Role of Mean Platelet Volume (MPV) as a Predictive Marker for Hypertensive Vascular Complications - A Cross-Sectional Study in a Tertiary Care Hospital

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ABSTRACT

BACKGROUND

Hypertension alone or in various combinations has been a major risk factor in ischaemic and haemorrhagic strokes. The mean platelet volume is a laboratory marker associated with platelet function and activity. Mean platelet volume is independently associated with Peripheral Artery Disease (PAD) and uncontrolled hypertension. We wanted to study the associated MPV levels in different grades (Grade I and Grade III) of hypertension in comparison with those of healthy normotensives.

METHODS

The current study was an analytical cross-sectional study, conducted in Velammal Medical College Hospital, Madurai, India, from October 2019 to December 2019. Patients with grade 1 and grade 3 hypertension as cases, and healthy individuals as controls were included in the study. Platelet parameters were assessed by the Beckman Colter haematology analyser (LH 750) by impendence technology. ANOVA was used to assess statistical significance. p-value < 0.05 was considered as statistically significant. IBM SPSS version 22 was used for statistical analysis.

RESULTS

Among the study population, 200 (57.14%) participants were controls, 100 (28.57%) participants were graded as 1 HT and 50 (14.29%) participants were grade as 3 HT. The Mean MPV (fL) among controls was 7.63 ± 1.13; it was 8.04 ± 0.91 in grade 1 HT group, and it was 10.05 ± 0.73 in grade 3 HT group and was statistically significant. The mean platelet count (1000 cells /cu. mm) among controls was 256.96 ± 62.78; it was 290.96 ± 79.77 in the grade 1 HT group and it was 295.68 ± 60.55 in grade 3 HT group and was statistically significant.

CONCLUSIONS

We conclude that MPV levels and platelet counts were increased with increasing severity of hypertension. MPV, as an important indicator of platelet activation can be used as a cost-effective diagnostic tool to identify hypertensive patients who are at increased risk for thrombotic vascular complications.

KEYWORDS

Mean Platelet Volume, Platelet Count, Hypertension, Thrombosis, Vascular Complications

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BACKGROUND

Hypertension alone or in various combinations has been a major risk factor in ischaemic and haemorrhagic strokes. In an analysis of worldwide data for the global burden of HTN, 20.6% of Indian men and 20.9% of Indian women were suffering from HTN in 2005. The rates for HTN in percentage are projected to go up to 22.9 and 23.6 for Indian men and women, respectively by 2025. Recent studies from India have shown the prevalence of HTN to be 25% in urban and 10% in rural people in India.[1] According to the WHO 2008 estimates, the prevalence of raised BP in Indians was 32.5% (33.2% in men and 31.7 % in women). However, only about 25.6% of treated patients had their BP under control, in a multicenter study from India.[2]

The ICMR multi-centric prospective case-control study of ischaemic strokes revealed that hypertension along with raised blood sugar, tobacco use, and low haemoglobin are important risk factors.[3] It is well known that up to a third of cardiovascular deaths can be avoided by proper treatment and control of hypertension and by addressing this risk factor we can significantly prevent premature (cardiovascular diseases) CVD mortality in India.[4] Suboptimal BP control is the most common attributable risk factor for CVD and cerebrovascular disease, including haemorrhagic (58%) and ischemic (50%) stroke, ischemic heart disease (55%), and other forms of CVD (58%), including heart failure and peripheral arterial disease.[5,6] Public health, health systems based as well as clinic-based interventions are needed to increase awareness, treatment, and control of hypertension.[7]

The mean platelet volume is a laboratory marker associated with platelet function and activity.[8] It is a blood parameter used for measuring platelet size and can be determined in routine blood tests. It is cost-effective and yields results in a short amount of time.[9] Increased MPV in thromboembolic disease is reflected as an important risk factor. Elevated MPV is associated with other markers of platelet activity, including increased platelet aggregation, increased thromboxane synthesis, increased β-thromboglobulin release, and increased expression of adhesion molecules.[10] MPV is a determinant of platelet activation and high sensitive C-reactive protein (hs-CRP) is the best candidate assay to identify and monitor the inflammatory response.[11] It is independently associated with peripheral artery disease (PAD and platelet size is an independent predictor of increased risk for PAD.[12] Varol E et al. showed that MPV was also higher in patients with hypertension than in patients with prehypertension.[13]
Patients with uncontrolled hypertension are at increased risk for cardiovascular events. MPV can be a useful screening test to antiplatelets for preventing cardiovascular diseases in uncontrolled hypertension patients. This study aims to assess the association of MPV levels in different grades (Grade I and Grade III) of hypertensive patients in comparison with healthy normotensive individuals.

METHODS

This is an analytical cross-sectional study conducted in Velammal Medical College Hospital, Madurai, Tamilnadu, India from October 2019 to December 2019.

Inclusion Criteria

Patients with Grade 1 hypertension and Grade 3 hypertension as cases and healthy individuals as controls were included in the study.

Exclusion Criteria

Subjects with renal diseases, pre-operated patients for CVD, on antiplatelet therapy, participants not willing to participate in the study.

Study Area

Patients reporting to the general medicine department of the Velammal Medical College Hospital, Madurai, Tamilnadu, India. Participants were randomly selected in that time frame who reported to the hospital. Controls were 200 (57.14%) participants, 100 (28.57%) participants were with grade 1 HT and 50 (14.29%) participants were with grade 3 HT.

Grading of hypertension was done by the following grading system (ESH/ESC 2013).[14]

Category	Systolic	Diastolic
Optimal	<120	<80
Normal	120-139	80-84
High normal	130-139	85-89
Grade 1 hypertension	140-159	90-99
Grade 2 hypertension	160-179	100-109
Grade 3 hypertension	≥180	≥110
Isolated systolic hypertension	≥140	<90

Grading of Hypertension (ESH / ESC 2013)

Study Procedure

The following information was collected from each subject through a validated questionnaire administered by the volunteers: name, age, sex, occupation, weight, height, history of diabetes, family history of hypertension, history of any examination of blood pressure and hypertension, or any it's complications, any symptom referable to target organ dysfunction, previous and present treatment profile, and addictions. Blood pressure was recorded in the sitting position for the right arm to the nearest 2 mmHg using the Mercury Sphygmomanometer (Diamond Deluxe BP apparatus, Pune, India). Blood pressure is measured for each participant, using the palpatory and auscultatory methods with a standardized calibrated mercury column type sphygmomanometer and an appropriate sized cuff encircling at least 80% of the arm in the seated posture, with feet on the floor and arm supported at heart level. Following a standardized protocol, three separate measurements with an interval of 5 minutes are recorded and the average of the three measurements after proper rest and due explanation to the examined participants about the

objective of the study. Blood samples are obtained after overnight fasting from mid-cubital vein in antecubital fossa making the subject sit comfortably in a chair. Through a sterile Dispovan syringe under sterile precautions, about three millilitres of blood is collected in EDTA coated vacutainers. Platelet parameters were assessed by the Beckman Colter haematology analyser of model number LH 750 by impendence technology.

Ethical Consideration

The study got approval from the institutional human ethics committee. Informed written consent was obtained from the participants and the confidentiality of the study participants was maintained throughout the study.

Statistical Analysis

Platelet count, MPV were considered as the primary outcome of interest. Descriptive analysis was carried out by frequency and proportion for categorical variables. The association between categorical explanatory variables and quantitative outcome was assessed by comparing the mean values. The mean differences along with their 95% CI were presented. ANOVA was used to assess statistical significance. The association between explanatory variables and categorical outcomes was assessed by cross tabulation and comparison of percentages. A Chi-square test was used to test statistical significance. P-value <0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

RESULTS

A total of 350 patients included in the final analysis. Among the study population, 200 (57.14%) participants were controls, 100 (28.57%) participants were graded 1 HT and 50 (14.29%) participants were grade 3 HT. The Mean age within controls was 48.62 ± 13.82, it was 53.79 ± 11.98 in grade 1 HT group and it was 59.22 ± 10.22 in grade 3 HT group. Taking controls as a baseline, the mean difference of age in grade 1 HT and grade 3 HT group was statistically significant (P-value <0.05). The difference in gender across the study groups was found to be insignificant with a P-value of 0.637, with a majority of 64% of participants were grade 1 HT group. (Table 1)

The Mean systolic blood pressure within controls was 117.6 ± 8.96, it was 140.6 ± 6.33 in grade 1 HT group and it was 193.6 ± 15.49 in grade 3 HT group. Taking controls as a baseline, the mean difference of systolic blood pressure in grade 1 HT and grade 3 HT group was statistically significant (p-value <0.05). The Mean diastolic blood pressure within controls was 74 ± 4.91, it was 89.2 ± 3.82 in grade 1 HT group and it was 105 ± 10.74 in grade 3 HT group. Taking controls as the baseline, the mean difference of diastolic blood pressure in grade 1 HT and grade 3 HT group was statistically significant (p-value <0.05). (Table 2)

The Mean MPV (fl) within controls was 7.63 ± 113, it was 8.04 ± 0.91 in grade 1 HT group and it was 10.05 ± 0.73 in grade 3 HT group. Taking controls as the baseline, the mean difference of MPV (fl) in grade 1 HT and grade 3 HT both were statistically significant (p-value <0.05). The Mean platelet count (1000 cells /cu. mm) within controls was 256.96 ± 62.78, it was 290.96 ± 79.77 in the grade 1 HT group and it was 295.68 ± 60.55 in grade 3 HT group. Taking controls as a baseline, the mean difference of platelet count (1000 cells /cu. mm) in grade 1 HT and grade 3 HT group was statistically significant (p-value <0.05). (Figure 3)

Parameter	Study Group Controls (N=200)	Grade 1 HT (N=100)	Grade 3 HT (N=50)	P-Value
Age (in years) (Mean ± SD)	48.62 ± 13.82	53.79 ± 11.98	59.22 ± 10.22	<0.001
Gender				
Male	122 (61%)	64 (64%)	28 (56%)	0.637
Female	78 (39%)	36 (36%)	22 (44%)	

Table 1. Comparison of Gender across the Study Groups (N=350)

Study Group	Mean ± SD	Mean Difference	95% CI Lower	95% CI Upper	P-Value
SBP in mm of Hg					
Controls	117.6 ± 8.96		(Baseline)		
Grade 1 HT	140.6 ± 6.33	23	20.70	25.30	<0.001
Grade 3 HT	193.6 ± 15.49	76	73.03	78.97	<0.001
DBP in mm of Hg					
Controls	74 ± 4.91		(Baseline)		
Grade 1 HT	89.2 ± 3.82	15.20	13.79	16.61	<0.001
Grade 3 HT	105 ± 10.74	31	29.18	32.82	<0.001

Table 2. Comparison of Mean SBP and DBP across the Study Groups (N=350)

Study Group	Mean ± SD	Mean Difference	95% CI Lower	95% CI Upper	P-Value
MPV (fl)					
Controls	7.63 ± 1.13		(BASELINE)		
Grade 1 HT	8.04 ± 0.91	0.41	-0.66	-0.17	0.001
Grade 3 HT	10.05 ± 0.73	2.42	2.10	2.73	<0.001
Platelet Count (1000 cells /cu. mm)					
Controls	256.96 ± 62.78				
Grade 1 HT	290.96 ± 79.77	34.005	17.68	50.33	<0.001
Grade 3 HT	295.68 ± 60.55	38.725	17.65	59.80	<0.001

Table 3. Comparison of Mean MPV (fl) and Platelet Count across the Study Groups (N=350)

DISCUSSION

Hypertension is an important risk factor for heart attack, stroke, and other vascular diseases.[15] Mean platelet volume (MPV) shown to be significantly increased in patients with hypertension, acute ischaemic stroke, especially in non-lacunar strokes.

Many indexes of platelet function have appeared as underlying prognostic markers of cardiovascular disease. However, most of the techniques used to analyse platelet activity are costly and time-consuming and require specialized techniques. In contrast to these methods, an approach considering MPV could be easily and cheaply made available. Elevated MPV indicates the presence of larger, more reactive platelets.[16] Larger and activated platelets secrete more prothrombotic material and express more substances than small platelets, which accelerate the formation of thrombus and increase the risk for several diseases. In fact, over the past decade, an accumulating

body of evidence has demonstrated that MPV is a predictive marker for stroke and coronary artery disease.[17]

In the current study, we observed that MPV levels were significantly increased in both grade 1 and 3 of hypertension when compared to controls. It is in line with Varol et al who conducted a case-control study and reported that the MPV values of patients with prehypertension and hypertension were significantly higher than those of the control group (8.4 ± 0.8 and 8.8 ± 0.7 versus 7.9 ± 0.5; $p<0.05$ and $p<0.001$ respectively). It was also higher in hypertensives than in pre-hypertensives (8.8 ± 0.7 versus 8.40.8; $p < 0.05$).[13] Similarly, Ian et al.[18] Conducted a case-control study investigated resistant hypertension and showed that MPV values in cases of resistant hypertension are higher than those in controlled-hypertensive cases or normotensive cases. These studies have shown that MPV is positively correlated with blood pressure. Whereas in a study conducted by Bath et al MPV was 7.7 fl vs. 7.8 fl, and platelet count 242 x 10(9)/l vs. 243 x 10(9)/l (2P=0.68) were similar in the hypertensive patients and normotensive subjects.[19] Another study by Butler et al concluded that there was no correlation between MPV and markers of end-organ damage in hypertensive patients which is not in line with our study.[20] In a study done by Pusuroglu H et al. on non-dipper and dipper hypertensive groups, they found significantly higher MPV levels than normotensives (8.4 ± 1 fL, 8.3 ± 1 fL, and 8.1 ± 0.6 fL, respectively, $p<0.001$) which is similar to our study.[21]

MPV, has been significantly higher in patients with prehypertension compared with control subjects and also in patients with hypertension than prehypertension.[13] MPV is one of the important platelet production indices that may relate to platelet function. It has been shown that platelet size, measured as MPV, correlates with their reactivity.[22] Larger and hyperreactive platelets accelerate intracoronary thrombus formation, which leads to a cascade of clinical events, such as acute coronary syndromes.[23] Nadar et al.[24] demonstrated that hypertensive patients with target organ damage including stroke, previous MI, angina microalbuminuria/proteinuria, and left ventricular hypertrophy, had higher MPV levels than hypertensive patients without target organ damage. There is also a role for evaluating MPV in patients with peripheral artery disease, unprovoked deep vein thrombosis, and pulmonary embolism.[25,26]

The present study showed significantly increased platelet count among grade 3 hypertensives which is in line with Gomi et al who reported increased platelet activation in hypertensive patients.[27] Shear forces, the renin-angiotensin system, endothelial dysfunction, elevated catecholamine levels, and the presence of comorbid conditions promotes the increased activation of platelets in hypertensive patients.[28] In a systematic review done by Chu SG et al. found that elevated MPV is associated with AMI, mortality following myocardial infarction, and restenosis following coronary angioplasty. It suggested that MPV is a potentially useful prognostic biomarker in patients with cardiovascular disease.[9] In a study done by Ntiaos et al on 636 subjects, they found that glucose, serum creatinine, haemoglobin, platelet count, and history of arterial hypertension were found to be significantly associated with MPV. On multivariate regression analysis, hypertension and platelet count remained as independent determinants of MPV.[29]

There is a lack of universal external calibration for MPV analysis. There can also be variability in the measurement of MPV depending on the instrument used.[30]

Platelet activation is believed to contribute importantly to the increased risk of thrombosis in essential hypertension, and this may be mediated through a variety of mechanisms. Neurohumoral activation is believed to play an important role in this. Increased activity of the sympathetic nervous system facilitates norepinephrine release from adrenergic nerve terminals and enhances the responsiveness of adrenergic receptors.[31] Importantly, increased sympathetic tone activates platelets, contributing to the hypercoagulability observed in hypertension.[32]

Although several authors have described MPV as a marker of platelet reactivity and risk factor for cardiovascular diseases, there is a higher variability in the literature. Although preanalytical variability is known from its introduction as standard laboratory value, no preanalytical standards have been introduced.[33]

The limitation of the study was that we did not evaluate other platelet activation markers such as mean platelet component, platelet component distribution width, and ADP or collagen-induced platelet activation. Secondly, the number of individuals in each group is different from each other. This case may attenuate the power of the statistical analyses which were used. And the smaller sample size affected the generalizability of results.

CONCLUSIONS

MPV levels and platelet counts were increased with increasing severity of hypertension. MPV, as an important indicator of platelet activation, can be used as a cost-effective diagnostic tool to identify hypertensive patients who are at increased risk for thrombotic vascular complications, and further studies are required to determine as to whether therapeutic modification of this marker will reduce these risks in hypertensive patients.

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