A study of association between platelet volume indices and ST elevation myocardial infarction

Bhawani Yasassri Alvitigala [a],[*],[1], Mohammedu Aroos Fathima Azra [a],[1], Darshana Udakara Kottahachchi [a],[1], Madduma Mudiyanselage Priyamali Thusharika Jayasekera [b],[1], Rajapaksha Arachchige Namal Kumarasiri Wijesinghe [c],[1]

[a] Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, General Sir John Kotelawala Defence University, Sri Lanka
[b] Department of Clinical Sciences, Faculty of Medicine, General Sir John Kotelawala Defence University, Sri Lanka
[c] Department of Clinical Sciences, Faculty of Medicine, General Sir John Kotelawala Defence University, Ratmalana, Sri Lanka

ARTICLE INFO

ABSTRACT

Introduction and objective: ST elevation myocardial infarction (STEMI) is caused by formation of a thrombus at a ruptured atheromatous plaque. Larger platelets are enzymatically and metabolically more active and play a crucial role in thrombus formation. Our objective was to study the association between platelet volume indices (mean platelet volume (MPV) and platelet distribution width (PDW)) and STEMI.

Methods: A hospital-based case control study to compare the platelet indices of 52 STEMI patients before commencing antiplatelet therapy and age and gender matched 52 controls who had no history of ischemic heart disease or antiplatelet therapy. Blood samples were collected to EDTA bottles and analyzed using Mindray BC 6800 automated analyzer.

Results: STEMI patients had significantly increased mean MPV and PDW compared to the control group ((8.22 ± 0.99 fL vs 7.74 ± 0.69 fL, $p = 0.005$) and (15.81 ± 0.41 fL vs 15.62 ± 0.33 fL, $p = 0.007$) respectively). Significant positive correlation existed between MPV and PDW ($R = 0.556$, $p = 0.000$) and weak negative correlation in platelet count with MPV ($R = -0.323$, $p = 0.019$) and PDW ($R = -0.309$, $p = 0.026$) of STEMI patients. Receiver Operating Characteristic (ROC) curves showed that MPV and PDW with cutoff values of 7.55 fL, 15.55 fL and with Area under the curve (AUC) of 0.640, 0.620 respectively. The sensitivities and specificities were found to be 73.1%, 69.2% and 61.5%, 55.8% for MPV and PDW respectively.

Conclusion: Increased MPV and PDW were found to have a significant association with STEMI and this test has the potential to be used as a preliminary test to identify high-risk patient for myocardial infarction.

1. Introduction

Myocardial infarction causes the most number of deaths in both developed and developing countries [1,2]. Sudden occlusion of the coronary artery by a thrombus leads to myocardial infarctions. According to the estimations of World Health Organization [3], 1 in every 3 people (31% of all deaths) die of cardiovascular diseases in developed countries and coronary artery disease is the most common cause for those. In Sri Lanka, 40% of deaths of non-communicable diseases were due to coronary artery disease [3]. Mortality due to coronary heart diseases in Sri Lanka is 25.7% (32,582 deaths) and the age adjusted death rate

was 154.7 per 100,000 of Sri Lankan populations which rank Sri Lanka in number 31 in the world [3].

Platelets play a crucial role in the thrombus formation after the rupture of an atherosclerotic plaque. There will be increased release of larger platelets with more dense granules that are highly active metabolically and enzymatically. Platelets with greater prothrombotic potential have higher levels of thromboxane A2, beta thromboglobulin, and intracellular and surface procoagulant proteins. More reactive platelets will undergo morphological changes in the cell by forming pseudopodia, thus participating in the thrombus formation. As a result, platelets will become larger and reactive, thus increasing the platelet volume indices; MPV and PDW [4,5].

MPV and PDW are platelet volume indices obtained from the full blood count (FBC). Although MPV measures the average size of platelets, it is also considered as a marker of platelet function and activation. High MPV values indicate hypercoagulability of the platelet or thrombosis [6–10]. PDW reflects the variance in platelet size due to

* Corresponding author at: 125/A, Thalawathugoda Road, Pitakotte 10100, Sri Lanka.
E-mail address: yasassri.alvitigala@gmail.com (B.Y. Alvitigala).
[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

active platelet release. The PDW increases when there are increased numbers of larger platelets as well as smaller platelets in the circulation. It indicates the heterogeneity of platelet sizes by providing the relative width of distribution of platelets by volume. It could also be used as a marker of platelet reactivity as well as an index for short term mortality of coronary artery disease and the risk of thrombolysis failure [11]. Further, PDW is considered as a more specific parameter for the activation than MPV, as it does not increase during simple platelet swelling [12–19].

Our aim was to study the association between platelet indices and STEMI patients compared to a control group and assess the possibility to use them in the preliminary diagnosis of STEMI.

2. Material and methods

A case control study was carried out at the Teaching Hospital, Kurunegala, Sri Lanka from 1st of June 2017 to 1st of October 2017. The ethical approval for the study was obtained from the ethical review committee of Teaching Hospital, Kurunegala.

The sample size was calculated to allow the detection of 30% difference in MPV and PDW between groups and α of 0.05. A total of 104 patients who presented to the emergency department were enrolled in the study.

Two groups were enrolled in the study, each consisting of 52 patients. Patients > 18 years were included in the study.

Group A: Patients presented with myocardial infarction for the 1st time and diagnosed as STEMI by 12-lead electrocardiogram were selected as the study group.

Group B: Age and gender matched controls who had no history of coronary artery diseases or other cardiac disorders and admitted only due to trauma were enrolled.

Patients having any previous long term medical problems and drug therapies, primary platelet disorders, bleeding/clotting disorders, any other cardiac related problems, cancers and chronic kidney disorders with eGFR<60 mL/min/1.73 m^2, pregnancy and blood transfusions within 3 months prior to the study were excluded.

Blood samples were collected to dipotassium ethylenedinitrotetraacetic acid (EDTA) tubes prior to the antiplatelet therapy. All the other data were obtained from the patient's history after getting their consent. Fully automated, daily quality control monitored 5-part Mindray 6800 BCE analyzer was used for full blood count analysis including platelet indices (platelet count, MPV and PDW).

2.1. Statistical analysis

All clinical and laboratory data analysis was done using statistical software; SPSS version 23.0.0.0 (released 2015, IBM statistics for Windows version 23, IBM Corp., Armonk, NY). Descriptive analysis was done for social-demographic characteristics and laboratory test data. Association between the parameters was analyzed using Paired t-test, one-way ANOVA and linear regression analysis. Receiver operating characteristic curve (ROC) were obtained for MPV and PDW.

The p-value < 0.05 was considered as a significant association between the parameters. Data were expressed as mean ± SD. Normal reference range of platelet count was taken as 150–450 × 10^9/L, for MPV; 6.1–12.0 fL and for PDW; 9–17 fL which were used as reference ranges at Teaching Hospital, Kurunegala.

3. Results

A total of 104 patients were selected and divided into two groups of 52 each, who were diagnosed as STEMI group and age and gender matched controls. Majority of the STEMI patients were males (83%). The baseline characteristics and platelet parameters were depicted in the Table 1.

Table 1
Baseline characteristics and platelet parameters in STEMI and controls.

	STEMI group (n = 52)	Control group (n = 52)	p value*
Gender			
Male	43 (83%)	43 (83%)	
Female	9 (17%)	9 (17%)	
Age (years)	55.9 ± 7.8	55.6 ± 8.0	0.054
Minimum	40	39	
Maximum	69	69	
Platelet count (×10^9/L)	233.9 ± 58.9	246.9 ± 67.4	0.276
Minimum	156	151	
Maximum	450	420	
MPV (fL)	8.2 ± 0.1	7.7 ± 0.7	0.005
Minimum	6.5	6.1	
Maximum	10.4	8.9	
PDW (fL)	15.8 ± 0.4	15.6 ± 0.3	0.007
Minimum	15.1	14.9	
Maximum	16.9	16.3	

fL: femtoliter, MPV: Mean Platelet Volume, PDW: Platelet Distribution Width.
Values are presented as mean ± SD.
*p < 0.05 was considered statistically significant.
All the individuals of the selected population were Sri Lankan Sinhalese.

Platelet count was not significantly different among groups (p = 0.276), although its value is slightly higher in controls than the STEMI group. MPV was significantly higher in STEMI patients than that of control group (p = 0.005). PDW was also significantly higher in STEMI group compared to the control group (p = 0.007) (Table 1).

Linear regression analysis was performed to determine the correlations between platelet count and platelet volume indices among both groups. Accordingly, there were statistically significant weak negative correlation between platelet count and MPV (r = −0.323, r^2 = 10.4%, p = 0.019), PDW (r = −0.309, r^2 = 9.6%, p = 0.026) and strong positive correlation between MPV and PDW (r = 0.556, r^2 = 31.0%, p = 0.000) of STEMI group. However, the correlation between platelet count and MPV (r = −0.254, r^2 = 6.4%, p = 0.069), and PDW (r = −0.166, r^2 = 2.8%, p = 0.240) were not significant in control group and there was a moderately positive correlation between MPV and PDW (r = 0.410, r^2 = 16.8%, p = 0.003) (Table 2).

Furthermore, ROC curve analysis was performed to obtain optimum cut-off values at maximum sensitivity and specificity that were useful diagnostic tool to detect STEMI cases from controls (area under curve (AUC) = 0.620, 95% confidence interval (CI) 0.513–0.727; AUC = 0.640, 95% CI 0.533–0.747 for PDW and MPV respectively). The best cut-off points, sensitivity, specificity for identifying STEMI for PDW and MPV were 15.55 fL, 69.2%, 55.8% and 7.55 fL, 73.1%, 61.5% respectively.

Table 2
Correlation between platelet parameters of STEMI and control groups.

	STEMI (n = 52)	Control (n = 52)
Platelet count and MPV		
r	−0.323	−0.254
r^2 (%)	10.4	6.4
p value*	0.019	0.069
Platelet count and PDW		
r	−0.309	−0.166
r^2	9.6	2.8
p value*	0.026	0.240
MPV and PDW		
r	0.556	0.410
r^2	31	16.8
p value*	0.000	0.003

MPV: Mean platelet volume, PDW: Platelet distribution width.
*p < 0.05 was considered statistically significant.

4. Discussion

Coronary artery disease is the leading cause of mortality and morbidity all over the world. Platelets play a major role in thrombus formation in the pathogenesis of myocardial infarction during atherosclerotic plaque rupture. Platelets become larger in size and become metabolically and enzymatically active due to formation of dense granules. The platelet size and reactivity can be easily measured by platelet volume indices, MPV and PDW, obtained from FBC.

The current study examined the association of MPV and PDW with STEMI patients at Kurunegala Hospital, Sri Lanka. There were two hypotheses developed in assessing the parameters. In the first hypothesis, activated platelets have an increase in size. Second, more platelet activation and aggregation will lead to release of younger platelets from bone marrow, hence there is a heterogeneity in the size of platelets in circulation. We found that the patients with STEMI had significantly higher MPV and PDW compared to the control group, while no statistical difference regarding platelet count although it is higher in controls than cases. Based on the results of MPV and PDW, it has clearly supported the confirmation of above hypothesis as high MPV indicates the increase in average size of platelets whereas high PDW indicated the reactivity and heterogeneity in size of platelets.

Both control and study populations of this study were selected from the emergency department of the same hospital to maintain the study population from the same area. Accordingly control group consisted of trauma patients admitted to the emergency department of the same hospital except the normal population. As traumatic patients didn't show any thrombotic conditions at the time of clinical diagnosis, their MPV and PDW values were in normal range.

However, in previous studies, there had been a significant difference of mean platelet counts between cases and controls [1,6,23]. Most of the studies have shown that MPV was significantly higher in cases than controls [1,6,22,23]. whereas in some it was not significant [20]. PDW is significantly higher [1,6,20–23] in cases than controls (Table 3).

Reddy et al. [21] selected 173 STEMI patients and 191 controls where MPV and PDW were significantly higher than controls and seem to be an independent risk factor for STEMI and correlated with the severity of the STEMI. They can be used as a simple, reliable, and economical method for predicting an impending acute coronary event. Similarly, Akula et al. [20] has done the study on 60 STEMI and 60 control individuals while Patil et al. (2017) had 25 individuals in each STEMI and control groups. Both these study have shown that MPV and PDW were significantly higher in STEMI than controls and hence could be used as a simple, reliable and readily available parameter in predicting the severity of STEMI (Table 3). The results of the above two studies including the population size were much comparable with the results of the present study. Hence, significance in MPV and PDW of present study could resemble the importance of those parameters in predicting the severity of STEMI as a simple and cost-effective method.

Moderately and strongly positive correlations between MPV and PDW in STEMI and control groups express that the parameters are directly associated with platelet characteristics. Highly prothrombotic larger platelets will increase MPV while simultaneously increasing the PDW as there are both smaller and larger platelets in circulation (heterogeneity in size).

As there was a significant difference between STEMI and the control group, establishment of a cutoff value for MPV (7.55 fL) and PDW (15.55 fL) would be beneficial to use them as screening parameters for CAD patients and contrast them from non-coronary artery disease patients in the routine practice. Since AUC values of MPV (AUC = 0.620) and PDW (AUC = 0.640) of our study were in the fair range of AUC interpretation, it is normal to have cut off values closer to the mean values of MPV and PDW of the control group. Other than above reason, the low values for AUC, fair sensitivity and specificity for above parameters may be due to the small sample size selected under a broad range of exclusion criteria. Our population was pure although the population size was small, as subjects were not under any drug therapy before the blood collection.

The measured parameters of MPV and PDW in current study are comparable with those of previous studies, which showed that those parameters can be used as diagnostic tests [1,6,13,15,16]. Platelet volume indices are markers that can be easily adapted in the routine clinical setup to assess the risk of a STEMI.

The limitations of this study include small size of the study population and not following-up the patients to examine the prognostic value of our findings. Further large-scale studies are required to evaluate the diagnostic and prognostic values of these parameters.

5. Conclusion

Current study clearly showed that MPV and PDW were significantly increased in STEMI patients than the control group. The developed cutoff values in a fair sensitivity and specificity could be used in clinical practice. Thus, the MPV and PDW has the potential to be used as a preliminary test to identify high-risk patients for myocardial infarction along with other supportive clinical investigations.

Measurements and abbreviations

MPV and PDW was expressed in fL (femtolitres). Platelet count was given in ($\times 10^9$/L).

MPV: Mean Platelet Volume; PDW: Platelet Distribution Width; STEMI: ST Elevated Myocardial Infarction

Funding

Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2018.09.001.

Table 3
Comparison of platelet parameters of previous studies.

Publisher	Parameter	Cases	Controls	P value
Sharma et al. [1]	Platelet count	264	285	0.001
	MPV	10.3	8.1	<0.001
	PDW	15.1	10.7	<0.001
Adel et al. [6]	Platelet count ($\times 10^9$/L)	261	252	0.002
	MPV (fL)	10.4	10.2	0.041
	PDW (fL)	15.3	15.5	0.030
Akula et al. [20]	Platelet count	–	–	–
	MPV	11.6	10.5	0.04
	PDW	17.3	15.2	0.0001
Cetin et al. [21]	Platelet count	278.1	27.1	0.532
	MPV	8.8	8.6	0.003
	PDW	17.2	16.4	<0.001
Patil et al. [22]	Platelet count	–	–	–
	MPV	10.5	9.7	0.000
	PDW	13.9	12.8	0.000
Reddy et al. [23]	Platelet count	273.7	257.1	0.017
	MPV	10.2	8.5	<0.005
	PDW	17.8	16.3	<0.001
Present study	Platelet count	233.9	246.9	0.276
	MPV	8.2	7.7	0.005
	PDW	15.8	15.6	0.007

fl: femtoliter, MPV: Mean Platelet Volume, PDW: Platelet Distribution Width.
Values are presented as mean ± SD.
*$p < 0.05$ was considered statistically significant.

References

[1] D. Sharma, M. Pandey, J. Rishi, Study of platelet volume indices in patient of coronary artery diseases, J. Sci. Innov. Res. 5 (5) (2016) 161–164.

[2] E. Vagdatli, E. Gounari, E. Lazaridou, et al., Platelet distribution width: a simple, practical and specific marker of activation of coagulation, Hippokratia 14 (1) (2010) 28–32.

[3] World Health Organization, Non-Communicable Diseases: Country Profiles 2014, Available from: http://www.who.int/nmh/countries/lka_en.pdf?ua=1 2014, Accessed date: 2 February 2017.

[4] M.M. Khandekar, A.S. Khurana, S.D. Deshmukh, et al., Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario, J. Clin. Pathol. 59 (2) (2006) 272–275.

[5] R. Pal, R. Bagarhatta, S. Gulati, et al., Mean platelet volume in patients with acute coronary syndrome: a supportive diagnostic predictor, J. Clin. Diagn. Res. 8 (8) (2014) (MC01-04).

[6] M.H. Adel, M. Seyedian, M. Jafarsalehi, et al., Is any correlation between platelet indices with extent of coronary artery involvement in ischemic heart diseases? Health 8 (12) (2016) 1266–1274.

[7] A. Bekler, M.T.A. Ozkan, E. Tnekecioglu, et al., Increased platelet distribution width is associated with severity of coronary artery disease in patients with acute coronary syndrome, Angiology 66 (7) (2014) 638–643.

[8] S.B. Biradar, S.V. Kashinakunti, R. Manjula, Platelet volume indices in acute coronary syndrome – a case control study, Int. J. Adv. Med. 3 (2) (2016) 349–352.

[9] M. Cetin, E.F. Bakirci, E. Baysal, et al., Increased platelet distribution width is associated with ST-segment elevation myocardial infarction and thrombolysis failure, Angiology 65 (8) (2014) 737–743.

[10] D.H. Choi, S.H. Kang, H. Song, Mean platelet volume: a potential biomarker of the risk and prognosis of heart disease, Korean J. Intern. Med. 31 (6) (2016) 1009–1017.

[11] R. Surendran, K. Ganesamoorthy, Relationship of platelet distribution width and white blood cell count on admission with ST-segment resolution in patients with ST-elevation myocardial infarction thrombolysed with streptokinase, J. Med. Dent. Sci. 15 (8) (2016) 147–172.

[12] H.R. Varasteh-ravan, S. Ali-Hassan-Syegh, S. Shokraneh, et al., Relationship of admission mean platelet volume, platelet distribution width and white blood cells with ST resolution in patients with acute ST segment elevation myocardial infarction treated with streptokinase without history of previous cardiovascular surgery, Perspect. Clin. Res. 4 (2) (2013) 125–129.

[13] M.R. Dehghani, L. Taghipour-sani, Y. Rezaei, et al., Diagnostic importance of admission platelet volume indices in patients with acute chest pain suggesting acute coronary syndrome, Indian Heart J. 66 (2014) 622–628.

[14] I.I. El-Dosouky, I.E. Shehata, Value of the mean platelet volume in evaluation of patients with acute coronary syndrome, J. Med. Diagn. Methods 5 (1) (2016) 1–5.

[15] V. Khode, J. Sindhur, D. Kanbur, et al., Mean platelet volume and other platelet volume indices in patients with stable coronary artery disease and acute myocardial infarction: a case control study, J. Cardiovasc. Dis. Res. 3 (2012) 272–275.

[16] A.Z. Mirzaie, A. Abolhasani, B. Ahmadinejad, et al., Platelet count and MPV, routinely measured but ignored parameters used in conjunction with the diagnosis of acute coronary syndrome: single study center in Iranian population, 2012, Med. J. Islam Repub. Iran 26 (1) (2012) 17–21.

[17] A. Maseri, S. Chierchia, G. Davis, Pathophysiology of coronary occlusion in acute infarction, Circulation 73 (2) (1986) 233–239.

[18] U.K. Ranawaka, C.N. Wijekoon, A. Pathmeswaran, et al., Risk estimates of cardiovascular diseases in a Sri Lankan community, Ceylon Med. J. 61 (2016) 11–17.

[19] M. Cetin, E.F. Bakirci, E. Baysal, et al., Increased platelet distribution width is associated with ST-segment elevation myocardial infarction and thrombolysis failure, Angiology 65 (8) (2014) 737–743.

[20] S.P. Akula, V.S.K. Krishana, J.R. Krishna, et al., A study of platelet indices in acute myocardial infarction: an observational study, J. Med. Dent. Sci. 16 (6) (2017) 10–13.

[21] S.R. Reddy, R. Shetty, S. Marupuru, et al., Significance of platelet volume indices in STEMI patients: a case-control study, J. Clin. Diagn. Res. 11 (4) (2017) LC05–LC07.

[22] S.K. Patil, S.D. Karchi, A comparative study of platelet indices in acute coronary syndrome, Int. J. Contemp. Med. Res. 4 (3) (2017) 77–83.

[23] M.S. Certin, E.H.O. Cetin, A. Akdi, et al., Platelet distribution width and plateletcrit: novel biomarkers of ST elevation myocardial infarction in young patients, Kardiol. Pol. 75 (10) (2017) 1005–1012.