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Research Article

UTILITY OF PLATELET INDICES IN THROMBOCYTOPENIA

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ABSTRACT

Objectives: The objectives of the study were to know the role and utility of platelet indices (MPV and PDW) in differentiating the etiology of thrombocytopenia.

Methods: This was a prospective and retrospective study of 400 cases of thrombocytopenia and 100 controls conducted over a period of 17 months from September 2020 to February 2022 at tertiary care hospital, Ahmedabad, Gujarat, India. All patients meeting inclusion criteria were included in the study. Exclusion criteria were radiation/chemotherapy, antiplatelet drugs induced thrombocytopenia, etc. EDTA blood samples were collected and further processed with a Sysmex KX-21 automated hematology analyzer. Platelet count, mean platelet volume (MPV), and platelet distribution width (PDW) were noted and data were statistically analyzed between groups using t-tests.

Results: Out of 400 cases, 304 belong to Group A (increased destruction of platelets) and the remaining 96 were in Group B (decreased production of platelets). Among Group A, causes were classified into immune thrombocytopenic purpura and others. Various infections resulting in thrombocytopenia were in the majority among other causes in Group A. Group B was comprised megaloblastic anemia as the leading cause responsible for thrombocytopenia. MPV and PDW values were high in hyperdestructive Group A compared to Group B and were found significant between various groups.

Conclusion: MPV and PDW along with platelet count can be used as an adjunct laboratory tool for early screening of the underlying cause of thrombocytopenia, which helps clinicians with targeted therapies in clinical management.

Keywords: Thrombocytopenia, Platelet indices, Platelet count, Mean platelet volume, Platelet distribution width.

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INTRODUCTION

Thrombocytopenia is defined as a reduced number of platelets in peripheral blood. According to the literature, a platelet count (PC) of $<150\times10^3/\mu L$ constitutes thrombocytopenia and is the most common cause of abnormal bleeding. While there are a variety of disorders that cause thrombocytopenia, it typically results from four processes: Thrombocytopenia caused by artifacts, decreased platelet production, accelerated platelet destruction, and abnormal distribution or pooling of the platelets within the body [1]. Most commonly, platelet destruction leads to the stimulation of thrombopoiesis. A result of accelerated thrombopoiesis is an increase in the number, size, and rate of maturation of the precursor megakaryocytes [1-3]. Several conditions can accelerate the destruction of platelets, both immunologic and non-immunologic. Immunologic causes include autoimmune, idiopathic, secondary infections, pregnancy, and collagen vascular disorders. Non-immunologic processes include thrombotic microangiopathies, disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura, and hemolytic-uremic syndrome [1]. Low platelet production may be caused by hypoplasia of megakaryocytes, ineffective thrombopoiesis, or hereditary conditions such as megaloblastic anemia, aplastic anemia, myelofibrosis, myelodysplastic syndrome, metastasis, leukemia, lymphoma, multiple myeloma, alcoholic liver disease, and infection [1].

The distinction of these two processes has a major effect on the management of patients. Bone marrow examination (BMA) has a paramount role in assessing the mechanism of thrombocytopenia but it is a time consuming, invasive, risky, and expensive procedure where chances of bleeding exist in severe thrombocytopenia [4]. Recent advances in automated hematology analyzers are capable to measure various platelet activation parameters that are helpful for diagnosing the underlying cause of thrombocytopenia [1-5]. They are mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet-large cell ratio (P-LCR). Estimation of these parameters by current automated analyzers is superior than manual estimation as it is a quick, automated, and cost-effective way which eliminates observer bias and artifacts [5]. MPV and PDW are derived from the platelet distribution curve, which suggest changes in platelet size and shape, respectively [1]. These platelet parameters help in classifying thrombocytopenia cases into hypoproductive and hyperdestructive groups which aid in clinical management as well as guide the clinician to assess morbidity and mortality.

Objective

The objective of the study was to find out the role and relationship of platelet indices (MPV and PDW) in determining the underlying etiology of thrombocytopenia.

METHODS

Study design

It was a retrospective (September 2020–March 2021) and prospective (April 2021–February 2022) study carried out for a period of 17 months at Central Hematology Laboratory of the Pathology Department at a tertiary care hospital, Ahmedabad, Gujarat, India. The study was ethically approved by the Institutional Ethical Committee (GCSMC/EC/Research Project/APPROVE/2020/293 dated March 26, 2021).

Study groups

A total of 400 EDTA blood samples of patients with PC <150×10³/μL and 100 healthy control samples with PC ≥150×10³/μL were included in the study.

Inclusion criteria

All adult patients aged >18 years of both sexes with a PC <150×10³/μL.

Exclusion criteria

Patients aged <18 years, previous history of blood transfusion, on antiplatelet drugs, chemotherapy, radiotherapy, and other medications causing thrombocytopenia (drugs such as furosemide, phenytoin, and fluconazole).

Study methods and data collection

A 2–4 ml of venous blood was collected in EDTA Vacutainer. Analysis was done by the 3-part automated hematology analyzer Sysmex KX-21, within 2–4 h of blood collection. The PC was reconfirmed on peripheral blood smear examination on field stained slide in all thrombocytopenia cases by two pathologists with consensus reporting using Nikon E 200 Light Microscope. Pseudothrombocytopenia and artifacts were ruled out. All data including age, sex, clinical signs and symptoms, and provisional clinical diagnosis were collected from clinical case records of patients. From the analyzer generated reports, hemoglobin, total WBC count, PC, MPV, and PDW were noted for all cases and controls. All the patients were divided into Group A (hyperdestruction of platelets) and Group B (decreased production of platelets) based on clinical and hematological details.

Statistical analysis

Demographic data were analyzed for frequency distribution. Platelet parameters (PC, MPV, and PDW) were calculated for each group with a median interquartile range (IQR). They were compared between various groups as well as with control using standard t-tests. The results were tabulated and analyzed. Detailed various comparisons were made using a Kruskal–Wallis test and *post hoc* testing. This aided them to decide whether there was significance of MPV and PDW among groups with the help of calculating p values. p<0.05 was considered statistically significant. For data analysis, SPSS version 26 (trial version) was used.

RESULTS

In the present study, a total of 500 samples were included in the study. Out of 500 samples, 400 samples were thrombocytopenia patients (cases) and 100 samples were healthy control with normal PC. Among the 400 thrombocytopenia cases, 304 (76%) were in Group A (increased megakaryocytes in marrow) and 96 (24%) were in Group B (decreased megakaryocytes in marrow). Out of 400 thrombocytopenia cases, 349 cases had all the clinical and hematological details. Fifty-one cases not showing any platelet parameters from the analyzer were not included in MPV and/or PDW data analysis. According to age distribution, the maximum number of patients was between 18 and 40 years (56%), including Group A and Group B (Fig. 1).

The majority of the patients of the study population were 240 (60%) males and the remaining 160 (40%) were females. The male-to-female ratio was 1.5:1 (Fig. 2).

Fig. 3 shows subdivision of frequency of each cause in Groups A and B. In Group A, the majority of causes were of non-immune thrombocytopenic purpura (ITP), such as others (infections, sepsis, shock, kidney, lung and liver diseases, pregnancy, and diabetes). Group B had megaloblastic anemia as the most common etiology. Median (IQR) values of PC, MPV, and PDW of both the groups in detail are shown in Table 1.

Group A showed higher values for MPV and PDW, while Group B had lower values in most cases. Values of MPV and PDW (median – 13.35 and median – 15.9, respectively) were also high in ITP cases (Table 1). The comparison was done between Groups A and B and control. Table 2 shows that PC, MPV, and PDW were statistically significant (p<0.05) in Groups A and B when compared with each other as well as with the control group.

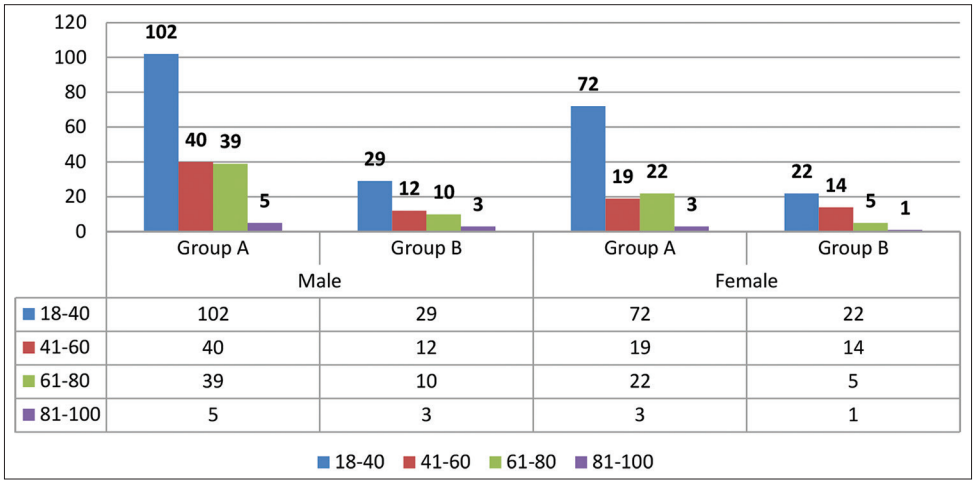
DISCUSSION

Megakaryocytes produce platelets which play a crucial role in clotting of blood. PC <150×10³/μL is referred to as thrombocytopenia. The

Table 1: Causes of thrombocytopenia under each group with median values of platelet parameters

	Platelet count (/μL)	MPV (fl)	PDW (fl)
	Median	Median	Median
Group A			
ITP	25,700	13.35	15.95
Other	94,500	10.9	15.2
Group B			
Megaloblastic anemia	83,000	11.25	15.45
Aplastic anemia	6000	-	-
Carcinoma	51,000	9.7	11.6
Leukemia	54,000	10	11.2
Lymphoma	117,000	9.25	10.8
MDS	31,500	11.5	12
Metastasis	56,000	15.6	16.7
Multiple myeloma	87,000	9.3	10.2

MPV: Mean platelet volume, PDW: Platelet distribution width, ITP: Idiopathic thrombocytopenic purpura, MDS: Myelodysplastic syndrome



	Male		Female	
	Group A	Group B	Group A	Group B
18-40	102	29	72	22
41-60	40	12	19	14
61-80	39	10	22	5
81-100	5	3	3	1

Fig. 1: Age distribution of 400 cases

Table 2: Comparison of median values of platelet count, mean platelet volume, and platelet distribution width between various groups

Parameters	Group Az	Group B	Control©	A versus B	A versus C	B versus C
PC median (IQR) (/µL)	90,000 (65,750)	65,500 (67,500)	296,000 (116,500)	<0.008	<0.0001	< 0.008
MPV median (IQR) fl	11 (2.8)	10.4 (2.8)	9.36 (1.2)	<0.0001	<0.024	<0.0001
PDW median (IQR) fl	15.2 (5.3)	13 (6.05)	11.6 (2.53)	<0.0001	<0.0001	<0.0001

PC: Platelet count, MPV: Mean platelet volume, PDW: Platelet distribution width, IQR: Interquartile range, fl: Femtoliter

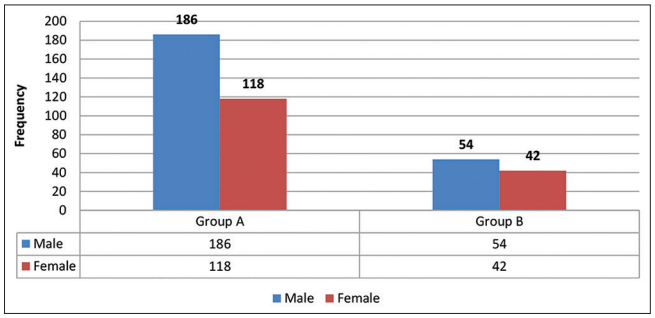


Fig. 2: Sex distribution of 400 cases

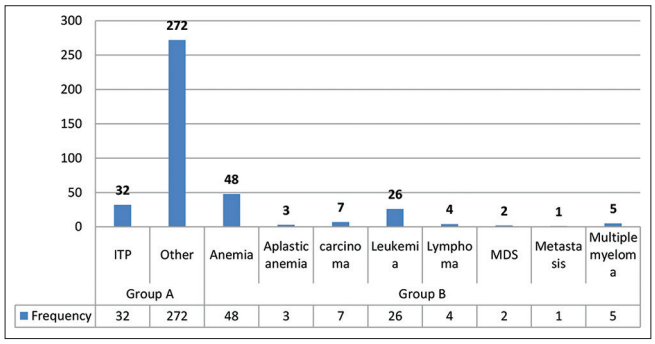


Fig. 3: Frequency distribution of each cause in Groups A and B. ITP: Immune thrombocytopenic purpura, MDS: Myelodysplastic syndrome

main causes of thrombocytopenia are increased destruction or decreased production and so are classified in the study. Increased platelet destruction is due to extracorpuscular platelet destruction or consumption with increased marrow production of megakaryocytes. Decreased production is due to various primary or secondary bone marrow diseases such as megaloblastic anemia, aplastic anemia, leukemia, multiple myeloma, lymphoma, and metastasis [1,4,6,7]. It is difficult to assess the mechanism of thrombocytopenia by clinical methods. Hence, platelet indices play a major role in identifying this mechanism which facilitates further management [4,6].

A well-prepared peripheral blood smear can be used to evaluate the platelet number, size, distribution, and morphology under microscopy, but it has many limitations. Delays in peripheral blood smear preparation after blood collection may change morphology with artifact generation in platelet diameter due to increased adhesiveness of them to smears [1,4]. Widespread availability of particle counters in the clinical hematology laboratory allows the accurate measurement of platelet volume on a routine basis [1]. MPV is a machine calculated measurement of average size of platelets found in blood with normal range of 9.4–12.4 fl. MPV is increased due to the presence of large numbers of megathrombocytes in peripheral blood as a compensatory hyperproduction in disorders associated with increased platelet destruction [1,6,7]. In general, normal or decreased values of MPV are seen in patients with deficient platelet production and in some patients with splenomegaly [1,6,7]. PDW is an indicator of variation in size of platelets called as anisocytosis. As per the operator manual of Sysmex KX-21 hematology analyzer, the normal range of PDW is 9–14 fl. Anisocytosis and greater PDW values are caused by platelet activation, which causes an increase in size and the development of pseudopodia. Thus, high PDW values are commonly seen in diseases with increased platelet destruction [1,8].

The present study showed the maximum number of cases in 18–40 years. Males (60%) were predominant with an M: F ratio of 1.5:1 (Fig. 2), which was identical to other studies by Reddy *et al.* [8] and Mala *et al.* [6].

Group A (76%) had the maximum number of cases in contrast to Group B (24%), which was the same as findings in studies by Parveen and Vimal [4], Reddy *et al.* [8], and Katti *et al.* [9] but differs with studies of Chaitra *et al.* [7] and Al-Sharifi [10]. In Group A, maximum cases showed non-ITP etiology mainly infections. This finding in the present study was observed as it was conducted in the SARS-CoV-2 era (September 2020–February 2022) where various bacterial, viral, and fungal (mucormycosis) infections were prevalent. Virus destroys platelets directly and, in some cases, leads to impaired production of megakaryocytes, leading to thrombocytopenia. Disseminated intravascular coagulation (DIC) due to Gram-negative and/or Gram-positive septicemia leads to splenic sequestration of platelets along with coagulopathy responsible for thrombocytopenia [1]. The above finding was identical with other studies [4,6,8]. Table 1 shows that MPV and PDW were significantly higher in Group A in contrast to Group B, which was close to other studies [4,6,8-13]. ITP cases of Group A also showed higher values of MPV and PDW, which were comparable to various studies [4,6,8-13]. This increase in MPV and PDW is due to compensation of immune destruction of platelets, leading to accelerated production of larger, younger immature platelets of varying sizes in bone marrow [4,6,7]. Group B included cases with defective or impaired production of platelets from bone marrow (24%). The majority of the cases were of megaloblastic anemia, similar to other studies [4,6,8]. Leukemia was the second leading cause for impaired production of platelets due to blast cell infiltration in bone marrow, leading to proportional reduction in megakaryopoiesis. The same findings were also observed in many studies [4,6,9]. Lower MPV and PDW values were noted in Group B (Table 1) compared to Group A and this was identical to other studies [4,6,8-13]. These decreased values are due to impaired production of smaller aged platelets from bone marrow because of deficiency of thrombopoietin [1,6]. Table 2 shows that MPV and PDW median (IQR) values in Group A were 11 (2.8) fl and 15.2 (5.3) fl, in Group B 10.4 (2.8) fl and 13 (6.05) fl, respectively. Similar ranges of values were also found in various studies [4,8,13]. However, in contrast, a study by Farweez *et al.* [2] showed no significant difference in MPV values between various groups. These variations between different studies may be due to the use of different analyzers with different working principles, regional prevalence of disorders, and proportion of diseases included [14].

Limitations

Bone marrow analysis was performed in a limited number of cases due to financial constraints. The present study has not analyzed some of the platelet parameters such as PCT and P-LCR. This may limit the application of findings to the larger community.

CONCLUSION

Platelet activation parameters such as MPV and PDW are high in hyperdestructive and low in hypoproductive etiologies of thrombocytopenia. Their application may avoid invasive and

expensive procedures like BMA. In ITP cases, they prevent undesirable transfusion of platelets among hyperdestructive groups. The scope for further research is open. The latest techniques have arrived, such as fluorescent staining and optical light scatter, which should be analyzed in detail. The cutoff values for each analyzer are to be established which facilitates clinical management of patients with thrombocytopenia. The precise differentiation of hypoproductive and hyperdestructive etiologies can be obtained with combined usage of MPV, PDW, PCT, and P-LCR by higher version hematology analyzers.

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AUTHORS' CONTRIBUTIONS

AKP and RJS conceptualized and designed study. AKP, NP, and KP collected and analyzed the data. RJS, SSB, and NAS prepared the manuscript. Final proofreading was done by all the authors.

CONFLICTS OF INTEREST

Nil.

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