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Original Article

Validity of Mean Platelet Volume to Detect Hyperdestructive & Hypoproductive Thrombocytopenia in Tertiary Care Setting

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Abstract:
Objective: Determine the validity of mean platelet volume (MPV) to detect hyper-destructive & hypo-productive thrombocytopenia, keeping bone marrow aspiration and biopsy as gold standard.
Study Design: Cross sectional (Validation) study.
Material and Methods: A total number of 147 patients of thrombocytopenia were enrolled.CBC of the patient was done using an EDTA sample. Bone marrow aspiration and biopsy was also performed. Keeping aspiration results as gold standard specificity and sensitivity of MPV was validated in diagnosing the type of thrombocytopenia.
Results: Mean platelet volume has a Sensitivity 95%, Specificity 15.7%, Positive Predictive Value64%, Negative Predictive Value 69.2% in detecting Hyper-destructive thrombocytopenia. It has a Sensitivity of 15.7%, Specificity 95.5% with a Positive Predictive Value of 69%and Negative Predictive Value of 64% in detecting Hypo-productive thrombocytopenia.
Conclusion: Mean platelet volume has limited sensitivity and specificity and can be used as an initial indicator but bone marrow aspiration and biopsy remains the gold standard for distinguishing between hyper-destructive and hypo-productive thrombocytopenia.
Keywords: Thrombocytopenia, hyper-destructive & hypo-productive thrombocytopenia, Mean platelet volume

Introduction

The main function of platelets is to regulate primary haemostasis[1]. The normal platelet count is between 150 x 10^9/L and 400 x 10^9/L[1]. Platelet count is gender dependent and it is slightly increased in females. Thrombocytopenia is defined as platelet count less than 150 x 10^9/L or platelet count below the normal range for population (+2SD) and is considered to be one of the most common causes of abnormal bleeding[2]. 5% of the population by definition will fall outside this range.[1] It can occur at any age, can be isolated or there can be bicytopenia or pancytopenia. Incidence in literature is 35-44%in critically ill patients.[3]Pathophysiologically thrombocytopenia is divided into two categories.

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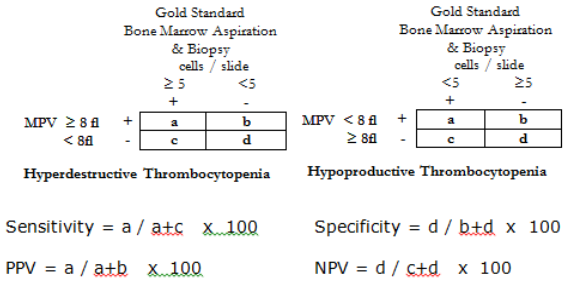
Hypoproductive thrombocytopenia and hyperdestructive thrombocytopenia.[4]It is associated with many conditions and in our country megaloblastic anemia, viral and bacterial infections are the common causes[5]. Thrombocytopenia are differentiated by the megakaryocyte count in the bone marrow aspiration and biopsy. Hyperdestructive thrombocytopenias are caused by extramedullary destruction of platelets with normal or increased bone marrow production and aspiration and is defined as a presence of a normal or an increased number of megakaryocytes in bone marrow (≥ 1 cell per low-power field or ≥ 5–10 cells per slide)[2], whereas Hypoproductive thrombocytopenias are caused by a decreased bone marrow production of platelets because of primary or secondary bone marrow diseases[2]and is defined as a presence of a decreased number of megakaryocytes (<1 cell per low-power field or <5–10 cells per slide) or a presence of dysmegakaryocytes in bone marrow. But these procedures are invasive, time consuming, and results can only be interpreted by a hematologist[2]. The mean

platelet volume can significantly indicate the presence or absence of bone marrow disease in thrombocytopenic patients. Hyperdestructive thrombocytopenia results in increased platelet production by hyperactive bone marrow, so there will be high values of MPV whereas in hypoproductive thrombocytopenia there is inadequate bone marrow platelet production so MPV will be low when compared with normal reference values[2].

The aim of the study is to use mean platelet volume as a discriminating factor between the hyperdestructive and hypoproductive thrombocytopenia. Mean platelet volume, measured by haemotology analyzer indicates platelet function.[6] Normally it has an inverse nonlinear relationship with platelet count.[7]From previous studies we have come to know that it alters in different manner in different causes of thrombocytopenia. It can be used as initial indicator of bone marrow pathology in thrombocytopenic patients. In early 80s it was discovered that mean platelet volume is a useful discriminator in thrombocytopenic patients between those who bleed and those who don't.[8] It is also a reliable marker in monitoring the recovery of thrombocytopenia as there is early rise of MPV than platelet count. MPV is increased in some non haematological diseases including diabetes, acute MI, Acute ischemia, pre-eclampsia, renal artery stenosis and hypercholestolemia. In coronary artery disease patient, raised MPV is a risk factor for MI. Patients of Hepatitis B carriers have increased MPV so more athrothrombotic risk.[9,10,11,12] The large range of normal value decreases its sensitivity. MPV is increased when there is increase turnover. IL6,11 and thrombopoietin are thought to be involved in the process.MPV is noninvasive, cost effective, quick and is measured by automated cell counter which is available in majority of the hospitals[5,13]. The specificity of mean platelet volume is 89.6%and sensitivity is 82.7% in differentiating between the two as in previous studies[14].

Material & Methods

It was a cross-sectional study conducted in 12 months in department of Pathology ,Benazir Bhutto Hospital .It is a tertiary care teaching hospital. 147 patients of thrombocytopenia (platelet count <150 x 10^9/L) were enrolled in the study. Sampling technique was non probability (consecutive sampling). An informed consent was obtained and a proforma was completed for all individuals . After patient reassurance and consent, sample was taken for complete blood picture and peripheral filmexamination,to rule out pseudothrombocytopenia . Sample was taken in EDTA. CBC and MPV analysis was done by using SYSMEX-KX-21, (the Automated Haematology Analyzer). After that Bone Marrow Examination was performed. All data collected was entered and analyzed in statistical package for social sciences (SPSS) version 10.0. Mean and Standard deviation werecalculated for numerical variables i.e. age. Frequency and percentages were presented for categorical variables i.e. gender. Sensitivity, specificity, Positive predictive value and Negative predictive value of MPV were calculated.



Results

A total of 147 patients of thrombocytopenia were enrolled in the study. Age of the patients ranged from 2months to 80 years Summary of age statistics & gender distribution is shown below in table 1& 2.Out of total of 147 patients ,90 patients had hyperdestructive thrombocytopenia while 57 had hypoproductive thrombocytopenia based on results of bone marrow biopsy. Then MPV was used to differentiate between hyperdestructive and hypoproductive thrombocytopenia. In hyperdestuctive thrombocytopenia MPV showed sensitivity and specificity of 95% and 15.7% while in hypoproductive thrombocytopenia it showed sensitivity and specificity of 15.7% and 95.5%., as shown in tables 3,4 5 & 6.

Table 1: Summary of age Statistics

Number of Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
147	2 months	80 Years	22.4 Years	21.0 Years

Table-2: Mean Platelet Volume in Hypoproductive Thrombocytopenia

Number of Patients	Minimum MPV	Maximum MPV	Mean	Standard Deviation
57	7FL	10.3FL	8.8FL	0.76

Table-3: Mean Platelet Volume in Hyperdestructive Thrombocytopenia

Number of Patients	Minimum MPV	Maximum MPV	Mean	Standard Deviation
90	7FL	12FL	9.72FL	1.04

Table-4: Results of Hyperdestructive Thrombocytopenia

	Bone Marrow	
	+VE	-VE
+VE MPV-VE	86	48
	4	9

Sensitivity = 95%, Specificity = 15.7%, Positive Predicted value = 64%, Negative Predicted Value = 69.2%

Table-5: Results of Hypoproductive Thrombocytopenia

	Bone Marrow	
	+VE	-VE
+VE MPV-VE	9	4
	48	86

Sensitivity = 15.7%, Specificity = 95.5%, Positive Predicted value = 69%, Negative Predicted Value = 64%

Discussion

The main function of platelets is to regulate haemostasis. Thrombocytopenia i.e. platelet count < 150 x 10^9/l is a most common cause of bleeding. Pathophysiologically, thrombocytopenia is divided into hyperdestructive and hypoproductive thrombocytopenia.[2] Bone Marrow examination is considered as a gold standard in distinguishing between the two categories. As it is an invasive time consuming procedure, in recent year's studies have been done to validate the specificity and sensitivity of MPV as an alternative method. MPV is measured by haematological analyzers. It indicates platelet function. It alters in different manner in different causes of thrombocytopenia. This study included 147 patients of thrombocytopenia. Bone marrow aspiration and biopsy was used as gold standard for classifying into two categories internationally many studies have been conducted on this subject, like the study done by Ntaiob-G in 2008 showed that MPV can be relied for the diagnosis of immune thrombocytopenic purpura. Another study done by Bowles KM and Cooke LJ showed that patients with marrow disease had MPV 8.1fl and without marrow disease 9[5].8fl But in some studies it was seen that 8.1fl cut off value has not high significance with a sensitivity of 67.7% and specificity of 65%. The results of this study showed that MPV with bone marrow disease was 7.3fl and without bone marrow disease was 8.62fl, so they stated that it can be used as an initial indicator but bone marrow aspiration and biopsy remain the gold standard.[15]

Study by Aksoyetal showed that MPV 7.4 fl cut offvalue has sensitivity 82.7%and specificity 89.6% and can be used in patients of solid tumors as a marker of presence or absence of bonemarrow metastasis[16].According to this study MPV of thrombocytopenic patients with bone marrow disease ranges from 7fl to 10.3fl with Mean value of 8.8fl and without bone marrow disease range from 7fl to 12fl with Mean value of 9.72. A value of 8 has no high significance. The most common causes of thrombocytopenia in our study were:

- Megaloblastic Anaemia (n)= 39
- Infective Process (n)=34
- Mixed deficiency Anaemia(n)=29

In patients of leukemia, aplastic anaemia and hypocellular marrow the MPV is decreased as compared to megaloblastic anaemia.[17]It was in close relation with a local study which concludes that in our setup infection and megaloblastic anemia are the most common causes of thrombocytopenia while in another International study it was concluded that 78% cases of isolated thrombocytopenia were of ITP. In this study it was also seen that patients of Megaloblastic anemia had high MPV levels, which was related to an international study with same results.[15,17] Iron deficiency anaemia is usually associated with thrombocytosis. The result of previous studies show that thrombocytopenia is not rare in patients of iron deficiency anaemia.[18]Thrombocytopenia reverses in these patients with the use of iron supplements.[19,20,21]

Conclusion

Mean platelet volume can be used as an initial indicator of the underlying cause of thrombocytopenia as it is rapid, easy and checked at bed side of patient but it is not as sensitive and specific as bone marrow examination .So Bone marrow examination remains the gold standard test for differentiating between hyporproductive thrombocytopenia and hyperdestructive thrombocytopenia.

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B. Experimentation/Study Conduction
C. Analysis/Interpretation/Discussion
D. Manuscript Writing
E. Critical Review
F. Facilitated for Reagents/Material/Analysis