

Comparative study of platelet indices in coronary artery diseases

Gururajaprasad. C^{1,*}, Ishita Maheshkumar Kaneria², Akkamahadevi. P³, Manjappa Mahadevappa⁴

¹Associate Professor, ²Post Graduate, ³Professor and HOD, ⁴Assistant Professor, ^{1,2}Dept. of Pathology, ³Dept. of Emergency Medicine, ⁴Dept. of Cardiology, J.S.S Medical College, J.S.S. University, Mysore, Karnataka, India

***Corresponding Author: Gururajaprasad. C**

Email: geepee111@yahoo.co.in

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Abstract

Introduction: With urbanization and increase in sedentary lifestyle, prevalence of CAD (Coronary artery disease) is looming large as the new epidemic afflicting Indians. Altered platelet morphology and functions have been linked with the formation and propagation of thrombotic event. Platelet indices (Mean platelet volume - MPV, Platelet distribution width - PDW, Platelet large cell ratio - PLCR) are determinants of platelet functionality.

Aims and Objectives: 1. To study platelet indices (MPV, PDW, P-LCR) in CAD; 2. To compare platelet indices in patients with myocardial infarction, stable CAD and control population.

Material and Methods: A comparative and prospective study was conducted on 100 patients each of MI & stable CAD on antiplatelet therapy and 100 age and sex matched healthy individuals as controls. Platelet indices were measured using an Automated Blood Counter SYSMEX XN-1000. Troponin T and CK-MB levels were collected from clinical data in MI cases.

Results: Platelet indices were significantly higher in MI patients in comparison to stable CAD and control groups. Stable CAD patients also showed significantly higher platelet indices in comparison to control groups. (p value <0.001)

Conclusion: The present study showed a significantly higher MPV, PDW and P-LCR in CAD patients in comparison to control group. Among CAD patients, MI patients had significantly higher platelet indices than stable CAD patients. Hence platelet indices can be used as simple and cost effective predictive parameters to predict CAD. Their use in a risk stratification system to predict MI and in response to intervention are worthy of consideration.

Keywords: Coronary artery diseases, Platelet indices, Mean platelet volume, Platelet distribution width, Platelet large cell ratio.

Introduction

The leading cause of mortality and morbidity in the world is Coronary artery disease (C.A.D). The commonest causes of mortality in patients with CAD are acute coronary syndromes (ACS), which encompass unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI). Indians have a very high incidence of the prevalence of CAD and the incidence of ACS.¹⁻⁵ The highest burden of CAD in the world is seen in India.⁶ In Indians, the rising incidence of CAD may be related to the changes in the lifestyle, the westernization of the food practices, the increasing prevalence of diabetes mellitus and probably genetic factors.⁷

Pathogenesis of CAD is attributed to the altered platelet morphology and functions. Hyperactivity of platelets has an important role in the initiation of atherosclerotic lesions and coronary thrombogenesis. As compared to smaller sized platelets, larger platelets are more active enzymatically and metabolically and have higher thrombotic ability.^{8,9}

The Platelet indices (Platelet count, Mean platelet volume - MPV, Platelet distribution width - PDW and Platelet large cell ratio - PLCR) determine platelet function. An increased mean platelet volume (MPV) and platelet distribution width (PDW) have been found to be important contributory factors causing thromboembolism.⁸

On routine hematological analysis, larger platelets can be identified and could possibly benefit from preventive/therapeutic treatment.

Coronary artery disease is such a huge public health problem and platelet volume indices are an important, simple and cost-effective tool in predicting the possibility of coronary artery disease, with simple hematological analysis, possible preventive/therapeutic measures can be taken. This study is aimed at finding a link between CAD and platelet indices.

Objectives of the Study

1. To study platelet indices (Platelet count, MPV, PDW, P-LCR) in coronary artery diseases.
2. To compare platelet indices in patients with myocardial infarction, stable CAD and control population.

Materials and Methods

Source of Data: The present study was undertaken in the Department of Pathology, JSS Medical College and Hospital, Mysore.

Method of Collection of Data:

1. Study period: October 2015 to September 2017.
2. Study design: Analytical study

Sample size and Study Subjects:

Group 1: 100 Myocardial infarction patients not on antiplatelet treatment.

Group 2: 100 Stable CAD patients on antiplatelet treatment.

Group 3: 100 age and sex matched healthy individuals.

Inclusion Criteria: Diagnosed cases of coronary artery diseases.

Exclusion Criteria: Patients with a history of renal disease or of past coronary intervention or coronary arterial bypass grafting, inflammatory rheumatic disease, chronic obstructive pulmonary disease and taking oral anticoagulants were excluded. Myocardial infarction patients pretreated or loaded with antiplatelet drugs were excluded.

Method of Collection of Data:

1. Data collection was done in a predesigned proforma.
2. Venous blood samples were collected in a vacutainer containing di-potassium EDTA and processed within 2 hours of sample collection.
3. Platelet indices (PC, MPV, PDW, P-LCR) were measured in cases and control groups using an Automatic Blood Counter (SYSMEX, XN-1000)
4. Serum Troponin T and CK-MB levels of MI patients were collected from clinical data.

Statistical Methods

Descriptive statistics such as numbers and percentages were used to describe categorical variables. Mean and standard deviations were used to describe continuous variables like platelet count, MPV, PDW and P-LCR. Independent sample t-test was applied to find out the significant difference in platelet count, MPV, PDW and P-LCR between the cases and controls. Pearson's correlation was used to analyse association between different variables. Statistical significance was determined at 5% level of significance (i.e. < 0.05 is significant). Statistical analysis was done using Statistical package for social sciences (SPSS version 22) software. Microsoft word and Excel have been used to generate graphs, tables etc.

Investigations

1. Complete blood count/ complete hemogram
2. Serum Troponin T
3. Serum CK-MB

Results

The present study included 100 cases each of myocardial infarction, stable CAD diagnosed at JSS hospital, Mysore from August 2015 to September 2017. Platelet indices, ECG and serum markers were recorded in a proforma. The details were then transcribed into master chart and analyzed.

Age Distribution: Age of myocardial infarction patients ranged from 32 years to 85 years with mean age of 64.2 ± 11.52 years. Age of stable CAD patients ranged from 25 years to 81 years with mean age of 61.7 ± 11.88 years. Age of controls ranged from 52 years to 89 years with mean age of 67.6 ± 10.71 .

Sex Distribution: Out of 100 MI cases, number of males and females were 64 and 36, respectively. Out of 100 stable CAD cases, number of males and females were 67 and 33 respectively. Controls had 59 males and 41 females.

Subtypes of Myocardial Infarction Cases: Out of 100 MI cases, 78 were ST elevation MI (STEMI) and 22 were Non-ST elevation MI (NSTEMI).

Serum Markers in Myocardial Infarction Patients: Serum Troponin T and CK-M levels were available for all MI cases. Mean Troponin T and CK-MB levels were 1.16 ng/ml and 28.9 ng/ml, respectively. Mean CK-MB level was higher in NSTEMI (38.51 ng/ml) than STEMI (26.19 ng/ml). However, there was no significant difference between CK-MB levels in these two groups. ($p > 0.05$).

Mean Troponin T levels of STEMI and NSTEMI were almost similar i.e. 1.15 and 1.17 ng/ml, respectively with no significant difference ($p > 0.05$).

Platelet Count in all 3 Study Groups: Mean platelet count of MI, stable CAD and controls were 2.78 ± 0.77 , 3.32 ± 0.86 and 2.9 ± 0.65 ($10^6/L$), respectively with no significant difference (p value – 0.41).

MPV in all 3 Study Groups: Mean MPV of MI, stable CAD and controls were 10.5 ± 0.76 , 10.2 ± 0.87 , 9.4 ± 0.7 fL, respectively. There was a significant difference between MPV of these groups ($p < 0.001$) with highest mean MPV being of MI group.

PDW in all 3 Study Groups: Mean PDW of MI, stable CAD and controls were 12.1 ± 1.68 , 11.8 ± 2.22 and 9.8 ± 1.4 fL, respectively. PDW was found to be significantly higher in MI group compared with stable CAD and control group, $p < 0.0001$.

P-LCR in all 3 Study Groups: Mean P-LCR in MI, stable CAD and controls were 28.3 ± 5.87 , 26.6 ± 7.22 and $20.1 \pm 5.84\%$, respectively. P-LCR was significantly higher in MI group in comparison to stable CAD and control group ($p < 0.0001$).

Platelet Indices in MI Subtypes: STEMI and NSTEMI cases had mean platelet count of 2.8 ± 0.77 and 2.9 ± 0.8 , mean MPV of 10.5 ± 0.74 and 10.5 ± 0.85 , mean PDW of 12.1 ± 1.68 and 12.18 ± 1.76 and mean P-LCR of 28.6 ± 6.07 and 27.5 ± 5.12 , respectively. However, there was no significant difference between all platelet indices of STEMI and NSTEMI cases.

Platelet indices and Serum Markers of MI: There was no significant correlation of platelet indices with serum Troponin T and CK-MB levels. ($p > 0.05$).

Discussion

CAD is the most leading cause of mortality and morbidity in India⁴ and has highest burden of CAD in the world.⁶ The increasing incidence of CAD amongst Indians may be related to the changes in the lifestyle, the westernization of the food practices, the increasing prevalence of diabetes mellitus and probably genetic factors.⁷

Pathogenesis of CAD is linked with the altered platelet morphology and functions. The platelets become hyperactive and larger in size when they come in contact with ruptured plaque. These larger platelets are more active metabolically and enzymatically and have higher thrombotic ability as compared to small sized platelets because of higher production of thromboxane A₂.^{8,9}

In addition to generation of thromboxane A₂, activation of platelets leads to conformational change in GP IIb/IIIa receptors. These receptors develop a high affinity for fibrinogen. Multivalent molecule Fibrinogen can bind to two different platelets at a time and results in platelet cross-linking and aggregation.^{10,17} Hence an increase in platelet consumption at the site of the atherosclerotic plaque occurs which causes larger platelets to be released from the bone marrow.^{18,19}

At the site of plaque, the thrombus composed of platelet aggregates and fibrin strands traps red blood cells and thus can reduce coronary blood flow, leading to the clinical manifestations of myocardial ischemia.¹⁰

Total or partial thrombosis superimposed on a disrupted plaque is a core factor in acute coronary syndromes.¹¹ Platelet reactivity is most important in the formation and propagation of intracoronary thrombus mainly due to their proinflammatory effects by recruiting white blood cells (WBC) at vascular injury sites, thus directly increasing the plaque burden.²⁰⁻²³

The larger platelets can be identified in routine hematological analysis by platelet volume indices (Platelet count, Mean platelet volume, Platelet distribution width and Platelet large cell ratio).⁸

The present study was conducted to determine the relationship of platelet indices with CAD and to compare the platelet indices in myocardial infarction, stable CAD and control population. 100 cases of each MI, stable CAD cases and age and sex matched controls were studied in present study.

Age Distribution

- Myocardial Infarction Cases:** Majority of patients fell into age group of 61 years to 70 years with mean age being 64.2 yrs.
- Stable CAD Cases:** Majority of patients were in the age group of 61 years to 70 years with mean age being 61.7 years. This age distribution of MI

and stable CAD show that with increase in age, the risk of developing CAD increases. This may be due to age dependent increase in risk factors like diabetes mellitus, hypertension and hyperlipidemia.

Sex Distribution: A male preponderance was observed in patients with CAD with the male to female ratio being 1.8:1 & 2:1 among the patients with M.I and stable CAD respectively. This shows males are more prone to the development of CAD than females.

MI Subtypes: Among 100 M.I patients, 78 were STEMI and 22 were NSTEMI. Many studies have found similar results.^{20,68,70,74} However, Ahmed et al⁸⁶ found more NSTEMI cases than STEMI cases.

Serum markers of MI: Mean Troponin T and CK-MB levels were 1.16 ng/ml and 28.9 ng/ml, respectively. When the NSTEMI & STEMI subgroups were compared, there were no significant differences in the levels of Troponin T & CK-MB which correlated with the study conducted by Orak et al.⁹¹

Platelet count and CAD: Mean platelet count was seen to be lowest in MI patients(2.78± 0.77) in comparison to the stable CAD patients which probably is due to immediate increased consumption of platelets at the site of plaque rupture.⁷² But there was no significant difference among mean platelet count of all the 3 groups. This finding was supported by Khode et al⁸¹ (2.89± 1.04) and Sharma et al¹⁸ (2.63 ± 0.33) but it was in contrast to studies conducted by Khandekar et al¹⁹ (2.32 ± 0.84), Ranjith et al⁷² (2.01 ± 0.13) and Amraotkar et al⁷⁰ (2.14± 0.69).

MPV and CAD: A significant difference was seen in the mean MPV of MI and stable CAD (10.45 ± 0.76 and 10.21 ± 0.87, respectively). This was further supported by Amraotkar et al,⁷⁰ Khode et al⁸¹ and Ranjith et al.⁷² An Increase MPV seen during MI may be due to increased platelet reactivity, which in turn increases platelet surface expression of IIb/IIIa receptors and P selectin proteins. According to our study results, MPV was higher in patients with stable CAD compared with the normal population. A possible explanation for an increased platelet volume and MPV is an increased activity of platelets and activation of the coagulation cascade due to enhanced vasoconstrictor substances.⁷²

Table 1

Study	Year	Mean MPV (fL)		P value
		MI	SCAD	
Khandekar et al ¹⁹	2009	10.43 ± 1.03	9.37 ± 0.99	< 0.001
Khode et al ⁸¹	2012	9.65 ± 0.9	9.38 ± 0.8	0.025
Ranjith et al ⁷²	2015	10.97 ± 0.58	10.03 ± 0.23	< 0.001
Sharma et al ¹⁸	2016	10.29 ± 1.12	9.19 ± 0.62	< 0.001
Amraotkar et al ⁷⁰	2017	9.18 ± 1.21	8.13 ± 0.66	0.003
Present study	2017	10.45 ± 0.76	10.21 ± 0.87	0.000

PDW and CAD: Mean PDW of MI and stable CAD were 12.06 ± 1.69 and 11.77 ± 2.22 , respectively. This is in concordance with studies conducted by Khandekar et al,¹⁹ Ranjith et al⁷² and Sharma et al.¹⁸ However, Khode et al⁸¹ did not find any significant difference in

PDW among these groups. It is argued that this platelet volume distribution provides a cause for the prethrombotic state in IHD. So, considering that PDW is an index of platelet heterogeneity, this might explain the above witnessed increase in MI.⁷²

Table 2

Study	Year	Mean PDW (fL)		P value
		MI	SCAD	
Khandekar et al ¹⁹	2009	13.19 ± 2.34	11.35 ± 1.95	< 0.001
Khode et al ⁸¹	2012	10.84 ± 2.2	10.65 ± 1.7	0.376
Ranjith et al ⁷²	2015	14.63 ± 0.64	12.43 ± 0.62	< 0.001
Sharma et al ¹⁸	2016	15.11 ± 0.88	13.25 ± 0.44	< 0.001
Present study	2017	12.06 ± 1.69	11.77 ± 2.22	0.000

P-LCR and CAD: Mean P-LCR of MI and stable CAD were 28.32 ± 5.87 and 26.59 ± 7.22 , respectively difference is significant. This was further supported by

Khandekar et al¹⁹ and Ranjith et al.⁷² However, Khode et al⁸¹ did not find any significant difference in P-LCR among these groups.

Table 3

Study	Year	Mean P-LCR (%)		P value
		MI	SCAD	
Khandekar et al ¹⁹	2009	29.4 ± 7.38	22.55 ± 6.65	< 0.001
Khode et al ⁸¹	2012	21.58 ± 6	20.92 ± 6.4	0.315
Ranjith et al ⁷²	2015	32.23 ± 1.94	26.77 ± 1.08	< 0.001
Present study	2017	28.32 ± 5.87	26.59 ± 7.22	0.000

Platelet Count and MI Subgroups: The mean platelet count of STEMI and NSTEMI were noted to be 2.81 ± 0.77 and 2.89 ± 0.79 , respectively with no significant difference. (p value - 0.65). This was in concordance with Salim et al⁸⁷ and Rifat et al⁸⁹

MPV and MI Subgroups: Mean MPV of STEMI and NSTEMI patients were 10.46 ± 0.74 and 10.45 ± 0.85 , respectively with no significant difference (p value - 0.95). This finding was further supported by Salim et al,⁸⁷ Manchanda et al.²⁰

Table 4

Study	Year	Mean MPV (fL)		P value
		STEMI	NSTEMI	
Rifat et al ⁸⁹	2011	8.7 ± 1	7.9 ± 0.7	< 0.001
Salim et al ⁸⁷	2013	10.9 ± 0.7	10.7 ± 0.6	0.32
Manchanda et al ²⁰	2015	9.67 ± 0.82	9.54 ± 0.76	> 0.05
Ahmed H et al ⁸⁸	2017	10.32 ± 0.78	9.22 ± 0.53	< 0.05
Patil et al ⁹⁰	2017	10.48 ± 1.42	9.73 ± 1.15	0.001
Present study	2017	10.46 ± 0.74	10.45 ± 0.85	0.95

PDW and MI Subgroups: Mean PDW of STEMI and NSTEMI were noted to be 12.07 ± 1.68 and 12.05 ± 1.76 , respectively. However, no significant difference

was noted in mean PDW of these two groups which was in concordance with Salim et al⁸⁷ and Manchanda et al.²⁰

Table 5

Study	Year	Mean PDW (fL)		P value
		STEMI	NSTEMI	
Salim et al ⁸⁷	2013	21.5 ± 1.7	21.9 ± 0.6	0.58
Manchanda et al ²⁰	2015	13.66 ± 3.55	13.24 ± 3.46	> 0.05
Patil et al ⁹⁰	2017	13.92 ± 1.57	12.84 ± 1.54	0.001
Present study	2017	12.07 ± 1.68	12.05 ± 1.76	0.97

P-LCR and MI Subgroups: Mean P-LCR of STEMI and NSTEMI patients were 28.55 ± 6.07 and 27.47 ± 5.11 , respectively with no significant difference (p value = 0.49). This finding was further supported by Manchanda et al.²

Conclusion

The present study showed a significantly higher MPV, PDW and P-LCR in CAD patients. MI patients had significantly higher platelet indices than stable CAD patients.

Platelet indices can be used as simple and cost effective predictive parameters with other laboratory tests in the emergency department (particularly in remote centres and where cardiac serum markers are not readily available) to predict the development of acute coronary events.

Use of platelet indices in future studies of risk stratification system to predict MI as well as in response to intervention are also worthy of consideration.

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