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A PROSPECTIVE STUDY TO DISCRIMINATE HYPOPRODUCTIVE THROMBOCYTOPENIA FROM HYPERDESTRUCTIVE THROMBOCYTOPENIA USING MEAN PLATELET VOLUME (MPV).

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Abstract:

Objective: *to determine the diagnostic accuracy of MPV in differentiating hypersestructive thrombocytopenia from hypoproductive thrombocytopenia, keeping bone marrow examination as the gold standard diagnostic tool.*

Material & Methods: *this crossectional validation study was conducted at the department of Pathology , Shekh Zaid Medical College and Hospital Rahim Yar Khan over a period of 6 months. A total of 200 patients 18 years and above were included in the study. Automated haematology analyser was used to measure MPV. The BM aspiration and trephine biopsy was performed by Haematologist. Data was analysed by using SPSS version 16. For quantitative variables 2X2 table was was made to calculate sensitivity, specificity, positive predictive value , negative predictive value and MPV.*

Results: *Out of 200 patients 94 (47%) were males and 106 (53%) females. Sensitivity, specificity and diagnostic accuracy of MPV differentiating HDT and HPT was 95.7%, 67.9%, and 74.5% respectively. Positive predictive value was 47.8% and negative predictive value was 98.1%. On BM examination 47 cases were HDT and 153 were HPT. True positive cases were 45, false positive cases 49, false negative cases were 2 and true negative cases were 104.*

Conclusion: *This study concluded that although MPV may provide a small initial insight into the aetiology of thrombocytopenia, it is limited by insufficient specificity and positive predictive value to distinguish hypoproductive from hypodestructive thrombocytopenias. A bone marrow examination continues to be the gold standard to differentiate the hypoproductive and hyperdestructive thrombocytopenias.*

Key words: *Hypoproductive thrombocytopenia, Hyperdestructive thrombocytopenia, sensitivity, specificity, positive predictive value.*

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INTRODUCTION:

Platelets are important components of blood cells which take active part in haemostasis. When they become active their size inceases along with their enzyme and metabolic activity[1]. Haematology analysers are available by which platelets size can be measured as mean platelet volume (MPV). Higher MPV is associated with active platelets resulting in more complications.

Hypoproductive thrombocytopenia (HPT) and hyperdestructive thrombocytopenia (HDT) should be evaluated and managed accordingly. For this purpose patient has to under go bone marrow (BM) aspirate and trephine biopsy along with a long series of tests. Studies have shown that MPV is increased in HDT[2]. MPV is a simple diagnostic parameter and may be used in distinguishing these two types of thrombocytopenias and a value above 7.9 fl can be taken as cutoff value and could predict HDT[3]. In southern Punjab very limited resources are available especially for the diagnosis of haematological diseases. We conducted this study to diffentiate between these two thrombocytopenias so that unnecessary BM procedures can be avoided for this purpose, in view of the easy availability and cost effectiveness of MPV estimation.

MATERIAL AND METHODS:

After ethical approval this study was conducted at department of Pathology Sheikh Zaid Medical College Rahim Yaar Khan and BVH Bahawalpur. This was a cross sectional validation study and was carried out over a six month period from 07/07/2015 to 06/01/2016. Total sample size was 200. Sampling technique was non probability consecutive. All patients aged 18 and above with thrombocytopenia (platelet count <50 $X10^3$ / cu.mm) were included. All patients with diabetes mellitus, ischaemic heart disease, obesity, smoking and hyperlipidemia were excluded.

After an informed consent samples for a complete blood count (CBC) was collected in EDTA containing tube. All the samples were analysed within 3 hours of collection to eliminate the possibility of platelet swelling in EDTA. Automated haematology analyser Sysmex KX-21 was used to measure MPV. Peripheral blood smear was evaluated to exclude pseudothrombocytopenia. The BM aspiration and trephine biopsy was performed by Haematologist under local anaesthesia from posterior superior iliac spine. Haematologist was unaware of MPV at the time of reporting BM. Data was analysed by using SPSS version 16. For quantitative variables 2X2 table was was made to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and MPV[4,5] (Table 1).

Table 1

Sensitivity	$\frac{\text{True Positive}}{\text{True Positive + True Negative}}$	x	100
Specificity	$\frac{\text{True negative}}{\text{True Negative + False Positive}}$	x	100
Positive Predictive Value	$\frac{\text{True Positive}}{\text{True Positive + False Positive}}$	x	100
Negative Predictive Value	$\frac{\text{True Negative}}{\text{True Negative + False Negative}}$	x	100
Diagnostic Accuracy	$\frac{\text{True Positive + True negative}}{\text{True Positive + True Negative + False Positive + False Negative}}$	x	100

Effect modifiers like age, gender and duration of disease was controlled through stratification. Post stratification Chi square test was applied by taking p value ≤ 0.05 as significant.

RESULTS:

Out of 200 patients 94 (47%) were males and 106 (53%) females and majority of patients were between 31-60 years of age with mean age 36±9. On BM examination 47 cases were HDT and 153 were HPT. True positive cases were 45, false positive cases 49, false negative cases were 2 and true negative cases were 104. Sensitivity, specificity and diagnostic accuracy of MPV differentiating HDT and HPT was 95.7%, 67.9%, and 74.5% respectively. Positive predictive value was 47.8% and negative predictive value was 98.1%. All values are given in detail in table2 to table 6.

Table 2. Stratification with regard to gender

Gender	Thrombocytopenia		Total
	Hyper destructive	Hypo Productive	
Male	43	51	94
Female	51	55	106
Total	**94**	**106**	**200**

Chi square = 0.035, P Value = 0.852

Table 3. Stratification with regard to age

Age	Thrombocytopenia		Total
	Hyper destructive	Hypo Productive	
18 - 30	22	41	63
31 - 60	72	65	137
Total	**94**	**106**	**200**

Chi square = 50387, P Value = 0.020

Table 4. Comparison of Mean Platelet Volume (MPV) vs bone marrow examination in differentiating Hyper destructive and Hypo productive Thrombocytopenia n=200

MPV	Bone marrow examination (Gold Standard)		Total
	Hyperdestructive	Hypoproductive	
Hyperdestructive	45 (TP)	49 (FP)	94
Hypoproductive	2 (FN)	104 (TN)	106
Total	**47**	**153**	**200**

TP = True Positive, FP = False Positive, FN = False negative, TN = True negative

Table 5. Sensitivity, specificity and diagnostic accuracy of MPV in differentiating Hypoproductive and hyper destructive thrombocytopenias

Sensitivity rate	$\frac{\text{True Positive}}{\text{True Positive + True Negative}}$	x	100	=	
	$\frac{45}{45 + 2}$	x	100	=	95.70%
Specificity rate	$\frac{\text{True negative}}{\text{True Negative + False Positive}}$	x	100	=	
	$\frac{104}{104 + 49}$	x	100	=	67.90%
Diagnostic Accuracy	$\frac{\text{True Positive + True negative}}{\text{True Positive + True Negative + False Positive + False Negative}}$	x	100	=	
	$\frac{45 + 104}{45 + 104 + 49 + 2}$	x	100	=	74.50%

Table 6. Positive predictive value and negative predictive value of MPV in differentiating hypoprodutive thrombocytopenia and hyperdestructive thrombocytopenias

Predictive Value of Positive test	$\frac{\text{True Positive}}{\text{True Positive + False Positive}}$	x	100	=	
	$\frac{45}{45 + 49}$	x	100	=	47.8%
Predictive value of Negative test	$\frac{\text{True negative}}{\text{True Negative + False Positive}}$	x	100	=	
	$\frac{\text{True negative}}{\text{True Negative + False Negative}}$				
	$\frac{104}{104 + 2}$	x	100	=	98.%

DISCUSSION:

Thrombocytopenia is one of the most critical and difficult clinical condition to manage, therefore the size of the platelets has interested physicians for the last three decades. The recent advances in haematology analysers have added new dimensions to the platelets indices especially MPV to discriminate the cause of thrombocytopenia[6].

As far as we are aware, this is the first study of its kind in southern Punjab. In this study sensitivity, specificity and diagnostic accuracy of MPV differentiating HDT from HPT was 95.7%, 67.9%, and 74.9% respectively. These results are comparable with the results of Khanna et al.[5] Although another study demonstrated MPV predicted HDT with a sensitivity of 82.3% and specificity of 92.5%. This difference could be because of the different analyser LH 750 (Beckman-Fullerton).

One of the limitations of this study was a small sample size and secondly the other platelet indices apart from MPV such as PDW (Platelet Distribution Width), platelet histogram and Platelet Large Cell Ratio (P-LCR) were not analysed. This was done intently just to concentrate only on one parameter although P-LCR was not provided by the analyser. In another study PDW was shown to discriminate the aetiology of thrombocytopenia[7]. Niethammer et al upheld the diagnostic value of platelet histogram maximum rather than MPV to differentiate between idiopathic thrombocytopenic purpura HPT[8]. In another study Ntaios et al found a combination of MPV and PDW superior to P-LCR[9].

By using RNA-binding dyes and flow cytometric analysis the reticulated platelets were assessed in another study to differentiate the different causes of thrombocytopenia[10]. However, this test is expensive, requires extensive quality control measures and is relatively time consuming. When the negative predictive value for bone marrow disease was analysed at different MPV threshold levels, it was noted that an increase in parallel with increasing MPV threshold. But with positive predictive value similar correlation did not exist. This finding in our study was similar to Khanna et al.[7]

It has been reported that although MPV may be used as an initial suggestion of bone marrow disease in thrombocytopenic patients, it has limited sensitivity and specificity[11]. MPV is of limited value in identifying mechanism of chemotherapy induced thrombocytopenia[12]. Similarly, MPV cannot be used to identify the aetiology of thrombocytopenia in the babies of preeclamtic mothers[13].

CONCLUSION:

This study concluded that although MPV may provide a small initial insight into the aetiology of thrombocytopenia, it is limited by insufficient specificity and positive predictive value to distinguish HDT from HPT. A bone marrow examination continues to be the gold standard to differentiate the hypoproductive and hyperdestructive thrombocytopenias.

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