Original Article

Evaluation of Platelet Indices in Acute Coronary Syndromes and Diabetes Mellitus

Mathumithra. T[1]*, Roopa Urs[1], Shreya[2], Bhavani S[1] and Dhananjay Kotasthane[1]

[1]Department of pathology, Mahatma Gandhi Medical College and Research Institute, Puducherry, INDIA.
[2]Mahatma Gandhi Medical College and Research Institute, Puducherry, INDIA.

Keywords: *Acute Coronary Syndromes, Mean Platelet Volume.*

ABSTRACT

Background: Acute Coronary Syndrome (ACS) is the most common cause of adult mortality worldwide. Atheromatous plaque with superimposed thrombus is the commonest underlying cause. Platelets play a pivotal role initiating a thrombus, larger platelets being metabolically more active than the smaller ones. Hence the aim is to study the changes in platelet volume indices and platelet count in acute coronary syndromes and diabetes mellitus.

Methods: This was a comparative study of 120 people (60 controls, 60 with ACS). ACS patients were subdivided as those with and without diabetes. Blood was collected in EDTA anticoagulated tubes. The platelet indices and platelet count were assayed using 8 part hematology analyzer (HORIBA) and compared among the groups.

Result: Mean platelet volume (MPV) and platelet distribution width (PDW) were significantly raised in ACS patients, being higher in ST elevation Myocardial infarction(STEMI) followed by Non-ST elevation Myocardial infarction (NSTEMI), unstable angina(UA) and controls. The mean values of MPV and PDW were 8.86fl and 15.24% in STEMI, 8.76fl and 14.62% in NSTEMI, 8.17fl and 13.54% in UA, 8.04fL and 12.74% in controls respectively. Plateletcrit and platelet count did not show significant variation among the groups. Both MPV and PDW were higher in diabetic ACS patients (8.66 fl and 15.71%) than the non-diabetics(8.17 fl and 14.2%).

Conclusion: Patients with acute coronary syndromes and diabetes had higher MPV and PDW compared to the controls. Measurements of platelet volume indices may be of some benefit in detecting those patients at higher risk for acute coronary events.

***Corresponding author:**
Dr. Mathumithra.T, No.89, High school road, Kirumampakkam, Puducherry, 607402 India.
Phone: +91 8870181486, 0413-2611123
Email: madhumithra59@yahoo.com

Introduction

Thrombosis and its complications like embolism are a global pandemic contributing significantly to adult mortality worldwide.[1] In the new era of non-communicable diseases, the problem of coronary artery disease(CAD) and its related emergency like acute coronary syndromes(ACS) balloons out huge afflicting significantly a large proportion of Indians.[2] The spectrum of ACS includes unstable angina (UA), Non-ST Elevation Myocardial infarction (NSTEMI), ST Elevation myocardial infarction (STEMI). The most common cause underlying ACS is a ruptured or complicated atherosclerotic plaque with a superimposed thrombus.[3,4] It is well known that platelets are activated along with the coagulation cascade at the onset of thrombosis. During activation, the platelets change their morphology, develop pseudopodia and release a number of substances enhancing the formation of thrombus. Larger platelets are haemostatically more active and are a risk factor for developing coronary thrombosis, leading to myocardial infarction. Platelet indices also vary in diseases like diabetes, hypertension, obesity, hyperlipidemia etc. [5] Hence it is wise to study the distribution of platelet indices in patients with established clot activation and analyze whether they change significantly in comparison to healthy adults.

Hence our aims were to study and compare the distribution of platelet count and platelet indices

- In patients with acute coronary syndromes, unstable angina (UA), Non-ST Elevation Myocardial infarction (NSTEMI), ST Elevation myocardial infarction(STEMI)) in comparison to the age and sex matched controls.
- In diabetic ACS patients Vs non-diabetic ACS patients

Materials and Methods

A prospective comparative hospital-based study was carried out on 60 ACS patients and 60 matched controls for a period of three months (from July 2016 to September 2016). All patients diagnosed with ACS were included in the study and compared with the controls. Sex and age matched non-diabetic patients admitted in the hospital for other non-thrombotic diseases with no cardiac symptoms, no history of ischemic heart disease and normal electrocardiogram were included as controls. The study was approved by the Institute Ethics Committee.

Inclusion criteria

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

Exclusion Criteria: Patients with bleeding diathesis, major operations or trauma (in past two weeks), malignant hypertension (>180/110mm of Hg). Patients presenting with Acute Coronary Syndromes within 24 hours were inclued. All subjects (both cases and controls) were inter-viewed as per the pre-prepared proforma. The blood samples of the patients on admission (before treatment) were collected as a part of emergency protocol and sent for complete blood count(CBC) and cardiac marker analysis. Samples for CBC were collected in EDTA coated vaccutainers. The sample was run within two hours of venepuncture using the 8 part differential automated Hematology analyzer (HORIBA) and complete blood count analysis of the sample was made including the platelet indices (MPV, PDW, Plateletcrit). Relevant investigations like electrocardiogram and cardiac enzymes (Creatine Kinase-MB and Troponin T) 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. All parameters were compared between the two groups of cases and controls.

Statistical Analysis: The categorical variables were expressed as frequencies or percentages. Quantitative variables were expressed as mean ± standard deviation. The means of continuous variables were compared using independent samples t-test (between two groups ACS and controls, diabetics and non-diabetics). One way ANOVA was used for comparing the continuous variables among the various subgroups of ACS. All the tests were two-tailed; $p<0.05$ was considered statistically significant.

Result

Of the 60 cases, 46 were males and 14 females. The mean age of patients was 57±11.6years. Among the ACS patients, 13(21.6%) had unstable angina, 20(33.3%) had NSTEMI and 27(45%) had STEMI. 38/60(63.3%) patients had diabetes mellitus. The cardiac markers, Troponin T was increased in 26 (43.3%) patients and CKMB in 31(51.6%) patients. The most common risk factor for ACS syndromes, next to diabetes was hypertension followed by smoking. 34(56.6%) patients were hypertensives and 23(38.3%) were smokers.

The platelet count, 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 controls. The mean of MPV and PDW for the control group, for unstable angina,

for STEMI & NSTEMI is shown (Table 1). The MPV(in fl) was highest in ST-Elevation Myocardial Infarction group (8.86±0.96)followed by Non-ST-Elevation Myocardial Infarction(8.76±1.04) and unstable angina (8.17±0.77) when compared to the control group(8.04±.59) and this was statistically significant (p-0.000).Similarly, the PDW (in %) was highest in ST-Elevation Myocardial Infarction group (15.24±2.295)followed by Non-ST-Elevation Myocardial Infarction(14.62±2.14) and unstable angina (13.74±.89) when compared to the control group(12.54±0.81). The p value was 0.000.

Similarly platelet count and plateletcrit was compared among the groups .The platelet count was lowest in STEMI compared to the NSTEMI, unstable angina and controls but was not statistically significant (Table 1). In contrast, Plateletcrit was lower among the controls than the cases.

The ACS patients were subcategorized as those with and without diabetics and their platelet indices were compared and also with the controls. Among the indices, MPV and PDW was higher in the diabetics compared to the non-diabetics and controls (p value-0.000) whereas the platelet count and plateletcrit failed to prove such significance (Table 2).

Table 1: Distribution of platelet indices.

Parameters	Controls (n=60)	Unstable angina (n=13)	NSTEMI* (n=20)	STEMI** (n=27)	p value (among 4 groups)	Cases (n=60)
Platelet count(lakhs/cmm)	2.8±1.06	2.9±0.5	2.87±0.91	2.6±0.71	0.791	2.78±0.75
MPV(fl)	8.04±0.59	8.17±0.77	8.76±1.04	8.86±0.96	0.000	8.68±0.97
PDW(%)	12.54±0.8	13.74±.897	14.62±2.14	15.24±2.295	0.000	14.7±2.07
PLCT(%)	0.22±0.07	0.24±0.07	0.26±0.08	0.25±0.06	0.2	0.25±0.076

*- Non-ST segment elevation Myocardial Infarction.; **- ST segment elevation Myocardial Infarction.

Table 2: Distribution of platelet indices.

Parameters	Controls (n=60)	Diabetic ACS* (n=38)	p value (among 2 groups)	Non-diabetic ACS* (n=22)	p value (among 3 groups)
Platelet count (lakhs/cmm)	2.84±1.06	2.67±0.56	0.31	2.98±0.99	0.43
MPV(fl)	8.04±0.59	8.66±0.94	0.000	8.17±1.04	0.000
PDW(%)	12.54±0.81	15.71±1.9	0.000	14.2±2.3	0.000
Plateletcrit(%)	0.22±0.07	0.24±0.06	0.17	0.27±0.09	0.06

*- acute coronary syndromes.

Discussion

The burden of cardiovascular diseases is increasing globally, accounting for approximately 12 million deaths annually.[6] Though multifactorial in etiology, many risk factors are strongly associated with ischemic heart disease (IHD) and henceforth atherosclerotic plaque formation, during which platelets play a vital role. Studies prove larger platelets have more prothrombotic activity, because of more dense granules.[7] In such a scenario (Acute coronary syndromes in our study) it is logical to reason out the increase in MPV and PDW. Inspite of the small sample size of our study, our results corroborate findings in previous studies emphasizing MPV and PDW as hematolological markers to assess thrombotic risk.

In our study, MPV and PDW was highest among the MI patients compared to those of unstable angina and age and sex matched controls. Studies in literature support the same. In a study by Manchanda et al, [6] MPV and PDW was highest in NSTEMI, followed by STEMI and unstable angina. In our study no significant reduction in plateletcrit was obtained. In a study by Costa et al,[8] similar findings were obtained whereas a study by Pipliwal et al[9] showed significant lowering of plateletcrit in ACS patients compared to the controls. Platelet large cell ratio is yet another controversial platelet index measured only in some hematology analyzers. Discordant results were obtained in literature search, with few studies demonstrating increase in P-LCR in ACS patients with reference to the controls and others showing nil significance.[6,9,10]

Though controversial, platelet count was evaluated along with the platelet indices in most such studies. Our study showed no significant difference in platelet count between the controls and ACS patients and among the sub-categories of ACS. A study by Assiri et al[11] shows similar results whereas many studies also show significant lowering of platelet count.[8,9, 12]

Most studies show MPV as a reliable marker of predicting cardiovascular risk and also the treatment outcomes. [5,13,14] Chu et al. present a systematic review and a meta-analysis emphasising the value of MPV as a predictor of

cardiovascular risk.[15] In a study by Slavka et al, MPV is shown to predict the vascular mortality following ischemic heart disease.[16] Another study showed MPV as a predictor of acute stent thrombosis in ACS patients.[14] In our study, follow up of the patients was not done.

Inspite of so many studies demonstrating the utility of MPV as a predictive marker, in

reality, it is a parameter which is subjected to biological and technical variations.[5]The platelet parameters derived by the automated cell counter are highly specific to the individual technologies developed for each type of analyzer.[5] With impedance counting, the MPV increases over time as platelets swell in EDTA, with increases of 7.9% within 30 min having been reported and an overall increase of 13.4% over 24 hours, although the majority of this increase occurs within the first 6 hours.[17] Conversely when MPV is measured by an optical light scatter system derived from the modal platelet size, the MPV decreases over time, possibly as a result of the dilution of cytoplasmic contents leading to a decrease in light scatter. [5] Second, MPV values can be influenced by type of anticoagulant used and the delay in time from sampling to analysis. In a study by Vagdatli et al,[18] where MPV was recorded hourly for four hours, there was a steady increase in MPV in EDTA anticoagulated blood. The reason is that platelets swell with time in EDTA blood. Hence, by standardizing the time delay between sampling and analysis and by using a alternative anticoagulant (like citrate), MPV can be reliably measured. [5]Over the past 20 years, platelet analyzers have been developed. Additional analyzer derived platelet parameters have been developed, such as the measurement of an immature platelet fraction and platelet large cell ratio, may provide information comparable to the MPV.[19]

In addition to the technical variation, MPV is influenced by a variety of hematological (eg-platelet function disorders, ITP etc) and non-hematological disorders like diabetes, hypertension, COPD, drug intake etc.[5,20,21] Studies prove increased MPV values in patients with diabetes mellitus compared to the controls. Diabetics with complications had a higher MPV compared to those without complications.[22]Our study also proves the same. When these variations are given a thought, appropriate measures taken and then analyzed in special settings like acute coronary syndromes, it will definitely prove a specific and reliable assessement marker.

Our study has some limitations. Owing to the short duration of study period, sample size was small. Follow up of the patients was not done hence implication of the platelet indices on the treatment outcome and overall morbidity and mortality was not assessed. Platelet function tests was not done to support the prothrombotic nature of the disease.

Conclusion

We conclude saying MPV and PDW is increased in ACS patients compared to the controls, values being higher in MI group than those with unstable angina. Both the parameters were also higher in the diabetic patients than the non-diabetics. Hence, the results of the present study appear to substantiate that increased MPV can serve as a predictive marker of prothrombotic state in ACS patients.

Acknowledgements

Dr. Dhananjay Kotasthane, Professor and head, Department of Pathology, Mahatma Gandhi Medical College and Research Institute, Puducherry-607 402, India

Funding

None

Competing Interests

None Declared

References

1. Lippi G, Filippozzi L, Salvagno GL, Montagnana M, Francwhini M et al. Increased Mean Platelet Volume with Acute Coronary Syndromes. Arch Pathol Lab Med 2009;133:1441-3.
2. Gupta R. Burden of coronary heart disease in India. Indian Heart J 2005;57:632-8
3. Obeidi SR, Ahmedm SH, Obeid FA. Evaluation of Platelet Indices in Patients with Acute Coronary Syndrome. Mustansiriya Medical Journal 2013; 12 :58 -64.
4. Kumar V, Abbas AK, Fauselto N, Aster JC. Robbins and Cotran Pathologic Basis of Disease. Eighth edition. New Delhi.2010:547-558.
5. Machin SJ, Briggs C. Mean platelet volume: a quick, easy determinant of thrombotic risk? J Thromb Haemost 2010;8:146–7.
6. Manchanda J, Potekar RM, Badiger S, Tiwari A.The study of platelet indices in acute coronary syndromes. Annals of pathology and laboratory medicine 2015;2:30-5.
7. Bray PF .Platelet Hyperreactivity: Predictive and intrinsic properties. Hematol Oncol Clin North Am. 2007;21:633–6.
8. Costa SC, de Matos Vinagre CG, Chacra APM , de Azevedo MRA. Platelet Indices in Patients with Acute Coronary Syndrome. Journal of Biosciences and Medicines 2015;3:71-6.

9. Pipliwal PS, Singh G, Ishran R, Bansal S. Mean platelet volume and other platelet volume indices in patients with acute myocardial infarction: A case control study. Journal of Dental and Medical Sciences Volume 2015;14: 35-8.
10. Khandekar MM, Khurana AS, Deshmukh SD, Kakrani A L, Katdare A D, Inamdar A K Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario. J Clin Pathol 2006;59:146–9.
11. Assiri AS, Jamil AM, Mahfouz AA, Mahmoud ZS, Ghallab M. Diagnostic importance of platelet parameters in patients with acute coronary syndrome admitted to a tertiary care hospital in southwest region, Saudi Arabia.J Saudi Heart Assoc 2012;24:17–21.
12. Yaghoubi A, Golmohamadi Z, Alizadehasl A, Azarfarin R. Role of platelet parameters and haematological indices in myocardial infarction and unstable angina. J Pak Med Assoc 2013;63:1133-7.
13. Balli M, Taşolar H, Çetin M, Cagliyan CE, Gözükara MY, Yilmaz M et al. Relationship of platelet indices with acute stent thrombosis in patients with acute coronary syndrome. Postep Kardiol Inter 2015;11:224–9.
14. Ranjith MP, DivyaRaj R, Mathew D et al. Mean platelet volume and cardiovascular outcomes in acute myocardial infarction. Heart Asia 2016;8:16–20.
15. Chu SG, Becker MD, Berger PB, Bhatt DL, Eikelboom JW, Konkle B et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. J. Thromb Haemost 2009;8:148–56.
16. Slavka G, Perkmann T, Haslacher H, Greisenegger S, Marsik C,Wagner OF .Mean Platelet Volume May Represent a Predictive Parameter for Overall Vascular Mortality and Ischemic Heart Disease. Arterioscler Thromb Vasc Biol. 2011;31:1215-8.
17. Bowles KM, Cooke LJ, Richards EM, Baglin T. Platelet size has diagnostic predictive value in patients with thrombocytopenia. Clin Lab Haematol 2005;27:370-3.
18. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. Hippokratia 2010;14:28-32.
19. Briggs C, Kunka S, Hart D, Oguni S, Machin SJ. Assessment of an immature platelet fraction (IPF) in peripheral thrombocytopenia. Br J Haematol 2004;126:96–9.
20. Papanas N, Symeonidis G, Maltezos E, Mavridis G, Karavageli E, Vosnakidis T. Mean platelet volume in patients with type 2 diabetes mellitus. Platelets 2004;15:475-8.
21. Hekimsoy Z, Payzinb B, Ornek T, Kandogan G. Mean platelet volume in type 2 diabetic patients. J Diabetes Complications. 2004;18:173–6.
22. Badiger R, Hosalli A, Ashwin S, Dinesha SV, Abhishek, Vijayalakshmi. Platelet indices in patients of acute coronary syndrome patients in tertiary care hospital. International Journal of Applied Research 2015;1:731-4.