peripheral Thrombocytopenia. Br J Haematol 2004;126:93–9.
16. Ibrahim H, Schutt RC, Hannawi B, DeLao T, Barker CM, Kleiman NS. Association of immature platelets with adverse cardiovascular outcomes. J Am Coll Cardiol 2014;64:2122–9.
17. López-Jiménez RA, Martín-Herrero F, González-Porras JR, Sánchez-Barba M, Martín-Luengo C, Pabón-Osuna P. Immature platelet fraction: a new prognostic marker in acute coronary syndrome. Rev Esp Cardiol (Engl Ed) 2013;66:147–8.
18. Schröder R. Prognostic impact of early ST-segment resolution in acute ST-elevation myocardial infarction. Circulation 2004;110:e506-10.

ISSN (O): 2687-5365; ISSN (P): 2753-6556