Original Article

Frequency of Increased Mean Platelet Volume in Patients Suffering From Hypertensive Retinopathy

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ABSTRACT

Introduction: The pathophysiological mechanism of hypertensive retinopathy is not fully established. It is thought that increased platelet activation may play a role in its pathogenesis. As mean platelet volume is a marker of platelet activation, so this study was designed to answer the question: does mean platelet volume increase in hypertensive retinopathy.

Objective: To determine frequency of increased mean platelet volume in hypertensive retinopathy. **Study Design:** Cross-sectional study**.**

Study Duration: Six months. **Setting:** Outpatient department of Medical unit III, Allied Hospital, Faisalabad. **SUBJECTS AND METHODS:** 138 patients of essential hypertension with hypertensive retinopathy of all ages and both sexes were included. For grading of hypertensive retinopathy according to the Keith Wagener classification, direct ophthalmoscopy was performed in all the subjects and mean platelet volume was measured after taking the blood sample. **Results:** The mean platelet volume was found to be normal (≤10 fl) in 97 patients (70.3%), among them 53 were males and 44 were females. Elevated levels of mean platelet volume (>10 fl) were found in 41 patients (29.7 %), of these 19 were males while 22 were females. In patients of grade 1 hypertensive retinopathy, the mean platelet volume was 9.1 ± 0.6 fl. In grade 2, 3 and 4 hypertensive retinopathy the values of mean platelet volume were 9.6 ± 0.5 fl, 10.1 ± 0.3 fl and 10.7 ± 0.6 fl respectively. **Conclusion:** This study concluded that frequency of mean platelet volume is increased in patients of hypertensive retinopathy and frequency increases with increasing the severity of hypertensive retinopathy.

Key words: mean platelet volume, platelet activation, essential hypertension, retinopathy.

INTRODUCTION

Hypertension is associated with increased cardiovascular risk leading to systemic end-organ damage, including retinopathy.[1,2] Prevalence of hypertensive retinopathy (HR) among hypertensive patients is quite high, seen in both sexes and almost in all age groups. It increases with duration of the disease and is maximum in patients with duration of 10 years or more.[3] The pathophysiological mechanism of hypertensive retinopathy is not fully established.

Platelets normally circulate in a quiescent disc shaped state and as they activate they undergo a disc to sphere transformation with the development of pseudopodia, causing a subsequent increase in size. So, mean platelet volume (MPV) is a marker of platelet activation.[4] It has been reported that platelet activation and aggregation are central processes in the pathophysiology of coronary heart disease.[5]

In hypertensive retinopathy, elevated blood pressure alone does not fully account for the extent of retinopathy, so other pathogenic mechanisms may be involved, such as increased platelet activation. It was shown that the level of mean platelet volume in grade 2 hypertensive retinopathy was significantly higher than in grade 1 hypertensive retinopathy.[6] As strong association between platelet activation and other vascular diseases such as coronary heart disease has been described, we want to determine whether the phenomenon of platelet activation is associated with hypertensive retinopathy.

Patients with larger platelets can easily be identified during routine haematological analysis and could possibly benefit from preventive treatment. Thus, MPV is an important, simple, effortless, and cost-effective tool that should be used and explored extensively, especially in countries like Pakistan, for predicting the possibility of vascular complications.[7]

Rationale of this study is detection of hypertensive retinopathy by using MPV, a cheap routine test, as an indicator of hypertensive retinopathy. This study will

help us identify the cases of hypertensive retinopathy (which is a commonly ignored complication of hypertension) among the known essential hypertensive patients, so that measures would be taken to prevent this complication.

MATERIAL AND METHODS

Setting: This study was carried out in Outpatient department of Medical unit III, Allied Hospital, Faisalabad. This is a tertiary care teaching hospital, attached to the Punjab Medical College, Faisalabd having 1100 beds. Faisalabad is the third biggest city of Pakistan and Allied hospital is the main referral teaching hospital for the whole district and the surroundings.

Duration of study: The duration of the study was six months, from May 2009 to Oct 2009.

Sample size: 138 patients

Study Design: It was a Cross-sectional study.

Sampling Technique : Technique used was Non probability purposive sampling.

Sample Selection

Patient selection was done in a meticulous manner for which an inclusion and exclusion criteria was delineated.

Inclusion Criteria

Known essential hypertensive patients of all ages and both sexes with hypertensive retinopathy.

Exclusion Criteria

- Diabetes mellitus (fasting blood sugar >126 mg/dl).
- Dyslipidemia .
- Obesity (body mass index>30 kg/m^2).
- Recent major surgery or illness within last six months.
- Patients on drugs affecting platelet function (heparin, aspirin, clopidogrel, warfarin).

Data Collection Procedure

The patients were selected from OPD of medical unit III of Allied hospital, after approval of Ethical Review Committee, Punjab Medical College, Faisalabad. Informed consent was obtained from all the subjects. All of them gave a detailed history and underwent weight and height measurements for the calculation of body mass index (BMI=weight/height). Those having BMI > 30 kg/m^2 or giving a history of using the drugs affecting platelet function, were excluded from the study. Arterial BP was recorded with a mercury sphygmomanometer after the patient had taken 5 minutes rest. For each subject, the average of two readings were obtained. Hypertension was defined as systolic blood pressure≥140 mmHg or diastolic blood pressure≥90 mmHg.

The patients were called back and blood samples were drawn after a fasting period of 12 hours. Enzymatic colorimetric assay method was used to measure fasting lipid profile (triglycerides, total cholesterol and HDL-cholesterol) and fasting plasma glucose levels. Those suffering from diabetes (fasting blood sugar>126mg/dl) or dyslipidemia (HDL<40 or >60 mg/dl, LDL >100 mg/dl, triglycerides >150 mg/dl or total cholesterol >200 mg/dl) were excluded from the study. The patients were then sent to the pathology laboratory in the Allied hospital where the pathologist measured the mean platelet volume after taking the blood sample and collecting it in citrate (1:4 v/v) in order to reduce platelet swelling, induced by EDTA.

For the evaluation of hypertensive retinopathy, direct ophthalmoscopy was performed in all subjects using the ophthalmoscope (Model NEITZ RP BXα Tokyo Japan, AC 230 V, 50/60 Hz, 0.3 W) after dilatation of pupils with 1% Mydriacyl eye drops.

138 known cases of essential hypertension with hypertensive retinopathy were included in the study.

Data analysis

Statistical analysis was done by using SPSS-12 version. The quantitative variables were presented as Mean ± SD i.e age and mean platelet volume. Frequency and percentages were presented for categorical variables i.e gender and grades of hypertensive retinopathy. One way ANOVA test was used to compare mean platelet volume in all grades of hypertensive retinopathy.

RESULTS

A total number of 138 patients who were known cases of essential hypertension with variable degrees of hypertensive retinopathy were included in the study. These patients were distributed in 5 different age groups. Group 1 (31-40 years) had 20 patients(14.5 %), Group 2 (41-50 years) had 34 patients(24.6 %), Group 3 (51-60 years) had 32 patients(23.2 %), Group 4 (61-70 years) had 44 patients(31.9%) and Group 5 (71-80 years) had 8 patients(5.8%). This showed a maximum distribution of patients of hypertensive retinopathy in age groups 41 to 70 years. These patients had a mean age of 54.1 ± 11.7 years (see TABLE No 1).

The mean platelet volume was found to be normal (≤10 fl) in 97 patients (70.3 %), among them 53 were males and 44 were females. Elevated levels of mean platelet volume (> 10 fl) were found in 41 patients (29.7 %), of these 19 were males while 22 were females.

The patients were examined by direct ophthalmoscopy and were classified in four different grades of hypertensive retinopathy, according to Keith Wagener Classification.

Patients of Grade 1 retinopathy were 58 (42 %) in total while those of grade 2, 3 and 4 were 62 (44.9 %), 14 (10.1 %) and 4 (2.9 %) respectively. This data showed that the maximum number of patients were falling in the grade 2 hypertensive retinopathy. Also we can conclude that most of the patients i.e 86.9 % were either of grade 1 or grade 2 hypertensive retinopathy. Patients with grade 4 retinopathy constituted a very small group (< 3 %).

Oneway Anova test was used to assess the hypothesis (i.e the frequency of mean platelet volume increases with the increase in the degree of hypertensive retinopathy). This test showed $p< 0.0005$ and strongly supported our hypothesis. In patients of grade 1 HR, the MPV was 9.1 ± 0.6 fl. In grade 2, 3 and 4 hypertensive retinopathy the values of MPV were 9.6 ± 0.5 fl, 10.1 ± 0.3 fl and 10.7 ± 0.6 fl respectively. These progressively increasing mean values of the MPV in different grades of hypertensive retinopathy (as shown in TABLE No. 2) also strengthens the hypothetical statement.

In grade 1 HR, 49 patients had normal MPV while 9 patients (15.5 %) had increased MPV values. Similarly, in grade 2 HR, 41 cases had normal and 21 (33.9 %) had increased MPV. Grades 3 and 4 patients had even higher percentages i.e 57.1 % and 75 % respectively (see TABLE No.3).

Table 1:
Distribution of patients according to age

Age group (years)	Frequency	Percent
31-40	20	14.5
41-50	34	24.6
51-60	32	23.2
61-70	44	31.9
71-80	8	5.8
Total	138	100.0

Mean ± S.D= 54.1 ± 11.7 years

Table 2: Oneway Anova Test

MPV	Sum of squares	df	Mean Square	F	Sig
Between groups	19.670	3	6.557	21.287	0.0005
Within groups	41.275	134	.308		
Total	60.945	137			

Mean platelet volume

Mean ± S.D in Grade 1 HR = 9.1 ± 0.6 fl.
Mean ± S.D in Grade 2 HR = 9.6 ± 0.5 fl.
Mean ± S.D in Grade 3 HR = 10.1 ± 0.3 fl.
Mean ± S.D in Grade 4 HR = 10.7 ± 0.6 fl.

Table 3: Groups of mean platelet volume according to grades of hypertensive retinopathy

Grades of HR	Count/ %	Groups of mean platelet volume		Total
		normal	increased	
1	Count	49	9	58
	% within grades of hypertensive retinopathy	84.5%	15.5%	100.0%
2	Count	41	21	62
	% within grades of hypertensive retinopathy	66.1%	33.9%	100.0%
3	Count	6	8	14
	% within grades of hypertensive retinopathy	42.9%	57.1%	100.0%
4	Count	1	3	4
	% within grades of hypertensive retinopathy	25.0%	75.0%	100.0%
Total	Count	97	41	138
	% within grades of hypertensive retinopathy	70.3%	29.7%	100.0%

DISCUSSION

Platelet abnormalities have been described in hypertension especially in the presence of target organ damage.

Our study results showed that the level of MPV was higher in grade 2 HR than in grade 1 HR (9.6 ± 0.5 fl vs 9.1 ± 0.6 fl) and that MPV in grade 3 HR was greater than in grade 2 HR (10.1 ± 0.3 fl vs 9.6 ± 0.5 fl), and finally grade 4 HR showed the highest value of MPV among all the grades. We found that the level of MPV increased as the degree of HR increased, in other words MPV showed positive correlation with the severity of HR. Our study results are comparable with those reported by Coban and his colleagues. They found a higher MPV in grade 2 HR (8.9 ± 0.8 fl) than in grade 1 HR (8.3 ± 0.8 fl). Moreover MPV values were higher in grade 1 HR than in normotensive control group who were not suffering from any retinopathy. They proved a positive correlation between MPV and the grades of HR.[6]

Carraro and colleagues found a strong association of different platelet parameters including mean platelet volume (MPV), platelet counts, platelet distribution width and the platelet–large-cell ratio with retinopathy.[8]

Nadar et al. found that MPV in patients with hypertension was significantly higher than in normotensive control subjects and within the hypertensive group those with evidence of target organ damage had significantly larger platelets with a greater mass than those without target organ damage. (Stroke, Previous myocardial infarction, angina, left ventricular hypertrophy).[9]

Scuteri et al. reported that MPV seem to be associated with increased left ventricular mass and inter ventricular septum thickness in middle aged elderly hypertensive patients.[10]

Platelet activation and hyperactivity has been proved by Varol et al. as one of the possible mechanisms causing hypertensive target organ damage e.g myocardial infarction. There is transient occlusion of the infarct-related artery owing to platelet hyperactivity and thrombosis. Mean platelet volume (MPV), an indicator of platelet activation, has been shown to be elevated in patients with unstable angina and myocardial infarction. In this study the MPV values of patients with myocardial infarction with normal coronary arteries were significantly higher than those of the control group (9.1±1.8 and 9.4±1.0 versus 8.3±1.4 fl; $p<0.05$ and $p<0.001$, respectively).[11] These mean values of MPV (9.1 and 9.4 fl) are very much close to our values (9.1 and 9.6 fl) in grade 1 and grade 2 hypertensive retinopathy. Thus both of these studies favour an increased MPV levels in target organ damage due to hypertension i.e myocardial infarction and hypertensive retinopathy respectively.

In another study, Coban et al. evaluated MPV as one possible mechanism by which white coat and essential hypertensive subjects might be at increased risk to develop microvascular complications. He described that MPV was significantly higher in essential hypertensives and white coat hypertensives than in normotensives; it was also higher in essential hypertensives than in white coat hypertensives. Moreover, MPV was positively correlated with ambulatory diastolic blood pressure in essential hypertension and white coat hypertension groups.[12] A very similar study narrated that MPV values were significantly higher in the prehypertensive group than in the control group (respectively, 10.41 ± 0.93 fl vs. 9.56 ± 1.04 fl, $p < 0.01$). Additionally, MPV was positively correlated with the systolic blood pressure. This study displayed a significant increase in MPV in prehypertensive subjects.[13] As it has already been established that degree of HR is significantly related to the pressure and severity of hypertension[14], so the similarity between our study and two of the above mentioned studies is that the MPV levels increase gradually as the severity of hypertension (and hence the severity of HR) increases.

Papanas also described an increased mean platelet volume in microvascular complications like peripheral neuropathy[15] and indirectly acknowledged the role of platelet activation in the pathogenesis of vascular lesions in different organs which share a common pathophysiology.

HR is among the vascular complications of essential hypertension. It is known that the autoregulation of retinal circulation fails as blood pressure increases beyond a critical limit however elevated blood pressure alone does not fully account for the extent of HR. There are cases in which retinopathy was resolved despite the persistence of high BP.[16,17] In addition to the effect of high BP, increased platelet activation plays an important role in the pathogenesis of HR.[18] Thus, the presence of high MPV levels in HR and the correlation of the increased MPV with the severity of HR imply that MPV may be involved in the mechanism of HR.

This study indirectly suggests a relationship between hypertensive retinopathy and platelet activation in essential hypertension. Platelet activation, a mechanism known to be involved in vascular lesions, may promote the development of HR.

CONCLUSION

This study concluded that frequency of mean platelet volume is increased in patients of hypertensive retinopathy and MPV increases with increasing the severity of hypertensive retinopathy.

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