Original Research Article

A study on mean blood platelet volume levels in patients with depression and generalized anxiety disorder

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Abstract
Background: *Stressful events, depression and anxiety usually elevate circulating levels of blood catecholamines which causes an increase in platelet activity and sympathoadrenal activation is thought to stimulate platelet through the α -2 receptors resulting in an increase in platelet volume.*
Aim: *To estimate the mean blood platelet volume levels in depressive disorder and generalized anxiety disorder patients.*
Methods: *The study was a hospital based cross sectional study conducted in the Department of Psychiatry, Assam Medical College and Hospital, Dibrugarh, Assam during the time period of June 2018 to May 2019 (1 year) after obtaining ethical clearance from the Institution Ethics Committee.*
Results: *Mean MPV level of Depression cases (13.25 ± 1.31 fl) was higher than GAD cases (11.79 ± 1.71 fl). It was statistically found to be significant (p value <0.001).*
Conclusion: *To the best of our knowledge no study till date studied the interrelationship among MPV, severity of Depression and GAD.*
Keywords: *Depression, generalized anxiety disorder, mean blood platelet volume.*

Introduction

Major depressive disorder is reported to be the most common mood disorder[1]. A major depressive disorder occurs without a history of a manic, mixed or hypomanic episode. It must last for at least 2 weeks [2]. The individual usually suffers from depressed mood, loss of interest and enjoyment, reduced energy leading to increased and easy fatigability with diminished activity[3]. Major depressive disorder has the highest lifetime prevalence (almost 17%) of any psychiatric disorder. There is two-fold greater prevalence of major depressive disorder in women than in men[2].

Anxiety is an emotion that predates the evolution of man[4]. GAD is characterized by an uncontrollable worry, more days than not, lasting greater than 6 months, and causing significant impairment[5]. Generalized anxiety disorder is a common condition; reasonable estimates for its 1year prevalence range from 3% to 8%. The women to men ratio is 2:1. About 25% of anxiety disorder patients have generalized anxiety disorder[6].

Platelets are disc shaped anucleate cell fragments that are shed from megakaryocytes in the bone marrow in the blood stream. The transport, metabolism, and release of several bio aminergic neurotransmitters (e.g. serotonin) are similar in platelets and neurons and thus platelets serve as a diagnostic tool and an interesting research model in several psychiatric disorders [7]. MPV has been found to be elevated in various mental disorders. The relationship between anxiety disorders, bipolar disorder, schizophrenia, major depression and increased platelet activity has been reported by several studies [8-12].

The exact mechanism of increased platelet activity after mental stress remains unclear. Stressful events, depression and anxiety usually elevate circulating levels of blood catecholamines. Increased catecholamine levels are thought to increase thrombosis by causing an increase in platelet activity and sympathoadrenal activation is thought to stimulate platelet through the α -2 receptors resulting in an increase in platelet volume [13,14].Treatment with SSRIs may lead to a decrease in platelet activity[15]. Mean blood platelet volume which is indicative of platelet size, is accepted as an indication of platelet activity [16]. MPV levels in generalized anxiety disorder supports the hypothesis of increase platelet activation due to sympathetic system activation[7]. The relationship between depression and platelet function has been in focus, because platelet share many similarities with the neuronal monoamine system in the central nervous system [17].

As there are limited studies on platelet parameters in psychiatric disorders like depression and GAD in our region as well as in rest of India, it has prompted us to take up this study.

Materials and Methods

This study was a hospital based cross sectional study conducted in the Department of Psychiatry, Assam Medical College and Hospital, Dibrugarh, Assam, during the time period of June 2018 to May 2019 (1 year) after obtaining ethical clearance from the Institution Ethics Committee.

Patients attending psychiatric services in the Department of Psychiatry, AMCH and diagnosed as Depression & Generalized Anxiety Disorder (GAD) as per ICD-10, fulfilling inclusion and exclusion criteria, and confirmed by a consultant psychiatrist were taken for the study as Group A (50 cases) &Group B (42 cases), respectively. Patients of all ages and both genders were included in the study. The patients with the following conditions were excluded from both the study groups which might cause altered mean blood platelet volume (MPV) level-those with comorbid mental illness; those with comorbid physical illness; patients on anti-platelet drugs like- aspirin, clopidogrel, ticlopidine, prasugrel, abciximab, etc.; patients on furosemide, penicillin, quinidine, quinine, ranitidine, sulphonamides, linezolid, etc.; patients on cytotoxic chemotherapy, post splenectomy patients; and pregnancy. An informed consent was taken from each participant. Socio demographic data of each patient was recorded in the demographic sheet.

Mean blood platelet volume (MPV) levels were estimated in all respondents prior to administration of pharmacological therapy. About 5 ml of venous blood were collected from each patient and analysed within 2-4 hours of sample collection by the Sysmex automated haematology analyser in the Clinical Haematology Laboratory in the Department of Pathology, AMCH, Dibrugarh. The mean platelet volume (MPV) is measured using impedance technology and is derived from the impedance platelet size distribution curve. The MPV is very dependent on the technique of measurement and on the length and conditions of storage before the blood is tested. It is calculated by dividing plateletcrit by platelet count[18]. The normal reference value is 6.5-11 fl (this normal reference range is set (fixed) in the Sysmex automated haematology analyser machine in the Clinical Haematology Laboratory of Department of Pathology, AMCH, Dibrugarh). All derived platelet parameters are highly specific to the individual technologies, with different analysers having different normal range[18] .

Severity of depression and GAD were assessed by Hamilton Depression Rating Scale (HAM-D) &Hamilton Anxiety Rating Scale (HAM-A), respectively.

The statistical analysis of data was performed using the computer program, Statistical Package for Social Sciences (SPSS for Windows, version 21.0. Chicago, SPSS Inc.) and Microsoft Excel 2010. Student t test was performed to compare two mean values. Results on continuous measurements are presented as mean ± standard deviation are compared using Analysis of Variance (ANOVA). Discrete data are expressed as number (%) and are analysed using Chi square test and Fischer's exact test (where the cell counts were <5 or 0). Pearson's correlation coefficient (r) was used to measure the associations among continuous variables. For all analyses, the statistical significance was fixed at 5% level (p value <0.05).

Results

Mean age of the depression cases was 37.12 ± 13.58 years and GAD cases was 35.05 ± 11.43 years. Majority of the patients of depression (30%) and GAD (38.10%) belonged to 20-29 years age group (table 1). It was found that majority were females in both the groups, with 58% in depression and 54.76% in GAD (table 1).Mean MPV level of Depression cases (13.25 ± 1.31 fl) was higher than GAD cases (11.79 ± 1.71 fl). Student t test was performed and it was statistically found to be significant (p value <0.001) (table 2).In our study, mean MPV level was found to be most elevated in severe depression (14.27 ± 0.81 fl), followed by very severe depression (13.91 ± 1.10 fl), moderate depression (12.77 ± 1.01 fl) and mild depression (11.20 ± 1.64 fl). So, here the mean MPV level increased with increase in severity of depression. By performing ANOVA test, these findings were statistically found to be significant (p value <0.001) (table 3).A strong positive correlation between MPV level and severity of Depression

(r=0.5085) was found and it was statistically significant (p value = 0.000163). It indicated that there was a linear increase in MPV level with increase in severity of Depression (Fig-1). In our study, mean MPV level was found to be most elevated in severe cases of GAD (12.71 ± 1.43 fl) followed by moderate cases of GAD (11.34 ± 1.71 fl) and mild cases of GAD (11.20 ± 1.68 fl). So, here the mean MPV level is increased with increase in severity of GAD. By performing ANOVA test, these findings were statistically found to be significant (p value <0.05) (table 3).It was found that there was a positive correlation between MPV level and severity of GAD (r =0.3898) and this positive correlation was found to be statistically significant (p value=0.010717). It indicated that there was a linear increase in MPV level with increase in severity of GAD (Fig-2).

**Table 1:** Distribution of cases on the basis of age and gender

AGE GROUP (in years)	GROUP–A		GROUP–B	
	n	%	n	%
<20	2	4.00	2	4.76
20–29	15	30.00	16	38.10
30–39	13	26.00	10	23.81
40–49	11	22.00	7	16.67
50–59	5	10.00	6	14.29
≥ 60	4	8.00	1	2.38
TOTAL	50	100.00	42	100.00
MEAN ± S.D (in years)	37.12 ± 13.58		35.05 ± 11.43	
p value	0.1521956			
GENDER	GROUP–A		GROUP–B	
	n	%	n	%
Male	21	42.00	19	45.24
Female	29	58.00	23	54.76
TOTAL	50	100.00	42	100.00
p value	0.75498			

Table 2: Comparison of MPV level in patients of depression and generalized anxiety disorder

	DEPRESSION	GAD
TOTAL CASES (n)	50	42
MEAN MPV LEVEL (*fl*) (Mean ± S.D.)	13.25 ± 1.31	11.79 ± 1.71
p value	< 0.001	

Table 3: Comparison of MPV level and severity of depression (as per HAM-D score) and generalized anxiety disorder (as per HAM-A score)

SEVERITY OF DEPRESSION	NUMBER OF CASES (*n* = 50)	MPV LEVEL (MEAN ± S.D) (*fl*)	*p value*
Mild	3	11.20 ± 1.64	<0.001
Moderate	23	12.77 ± 1.01	
Severe	7	14.27 ± 0.81	
Very severe	17	13.91 ± 1.10	
SEVERITY OF GAD	NUMBER OF CASES (n=42)	MPV LEVEL (MEAN ± S.D) (fl)	*p value*
Mild	11	11.20 ± 1.68	0.0304
Moderate	16	11.34 ± 1.71	
Severe	15	12.71 ± 1.43	

Fig–1
Clinical correlation between MPV level and severity of depression (HAM-D score)

Fig–2
Clinical correlation between MPV level and severity of GAD
(HAM-A score)
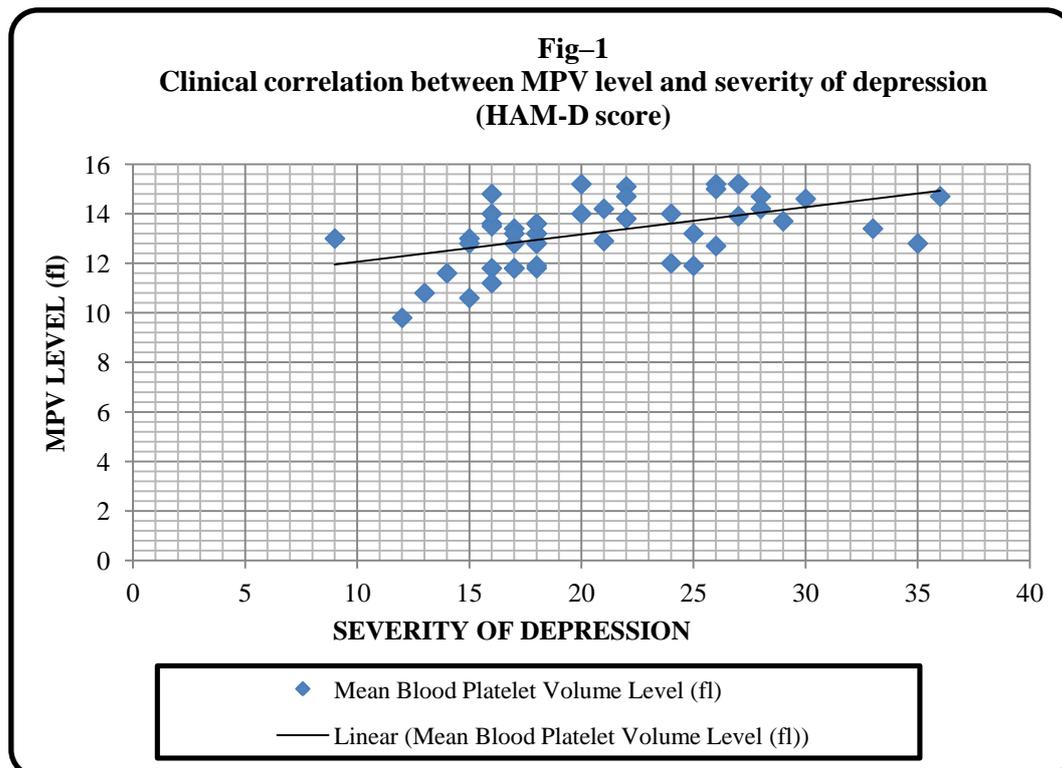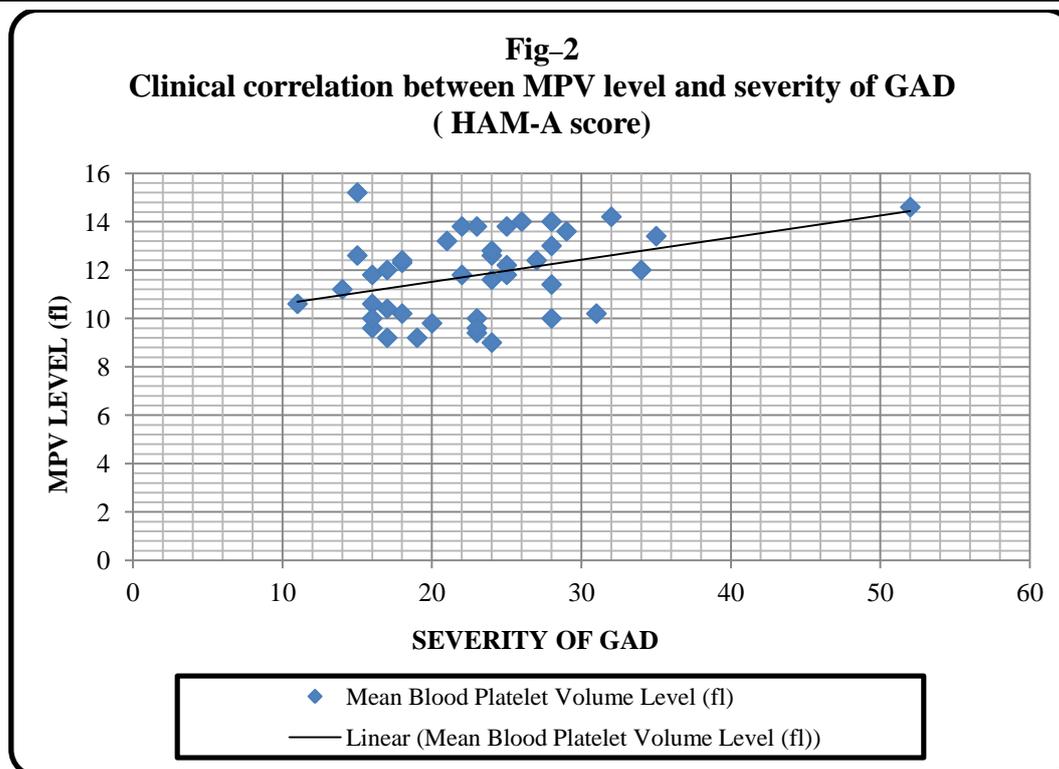
Discussion

In our study majority of the patients, 30% of depression cases and 38.10% of Generalized Anxiety Disorder cases, belonged to 20-29 years age group. According to DSM-5 the most common age of depression is 18-29 years age group which is quite similar to our findings[19]. Mean age of the Depression cases was 37.12 ± 13.58 years and GAD cases was 35.05 ± 11.43 years in our study which is similar to the findings by Bondade et al.[20] Ataogluet al.[21], found mean age of depression cases to be 37.1 ± 10.3 years in his study. Almis BH et al.[10], found that mean age for GAD cases in their study was 38.35 ± 18.97 years.

Majority of the Depression (58%) and GAD (54.76%) cases were females in our study. Depression was found to be very high among females in a study by Bondade et al.[20] which is consistent with our study. GAD was found to be high among females in the studies by Reddy and Chandrashekar et al. (1998)[22], Almis BH et al. (2017)[10].

The mean MPV level of depression patients (13.25 ± 1.31 fl) was significantly (p value <0.001) elevated than GAD patients (11.79 ± 1.71 fl). In the study by Bondade et al.[20], MPV was significantly (p<0.001) more in depressive disorder (9.73±1.23 fl) and anxiety disorder (9.84±1.3 fl) than in the controls (8.77±0.44 fl) and when the mean MPV levels were compared between depressive disorder and anxiety disorder, no statistically significant difference was found which is contrary to our study. In another study Canan F et al.[22] reported that patients with major depression were found to have increased MPV levels in comparison with controls. Almis and Aksoy et al.[10] found increased MPV levels in GAD patients as compared to healthy controls.

The mean MPV level was increased significantly (p value <0.001) with increase in severity of Depression (HAM-D score) and found a strong positive correlation between MPV level and severity of Depression (R =0.5085; p value <0.001). Similarly, Bondade et al. [20] found a positive correlation between HAM-D scores and MPV (r = +0.312). Here, the mean MPV level increased significantly (p value= 0.0304) with increase in severity of GAD (HAM-A score). There was a positive correlation between MPV

level and severity of GAD (r=0.3898; p value =0.010717) which is consistent to the findings by Bondade S et al.[20].

Conclusion

From our findings, it can be concluded that mean blood platelet volume (MPV) level was elevated significantly in Depression and GAD and elevation in depression patients were more than GAD patients. There was also a significantly positive linear correlation between mean blood platelet volume (MPV) level and severity of Depression and GAD.

Strengths of the Study

1) This study was a comparative study and it has evaluated the biological parameter mean blood platelet volume in patients of Depression and GAD.
2) This is the first study of its kind in Indian context. To the best of our knowledge no study till date studied the interrelationship among MPV, severity of Depression and GAD.
3) Detailed clinical assessment was conducted and laboratory investigations were performed in the Clinical Haematology Laboratory, Department of Pathology, Assam Medical College & Hospital, Dibrugarh. It was a sincere effort to estimate mean blood platelet volume levels in depression and generalized anxiety disorder patients attending psychiatric services in Assam Medical College and Hospital, Dibrugarh.

Limitations

1) This was an one-time cross sectional assessment study which lacked follow up.
2) The sample sizes of the study groups were relatively small and it is a hospital based study. So, the findings cannot be generalized to a larger community population.
3) The study groups were not compared to age and sex matched control groups.

Future Implications

The results of our study suggest that platelets are affected by diverse psychological stressors. The relation between MPV, depression and GAD raised the possibility of future research, theories and treatment options. The exact mechanism how MPV is associated with Depression and GAD is still unclear and needs to be found out and this can prove to be of immense value in the approach to the disease. Further research for the estimation of MPV as a tool for neuropsychiatry and psychopharmacology to examine how certain mental illnesses and medications influence the central nervous system is required.

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