Original Article

The study of platelet indices in acute coronary syndromes

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Abstract

Background: Platelets have been implicated in the pathogenesis of cardiovascular disorders including atherosclerosis and its complications such as acute myocardial infarction (MI), unstable angina and sudden cardiac death. Platelet indices correlates with functional status of platelets and is an emerging risk marker for atherothrombosis

Methods: A prospective hospital based study was carried out on 175 cases diagnosed with Acute Coronary Syndromes and 175 controls from October 2011 to March 2013 considering the inclusion and exclusion criteria**.**

Results: The incidence of ACS in males (62.86%) was more as compared to females (37.14%).The average age with which the patient presented with ACS was 57.76 ± 13.19 years. The commonest manifestation of ACS was ST elevation MI. Analysis of PVI indicated MPV & PDW as significant risk factor for developing a myocardial infarction. This was in concordance with the elevated cardiac enzymes levels.

Conclusion: The study concludes that Platelet Indices especially MPV & PDW is raised in patients who have suffered STEMI & NSTEMI as compared with patients diagnosed with unstable angina.

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Introduction

Ischaemic Heart Disease is defined as myocardial impairment due to imbalance between coronary blood flow and myocardial requirement. Cardiovascular diseases accounts for approximately 12 million deaths annually and is the commonest cause of death globally.[1]

Patients with Ischaemic Heart Disease fall into two large groups:

1. Patients with stable angina secondary to Coronary Artery Disease
2. Patients with Acute Coronary Syndromes

The latter group, in turn, is composed of patients with Acute Myocardial Infarction with ST-segment elevation on their presenting electrocardiogram and those with Unstable Angina and Non-segment elevation myocardial infarction.[2] Conventional risk factors for atherosclerosis include smoking, diabetes mellitus, hypertension, hyperlipidemia, obesity and stress which either acting singly or in combination increase the chances of developing coronary atherosclerosis. However, they only explain part of the cases and other relevant risk factors need to be identified for an accurate calculation of an individual's risk for myocardial infarction.

Platelet indices viz – Mean platelet volume (MPV), Platelet distribution width (PDW) and Platelet large cell ratio (P-LCR) have been well utilized for certain conditions like Idiopathic Thrombocytopenic Purpura (ITP), Aplastic anemia and other haemotological and myeloproliferative disorders to assess the prognosis but are underutilized for cardiovascular disorders.[3] Platelets have been implicated in the pathogenesis of cardiovascular disorders including atherosclerosis and its complications such as acute myocardial infarction, unstable angina and sudden cardiac death. Platelet hyperactivity and local platelet activation have been suggested to play a role in acute coronary events. Platelet size has been shown to reflect platelet activity which is indirectly measured by the parameters. Larger platelets are metabolically and enzymatically more active than small platelets.[4] Platelet indices correlates with functional status of platelets and is an emerging risk marker for atherothrombosis.[5]

The most sensitive and specific biomarkers of myocardial damage are Troponin I and Troponin T, levels of both begin to rise at 2 to 4 hours and peak at 48 hours. Creatine Kinase enzymes begins to rise within 2 to 4 hours of the onset of myocardial infarction, peaks at about 24 hours and returns to normal within approximately 72 hours.[6] Platelet parameters can be detected earlier as compared to specific and non specific markers of Myocardial Infarction. Platelet indices are easily recorded by automated cell counter and are routinely available in most clinical laboratories. There is scope to make better use of the platelet parameters generated, as patients with larger platelets can easily be identified during routine haematologial analysis and could possibly benefit from timely treatment.[4] The study was undertaken to account the efficacy of platelet parameters in Acute Coronary Syndromes.

Materials and Methods

A prospective hospital based study was carried out on 175 patients admitted from October 2011 to March 2013 considering the inclusion and exclusion criteria. All the patients diagnosed with Acute Coronary Syndromes were included in the study and compared with age and sex matched controls having a normal electrocardiogram and no past history of Ischaemic heart disease.

Method of collection of data: The study was carried out on patient presenting with Acute Coronary Syndromes within 24 hours. All subjects were interviewed as per the prepared proforma and then complete clinical examination was done. The blood samples of the patients were drawn from the antecubital vein using a 5ml syringe and immediately mixed in EDTA vacuutainers. The sample was run within two hours of venepuncture using the 3 part differentiated automated Hematology analyzer (Sysmex KX-21) and complete blood count analysis of the sample was made including the platelet indices (MPV, PDW, P-LCR). Relevant investigations like electrocardiogram and cardiac enzymes were analysed for confirmation of the diagnosis. Trop T Sensitive kit was used as an aid in the diagnosis of myocardial injury. Detection of rise or fall in cardiac biomarker Troponin T with at least one value above 99th percentile of upper limit was considered diagnostic.

Inclusion criteria:

1. Patients diagnosed with unstable angina (UA), ST segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI).
2. Patients more than 18 years of age

Exclusion criteria:

1. Patients with bleeding diathesis, previous stroke, major operations or significant trauma in the past two weeks or hypertension(>180/110 mm of Hg)
2. Patients less than 18 years of age
3. Patients with non-cardiac chest pain

Values were expressed as mean ± standard deviation. Chi square tests were used to compare categorical variables such as status of smoking, diabetes, hypertension, family history and alcohol consumption. $P < 0.05$ was considered statistically significant.

Result

A total of 350 cases were studied and were divided further into two groups of 175 patients each, who were patients diagnosed with ACS and age and sex matched controls. The mean age of patients in our study was 57.76 ± 13.19 years. Majority of patients diagnosed as Acute Coronary Syndrome belonged to the 5th decade of life (29.71%), followed by 6th decade (22.86%) and 4th decade (18.86%) of life. In the present study, total number of males including both cases and controls were 223 (63.71%) and number of females were 127 (36.28%).The number of males in the MI group were 110 (62.86%) compared to non - MI group 113 (64.57%). The numbers of females in the MI group were 65 (37.14%) compared to non - MI group 62 (35.42%).

In our present study risk factors were evaluated. Significantly, more number of patients who were smokers and alcoholics and had diabetes were present in cases as compared to controls. Family history and hypertension did not contribute significantly to the risk of myocardial infarction in our model and were thus excluded. (Table 1)

Table 1: distribution of risk factors

Risk factor	Cases (n=175)	Controls (n=175)	Odds Ratio	P value
Positive family history	4 (2.3%)	1 (0.5%)	4.07	0.211
Cigarette	52 (29.7%)	30 (17.0%)	2.04	**0.005**
Alcohol	82 (46.9%)	13 (7.2%)	10.99	**<0.0001**
Diabetes	34 (19.4%)	12 (6.7%)	3.28	**<0.005**
Hypertension	31 (17.7%)	43 (24.3%)	0.66	0.118

TABLE 2: distribution of platelet indices

Platelet indices	Unstable angina (n=58)	STEMI (n=79)	NSTEMI (n=38)	Control (n=175)	Overall (cases) (n=175)
PDW (fL)	13.41 ±4.02	13.66 ±3.55	13.24 ±3.46	12.23 ±3.13	13.49 ±3.67
MPV (fL)	8.53 ±0.54	9.67 ±0.82	9.54 ±0.76	8.14 ± 0.67	09.27 ±0.89
P-LCR (%)	18.57 ±3.70	22.09 ± 4.89	22.36 ±4.95	18.12 ±3.54	20.99 ±4.83

The platelet indices; Mean platelet volume (MPV), Platelet distribution width (PDW) and Platelet large cell ratio (P-LCR) were studied among patients with ACS and compared with age and sex matched control groups. (Table 2) The mean of the MPV for the control group in our study was 8.14 ± 0.67 fL, for unstable angina it was 8.53 ± 0.54fL, 9.67 ± 0.82 fL for STEMI & 9.54 ± 0.76 fL for NSTEMI (Table 2). The MPV was highest in ST-Elevation Myocardial Infarction group 9.67 ± 0.82 fL followed by Non-ST-Elevation Myocardial Infarction 9.54 ± 0.76 fL when compared with patients diagnosed as unstable angina 8.53 ± 0.54 fL which was close to the MPV values recorded in the control group.

Table 3: distribution of cases according to MPV & PDW values

Parameter	value	CLINICAL DIAGNOSIS			
		Unstable Angina (n=58)	STEMI (n=79)	NSTEMI (n=38)	Total (n=175)
MPV	**<9.6**	56	35	14	105
	≥9.6	2	44	24	70
PDW	**<12.8**	21	51	24	97
	≥12.8	37	28	14	78

Based on previous similar studies done on platelet indices & CVD, a cut-off value of 9.6 fl was taken to make it a dichotomous variable for calculating the statistical association between MPV recorded and the clinical diagnostic category. We found it to be highly significant for both category (STEMI & NSTEMI) with p value ($p < 0.0001$) at 2 degrees of freedom and 95% Confidence level control in comparison to patients diagnosed with unstable angina (Table3). Our study showed that the association between Mean

Platelet Volume and Cardiac Troponin T is statistically significant (p=0.031) at 1 degree of freedom and 95% confidence level for the STEMI group as 95% of cases here had larger value of MPV and had cardiac enzyme Troponin T positive, for the NSTEMI group about 87% cases had both the larger indices and positive Troponin Value but it was not statistically significant (p= 0.603) (Table 4).

Table 4: Association between Mean Platelet Volume & Cardiac Troponin T

MPV	Troponin in STEMI			Troponin in NSTEMI		
	Positive	Negative	Total	Positive	Negative	Total
<9.6fl	28 (80.0)	7 (20.0)	35	12 (92.9)	1 (7.1)	14
≥9.6fl	42 (95.4)	2 (4.6)*	44	21 (87.5)	2 (12.5)	24
Total	70	9	79	34	4	38
Chi-square	4.612	p=0.031		0.269	p=0.603	

Table 5: Association between Platelet Distribution Width and Cardiac Troponin –T Results

PDW (fl)	Troponin-T in STEMI			Troponin-T in NSTEMI		
	Positive	Negative	Total	Positive	Negative	Total
<12.8	33 (82.50)	7 (17.5)	40	22 (91.67)	2 (8.33)	24
≥12.8	37 (94.87)	2 (5.13)*	39	12 (85.71)	2 (14.29)	14
Total	70	9	79	34	4	38
Chi-square	4.87	p=0.027		5.6	p=0.018	

The PDW in our study for the control group was 12.23 ± 3.13 fL. The mean of the PDW values for unstable angina was 13.41 ± 4.02 fL, 13.66 ± 3.55 fL for STEMI & 13.24 ± 3.46 fL for NSTEMI . (Table 2) To convert it into a dichotomous variable for calculating the statistical association between PDW and clinical category & also with cardiac enzymes, PDW with the value of <12.8 & PDW >=12.8 was taken (Table 3).

Here in the STEMI group 95 % cases were Troponin-T positive with PDW ≥ 12.8 and only 5% were Troponin-T negative which is statistically significant (p=0.027). Among the NSTEMI group, there was

86% enzyme positive with PDW≥12.8 against 14% cases with Troponin-T negativity with PDW ≥12.8. This association was again statistically significant (p=0.018), suggesting that PDW ≥12.8 with Troponin-T positivity is indicative of an impending acute coronary event (Table 5).

The P-LCR recorded in our study for MI group was higher and (22.36±4.95fL), in comparison to the non-MI group 18.57±3.70fL the control group (18.12 ± 3.54fL). The p-value for P-LCR was however not statistically significant for evaluating a cardiovascular patients profile.

Discussion

Myocardial Infarction is a major cause of morbidity & mortality in industrialized countries .[2]Though a large number of risk factors are known, they explain only a part of the cases .[1] The aeitology of Ischaemic Heart Disease, is without doubt multifactorial.[7] It is likely that platelet activation plays a central role in the transformation of atherosclerotic cardiovascular disease (CVD) into its potentially major adverse clinical events, such as ischemic stroke and myocardial infarction.[8] Ischaemic Heart Disease is defined as myocardial impairment due to imbalance between coronary blood flow and myocardial requirement. Cardiovascular diseases accounts for approximately 12 million deaths annually and is the commonest cause of death globally.[5]

The MPV values evaluated in our study were 8.14 ± 0.67fl for the control group, 8.53 ± 0.54fl for unstable angina, 9.67 ± 0.82fl for STEMI & 9.54 ± 0.76 for NSTEMI. We found that MPV was raised in patients who have suffered an acute coronary event when compared with controls and those with unstable angina. This is in agreement with the results of similar studies by other workers. (Table 6)

In ACS, rupture of unstable atherosclerotic plaque triggers a thrombogenic cascade leading to clinical events. However, platelet reactivity is critically important in the formation and propagation of intracoronary thrombus.[11] MPV, one of the markers indicating the function of platelets, is a simple and easy measurement .[17]

Increased MPV was found to be associated with coronary artery disease, acute MI, congestive heart failure and hypertensive patients with evidence of target organ damage and cerebrovascular disease,[18] an important complication of atherosclerosis. Sub-

stantial evidence indicates that platelets and their interaction with the coronary arterial wall are of pathogenic importance in coronary atherosclerosis and its complications. After erosion or rupture of atherosclerotic plaques in coronary arteries, platelet activation plays a crucial role in the prothrombotic events leading to MI. Increased platelet reactivity is associated with increased platelet volume.[4,5,17] As mentioned earlier large platelets that contain more dense granules are metabolically and enzymatically more active than small platelets and have higher thrombotic potential .[4] The size of platelets has been found to associated with an increased number of megakaryocytes. The increased ploidy of megakaryocytes is correlated with megakaryocyte and platelet volume.[19,20,21,22] Elevated levels of CD40 ligands, which are expressed by activated platelets, have been found in atheromatous plaques.[23] Pizulli et al suggested that because platelets stay in the circulation for 7–11 days, they might be detected days before symptoms appear.[14]

Table 7: comparison of MPV in AMI and controls in different studies

Publication	Cases	MPV	Controls	MPV	p Value
O'Brien et al[9] (1973)	23	8.10	36	7.01	<0.001
Cameron et al [10] (1983)	100	9.07	200	8.32	<0.001
Martin et al[11] (1983)	15	7.3	22	6.32	0.05
Martin et al [12] (1991)	126	10.09	1590	9.72	<0.001
Smyth et al [13] (1993)	24	8.54	23	8.1	0.04
Pizulli et al [14] (1998)	108	9.4	97	8.2	<0.001
Khandekar et al [4] (2006)	94	10.43	30	9.2	<0.001
Lippi et al[5] (2009)	456	7.4	1848	8.0	<0.001
Chu et al[15] (2010)	911	9.24	1898	8.48	<0.001
Khode et al[16] (2012)	*39*	*9.65*	*65*	*9.21*	*0.018*
Present Study	175	9.605	175	8.33	<0.0001

Chu H et al showed MPV is significantly associated with ACS in patients with acute chest pain and is an early and independent predictor.[24] Chu SG et al review demonstrated that elevated MPV is associated with acute MI, mortality following MI, and restenosis following coronary artery intervention.[15] Mathur et al studies have shown higher MPV values in pa-

tients with UA (10.7fl) than those with MI(9.8fl),[25] but our study found no such difference which compares well with a study by Senaran et al in which Mean platelet volume was found to be elevated in patients with AM1 (8.2 ± 0.8 fl) and UA(7.7 ± 0.5fl) compared with control subjects (6.6 ± 0.6 fl).[26]

The role of PDW specifically in patients with CAD and acute coronary events is yet to be explored.[4] Nevertheless our observations showed that PDW was significantly elevated among the patients as compared to the non-MI patients and the control group.

The PLCR parameter is generated by only a few machines, with the Sysmex analyser being one of them. It is not often quoted in the literature, probably because it is a relatively new PVI parameter.[4] Our study shows that P-LCR is not a reliable marker for predicting an acute coronary event. This is in agreement with the studies by Khode et al [16] and Bhayana et al. [21] However these results are in contrast to study of Khandekar et al. [4]

Limitations of the study

- Follow up of the patients was not possible to examine the prognostic value of our findings.
- Patients with qualitative disorders and causes of reactive platelets were not assessed.
- Platelet function tests could not be conducted on the sample to substantiate our findings further.

Conclusion

Our data suggest that the increased platelet volume indices contribute to the prethrombotic state in acute ischaemic syndromes and that larger platelets may play a specific role in infarction. Because larger platelets are haemostatically more active, the presence of larger platelets is probably a risk factor for developing coronary thrombosis and MI. Patients with larger platelets can easily be identified during routine haematological analysis because PVI are generated as a by product of automated blood counts. Thus, in conclusion, PVI provides an important, simple, effortless, and cost effective tool, which can be useful in predicting an impending acute coronary event.

Competing Interests

None declared

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