Significance of Platelet Volume Indices in Patients with Coronary Artery Diseases

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Abstract

Background: Platelets play an important role in the development of intravascular thrombosis, the major cause of acute coronary syndromes. Platelet size has been considered to reflect platelet activity.

Objectives: The aim of this study is to investigate the clinical value of platelet volume indices (PVI) in the spectrum of ischemic heart diseases and the possibility of being a risk factor for acute myocardial infarction (MI).

Patients &Methods: Thirty six (36) patients were included in the study: 22 of them have myocardial infarction (MI) and 14 have unstable angina (UA). Risk factors and history of stable angina (SA) were reviewed and studied by Chi square. Complete blood count and platelet volume indices (PVI): mean platelet volume (MPV), platelet large cell ratio (P-LCR), and platelet distribution width (PDW) were done using automated hematology analysis system and studied by t-test and correlation analysis. All P values were two sided and P value of < 0.05 was considered statistically significant.

Results: It is found that MPV and P-LCR were the most significant parameters that showed statistical difference between patient with UA and those with MI (P=0.042 & P=0.031) respectively unlike other parameters (platelets count or PDW) (P=0.703 & P=0.094). There were no correlations between MPV & other platelet indices with existing past history of SA as well as other risk factors for acute coronary syndrome (P=0.811).

Conclusion: Because it is simple, economic, and practical, MPV and P-LCR can be used in predicting the possibility of acute thrombosis in patients with coronary artery diseases.

Key words: Platelets, platelet volume indices, atherosclerosis, myocardial infarction, unstable angina, coronary artery disease.

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Introduction

Coronary atherosclerosis and its complication like myocardial infarction (MI) are the major causes of morbidity and mortality in industrialized countries. Endogenous and exogenous risk factors exist but they only explain part of the case, other relevant risk factors need to be identified [1, 2, 3].

Platelets have been implicated in the pathogenesis of cardio- vascular disorders including atherosclerosis and its complication like acute myocardial infarction (AMI), unstable angina (UA) and sudden cardiac death[8].

After rupture of arteriosclerotic plaque in coronary arteries, platelets hyperactivity and local platelets activation have been suggested to play a causal role in prothrmbotic events leading to MI [1, 2, 4, 5]. An increased platelet reactivity and shortened bleeding time are associated with increased platelet volume [6], therefore; platelet size has been considered to reflect platelet level of activity [2,4] as the large platelets are metabolically and enzymatically more active than small platelets [1,7] and they have a higher thrombotic potential due to high concentration of thromboxane A2 [1,2,4,8,9].

Various studies found an association between mean platelet volume (MPV) and coronary artery disease [10] or the occurrence of an acute MI [1,2,9,10,11], while others found no such effect [12].The biological and

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prognostic value of increased MPV is still controversial and the reason for high platelet size still unclear [1].

Automated cell counter have been made the platelet volume indices (PVI) like mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR) are routinely available. The MPV can reflect changes either in the level platelet stimulation and the rate of platelet production so platelet activation can be indirectly and simply measured via MPV [4].

Patients and methods

This study was designed as cross sectional study. 36 patients admitted to coronary care unit (CCU) in Al Kadhimiya teaching hospital with state of acute coronary syndrome at the period from April –May 2008. This study was approved by the local ethics committee. Patients were divided into 2 groups according to clinical data and patient history with support of cardiac enzyme assay and electrocardiographic (ECG) changes: First group is UA group including 14 patients; Second group is AMI group including 22 patients. All individuals were reviewed for established risk factors like (smoking, diabetes mellitus (DM), hypertension, a previous diagnosis of stable angina) in addition to age and gender. Lipid profile records were not available for most of patients in this study. Those with previous or recent AMI, or cerebrovascular event or valvular heart disease were excluded.

EDTA (ethylenediamino tetra acetic acid) samples of blood drawn at first day of admission of patients were analyzed in an automated hematology analysis system (Sysmex, serial number 1544, version no. 00-17, UA). All patient samples were processed within 2 hours of venipuncture as recommended by Symth et al. [13] to avoid bias due to excessive platelet swelling which is reported in some studies secondary to effect of EDTA [14].

Statistical analysis was performed using statistical package for social science (SPSS v.10) on window XP. The chi square test used to compare differences of frequencies in patient characteristics in addition of t-test and correlation analysis. P value $\leq$ 0.05 or $\leq$ 0.001 were considered as statistically significant values accordingly.

Results

Thirty six (36) patients were included in this study, 16 were males and 20 were females. The first group, unstable angina (UA) patients, was 14 patients (38%), 4 of them were males (28.6%) and the rest were females (71.4%). Their age range was 40-65 years with mean age $\pm$ SD (standard deviation) of 52.57 $\pm$ 9.89 year. The second group, myocardial infarction (MI) patients, was 22 patients (62%), 12 were males (54.5%) while 10 were females (45.5%) with age range 46-80 years and mean $\pm$SD of 64.18 year $\pm$ 9.29 year. These two groups shows statistically significant differences concerning their age distribution (P= 0.001)

The baselines demographic data are shown in (Table 1) which demonstrate a statistically significant differences concerning the smoking history (P=0.011), and hypertension (P=0.032) with highly significant differences in cardiac enzyme elevation according to the underlying pathogenesis in the 2 groups (P=0.0001), however , there were no significant differences in terms of existing previous history of stable angina when compared with their recent presentation as acute coronary syndrome (P=0.629).

Platelets volume indices (PVI) were studied using t test between the above 2 groups of presentation and it is found that MPV and P-LCR were the most significant parameters that

showed statistical differences between patient with UA and those with MI (P=0.042andP=0.031) respectively unlike other parameters (platelets count or PDW)(P=0.703 and P=0.094) (Table 2).

It is found also that MPV will exceed 11.6 fl and 12.10 fl at percentile 95 in case of UA and MI respectively and similarly P-LCR will exceed 37.66 and 41.20 at percentile 95 in the above two groups respectively which may indicate a higher level of activity.(Table 3)

There were no correlation found between MPV and other platelets indices with existing past history of stable angina as well as other risk factors for acute coronary syndrome (P=0.811) i.e. these PVI did not altered significantly with these risk factors and their difference is related directly to acute events.

Discussion

The findings indicate that increased platelet volume is associated with a higher risk of suffering an acute coronary event independent of the extent of a previous coronary artery disease (CAD). Percentile 95 value will indicate a higher risk of getting acute coronary event with being increased platelet volume and a higher percentage of large size cells independent of existence of other risk factors. Thus MPV and P-LCR above these percentile values may represent an independent risk factors for MI similar to other studies [1, 2, 3], but there were no practical application of platelet count which had been demonstrated by Kilici-Cmur N. et al [2].

The mechanism for an increased platelet volume are not well fully understood, possibly cytokines may trigger the production of larger more reactive platelet following platelet destruction in peripheral blood including interleukin-6 (IL-6) [14], although, it is not settled completely [1].

In this study we neglected the drugs used by patients as there are limited data about the effect of pharmacological therapy on platelet count and size. It has been proved previously that standard medical treatment for coronary diseases did not significantly change platelet markers [3]. In previous studies, an increased MPV was found to be associated with coronary artery disease [10, 15, 16], UA [9, 10], AMI [1, 9] and even congestive heart failure [18] as well as in cerebrovascular diseases (18) and this can be explained on base of increased platelet hyperactivity after erosion or rupture of atherosclerotic plague leading to potentiated prothrombotic complication like MI or cerebrovascular events [1, 6].

Large platelets that contain more dense granules are metabolically and enzymatically more active than small platelet with a higher thrombotic capacity (1) as they express higher levels of prothrombotic substances, thromboxane A2, serotonin b, B-thromboglobulin and procoagulation surface protein such as P-selectin and glycoprotein IIIa [11]. An increased MPV decreases the inhibitory effectiveness of PG I_2 on both platelet aggregation and the release reaction [19]. Higher levels of P- selectin was previously reported to associate with acute MI and its measurement was promising as predictors of vascular risk due to platelet aggregation [20].

The size of platelet has been found to associate with an increased number of megakaryocyte [3]. In agreement with Kilicli-Camur observation, we did not report a significant correlation between MPV and history of stable angina, and this is in contrast to others findings like Endler G. et al and Erne P. et al [1, 17].

Similar to reported data, we found also that MPV was significantly higher in MI group than UA group (1, 2, 6, 17) but unlike the result of Mc Karns et al [3] and in contrast to finding of Mathur et al (21) who observed higher MPV in UA group than MI group. Similarly, it is noted that the time span between MI and laboratory testing did not influence platelet size and thus may suggest that MPV will not change during the acute phase reaction. The finding of this study confirm that increased MPV might be responsible for the prothrombotic state that eventually leads to thrombus formation after rupture of coronary plaque [10,16,21].

Little is known about the effect of aspirin and other platelets aggregation inhibitors on MPV (10), however, whether intervention with platelets aggregation inhibitors or other drugs are beneficial for patient with high MPV remain to be determined.

Conclusion

MPV might be a valuable risk factor for atherosclerosis and acute coronary syndrome. Since it is simple, economic & practical, MPV & P-LCR can be used in predicting the possibility of acute thrombosis in patients with coronary artery diseases.

Table 1: Demographic & clinical characteristics in the study population

Character		UA		MI		P value
		No	%	No	%	
Sex	Male	4	28.6	12	54.5	0.126
	Female	10	71.4	10	45.5	
Smoking	yes	-	-	8	36.4	0.011*
	no	14	100.0	14	63.6	
Diabetes mellitus	yes	10	71.4	14	63.6	0.629
	no	4	28.6	8	36.4	
Hypertension	yes	14	100.0	16	72.7	0.032*
	no	-	-	6	27.3	
History of CAD	yes	10	71.4	14	63.6	0.629
	no	4	28.6	8	36.4	
Cardiac Enzyme	Positive	2	14.3	18	81.8	0.0001*
	Negative	12	85.7	4	18.2	

*The Pearson Chi-Square statistic is significant at the 0.05 level.

Table 2: Distribution of hematological parameters.

Parameter	UA	MI	P value
	Mean ± SD (Min-Max)	Mean ± SD (Min-Max)	
Platelet count	280428.57 ± 76361.20 (158000-381000)	267545.45 ± 109062.55 (137000-522000)	0.703
Platelet distribution width(PDW)	13.62 ± 1.83 (10.5-15.5)	12.50 ± 1.96 (9.5-16.3)	0.094
Mean platelet volume (MPV)	10.53 ± 0.80 (9.4-11.6)	9.82 ± 1.07 (8.2-12.1)	0.041*
Platelet large cell ratio (P-LCR)	29.97 ± 5.31 (22.3-37.6)	24.43 ± 8.15 (11.6-41.2)	0.031*
ESR	35.29 ± 13.03 (12.0-55.0)	48.55 ± 35.47 (10.0-120.0)	0.190

*The Independent Samples Test statistic is significant at the 0.05 level.

Table 3: The percentile ratio of MPV & P-LCR

Diagnosis		UA	MI
Mean platelet volume	Percentile 50	10.90	9.20
	Percentile 75	11.20	10.70
	Percentile 95	11.60	12.10
	Percentile 99	11.60	12.10
Platelet large cell ratio	Percentile 50	32.40	20.10
	Percentile 75	33.90	31.40
	Percentile 95	37.60	41.20
	Percentile 99	37.60	41.20

References

1. Endler G, Klimesch A, Sunder-Plassmann H, Schillinger M et al: Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. British J. Haematology 2002; 117, 399-404.

2. Kilicli-Camur N, Demirtunc R, Konuralp C, Eskiser A, et al: Could mean platelet volume be a predictive marker for acute myocardial infarction?. Med Sci Monit. 2005; 11(8), CR 387-392.

3. McKarns S C, Smith C J, Payne V M and Dolittle D J: Blood parameters associated with atherogenic and thrombogenic risk in smokers and nonsmokers with similar life style. Modern Pathology. 1995:8,434-440.

4. Khandekar M M, Khurana A S, Deshmukh S D, Katadare A D, et al.: Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: Indian scenario: J. Clinical Path.2006;59,146-149.

5. Trip M D, Cats V K, VanCapelle F J L et al.: Platelet hyperreactivity and prognosis in survivors of myocardial Infarction. N E J M. 1990; 322, 1549-54.

6. Dalby K S, Milner P C, Martin J F: Bleeding time and platelet volume in acute myocardial infarction. A 2 year follows up study: Thrombos. Haemost. 1988; 59, 353-56.

7. Corash L, Tan H, Grolnick H R: Heterogeneity of human whole blood platelet subpopulation. : Blood. 1977; 49, 71-87.
8. Thompson C B, Elaton K A, Princiotta S M, et al.: Size dependant platelet subpopulation; Relationship of platelet volume to ultra structure enzymatic activity and function. : B J H.1982; 50, 509-20.
9. Senaran H, Ileri M, Altinbas A, et al: Thromboietin and mean platelet volume in coronary artery Disease: Clini. Cardio 2001; 24, 405-08.
10. Pizzulli L, Yang A, Martin J F, Luderitz B: Changes in platelet size and count in unstable angina compared to stable angina or non cardiac chest pain. : Eur. H. J. 1998; 19, 80-84.
11. Martin J F, Bath P M, and Burr M L: Influence of platelet size on outcome after myocardial infarction. : Lancet. 1991; 388(8780), 1409-11.
12. Halbamayer W M, Haushofer A, Radek J, et al: Platelet size, fibrinogen and lipoprotein (a) in coronary heart disease: Coronary Artery Disease. 1995; 6,397-402
13. Symth D W, Martin J F, Michalis L, et al: Influence of platelet size before coronary angioplasty on subsequent restenosis. : Eur. J. Clini. Invest. 1993; 23, 361-67.
14. Bath P M, Missouris C G, Backenham Tand MacGregor G A: Increased platelet volume and platelet mass in patient with atherosclerotic renal artery stenosis: Clini. Science. 1994; 87, 253-257.
15. Henning B F, Zidek W, and Linder B, Tepel M: Mean platelet volume andcoronary heart disease in hemodialysis patient. : Kidney Blood Press. Res. 2002; 25,103-08.
16. Kario K, Mastuo T, Nakao K: Cigarette smoking increases the mean platelet volume in elderly patient with risk factors for atherosclerosis: Clini. Lab. Haemat. 1992; 14, 281-87.
17. Erne P, Wardle J, Sanders K, et al: Mean platelet volume and size distribution and their sensitivity to agonist in patient with coronary artery diseases and congestive heart failure. : Thrombos. Haemost. 1988; 59, 259-63.
18. O'malley T, Lanhorne P, Elaton K A,Stewart C: Platelet size in stroke patient .: Stroke 1995; 26, 995-99.
19. Jackabowski J A, Adler B, Thompson C B, et al.: Infulence of platelet volume on the ability of prostocyclin to inhibit platelet aggregation and the release reaction. : J. Lab. Clini. M ed. 1985; 105, 271-76.
20. Tsiaria S, Elisat M, Anita J I and Mikhailidis D P: Platelet as predictors of vascular risk: Is there a practical index of platelet activity? Clini. Appl. Throbosis / Haemostasis. 2003; 9(3), 177-90.
21. Matheur A, Robinson M S, and Cotton J, et al.: Platelet reactivity in acute coronary Syndrome: Evidence for differences in platelet behavior between unstable angina and myocardial infarction. : Thromb. Haemost. 2001; 85, 989-94.