Original Article

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Role of Platelet Indices as a Predictive Tool in Hypoproliferative and Hyperdestructive Type of Thrombocytopenia

Pathology Section

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ABSTRACT

Introduction: Platelet count below 150×10^9/L defines thrombocytopenia, which can be due to hypoproliferation or peripheral hyperdestruction, distinction of which is made by bone marrow examination. Advances in automated blood cell analysers have made it possible to measure various platelet indices like Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Plateletcrit (PCT) which may be helpful in evaluating thrombocytopenia cases.

Aim: To investigate the role of platelet indices in discriminating hypoproliferative and hyperdestructive type of thrombocytopenia.

Materials and Methods: This was a cross-sectional study of 300 thrombocytopenia cases investigated with bone marrow examination over a period of four years from September 2015 to August 2019. Cases were divided into hypoproliferative and hyperdestructive types, Platelet indices (MPV, PCT, PDW) and platelet count were evaluated for any significant correlation between both types of thrombocytopenia and normal controls using student's t-test.

Results: Out of 300 cases of thrombocytopenia, 200 cases were hypoproliferative type and 100 cases were hyperdestructive type with their mean age of 40.03 years and 38.58 years; and male to female ratio of 1.59:1 and 1:2.57, respectively. Statistically significant correlation ($p\leq0.05$) was noted when means of platelet count, MPV, PDW and PCT of hypoproliferative and hyperdestructive group was compared with control group individually. When platelet parameters of hypoproliferative groups were compared with hyperdestructive group, only platelet count and MPV showed significant ($p\leq0.05$) correlation. Among the three platelet indices, only MPV showed significant correlation ($p=0.02$) among the study groups for which Receiver Operating Characteristic (ROC) curve analysis was performed with AUC (area under the ROC curve) of 0.591, sensitivity 57% and specificity 55% at MPV cut-off of 8.8 fl.

Conclusion: MPV can be useful as a screening test for differentiating hypoproliferative type of thrombocytopenia from hyperdestructive type and may help in avoiding or delaying irrelevant invasive procedure such as bone marrow aspiration or preventing useless transfusion of platelets among hyperdestructive thrombocytopenia patients.

Keywords: Bone marrow examination, Mean platelet volume, Megakaryocytes, Platelet destruction, Platelet transfusion

INTRODUCTION

Platelet count and morphology were the only vital information available initially, platelet count below 150×10^9/L defines thrombocytopenia but does not reveal the underlying pathogenic mechanism, which can be due to hypoproliferation (decreased number of megakaryocytes in marrow) or peripheral hyperdestruction of platelets (marrow showing increased number of megakaryocytes) [1-3]. Distinction of these two processes has an impact over the proper management of the patients and is made by time consuming bone marrow examination, an invasive as well as risky procedure with chances of bleeding in critical thrombocytopenia cases [3]. Advances in automated blood cell analysers have made it possible to measure various parameters. Platelet indices, such as MPV, PDW, and PCT, may provide some important information [1,4].

The usefulness of platelet parameters estimated by the automated analysers are being studied extensively and among them, MPV has been reported to differentiate hypoproliferative and hyperdestructive types of thrombocytopenia with sufficient predictive capacity, sensitivity and specificity [2,5]. Higher values of MPV suggests increased activity of megakaryocytes and lower MPV values indicates marrow suppression [2], but none of the studies have established a standard cut-off value for MPV for respective haematology analyser which can aid in making clinical decision without performing bone marrow examination. So, this study was done to investigate the role of platelet indices in discriminating hypoproliferative and hyperdestructive type of thrombocytopenia, assess sensitivity and specificity of statistically significant indices, and to obtain cut-off values in ADVIA 2120i haematology analyser, in an attempt to consider the use of these indices during initial evaluation of thrombocytopenic patients and avoid invasive procedures like bone marrow examination.

MATERIALS AND METHODS

This was a cross-sectional study that was conducted on all thrombocytopenia cases over a period of four years from September 2015 to August 2019 in the Department of Pathology, at NRI Medical College and General Hospital, Guntur, Andhra Pradesh, India. This study was approved by the Institutional Ethics committee (IEC registration number. ECR/1160/Inst/AP/2018).

All 300 cases reported as thrombocytopenia and further investigated with bone marrow examination during the study period were included in the study after getting informed consent. Age, sex, peripheral smear findings and bone marrow diagnosis were collected from the records. Platelet indices of the respective cases were retrieved from the Advia 2120i cell coulter analysis data of peripheral blood. Cases with no bone marrow examination or inconclusive reports or who had platelet transfusions were excluded from the study.

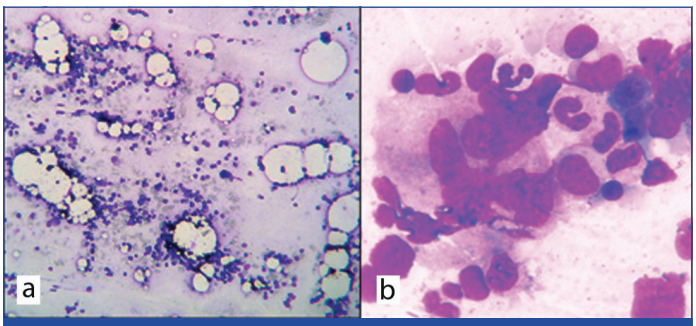
Frequency of various conditions leading to thrombocytopenia was listed in percentage. Thrombocytopenia cases were divided into hypoproliferative (Group A) and hyperdestructive types (Group B) after reviewing bone marrow examination. Hundred cases were taken as controls where platelet counts were normal, their indices were noted. All the platelet indices, MPV, PCT, PDW, and platelet count were evaluated for any significant correlation between both types of thrombocytopenia and with normal controls (Group C).

STATISTICAL ANALYSIS

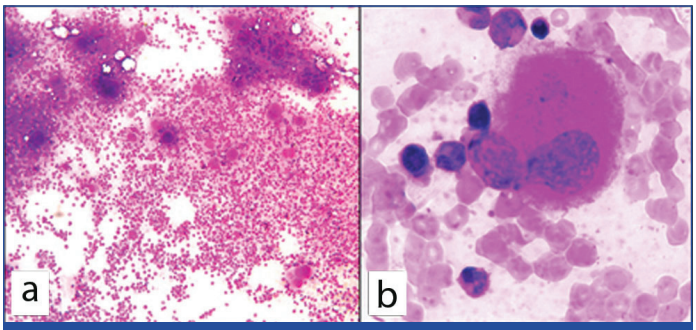
All data was statistically analysed applying Student's t-test (between study groups and with control group) and ANOVA using MedCalc software, version 19.1.1. The p-value of <0.05 was considered significant. Cut-off values of statistically significant platelet indices was derived from ROC curve analysis and, sensitivity and specificity was calculated and compared with the available data in literature.

RESULTS

Among the study group of 300 cases of thrombocytopenia, 200 cases were hypoproliferative type with decreased megakaryocytes in marrow [Table/Fig-1] and 100 cases were hyperdestructive type with increased megakaryocyte number in marrow [Table/Fig-2]. The male to female ratio among the study group was 1.01:1.



[Table/Fig-1]: Hypoproliferative type of thrombocytopenia with: a) Decreased number of megakaryocytes in bone marrow; b) Megakaryocyte with normal morphology. Leishman stain, x400 and x1000.



[Table/Fig-2]: Hyperdestructive type of thrombocytopenia with: a) Increased number of megakaryocytes in bone marrow; b) Hypolobated forms of megaryocytes. Leishman stain, x400 and x1000.

Different causes of thrombocytopenia with their frequencies, mean values of platelet count, MPV, PDW and PCT in both hypoproliferative and hypoproliferative types are depicted in [Table/Fig-3]. The mean age of hypoproliferative type was 40.03 years with male to female ratio of 1.59:1. The mean age of hyperdestructive type was 38.58 years with male to female ratio of 1:2.57.

Hundred cases were taken as control group with normal platelet count (>150×10^9/L) and their indices were noted. The comparison of mean values of platelet count, MPV, PDW and PCT between both the groups and control group are shown in [Table/Fig-4].

Statistically significant correlation (p≤0.05) was noted when means of platelet count, MPV, PDW and PCT of study groups, i.e., hypoproliferative (Group A) and hyperdestructive (Group B), was compared with control group (Group C) individually. When platelet parameters of hypoproliferative cases were compared with hyperdestructive cases only platelet count and MPV showed significant (p≤0.05) correlation.

Among the three platelet indices, only MPV showed significant correlation among the study groups for which ROC curve analysis was performed with AUC (area under the ROC curve) of 0.591 [Table/Fig-5]. The sensitivity and specificity for MPV cut-off value 8.8 was 57% and 55% respectively.

DISCUSSION

Thrombocytopenia diagnosis and management has become a growing component in haematology. In thrombocytopenia cases, the frequency of consultation with haematologists continues to increase with introduction of automated platelet indices like MPV, PDW, and P-LCR, although their clinical usefulness is yet to be achieved [1].

In the present study, hypoproliferative type (66.7%) of thrombocytopenia was more common than hyperdestructive type (33.3%), similar to Xu RL et al., [6], but in contrast to studies done by Parveen S and Vimal M, Reddy RS et al., Gulati I et al., who reported hyperdestructive type to be more common in their studies [3,7,8].

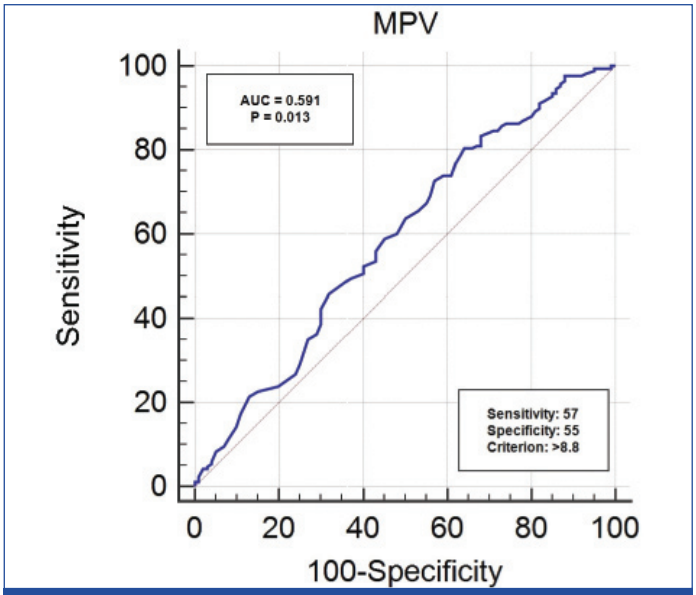
The mean age of hypoproliferative type (group A) was 40.03 years and hyperdestructive type (group B) was 38.58 years which was in contrast to studies done by Rajashekar RB et al., and Norrasethada L et al., who reported higher means in hyperdestructive type than hypoproliferative type [2,9].

Cause of thrombocytopenia	Number of cases (%) N=300 (100%)	Platelet count (mean±SD) (×10^9/l)	MPV (mean±SD) (fl)	PDW (mean±SD) (fl)	PCT (mean±SD) %
A. Hypoproliferative	200 (66.7)	48.7±33.0	9.2±2.0	52.1±25.9	0.04±0.03
Acute leukaemia, post chemotherapy	94 (31.3)	43.8±30.2	9.06±2.1	53.8±27.0	0.39±0.02
Hypoplastic/Aplastic marrow	39 (13)	41.0±35.6	8.56±1.8	46.1±25.4	0.03±0.03
Megaloblastic anaemia	32 (10.7)	63.8±32.6	10.3±2.1	53.6±25.1	0.06±0.03
Myeloma	13 (4.3)	61.9±36.7	8.7±0.9	48.2±23.3	0.05±0.03
Myelofibrosis	12 (4)	40.3±21.8	10.1±2.6	51.7±30.0	0.04±0.04
Metastasis/Lymphoma involvement	10 (3.4)	66.4±33.0	8.7±1.2	60.5±24.9	0.05±0.03
B. Hyperdestructive	100 (33.3)	35.6±27.3	9.8±2.7	48.2±24.9	0.03±0.03
Immune Thrombocytopenic Purpura (ITP)	31 (10.3)	21.6±18.4	9.7±2.5	39.1±24.7	0.02±0.03
Reactive marrow (infections, sepsis, pyrexia of unknown origin)	69 (23)	41.9±27.9	9.9±2.8	52.2±23.6	0.04±0.04

[Table/Fig-3]: Causes of thrombocytopenia under each group with frequency and mean values of platelet parameters.

Parameter	Group A	Group B	Group C	A vs. C	B vs. C	A vs. B
Platelet count (mean±SD) (×10^9/l)	48.7±33.0	35.6±27.3	257.4±53.2	p=0.0001	p=0.0001	p=0.0008
MPV (mean±SD) (fl)	9.2±2.0	9.8±2.7	8.0±1.0	p=0.0001	p=0.0001	p=0.02
PDW (mean±SD) (fl)	52.1±25.9	48.2±24.9	59.8±7.7	p=0.0042	p=0.0001	p=0.21
PCT (mean±SD) %	0.04±0.03	0.03±0.03	0.20±0.04	p=0.0001	p=0.0001	p=0.10

[Table/Fig-4]: Comparison of mean values of Platelet count, MPV, PDW and PCT between Hypoproliferative (A) and Hyperdestructive groups (B) and control group (C).



[Table/Fig-5]: ROC curve for MPV.

The overall male to female ratio of all 300 cases was 1.01:1 with mild male predominance similar to Reddy RS et al., and Gulati I et al., studies [7,8]. The hypoproliferative thrombocytopenia was more common in males with male to female ratio of 1.59:1 similar to Xu RL et al., and Norrasethada L et al., in validation set [6,9] but in contrast to Rajashekar RB et al., and Norrasethada L et al., in training set [2,9]. Among the hyperdestructive type, female predominance was noted with male to female ratio of 1:2.57 which is similar to Elsewefy DA et al., and in contrast to Xu RL et al., [1,6], Rajashekar RB et al., and Norrasethada L et al., [2,9].

The mean platelet count was significantly higher in group A compared to group B (p=0.0008) similar to Xu RL et al., study (0.003) [6], but in contrast no significance was reported in Elsewefy DA et al., Parveen S and Vimal M, Norrasethada L et al., and Kaito K et al., studies [1,3,9,10]. The mean platelet count of group A and group B when compared with group C (controls) individually, were found significant, similar to Elsewefy DA et al., study [1].

The mean MPV was significantly higher in hyperdestructive type when compared to hypoproliferative type (p=0.02) similar to studies done by Elsewefy DA et al., Parveen S and Vimal M, Xu RL et al., Norrasethada L et al., and Kaito K et al., [1,3,6,9,10]. In contrast, Nakadate H et al., reported no significant difference in MPV values between hyperdestructive type and hypoproductive type of thrombocytopenia [11]. In comparison with group C, there was significantly higher MPV in both group A (p=0.0001) and group B (p=0.0001) similar to Reddy RS et al., study [7], but in contrast Elsewefy DA et al., reported no significance when individual groups were compared with control group [1].

During platelet loss in hyperdestructive type, compensation occurs actively in the bone marrow resulting in release of larger younger platelets called as left shift. These platelets during the next 7-10 days life span become smaller in size [3,12].

Usage of different automated haematology analysers has lead to variation in mean MPV in each study. Although, across all studies, the mean MPV was higher type than that found in hypoproliferative type of thrombocytopenia [13-15].

In this study, mean PDW and mean PCT did not show any significance between group A and group B similar to Elsewefy DA et al., Parveen S and Vimal M, Reddy RS et al., and Nakadate H et al., [1,3,7,11]. In contrast, Mowafy NM et al., reported positive correlation between PDW in Immune Thrombocytopenic Purpura (ITP) and non-ITP cases [16]. ROC curves were not analysed nor cut-offs derived for PDW and PCT as there were no significant correlation between hyperdestructive and hypoproliferative groups.

Comparison of mean PDW of group A with control group showed significant p-value of 0.0042, in contrast no significance was reported when hypoproliferative group was compared with control group in studies done by Elsewefy DA et al., and Reddy RS et al., [1,17]. Mean PDW of group B in this study when compared with controls showed significant p-value of 0.0001 similar to Reddy RS et al., [17] and in contrast Elsewefy DA et al., reported no significance between mean PDW of hyperdestructive and control groups [1].

The ROC curve for PCT values showed area under the curve of 0.571 with sensitivity of 63% and specificity of 52% at cut-off value of ≤0.03. The ROC curve for PDW values showed AUC of 0.551 with sensitivity of 52% and specificity of 57% at cut-off value of ≤56.7. The significance level p for both PCT and PDW was >0.05, hence not useful in differentiating hypoproliferative and hyperdestructive types of thrombocytopenia.

The ROC curve from MPV values showed AUC of 0.591, similarly Norrasethada L et al., reported AUC of 0.57 in their study group [9]. The significance level p was 0.01 for MPV in the present study, hence helpful in differentiating hypoproliferative and hyperdestructive types of thrombocytopenia. The various cut-off values of MPV and its sensitivity and specificity in comparison with a concordant study done by Norrasethada L et al., [9] and discordant with other studies like Negash M et al., Gulati I et al., Khanna R et al., are shown in [Table/Fig-6] [5,8,18].

Other studies	MPV cut-off (fL)			Present study	
		Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Norrasethada L et al., [9]	8.0	75	30	71	36
Norrasethada L et al., [9]	8.8	60	50	57	55
Norrasethada L et al., [9]	9.0	50	54	52	60
Negash M et al., [5]	9.9	91	64	37	79
Negash M et al., [5]	11.0	67	95	27	86
Gulati I et al., [8]	8.5	92	100	60	51
Khanna R et al., [18]	9.3	69	55	45	67

[Table/Fig-6]: Comparison of sensitivity and specificity of various cut-offs of MPV with other studies [5,8,9,18].

The cut-off points, sensitivity and specificity vary among different studies, hence MPV interpretation should be done in correlation with physical examination, complete clinical history, which will lead to further appropriate management and investigations.

Study done by Baig MA on platelet indices among paediatric cases of thrombocytopenia showed inverse relationship with platelet count in linear relationship in hypoproliferative type and hyperdestructive type. Baig MA suggested combined usage of MPV, PDW and P-LCR in precise differentiation of ITP (hyperdestructive type) from acute leukemias and aplastic anaemias (hypoproliferative type) and reported that PCT was less sensitive aid in differentiating these types of thrombocytopenias [19].

There is a need for further research into MPV among specific diagnosis which will be more relevant in clinical practice like in patients with no leukemic blasts, normal haemoglobin and normal total leucocyte counts [10]. The advent of newer modalities for haemogram and platelet analysis has resulted in newer haematology analysers with different principles such as electrical impedance,

optical light scatter, and fluorescent staining should be studied and analysed individually and cut-off values should be established which can help in clinical practice.

Limitation(s)

The measurement time after venipuncture to analysis of blood sample was not considered in the study. Age adjusted analysis and platelet qualitative tests were not done in the study.

CONCLUSION(S)

MPV can be useful as a screening test for differentiating hypoproliferative type of thrombocytopenia from hyperdestructive type. It may help in avoiding or delaying unnecessary, invasive procedure like aspiration of bone marrow or preventing undesirable transfusion of platelets among hyperdestructive thrombocytopenia patients. Further research is needed to establish a cut-off value of MPV for a particular haematology analyser which can aid the clinician in management of patient and avoid unnecessary invasive procedure like bone marrow examination or unwanted platelet transfusions.

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