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Original Research Paper



EVALUATION OF PLATELET PARAMETERS IN PATIENTS OF ISCHEMIC HEART DISEASE AND ISCHEMIC STROKE

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ABSTRACT INTRODUCTION: Ischemic heart disease (IHD) and ischemic stroke are among the most common causes of morbidity worldwide. The aim of the current study is to evaluate the platelet parameters platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) and Platelet large cell ratio (P-LCR) as a risk factor in patients with IHD and ischemic stroke.

MATERIALS AND METHODS: Study included 200 healthy controls and 200 cases of Acute coronary syndrome and ischemic stroke during the period of April 2017 to October 2017. Total platelet count, MPV, PDW, PCT and P-LCR of all these patients were obtained and compared with normal healthy controls.

RESULTS: All indices excluding PLT and PCT were significantly raised among the cases (p < 0.0001). The risk of a thrombotic event in the high P-LCR group was 1.89 times higher (p < 0.05). Similarly, the risk of a thrombotic event in the high MPV group was 1.27 (p < 0.05) times, and in the high PDW group was 1.11 times higher (p < 0.05) than controls. There was negligible risk in cases that showed increased PCT and no risk in patients with high Platelet count.

CONCLUSION: High MPV, PDW and P-LCR is associated with increased risk of development of ischemic events. Hence evaluation of these parameters in high risk patients can predict the possibility of an impending thrombotic event.

KEYWORDS : Ischemic heart disease, ischemic stroke, platelet parameters

INTRODUCTION

Ischemic heart disease (IHD) and ischemic stroke are among the most common causes of morbidity worldwide, and is increasingly becoming common in India as well1. The underlying pathology is atherosclerosis and progresses chronically to manifest as acute coronary syndromes (ACS) and stroke. Conventional risk factors for atherosclerosis include smoking, diabetes mellitus, hypertension, hyperlipidemia, obesity and stress which either act singly or in combination to increase the risk of developing atherosclerosis. ACS and stroke depict an 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. It is unclear if certain platelet characteristics predispose some individuals with atherosclerosis to develop ACS and stroke. It is likely that different individuals have platelets of variable size, density, and reactivity. Larger the platelets, they are more likely to be metabolically and enzymatically active. It is known that large platelets are denser, aggregate more rapidly with sub endothelial collagen, produce more thromboxane A2 and express more glycoprotein Ib and glycoprotein IIb/IIIA receptors. These characteristics may lead to increased thrombosis, and possibly ACS2-6. Platelets play an important role by participating in the formation of thromboemboli and hence initiate the symptoms of stroke and ischemic heart disease. Activated platelets initiate the formation of a hemostatic plug and provide a scaffold for the activation of coagulation. Platelet parameters have been evaluated in some studies and correlated with the increased risk of ischemic stroke and IHD. Electronic cell counters have made it possible to measure platelet parameters, specifically mean platelet volume (MPV), and platelet distribution width (PDW), plateletcrit (PCT), Platelet large cell ratio (P-LCR). PDW reflects the platelet heterogeneity in circulation, the size of the

platelet distribution and the degree of dispersion; MPV reflects the overall situation of the platelet volume size in the body and the platelet formation in the bone marrow; meanwhile, P-LCR reflects the circulatory system in large volume platelet turnover situation.

The studies have evaluated MPV in most instances while some have included PDW, PCT, while few have included P-LCR. Patients with larger platelets can easily be identified during routine hematological analysis and could possibly benefit from preventive treatment. Thus, platelet parameters are an important, simple, effortless, and cost effective tool that should be used and explored extensively, especially in countries such as India, for predicting the possibility of impending acute events. The objective of this study is to measure the platelet parameters which include MPV, PDW, PCT and P-LCR in patients of IHD and ischemic stroke. This is an observational study and might serve as a prognostic tool to predict the possibility of impending acute cardiac or stroke events.

MATERIALS AND METHODS

This observational study was conducted in patients admitted to a tertiary care Hospital. As a part of routine evaluation, the IHD and ischemic stroke patients undergo complete hemogram among the other battery of investigations as a standard of care. Standardized EDTA tubes were used for sample collection and all samples were processed within 30 min after blood collection. The complete hemogram was performed using a fully automated five part Hematology Analyzer (Model- Sysmex Xt2000i). Our study included 200 healthy controls and 200 cases who were admitted to our hospital/ patient on follow up for Acute coronary syndrome and ischemic stroke during the period of April 2017 to October 2017. Total platelet count, MPV, PDW, PCT and P-LCR of all these patients were obtained and compared with normal healthy controls. The samples were obtained from patients

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(>18yrs) with IHD and ischemic stroke. The ethics committee of study centre approved the study in accordance with ethical standards of the Declaration of Helsinki.

INCLUSION AND EXCLUSION CRITERIA

Inpatients and outpatient of IHD or ischemic stroke were included. Cases of hemorrhagic stroke were excluded.

TABLE 1: REFERENCE RANGE FOR THE PARAMETERS ASSESSED

PLATELET PARAMETER	REFERENCE RANGE
PLT (Platelet Count)	$150 - 400 \mathrm{x} 10^{9} \mathrm{/L}$
MPV (mean platelet volume)	9-11.5 fL
PDW (Platelet distribution width)	9 – 14 fL
PCT (plateletcrit)	0.22 - 0.25%
P-LCR (platelet large cell ratio)	15-35%

RESULTS

GENERAL CHARACTERISTICS

The age of the patients ranged from 30 to 78 yrs with median age of 59 yrs. There were a total of 48 females out of 200 patients. There were 38 cases of ischemic stroke and 162 cases of ischemic heart disease.

TABLE 2: PLATELET PARAMETERS IN CASES AND CONTROLS

Parameters	CASES				CONTROLS				p-value
	Minimum	Maximum	Mean	Std. Deviation	Minimum	Maximum	Mean	Std. Deviation	
PLT (10 ⁹ /L)	141	601	258.53	89.30	70	555	258.93	76.77	0.1692
PDW (fL)	9.2	22.90	14.60	2.48	9.1	19.9	12.24	1.50	< 0.0001
MPV (fL)	8.5	15.9	11.37	1.17	8.20	12.9	10.47	0.79	< 0.0001
P-LCR (%)	14.5	51	34.14	6.35	12.40	52.00	28.31	5.88	< 0.0001
PCT (%)	0.15	0.63	0.28	0.07	0.11	0.45	0.27	0.67	0.543

determine the odds ratio (OR) between controls and cases. P-value was also calculated with this statistical analysis.

TABLE 3: ASSOCIATION OF PLATELET PARAMETERS WITH THE RISK OF ISCHEMIC STROKE AND IHDDETECTED BY LINEAR REGRESSION ANALYSIS

Parameter		Cases	Control	OR (95% CI)	P Value
PLT	Normal	192	186	1	0.92
	High	6	7	0.22 (0.10-1.88)	
	Low	2	7		
PDW	Normal	98	177	1	0.01
	High	102	23	1.11 (0.20-6.19)	
	Low	-	-		
MPV	Normal	138	178	1	
	High	60	18	1.27 (0.55-2.92)	0.045
	Low	2	4		
P-LCR	Normal	123	175		
	High	75	23	1.89 (0.66-3.54)	0.026
	Low	2	2		
PCT	Normal	56	58	1	
	High	109	118	1.003(0.61-1.62)	0.14
	Low	35	24		

Among the parameters obtained, linear regression analysis revealed the risk of a thrombotic event in the high P-LCR group was 1.89 times higher when compared to the controls. Similarly the risk of a thrombotic event in the high MPV was 1.27 times and while that of high PDW group 1.11 times higher than the controls. While there was a negligible risk in cases those showed increased PCT and no risk was identified in patients with high platelet counts.

DISCUSSION:

Atherosclerosis is the important and most of the times the primary cause of vascular occlusive disorders such as

THE RESULTS OF PLATELET INDICES:

The mean platelet count in the cases is $258.53 \pm 89.30 \times 10^{3}$ /L with the range being 141-601 ×10⁹/L while in controls the mean count was $258.93 \pm 76.77 \times 10^{9}$ /L with a range from 70-555 ×10⁹/L. The difference in platelet count between cases and controls was insignificant with the *p* value more than 0.05. The PDW in the cases is 14.6±2.48 fL with the range being 9.2-22.9 fL while in controls the mean was 12.24 ± 1.5 fL with a range from 9.1-19.9 fL and this difference is statistically significant with the *p* value less than 0.05.

The MPV in the cases is 11.37 ± 1.17 fL with the range being 8.5 - 15.9 fL while in controls the mean was 10.47 ± 0.79 fL with a range from 8.2 -12.9 fL and this difference is statistically significant with the *p* value less than 0.05. The PCT in the cases is 0.28 ± 0.07 % with the range being 0.15 - 0.63% while in controls the mean was 0.27 ± 0.07 % with a range from 0.11 - 0.45% and this difference is not statistically significant with the *p* value more than 0.05.

The P-LCR in the cases is 34.14 ± 6.35 % with the range being 14.5 - 51% while in controls the mean was 28.31 ± 5.88 % with a range from 12.40-52.0% and this difference is not statistically significant with the p value more than 0.05.

Subsequently linear regression analysis was used to

coronary artery disease and occlusive cerebrovascular events. Platelets play a pivotal role in formation of thrombus and the subsequent vascular events. Based on extensive laboratory and clinical experience, it is clear that platelet activation and aggregation play an integral role on two fronts: (a) in the cytokine-driven local inflammatory changes associated with plaque formation and growth, followed by (b) thrombus associated with plaque instability.

For an arterial thrombi to form, the activity of platelets is the first and foremost important requirement. The functional activity of platelets can be related to various platelet parameters as brought out by the previous studies^{1.7}. Platelets with high MPV, was supposedly more active functionally and are associated with increased platelet reactivity and this being a major risk factor for thrombotic phenomenon especially in a diseases atherosclerotic blood vessel. Studies have brought out the fact that high MPV levels were associated with overall increased mortality due to ischemic cerebrovascular and cardiovascular events ^{8:10}. Therefore, MPV has been suggested as a simple marker of functional status of platelets and may represent a risk factor for vascular adverse events.

The present study included almost all of the platelet parameters that can be measured by automated hematology analyzer and assess their role in risk assessment in cases of ischemic events. The various parameters assessed include MPV, PDW, PCT and P-LCR in patients with IHD and ischemic stroke. Evaluation of platelets parameters as an index of their activity could be useful in prediction of potential coronary or stroke eventssuch patients and might serve as a prognostic tool to predict patients with possibility of impending acute cardiac or stroke events.

In this pilot study, 200 patients who had an ischemic cardiac or cerebrovascular event were included and their platelet

parameters were compared with the healthy persons who did not have any ischemic events or any other ailments. Our findings revealed no significant differences in the platelet count or PCT among the patients and controls, however MPV, PDW and P- LCR were significantly higher in the cases as compared to the controls. Most of the studies in the literature have limited themselves to MPV, while our present study has included all available platelet parameters. We also attempted to assess the odds ratio for various parameters. Statistically significant results were noted for the three parameters namely MPV with increased risk of ischemic event (OR=1.27), high PCT (OR=1.11), whereas an elevated P-LCR had the highest risk with OR=1.89. The elevation of MPV has been found to significantly increase the risk of ischemic events. This finding is in unison with previous studies¹¹. As an important indicator that describes platelet function and activity, MPV is found to be positively associated with platelet reactivity. Large platelets, which contain more high-density granules and have higher activity, are much easier to form thrombi¹². At the time of platelet production in the bone marrow, the platelet size (i.e) MPV is determined and it is not altered after the production. Hence it is safe to infer that the hypercoagulable state is determined much before the onset of ischemic event. Elevated MPV has been shown to be associated with poor prognosis in patients with acute ischemic stroke13,14, but other studies identified no significant correlation between MPV and the prognosis of stroke¹⁵. Hence it was opt to carry out the present study. A similar study included MPV, PDW and P-LCR and showed significant correlation between MPV and P-LCR only¹⁶ while our study revealed significant correlation between all the three parameters namely MPV, PDW and P-LCR.

CONCLUSION

The current study had found out that high MPV, PDW and P-LCR is associated with increased risk of development of ischemic cardio vascular and cerebro vascular events. Hence evaluation of these parameters in high risk patients can predict the possibility of an impending thrombotic event.

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