Research Article

Evaluation of Platelet Indices in Patients with Acute Coronary Syndrome

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Date Submitted: 11.6.2012

Date Accepted:10.2.2013

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Abstract

Background and Aims: Platelets have a significant role in the pathogenesis of atherosclerosis and coronary artery disease. It is well established that large platelets are involved in the development of atherosclerotic plaque and acute coronary syndromes.

Aim: The aim of this study was to define the relationship between platelet volume indices and development of acute coronary syndrome.

Patients and Methods: Our study included 50 patients admitted to AL-Yarmouk teaching hospital with acute coronarysyndrome;20 patients had unstable angina (UA) and 30 patients had acute myocardial infarction (AMI) diagnosed on the basis of history, characteristic electrocardiographic changes, and increased cardiac biomarkers activities. Mean platelet volume (MPV), platelet crit (PCT), platelet count and platelet distribution width(PDW) were done using automatedhematology analysis and compared them with 50 age and sex matched healthy controls.

Results: All platelet volume indices—mean platelet volume (MPV), platelet distribution width (PDW), platelet count and platelet crit(PCT)—were significantly raised in patients with AMI and UA. In patients with myocardial infarction, the mean values of MPV, PDW, platelet count and PCT were 10.9fL, 21.6%, 352.2(x 10^9/L) and 0.171% respectively; while in normal healthy control the mean values of these indices were 7.1fL, 15%, 256.2(x 10^9/L) and 0.153% respectively. A statistically significant difference in mean values of these indices was found (p value < 0.001). Similarly, in patients of unstable angina mean values of MPV, PDW, platelet count and PCT were 11.1fL, 21.1%, 300.7(x 10^9/L) and 0.165% respectively. Statistically significant differences in mean values of these indices were found.

Conclusions: Larger platelets are haemostatically more active and are a risk factor for developing coronary thrombosis and subsequent acute coronary events (myocardial infarction and unstable angina). Patients with larger platelets can easily be identified during routine hematological analysis and could possibly benefit from preventive treatment.

Keywords: Acute myocardial infarction, unstable angina and platelet volume indices

INTRODUCTION

Platelet activation plays a central role in the transformation of atherosclerotic cardiovascular disease (CVD) into its potentially major adverse clinical events, such as ischemic stroke and myocardial infarction (MI) [1-3].Increased platelet activation may also represent the net patho-physiological effects of a number of CVD risk factors, such as smoking and raised cholesterol, thus representing a broad marker of CVD risk [4]. Platelet activation leads to changes in platelet shape (increasingly spherical) with increased platelet swelling leading to an increase in platelet mass and volume [4,5] .Traditional measures of platelet function/activation, such as the quantification of platelet derived metabolic products (e.g. beta thrombomoglobulin [bTG]), platelet surface receptors/proteins (e.g. soluble P selectin, fibrinogen) and the use of platelet aggregometry are technically difficult [6, 7]. Acute coronary syndrome (which include unstable angina, acute myocardial infarction and sudden cardiac death) result from acceleration of this chronic process

characterized by rupture or fissuring of an unstable atherosclerotic plaque, accompanied by a cascade of platelet reactions resulting into thrombus formation [8].

The WHO has drawn attention to the fact that CAD is a modern epidemic more in geriatric population i.e. people above 60 years of age. Large increase in CAD is projected and now it is the most common cause of death [9].Platelets play a crucial role in pathogenesis of atherosclerotic complications, contributing to thrombus formation or apposition after plaque rupture [10,11,12].After rupture of arteriosclerotic plaque in coronary arteries, platelets hyperactivity and local platelets activation have been suggested to play a causal role in prothrombotic events leading to MI[13].An increased platelet reactivity and shortened bleeding time are associated with increased platelet volume, therefore; platelet size has been considered toreflect platelet level of activity as the large platelets are more active than small platelets and they have a higher thrombotic potential due to high concentration of thromboxane A2[14].

PATIENTS AND METHODS

This study was done in the laboratories of AL-Yarmouk teaching hospital for the period between June 2012 to November 2012 .The subjects were divided into three groups:

(1) First group includes thirty patients were admitted to the coronary care unit, AL- Yarmouk teaching hospital with diagnosis of acute myocardial infarctions (AMI).

(2)Second group includestwenty patients were admitted to coronary care units diagnosed as having unstable angina.

(3)Third group includes fifty healthy control groups.

Data were translated into a computerized database structure. An expert statistical advice was sought for Statistical analyses were computer assisted using SPSS version 20 (Statistical Package for Social Sciences).The outcome quantitative variables were normally distributed and conveniently described by mean, SD (standard deviation) and SE (standard error), and the parametric statistical tests of significance were used. The independent samples t-test was used to test the statistical significance of difference in mean between 2 groups. ANOVA test was used to test the statistical significance of difference in mean between more than 2 groups. When ANOVA model showed a statistically significant difference, further exploration for the site of statistical significance between all possible paired combinations of study groups was performed by LSD (least significant difference test). P value less than the 0.05 level was considered statistically significant.

Criteria of inclusion of the subjects:

Patients with newly diagnosed acute myocardial infarction [STEMI andNSTEMI(cardiac enzyme activity positive)] and unstable angina(some patients had previous acute myocardial infarction).

Sample collection**:**

Blood samples were taken from both groups of patients and control. 2.5 ml of blood were withdrawn in syringes by clean venipuncture; blood was dispersed in ethylene diamine tetraacetic acid (EDTA) tube.

Methods: Blood sample(320microliter) from EDTA tube were put in automated analyzer for hematology(analysis system) called CELL –DYN RUBY; list number 08H56-02 made by USA.

RESULTS

A total of 100 subjects were analyzed, 50 healthy controls with a mean age of 57 year(± 15) and 30 MI cases with a mean age 63.6 (± 8.7) and 20 cases with unstable angina with a mean age of 54 (± 10.5). Male constituted 50% of healthy control, 40% of MI and 30% of cases with unstable angina .No important differences were observed between 3 study groups.The difference in mean platelet indices between the 3 study groups is shown in table 1that was significantly higher in MI and UA groups compared to healthy control. Meanplatelet count in control group is 256.2x10^9/L while in MI and UA groups are352.2, 300.7x10^9/L respectively. MPV in control group 7.1flwhile in MI and UA groups are 10.9, 11.1fL respectively, which is statistically significant, on other hand, there were no significant difference in MPV between MI and UA groups.PCT in control group 0.153% while in MI and UA are 0.171, 0.165% respectively, which is significant only in MI compared to healthy control.PDW in control group was 15 while in MI and UA were 21.6, 21.1 respectively,which is a statistically significant difference, on other hand,there were no significant difference in mean PDW between MI and UA groups. The difference in mean Platelets indices between MI subjects with STEMI and those NSTEMI are shown in table 3 which is not significant statistically. The receiver operator characteristic(ROC) area is used to distinguish between all parameters in table 3in which parameters has more or less validity to differentiate between ACS and healthy control (discrimination between cases with acute coronary syndrome (MI and UA) and healthy controls),

that mean any value nearest to (1) more validity to predict ACS. MPV and PDW had a very high validity (perfect test) in predicting ACS (=1), comparable to PCT and platelet count had an average validity (ROC area=0.733,0.731) respectively.

The cut-off value represented Validity parameters for Platelets count, MPV, PCT and PDWare shown in tables 4,5,6,and 7, when used as test to predict cases with coronary syndrome differentiating them from healthy controls .Cut-off taken as higher accuracy value, therefore; any value more than cut-off value predict ACS.

DISCUSSION

Platelet activation leads to the formation of free arachidonic acid, which can be transformed into prostaglandins, such as thromboxane A2, one of the most potent vasoconstriction and platelet-aggregating substances, or into leukotrienes, which can amplify the acute inflammatory response[10].

Platelet function and size correlate because larger platelets, produced from activated megakaryocyte in the bone marrow, are likely to be more reactive than normal platelets because large platelets contain more secretary granules and mitochondria and are known to be more active than small platelets (normal)(14). Consequently, larger and hyperactive platelets play a vital role in accelerating the formation and propagation of intracoronary thrombus, leading to the occurrence of acute thrombotic events [15] .

In our study the difference in mean platelet indices (MPV, PDW, platelet count, and PCT) between the 3 study groups are highly significant statistically ($p<0.001$), that MPV, PDW, platelet count, and PCT is higher in patients with unstable angina and MI compared to healthy controls [16-18). Our data suggest that the increased MPV and PDW contribute to the prothrombotic state in acute coronary syndromes and that larger platelets may play a specific role in infarction [13,19].The difference in mean platelet indices between MI subject with STEMI and those NSTEMI(ECG change and enzyme positive) was statistically not significant, similar to Indian study that was done by Khandekar that found no association between the type of infarction and MPV[20,21] .

Martin etal (India) found that MPV was significantly higher in those patients who has MI, compared with healthy group, which is confirmed by Senaran et al (India)(20,22),both studies are similar to our study.In our study, PDW increased in MI and UA compared to healthy control.While the role of PDW specifically in patients with coronary artery disease (CAD) are yet to be discussed in Indian study[22].

Van der Loo et al (Turkey) in their study suggested that platelet volume was an important biological variable to determine platelet reactivity .They also suggested that elevated platelet volume measured after MI might be a determinant factor for future ischemic episodes and death. In this study, itwas observed that platelet volume indiceswere increased in patients with ST-elevated myocardial infarction compared to normal population which is also significant similar to our study[23].

Butkiewicz(Turkey) there is no significant differencefound between unstable angina pectoris and healthy control in terms of MPV[24], while in our study statistically significant difference was found between unstable angina and healthy control in terms of MPV ($p<0.001$).

Mathur et al (Turkey) found platelet counts to be significantly lower and MPV to be higher in patients with unstable angina pectoris [25.Different to our study, platelet count is increased significantly in MI and UA($p<0.001$,$p=0.04$ respectively) .MPV, in our study, is higher in both MI and UA ($p<0.001$) which is similar to Mathur et al study.

Conclusions

1. Larger platelets are haemostatically more active and are a risk factor for developing coronary thrombosis, leading to myocardial infarction.(13,19).

2. The findings of our study, which was performed on the largest-ever sample of patients who were admitted to the (CCU) for a suspected diagnosis of ACS, indicate that MPV and PDW at admission are significantly higher in patients with diagnosed ACS than in those with chest pain of non-cardiac origin. For thispurpose, we think that MPVand PDW measurement, whichis a non-invasive and easy-to-perform method,may be an useful tool for the follow-up and further studies are needed to confirm these finding

Table 1. The difference in mean platelet indices between the 3 study groups.

	Study group			
	Apparently healthy controls (n=50)	MI (Myocardial infarction) (n=30)	Unstable angina (n=20)	P (ANOVA)
Platelets count (x 10^9/L)				<0.001
Range	(140 - 390)	(160 - 460)	(140 - 460)	
Mean	256.2	352.2	300.7	
SD	55	89.5	115.3	
SE	7.78	16.35	25.79	
P (LSD) for difference in mean between:				
Apparently healthy controls x MI (Myocardial infarction) <0.001				
Apparently healthy controls x Unstable angina = 0.04				
MI (Myocardial infarction) x Unstable angina = 0.029				
MPV (fl)				<0.001
Range	(6.1 - 8.5)	(9.8 - 12.1)	(10 - 12.1)	
Mean	7.1	10.9	11.1	
SD	0.7	0.7	0.6	
SE	0.1	0.12	0.14	
P (LSD) for difference in mean between:				
Apparently healthy controls x MI (Myocardial infarction) <0.001				
Apparently healthy controls x Unstable angina <0.001				
MI (Myocardial infarction) x Unstable angina = 0.3[NS]				
PCT (%)				0.008
Range	(0.125 - 0.199)	(0.141 - 0.23)	(0.017 - 0.24)	
Mean	0.153	0.171	0.165	
SD	0.019	0.022	0.043	
SE	0.0027	0.004	0.0097	
P (LSD) for difference in mean between:				
Apparently healthy controls x MI (Myocardial infarction) = 0.003				
Apparently healthy controls x Unstable angina = 0.08[NS]				
MI (Myocardial infarction) x Unstable angina = 0.42[NS]				
PDW				<0.001
Range	(10.5 - 19.3)	(18.3 - 24.5)	(17.9 - 23.6)	
Mean	15	21.6	21.1	
SD	2.3	1.5	1.6	
SE	0.32	0.28	0.36	
P (LSD) for difference in mean between:				
Apparently healthy controls x MI (Myocardial infarction) <0.001				
Apparently healthy controls x Unstable angina <0.001				
MI (Myocardial infarction) x Unstable angina = 0.43[NS]				

Table 2. The difference in mean Platelets indices between MI subjects with STEMI and those NSTEMI.

	ECG		
	STEMI (n=23)	**NSTEMI (n=7)**	**P (t-test)**
Platelets count (x 10^9/L)			0.93[NS]
Range	(160 - 460)	(170 - 440)	
Mean	352.9	350	
SD	92.6	85.5	
SE	19.3	32.32	
MPV (fl)			0.32[NS]
Range	(9.8 - 12.1)	(9.9 - 11.7)	
Mean	10.9	10.7	
SD	0.7	0.6	
SE	0.14	0.24	
			0.53[NS]
PCT (%)			
Range	(0.141 - 0.23)	(0.144 - 0.205)	
Mean	0.173	0.166	
SD	0.023	0.02	
SE	0.0047	0.0076	
PDW			0.58[NS]
Range	(18.3 - 24.5)	(20.8 - 22.8)	
Mean	21.5	21.9	
SD	1.7	0.6	
SE	0.36	0.24	

Table 3. ROC area for selected parameters when used in the context of discrimination between cases with coronary syndrome (MI and UA) and healthy controls.

		ROC area	**P**
1-	MPV (fl)	1	<0.001
2-	PDW	0.993	<0.001
3-	PCT (%)	0.733	<0.001
4-	Platelets count (x 10^9/L)	0.731	<0.001

Table 4. Validity parameters for Platelets count (x 10^9/L) when used as test to predict cases with coronary syndrome differentiating them from healthy controls.

				PPV at pretest probability=		
Positive if ≥ cut-off value	**Sensitivity**	**Specificity**	**Accuracy**	**50%**	**90%**	**NPV at pretest probability=10%**
142.5 Highest sensitivity	98.0	2.0	50.0	50.0	90.0	90.0
334.0 Optimum cut-off value	72.0	92.0	82.0	90.0	98.8	96.7
392.5 Highest specificity	34.0	100.0	67.0	100.0	100.0	93.2

Table 5. Validity parameters for MPV(fl)when used as test to predict cases with coronary syndrome differentiating them from healthy controls.

Positive if ≥ cut-off value	Sensitivity	Specificity	Accuracy	PPV at pretest probability= 50%	PPV at pretest probability= 90%	NPV at pretest probability=10%
9.15 Optimum cut-off value	100.0	100.0	100.0	100.0	100.0	100.0

Table 6: Validity parameters for PCT(%)when used as test to predict cases with coronary syndrome differentiating them from healthy controls..

Positive if ≥ cut-off value	Sensitivity	Specificity	Accuracy	PPV at pretest probability= 50%	PPV at pretest probability= 90%	NPV at pretest probability=10%
0.138 Highest sensitivity	98.0	22.0	60.0	55.7	91.9	99.0
0.156 Optimum cut-off value	72.0	70.0	71.0	70.6	95.6	95.7
0.200 Highest specificity	12.0	100.0	56.0	100.0	100.0	91.1

Table7: Validity parameters for PDW when used as test to predict cases with coronary syndrome differentiating them from healthy controls.

Positive if ≥ cut-off value	Sensitivity	Specificity	Accuracy	PPV at pretest probability= 50%	PPV at pretest probability= 90%	NPV at pretest probability=10%
17.8 Highest sensitivity	100.0	88.0	94.0	89.3	98.7	100.0
19.4 Highest specificity and Optimum cut-off value	94.0	100.0	97.0	100.0	100.0	99.3

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