(International Print/Online Journal)

SJIF IMPACT FACTOR: 4.617
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume2, Issue 3, Page No: 108-116
May-June 2019

A Comparative study of Platelet indices in Acute Myocardial Infarction and Stable Coronary Artery Disease patients

[1]Dr Swathi Sridharan, [2]Dr Shanmugapriya M*, [3]Dr Eswari V
[1]Postgraduate, [2]Associate Professor, [3]Professor and HOD
Department of Pathology, Meenakshi Medical College Hospital and Research Institute,
Kanchipuram-631552, Tamilnadu

***Corresponding Author:**

Dr Shanmugapriya M
Associate Professor, Department of Pathology,
Meenakshi Medical College Hospital and Research Institute

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

ABSTRACT

Introduction: Coronary Artery Disease is a leading cause of mortality worldwide which is caused by atherosclerosis and its complications. Platelets and their activity play an important role in the initiation of atherosclerotic lesions and formation of coronary thrombus. The aim of this study is to compare the changes in the platelet parameters among patients presenting with Stable Coronary artery disease and Acute Myocardial infarction.

Materials and Methods : A total of 100 cases were studied, 50 patients of acute myocardial infarction (AMI) and 50 patients of stable coronary artery disease consisting of those who had AMI at least 5 weeks prior or admitted for coronary angiography. Venous samples were drawn from the patients and collected in standardized EDTA sample tubes. Platelet indices were assayed using 3 part haematology analyser with regular quality control and further results were analysed using appropriate statistics.

Results : Among the platelet parameters, Platelet count was found to be increased in AMI patients(246.260 ± 85.05 x10^3 / microliter) as compared to stable CAD patients (211.520 ± 71.94 x10^3 / microliter).The difference was statistically significant between the two groups with a p value of 0.03. There was no statistically significant difference between other platelet indices like Mean platelet volume (MPV), Platelet distribution width (PDW) and Plateletcrit between the two groups.

Conclusion:

High platelet count in AMI seems to be an independent risk factor which correlated with severity of the coronary atherosclerosis. Platelet count can be used as an early biomarker in predicting impending acute coronary events.

Keywords: Acute myocardial infarction, Platelet indices, Stable coronary artery disease

INTRODUCTION

Coronary Artery Disease (CAD) is a well-known leading cause of mortality worldwide [1] and by the year 2020, will be first in the leading causes of disability [2]. Acute coronary syndrome (ACS) includes the full spectrum of clinical manifestations from unstable angina (UA) to non-ST segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI) [3]. Coronary artery disease is mainly caused by atherosclerosis and its complications. Platelets and

their activity play an important role in the initiation of atherosclerotic lesions and thrombus formation [4, 5].

Acute Coronary Syndrome results from rupturing of an unstable atherosclerotic plaque, followed by a cascade of platelet reactions resulting into thrombus formation. Platelets are heterogeneous blood elements with various sizes and densities which help in converting the chronic atherosclerotic plaque to an occluding thrombus. Large platelets are denser; aggregation rate is faster with sub endothelial collagen, higher production of thromboxane A2 and greater expression of glycoprotein Ib and glycoprotein IIb/IIIA receptors. All these features, increases the risk of thrombosis, and possibility of development of ACS[6].

Stable coronary artery disease (CAD) reflects the heterogeneous pathophysiology of epicardial, micro vascular and endothelial abnormalities in patients with stable angina. Stable CAD patients presents with recurrent, transient episodes of chest pain reflecting demand-supply mismatch as in Angina pectoris[7].Overall, Stable ischemic heart disease remains a worldwide public health problem of unmet need.

Platelet distribution width measures the variability in platelet size. The shape of the platelets is changed from discoid to spherical during activation. Hence, Platelet indices like MPV and PDW can be used to assess the degree of platelet activation and acts as an important predictor of ischemic events.

Platelet parameters can be detected earlier than markers of myocardial infarction which can be easily recorded by automated cell counter and is routinely available in most clinical laboratories. This study was undertaken to compare the changes in the platelet parameters among patients presenting with Acute Myocardial infarction and Stable Coronary artery disease patients and to assess whether they can be used as an independent biomarker in predicting the spectrum of CAD.

Materials and Methods:

This is an institutional based observational study carried out in the Department of Clinical Pathology at Meenakshi Medical College Hospital and Research Institute, Kanchipuram from June 2018 to December 2018.

A total of 100 cases were studied and were further subdivided into two Groups, Group 1 included 50 patients of acute myocardial infarction (AMI) and Group 2 included 50 patients of stable coronary artery disease consisting of those who had AMI at least 5weeks prior and either of those who were admitted for coronary angiography. Venous samples were drawn and collected in standardized EDTA sample tubes. Platelet count and platelet volume indices were assayed using 3 part haematology analyser with regular quality control and the results were analyzed using appropriate statistics.

Inclusion criteria:

Group 1: Patients admitted with Acute myocardial infarction (AMI)

Group 2: Patients of stable coronary artery disease who had AMI at least 5 weeks prior or those admitted for angiography.

Exclusion criteria:

Patients with severe hepatic impairment, patients with end stage renal disease, Thyroid disorders, Sepsis, Pregnant women, malignancies, autoimmune disorders like systemic lupus erythematosus, Rheumatoid arthritis etc., Recent history of Blood Transfusion ,Patients with active infection, Patients with cardiomyopathy, bleeding disorders like Idiopathic thrombocytopenic purpura and Thrombotic thrombocytopenic purpura (TTP).

Statistical Analysis:

The Results were expressed as mean ± standard deviation. Data was analyzed using SPSS version 20. Categorical variables were analyzed by chi-square test. Independent sample t test was used to compare the numerical variables. p value less than 0.05 was considered to be statistically significant. The data was statistically analyzed for various parameters like age, sex incidence, risk factors, and pre-existing conditions, mean PDW, mean platelet count, mean MPV, and mean plateletcrit and compared among group 1 and group 2.

Results:

A total of 100 cases were studied and further subdivided into two groups comprising 50 patients with acute myocardial infarction and 50 patients with stable coronary artery disease. In our study, the mean age of patients was 61.49 ± 12.20 years with a range

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from 27 to 89 years. Out of which, the mean age in group 1 was 60.98 ± 14.35 years and 62 ± 9.73 years in group 2.The most affected age group was elderly patients above 60 years of age and the least affected were 21-30 years age group patients(**Figure 1**).

Total number of males was 66 and number of females was 34 (**Figure 2**). The number of males in Group 1 was 28 compared to 37 in Group 2. The numbers of females in the group 1 were 22 compared to 13 in group 2.

Figure 1: Age distribution of Study patients

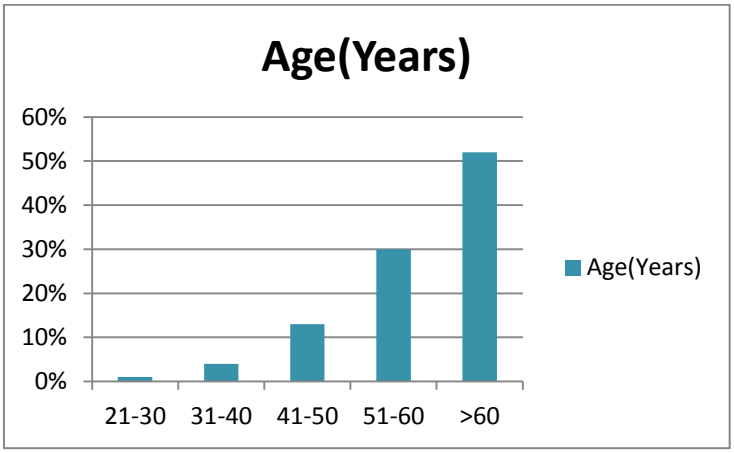
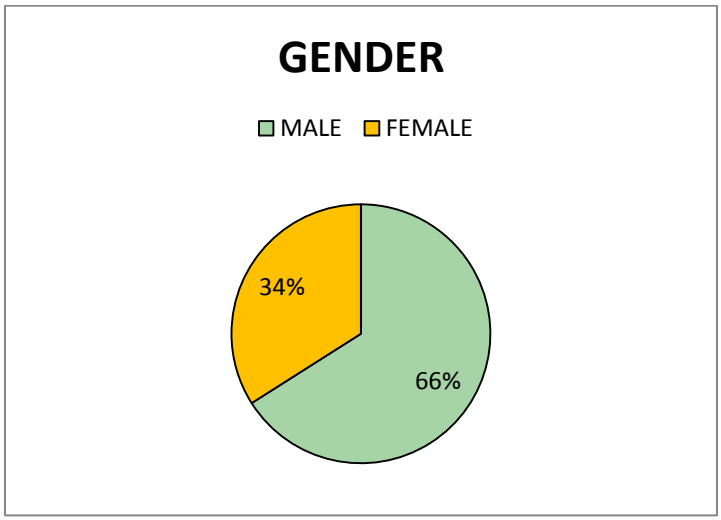


Figure 2: Gender distribution of Study patients



In our present study, various risk factors were evaluated **(Table 1).**A detailed clinical examination revealed that 68% of study patients were both hypertensive and diabetic which are the two most major risk factors for MI. Around 63% of patients were on regular treatment with antihypertensive drugs and 60% of the patients were on antidiabetic drugs. Chronic kidney disease was seen in 13% of the study patients accounting for second most common risk factor in our study. The third most common risk factor was pre-existing ischemic heart disease (IHD) which was seen in 12 % of the study patients. Chronic obstructive pulmonary disease (COPD) was present in 11% and Dyslipidemia in 3% of study patients. There was a statistically significant difference in hypertension as a risk factor between the two groups with a p value of 0.03. The other risk factors did not show statistically significant difference between the two groups (**Table 1**).

The patients presented with various chief complaints in Group 1 among which Chest pain and breathlessness were the most common complaints accounting for 31% followed by palpitations(14%) and sweating (12%)(**Figure 3**).The Group 2 patients did not present with specific complaints since most of them came for post-operative follow up or routine checkup.

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Among 50 AMI patients in Group 1, 22 patients were diagnosed with ST elevation myocardial infarction (STEMI) and 28 patients were diagnosed with Non ST elevation myocardial infarction (NSTEMI) **(Figure 4)**

FIGURE 3: Chief complaints of Group 1: AMI patients

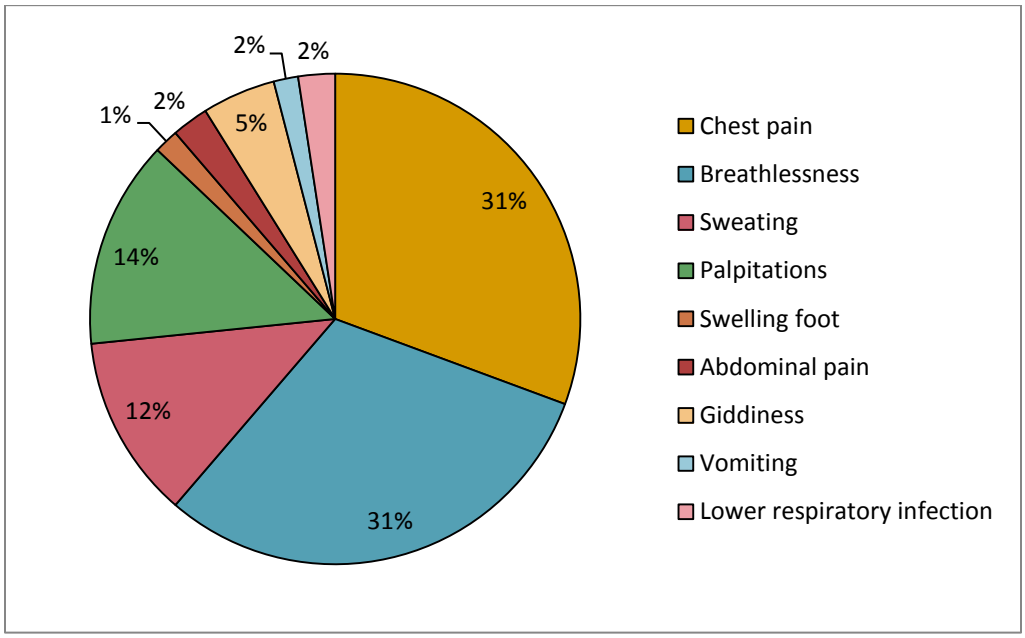
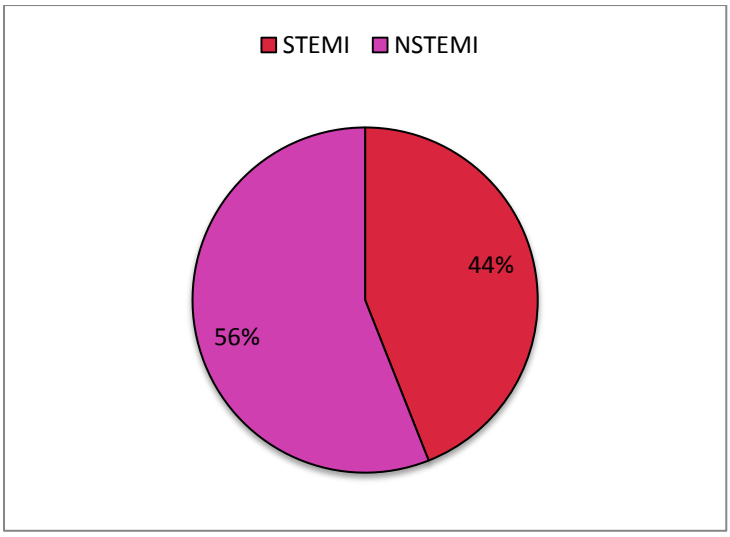


FIGURE 4: Type of MI in Group 1: AMI patients



The mean value of troponin-I was 4286.181 ng/dl. There was a significant increase in Troponin-I value (5310.53 ng/dl) in Group 1 compared to lesser value (3261.82 ng/dl) in group 2 cases. Troponin I values were increased in 48 out of 50 patients in group 1.In group 2, 22 patients had Troponin I value more than 100 ng/dl accounting for high risk of MI(**Table 2**).

Comparison of platelet indices between AMI and stable CAD cases were assessed by independent t test. Our study revealed that mean platelet count in AMI was 246.260 ± 85.05

($x10^3$ / microliter) and in stable CAD patients it was 211.520 ± 71.94($x10^3$ / microliter).We found that the difference was statistically significant between the two groups with a p-value of 0.03.There was no statistically significant difference between the other platelet indices like MPV, PDW and plateletcrit between the two groups(**Table 3**).

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TABLE 1: Comparison of Categorical variables in AMI and Stable CAD

RISK FACTORS	TOTAL	AMI	STABLE CAD	P VALUE
Sex:				
Male	**65**	**28**	**37**	**0.05**
Female	**35**	**22**	**13**	
Diabetes mellitus:				
Absent	**32**	**15**	**17**	**0.66**
Present	**68**	**35**	**33**	
Hypertension:				
Absent	**32**	**21**	**11**	**0.03**
Present	**68**	**29**	**39**	
Dyslipidemia:				
Absent	**97**	**48**	**49**	**0.55**
Present	**3**	**2**	**1**	
COPD:				
Absent	**89**	**44**	**45**	**0.74**
Present	**11**	**6**	**5**	
CKD:				
Absent	**87**	**42**	**45**	**0.37**
Present	**13**	**8**	**5**	
IHD:				
Absent	**88**	**45**	**43**	**0.53**
Present	**12**	**5**	**7**	

P value less than 0.05 is considered statistically significant

TABLE 2: Comparison of Troponin I values in AMI and Stable CAD

Troponin I (with reference range)	AMI	STABLE CAD
Negative(< 1.5 to 19 ng/dl)	0	4
Observation zone(>19 to 99 ng/dl)	2	24
Positive (100 to >100 ng/dl)	48	22

Positive Troponin I value indicates high risk of AMI

TABLE 3: Comparison of platelet indices between AMI and Stable CAD cases

Platelet indices	AMI	Stable CAD	P value
Platelet count ($x10^3$ / microliter)	246.260 ± 85.05	211.520 ± 71.94	0.03

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MPV(fl)	8.22 ± 0.86	8.24 ± 0.93	0.903
PDW (%)	11.296 ± 1.14	11.298 ± 1.27	0.99
Plateletcrit (%)	0.19 ± 0.06	0.16 ± 0.53	0.07

Values expressed as Mean ± SD

Discussion:

Platelets are cytoplasmic fragments of bone marrow megakaryocytes. Almost 1500–2000 of them are released from a single megakaryocyte into the bloodstream, where they circulate for 7–10 days. Platelets have a diameter of 3-5 µm and a volume of 4.5–11 fL .Inactivated platelets are discoid shaped and devoid of nucleus [8].

The primary function of platelets along with the coagulation factors, is haemostasis. Platelets become activated when they interact with each other or with leukocyte and endothelial cells and searches the vascular bed for sites of injury. The platelets undergo a shape change when stimulated thereby increasing their surface area and bioactive molecules stored within their alpha and dense granules molecules are rapidly secreted [9].

In Acute coronary syndrome, the activity of platelets is increased during atherothrombotic events thereby enhancing their size accordingly. The larger platelets are more reactive and produce more proinflammatory and prothrombotic mediators which further leads to coronary related clinical events.

The routine biochemical markers used to detect ACS are Troponin and the MB isoenzyme of creatine kinase (CK-MB). Out of which, Troponin I is considered as the most sensitive and tissue-specific cardiac marker and it is considered to be the gold-standard biochemical tool for ACS risk stratification. The major drawback of this marker is that it remains undetectable in about 40 - 60% of patients suffering from an ACS [10]. This emphasizes the usage of multimarker approach inorder to diagnose the spectrum of clinical manifestation in acute coronary syndrome. Platelet count and platelet indices are the routine, cost effective haematological investigations which can act as a good prognostic marker in ACS.

In the current study, the age of the patients ranged from less than 27 years to 89 years with maximum number of cases seen in above 60 years of age for both males and females. In a similar study done by **Kruthika S Patil et al [11]**, the age of the patients ranged from 30 to 93 years. The comparison of age between the present study and various studies is shown in **Table 4.**

In case of gender, 66 % cases were males and 34% cases were females showing male preponderance. Hence, Males were at more risk of MI compared to females in our study. Similar findings were seen in studies done by **Rabia Parveen et al [12]** and **Siva Prasad Akula et al [13].**

TABLE 4: Comparison of Age in Various Studies

Author	**Year**	**Mean age in years**	
		ACS	**STABLE CAD**
Vitthal Khode et al[22]	2012	54.77 ± 9.09	55.75 ± 11.06
Silpi Pervin et al[20]	2013	55.05±10.73	54.5 ± 10.39
Mohamed A.A et al[27]	2017	65.19 ± 10.95	62.84 ± 9.14
Present study	2019	60.98 ± 14.35	62 ± 9.73

Hypertension and Diabetes mellitus were the two major risk factors in our study. Similar findings were seen in a study done by **Kruthika S Patil et al [11]** in which Hypertension was the major risk factor. Another study done by **Jindal S et al [14]** concluded Diabetes mellitus as a prothrombotic state associated with accelerated atherosclerosis.

In our study, we found that the mean platelet count was significantly higher in AMI(246.260 ± 85.05) than stable CAD cases(211.520 ± 71.94).This was in concordance with the study done by **Paul GK et al**.

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in which the role of platelets in the pathogenesis of STEMI has been demonstrated. The patients with higher platelet count in AMI is associated with higher rate of adverse clinical outcome in ST elevation Myocardial infarction(STEMI) like heart failure, arrhythmia, re-infarction and death[15].

Dawod Sharif et al. found that patients with anterior STEMI treated by primary percutaneous intervention with lower platelet count at admission had higher left anterior descending artery diastolic velocities and better myocardial perfusion. This led to high coronary flow and better function of coronary microcirculation. Patients with higher platelet counts had lower left ventricular systolic function both at admission and before discharge which resulted in larger myocardial injury [16].

The study done by **Awad-Elkareem Abass et al.** found that there was no significant difference in platelet count between AMI and stable CAD cases[17].Another study done by **Abdullah S.Assiri et al(2011)** also did not detect any statistically significant difference in platelet count between three comparative groups comprising of MI, unstable angina and control groups[18].

Our study showed no statistically significant difference in PDW and MPV between the two groups, but few studies showed contrary results. **M.M.Khanderkar et.al [19]** found that among the platelet parameters, PDW and MPV were significantly raised in Acute MI patients when compared with stable CAD patients and control groups. **Silpi Pervin et al [20]** suggested that PDW can be used as an essential biomarker for early detection of ACS. **Vagdatli et al [21]** concluded that the combined usage of MPV and PDW could predict the platelet activation more efficiently. However, **Vitthal Khode et al** [22] found that there was no statistically significant difference in PDW among three groups of patients with AMI, stable CAD and controls.

The contrary results obtained in our study can be attributed to the usage of antihypertensive drugs in 60% of Group 1 patients and antidiabetic drugs in 72 % of group 1 patients. **Gomi T et al[23]** observed that platelet activation in patients with essential hypertension was suppressed by treatment with antihypertensive drugs like alpha blockers and ACE inhibitors which leads to decreased PDW.

Diabetes mellitus is an independent risk factor for cardiovascular disease. A study by **Gloria Formoso et al [24]** showed that antidiabetic drugs like Metformin can decrease platelet activation in Type 2 diabetes mellitus which led to decrease in PDW. Another similar study by **Ilhan Dolasik et al[25]** concluded that after 6 months of treatment with metformin, platelet activation is decreased thereby resulting in reduced MPV in regularly treated diabetic patients.

Plateletcrit is a parameter which gives data about the platelet mass. In our study, we found that the Plateletcrit value was slightly higher in AMI compared to stable CAD group though it was not statistically significant. Our finding was consistent with the study done by **Ugur et al** [26] who reported that high plateletcrit values on admission are independently associated with long-term adverse outcomes in patients with STEMI who undergo primary angioplasty.

In view of conflicting results from various studies, the role of these indices is still a matter of debate. The study has several limitations such as small sample size of the study population , confounding factors and not following-up the patients to examine the prognostic value of our findings. This emphasizes the need of further large scale studies inorder to evaluate the diagnostic and prognostic values of these parameters.

CONCLUSION:

The Cardiac markers are used in the diagnosis and risk stratification of patients with chest pain and suspected acute coronary syndrome. However, the currently available cardiac markers are not sufficiently sensitive in detecting the early stage of ACS.

High platelet count in acute MI seems to be an independent risk factor and correlated with the severity of the coronary atherosclerosis.

We conclude that the Platelet parameters, especially the Platelet count is an inexpensive and a good prognostic marker which can be easily adapted in clinical setup as a routine and economical test in detecting an impending acute coronary event.

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