## RESEARCH



# Platelet indices as a predictor in patients with aplastic anemia and immune thrombocytopenic purpura: a retrospective case-control study



Mahynour Z. Abdel Hi<sup>1\*</sup>, Safaa A. A. Khaled<sup>2</sup>, Dalia G Mahran<sup>3</sup> and Mai M. Aly<sup>2</sup>

## Abstract

**Background and objectives** Platelet indices are widely available and relatively cheap platelet parameters. The critical objective of this study is to assess the reliability of platelet indices as biomarkers for diagnosis and prognosis in adult thrombocytopenic patients.

**Methods** A retrospective case–control study, including 81 immune thrombocytopenia (ITP) cases, 50 aplastic anemia (AA) cases, and 150 participants as a control group. This study included patients admitted from 2016 to 2021 to the Clinical Hematology Unit, Department of Internal Medicine, University Hospital. The collected data included sociodemographic information, clinical data, laboratory data, and an assessment of the therapeutic response in the studied groups.

**Results** For the diagnosis of adult thrombocytopenic patients, platelet distribution width (PDW) showed the best diagnostic accuracy (85% for ITP and 91.9% for AA) at cutoff points of 14.9% and 17.2%, respectively. This was followed by mean platelet volume (MPV) with diagnostic accuracies of 77% for ITP and 89.3% for AA at a cutoff point of 9.4 fl. Platelet large cell ratio (PLCR) demonstrated insignificant accuracy in diagnosing either ITP or AA.

**Conclusion** Platelet indices can play a crucial influence in the diagnosis, not the prognosis, of adult thrombocytopenia.

Trial registration NCT05116033. https://classic.clinicaltrials.gov/ct2/show/NCT05116033

**Keywords** Immune thrombocytopenic purpura, Aplastic anemia, Mean platelet volume, Platelet distribution width, Platelet large cell ratio

## \*Correspondence:

Mahynour Z. Abdel Hi

mahynwrzghby@gmail.com; mahynwrzghby@aun.edu.eg

<sup>1</sup> Department of Family Medicine, Faculty of Medicine, Assiut University

Hospitals, Assiut University, Assiut, Egypt <sup>2</sup> Clinical Hematology Unit, Internal Medicine Department, Faculty

of Medicine, Assiut University, Assiut, Egypt

<sup>3</sup> Deventes and of Dublic Health and Construct

<sup>3</sup> Department of Public Health and Community Medicine, Faculty of Medicine, Assiut University, Assiut, Egypt

## Introduction

Thrombocytopenia is defined as a platelet count less than 150,000 cells per  $\mu$ L [1]. There are two fundamental causes of thrombocytopenia: an under-proliferative bone marrow or impoverished platelet production and excessive platelet decomposition. Hypo-proliferative bone marrow disorders incorporate aplastic anemia (AA), acute leukemia, and myelodysplastic syndrome (MDS). Peripheral disruption of platelets can be attributable to immune-mediated processes such as immune thrombocytopenia (ITP) or nonimmune-mediated processes



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

akin to disseminated intravascular coagulopathy (DIC), thrombotic thrombocytopenic purpura (TTP), or particular diseases [2].

ITP stands for isolated thrombocytopenia. It is an autoimmune illness [3]. Many ITP patients have minuscule bleeding symptoms such as purpura, petechiae, and mucosal bleed out, which could imply gingival and epistaxis. On the flip side, only a handful of patients incur crucial organ bleeding, such as gastrointestinal bleeding and intracerebral hemorrhage (ICH), which greatly increase morbidity and death [4].

AA is a scarce type of bone marrow failure syndrome (BMFS) that is distinguished by valuable pancytopenia and BM hypoplasia of varying severity [5].

A daily automated blood count carries earned variables such as platelet indices (PIs), which denote platelet activity. PIs are associated with platelet morphological concepts and growth kinetics [6].

MPV, PDW, a measure of platelet variety, and the platelet large cell ratio (P-LCR) were among the platelet indices [7].

Platelet distribution width (PDW) reflects the size distribution of megakaryocyte-produced platelets, which increases during platelet activation and serves as a marker of platelet anisocytosis. The evaluated studies found that in healthy adults, this number varied between 10 and 18% [6].

Platelet function and production rate were thought to be mirrored by platelet count, MPV, and PDW [8].

Another indicator of platelet activity is the platelet larger cell ratio (P-LCR), which is the proportion of all circulating platelets in the bloodstream that have a volume greater than 12 fl. Typically, it falls between 15 and 35% [6].

The current study aims to explore the validity of platelet indices as diagnostic and prognostic biomarkers in adult thrombocytopenic patients.

#### **Patients and methods**

#### Study design

A retrospective case–control study was done to achieve the aim of the diagnostic validity of platelet indices between control and patients with thrombocytopenia. A prospective case-series study was conducted to achieve the objective of the prognostic value of the platelet indices in thrombocytopenia patients.

#### Study site

The Clinical Hematology Unit of the Internal Medicine Department. This study was conducted from February 2022 to March 2023.

#### **Study participants**

The study included adult thrombocytopenic patients with a confirmed diagnosis of ITP or AA who were admitted to the Clinical Hematology Unit, Internal Medicine Department.

#### Inclusion criteria

These are age greater than 18 years old, irrespective of gender, platelet count less than 100,000/cu mm, verified diagnosis of AA or ITP, and age and gender match in the control group.

#### Exclusion criteria

These are patients who went through a platelet or blood transfusion within 2 weeks of the mean platelet volume (MPV) analysis, splenectomized patients, patients with chronic infections or inflammations, diabetics, patients with coronary artery disease, and patients taking antiplatelet or anti-inflammatory medications.

## Controls

The control group was collected from the attendants at the Outpatient Clinic at the Department of Internal Medicine. They were age and sex matched and did not fulfill the inclusion criteria of the case group. They were also free from hematological and chronic diseases.

#### Sample size calculation

Accordingly, the mean of platelet distribution width (PDW) in thrombocytopenic patients was  $14.4\pm1.7$ , and the mean in the nonthrombocytopenic group was  $13.7\pm2.1$  from a study that was done by H. Altaf Mali et al. (2021) [9]. By using Epi Info version 3 to calculate the sample size considering CI 95%, and power 80%, the calculated sample size with a 1:1 ratio in two groups was 236 patients, with 118 in each of the patients and control group and 131 thrombocytopenic patients with a total of 281.

#### Data collection for the cases group

The data was collected by 2 means: 104 cases were retrospectively collected from patient's records from 2016 to 2021, and the other part of data about 27 cases was collected by interviewing the patients from February 2022 to March 2023 at the Hematology Outpatient Clinic to achieve adequate sample size. Enrollment of cases after 3 months was done by inviting them by phone calls or waiting for them to get the treatment, so the follow-up visit was easy. A semi-structured questionnaire was designed, including the same data in the records, and filled in by personal interviews with the patients in addition to lab results from the lab at the university hospital. Data from the control group were also collected through personal interviews.

The collected data included sociodemographic data (name, age, and sex); clinical data, including clinical manifestation on admission and 3 months after therapy; and laboratory data, including complete blood counts of participants, including white blood cells, hemoglobin, platelet count, and platelet indices (MPV, PDW, and PLCR), one at admission (baseline) and another after 3 months. The device used in the analysis of blood samples was Sysmex XN-1000, and bone marrow studies include bone marrow cellularity and megakaryocytic abnormalities.

The therapeutic response in the studied patients was assessed using the clinical response for the ITP group, which was assessed according to the reduction of platelet and blood transfusion as the patient converted from transfusion dependent to independent. Hematologic response was assessed by increasing the platelet count (doubling of baseline count).

#### Statistical analysis

All data was entered using the Excel program, and data cleaning was done before transforming the data to SPSS. Data were analyzed by using SPSS (Statistical Package for the Social Science, version 20, IBM, Armonk, New York). The Shapiro test was used to determine the compliance of the data to normal distribution.

Nominal data were given as number (n) and percentage (%). Quantitative data with normal distribution were expressed as mean  $\pm$  standard deviation (SD) and compared with the Student *t*-test and ANOVA test. The chi-square test was implemented on such data. The accuracy of different platelet indices in the diagnosis of ITP and prediction of bleeding and transfusion dependency was determined by the receiver operator characteristics (ROC) curve. The level of confidence was kept at 95%, and hence, the *p*-value was considered significant if < 0.05.

#### **Ethical considerations**

The study was consistent with the Declaration of Helsinki for medical research.

### Result

#### Main laboratory data of the studied cohort

Data are presented in Tables 1, 2, 3, 4, 5, 6, and 7 and Fig. 1.

Table 2	Diagnostic acc	uracy of pla	telet indices	s in ITF	at C	Ilinical
Hematol	ogy Unit					

	MPV	PDW	PLCR
Sensitivity	47%	83%	66.7%
Specificity	93%	86%	79.3%
PPV	77%	47%	11%
NPV	76.4%	95%	98%
Positive LR	6.4	5.9	3.2
Negative LR	0.57	0.20	0.20
Accuracy	77%	85%	68%
Cutoff point	9.4	14.9	24.1
AUC	0.626	0.866	0.647
<i>p</i> -value	0.005	< 0.001	0.378

MPV Mean platelets volume, PDW Platelets distribution width, PLCR Platelets large cell ratio, ITP Immune thrombocytopenia purpura, PPV Positive predictive value, NPV Negative predictive value, LR Likelihood ratio, AUC Area under curve

Table 1 Baseline laboratory data and platelet indices in studied groups (ITP, aplastic anemia, and control groups) at the Clinical Hematology Unit

	ITP (n = 81)	Aplastic anemia (n = 50)	Control group ( $n = 150$ )	Total (n = 281)	Ρ	<i>P</i> 1	P2	Р3
Hemoglobin (g/dl)	11.01±2.62	7.75±2.47	12.95±1.47	10.57±2.19	< 0.001	< 0.001	< 0.001	< 0.001
Leucocytes (10 <sup>3</sup> /µl)	$9.79 \pm 1.46$	$2.64 \pm 0.55$	7.44±1.92	$6.62 \pm 1.31$	< 0.001	< 0.001	< 0.001	< 0.001
Platelets (10 <sup>3</sup> /µl)	$31.40 \pm 5.77$	$22.84 \pm 5.98$	267.87±61.07	107.3±24.27	< 0.001	0.31	< 0.001	< 0.001
MPV (fl)	$9.87 \pm 2.55$	$9.19 \pm 3.16$	10.71±1.06	$9.92 \pm 2.26$	< 0.001	0.06	0.04	< 0.001
PDW (%)	$28.78 \pm 6.66$	25.07±8.91	12.44±2.25	$22.10 \pm 5.94$	< 0.001	0.20	< 0.001	< 0.001
PLCR (%)	$24.66\pm6.90$	$30.71 \pm 3.45$	$30.51 \pm 8.04$	$28.63 \pm 6.13$	0.30	0.27	0.12	0.95

MPV Mean platelets volume, PDW Platelets distribution width, PLCR Platelets large cell ratio

\*ANOVA one-way test was used. A post hoc test was done for significance between groups

p-value compares between different groups

P1 value compares between ITP and aplastic anemia groups

P2 value compares between ITP and control groups

P3 value compares between aplastic anemia and control groups

**Table 3** Diagnostic accuracy of baseline platelets indices in AA

 at Clinical Hematology Unit

	MPV	PDW	PLCR
Sensitivity	78%	70.6%	60%
Specificity	93%	96.7%	69.3%
PPV	78%	71%	4.2%
NPV	93%	97%	97.2%
Positive LR	10.64	21.18	1.3
Negative LR	0.24	0.30	0.87
Accuracy	89.3%	91.9%	68.7%
Cutoff point	9.4	17.2	33.4
AUC	0.862	0.765	0.539
<i>p</i> -value	< 0.001	0.006	0.825

*MPV* Mean platelets volume, *PDW* Platelets distribution width, *PLCR* Platelets large cell ratio, *PPV* Positive predictive value, *NPV* Negative predictive value, *LR* Likelihood ratio, *AUC* Area under curve

 Table 4
 Accuracy of baseline platelet indices in prediction of bleeding in ITP

	MPV	PDW	PLCR
Sensitivity	81%	57%	65%
Specificity	36%	81%	50%
PPV	44%	57%	50%
NPV	75%	81%	65%
Positive LR	1.26	3.05	2
Negative LR	0.54	0.53	0
Accuracy	53.3%	59%	57%
Cutoff point	11.2	27	24.1
AUC	0.663	0.625	0.625
<i>p</i> -value	0.303	0.08	0.59

MPV Mean platelets volume, PDW Platelets distribution width, PLCR Platelets large cell ratio, ITP Immune thrombocytopenia purpura, PPV Positive predictive value, NPV Negative predictive value, LR Likelihood ratio, AUC Area under curve

This current study included 131 thrombocytopenic patients among these patients, 81 were ITP patients (G 1), 50 had AA (hypo-productive thrombocytopenia G2), and 150 participants as the control group (G3), and mean age ( $\pm$  standard deviation) of the studied groups was 32.49 ( $\pm$  11.12), 34.30 ( $\pm$  15.39), and 33.43 ( $\pm$  12.65) years respectively.

The majority of ITP and control groups were females, while the majority of the aplastic anemia group were males. Different groups had insignificant differences as regards mean age (p = 0.73). Meanwhile, there was a significant difference as regards sex distribution (p < 0.001), which did not affect the study results.

Patients with aplastic anemia have a significantly higher frequency of current bleeding (54.41% vs.

Table 5	Accuracy of baseline platelet indices in prediction of
bleedina	in AA at Clinical Hematology Unit

	MPV	PDW	PLCR
Sensitivity	75.7%	76.9%	33.3%
Specificity	38.5%	75%	100%
PPV	78%	91%	0.89
NPV	36%	50%	1.11
Positive LR	1.23	3.08	66.7%
Negative LR	0.63	0.31	29%
Accuracy	74%	76.5%	69%
Cutoff point	9	17.5	0.85
AUC	0.536	0.731	0.583
P value	0.702	0.101	0.632

*MPV* Mean platelets volume, *PDW* Platelets distribution width, *PLCR* Platelets large cell ratio, *PPV* Positive predictive value, *NPV* Negative predictive value, *LR* Likelihood ratio, *AUC* Area under curve

Table 6	Accuracy of	baseline pla	atelet indices	s in predio	ction o	f
transfusio	on depender	icy in ITP at	Clinical Hen	natology	Unit	

	MPV	PDW	PLCR
Sensitivity	83%	86%	66.7%
Specificity	37%	40%	40%
PPV	44%	35%	40%
NPV	79%	88%	66.7%
Positive LR	1.33	1.40	2
Negative LR	0.45	0.37	0.50
Accuracy	53.9%	54%	53%
Cutoff point	11.2	30	43.5
AUC	0.564	0.565	0.556
<i>p</i> -value	0.320	0.622	0.835

*MPV* Mean platelets volume, *PDW* Platelets distribution width, *PLCR* Platelets large cell ratio, *ITP* Immune thrombocytopenia purpura, *PPV* Positive predictive value, *NPV* Negative predictive value, *LR* Likelihood ratio, *AUC* Area under curve

45.59%; p < 0.001) and transfusion dependency (61.04% *vs.* 38.96%; p < 0.001) in comparison to those with ITP.

Table 1 showed that there were significant differences between different groups as regards hemoglobin, platelets, leucocytes, mean platelet volume (MPV), and platelet distribution width (PDW) (p < 0.001), but no significant difference was found between the groups as regards platelet large cell ratio (PLCR) (p = 0.30). With post hoc analysis, the control group has significantly higher platelets count in comparison to ITP (267.87 ± 61.07 vs. 31.40 ± 5.77 ( $10^3/\mu$ l); p < 0.001) and AA group (267.87 ± 61.07 vs. 22.84 ± 5.98 ( $10^3/\mu$ l); p < 0.001). Also, the control group has significantly higher MPV in comparison to ITP ( $10.71 \pm 1.06$  vs.

 Table 7
 Accuracy of baseline platelet indices in prediction of transfusion dependency in AA at Clinical Hematology Unit

	MPV	PDW	PLCR
Sensitivity	80%	81%	60%
Specificity	30%	40%	40%
PPV	44%	33%	39%
NPV	73%	70%	67%
Positive LR	1.29	1.33	1.88
Negative LR	0.40	0.30	0.49
Accuracy	52.5%	53%	51.55%
Cutoff point	10.55	24	34
AUC	0.570	0.600	0.524
<i>p</i> -value	0.564	0.987	0.087

*MPV* Mean platelets volume, *PDW* Platelets distribution width, *PLCR* Platelets large cell ratio, *PPV* Positive predictive value, *NPV* Negative predictive value, *LR* Likelihood ratio, *AUC* Area under curve



**Fig. 1** Accuracy of baseline platelet indices in diagnosis of ITP at Clinical Hematology Unit

 $9.87 \pm 2.55$  (fl); p = 0.04) and AA group  $(10.71 \pm 1.06 \text{ vs.}$  $9.19 \pm 3.16$  (fl); p < 0.001).

In contrast, the control group has significantly lower PDW in comparison to ITP ( $12.44 \pm 2.25 vs. 28.78 \pm 6.66$  (%); p < 0.001) and AA group ( $12.44 \pm 2.25 vs. 25.07 \pm 8.91$  (%); p < 0.001).

At the same time, no significant difference was found between ITP and aplastic anemia as regards platelets count (p=0.31), MPV (p=0.06), PDW (p=0.20), and PLCR (p=0.27).

#### Diagnostic functionality of platelet indices

On account of the diagnosis of ITP, in Table 2, it was found that PDW has the best diagnostic accuracy (85%) at a cutoff point of 14.9% with an area under the curve which was 0.866 followed by MPV at cutoff point 9.4 fl with an area under the curve which was 0.626 with 77% overall accuracy. ROC curve is illustrated in Fig. 1.

As regards the diagnosis of aplastic anemia (Table 3), it was found that PDW has the best diagnostic accuracy (91.9%) at a cutoff point of 17.2% with area under the curve which was 0.765 followed by MPV at cutoff point 9.4 fl with an area under the curve which was 0.862 with 89.3% overall accuracy. Meanwhile, PLCR had insignificant accuracy in the diagnosis of ITP or aplastic anemia (p=0.378 & p=0.825). (The figure of the ROC curve for aplastic anemia patients is shown in the supplementary material Fig. 1).

## Prognostic role of platelet indices (Pls) in thrombocytopenic patients

Tables 4 and 6 showed that all platelets' indices had insignificant values in the prediction of bleeding or transfusion dependency in ITP (p > 0.05). But PDW had the highest accuracy.

The same for AA, it was found that all platelets' indices had insignificant values in the prediction of bleeding or transfusion dependency in aplastic anemia (p > 0.05). However, PDW had the highest accuracy shown in Tables 5 and 7.

The correlation between platelets count and platelet indices is shown in supplementary Tables S2 and 3 and Fig. 2 in the supplementary material.

#### Discussion

This study was conducted to explore the validity of platelet indices as diagnostic and prognostic biomarkers in adult thrombocytopenic patients; to do so, data of the patients were collected retrospectively, while the data of control were collected by personal interview, and laboratory assessment for the indices was done for the control group.

In a comparison of platelet count between group I (ITP) and group II (hypo-productive, aplastic anemia), El Sewefy et al. (2014) and Mali et al. (2021) found that the platelet count was not significantly different statistically between destructive and hypo-proliferative categories similarly to this study [9, 10].

On comparison of platelet indices, El Sewefy et al. (2014) reported that PDW did not show significant

Page 6 of 8

differences between the two patient groups similar to this study but disagreed as regards MPV and P-LCR which were significantly higher in the ITP group compared with the AA group (hypo-productive), while Mali et al. (2021) found that the difference between the two patient groups was significant only in PDW [9, 10]. This study revealed that both groups had insignificant differences as regards MPV and PDW.

A study about the clinical relevance of extended platelet indices in the diagnosis of ITP conducted by A. Arshad et al. (2021) reported that mean hemoglobin, TLC, and PLT were significantly different in all ITP groups compared with healthy controls, and platelet parameters such as MPV and PDW also showed significant differences between the ITP patients and control group, the same as our study [11].

Khaleel et al. (2014), Negash et al. (2016), Al-Musawi et al. (2017), H. Khan et al. (2019), and J. Nayak et al. (2023) reported that all the indices were significantly higher in hyper-destructive thrombocytopenia compared to hypo-productive thrombocytopenia, and this disagreement may be due to difference in studied groups as a hypo-productive group not include aplastic anemia in Negash et al. study and a wide range of age of participants in Khaleel et al. and Khan et al. studies; otherwise, the hypo-productive category included megaloblastic anemia, acute leukemia, and myelodysplastic syndrome besides aplastic anemia in J. Nayak et al. study [1, 12–15]. But our study revealed no significant difference was found between ITP and AA as regards platelets count, MPV, PDW, and PLCR.

A study done by Sridhar Reddy et al. (2018) about mean platelet volume (MPV) in thrombocytopenia found that mean values for MPV show higher values for accelerated destruction in comparison to those of the impaired production group contrary to our study that revealed no significant difference was found between ITP and AA as regard platelets count, MPV, PDW, and PLCR. This can be explained in Reddy's study age range from 1 day to 90 years, and the study involved more categories in the destructive group rather than ITP, the same in the hypo-productive group [16].

This study concurred with the studies undertaken by Rana et al. (2019), and Bali et al. (2019) reported that platelet parameters assessed in the studies did not differ significantly in the groups of patients as defined by the pathogenic mechanism of thrombocytopenia [17, 18].

For diagnostic accuracy of PIs, Elsewefy et al. (2014) reported that diagnostic accuracy at a cutoff value greater than 9.7 fl for MPV yielded 70% diagnostic accuracy and a cutoff value greater than 33.6% for P-LCR yielded 99.6% diagnostic accuracy disagreeing with us [10].

Contrary to the current study, Rana et al. (2019) revealed that for the diagnosis of ITP in thrombocy-topenic patients, MPV and PDW were found to be not good parameters for the prediction of ITP [17].

As for sensitivity and specificity of the platelet indices for diagnosis of ITP, the current study found that PDW has the best diagnostic accuracy (85%), followed by MPV at cutoff point 9.4 with overall accuracy, and the study done by Negash et al. (2016) about diagnostic predictive value of platelet indices for discriminating hypoproductive versus immune thrombocytopenia purpura reported that at different cutoff points from ROC curve coordinates when MPV>9.95 fl is with sensitivity 91% and specificity 64% but our MPV at cutoff point 9.4 fl has sensitivity 47% and specificity 93%, then this difference can be explained as it is evident that Africans have higher MPV as compared to the other groups. Though they analyzed 42 healthy controls, the mean MPV was 10.3 fl which suggested that the actual size of the platelet in their study subjects could be higher [1].

H. Khan et al. (2019) also reported that the sensitivity and specificity of platelet indices to make a diagnosis of ITP were calculated under various cutoff ranges. When MPV cutoff value > 11-fl sensitivity was 73.33% and specificity was 80.0%, PDW cutoff value > 14-fl sensitivity was 86.67% and specificity was 93.3%. P-LCR cutoff value > 40% sensitivity was 100%, and specificity was 63.0%; different numbers with this study may be explained by the small sample size in their study of 30 patients in each group [14].

L. Al-Sharifi et al. (2018) agree with this study that regarding MPV and PDW, there is a significant difference between the control group and groups A (hypoproductive) and B (hyper-destructive) but disagree with this study in a cutoff value greater than 9.9 fl for MPV with100% sensitivity and 100% specificity for the diagnosis of ITP; this difference was explained by difference in a wide range of age group in their study from 1 to 80 years, and hypo-productive group includes other causes rather than aplastic anemia [19].

Gulati et al. (2017) reported in their study about the diagnostic implication of mean platelet volume in thrombocytopenia that a cutoff MPV value of 8.5 fl showed the maximum sensitivity (92.4%) and specificity (100%). The positive predictive value, negative predictive value, and diagnostic accuracy were 100%, 77.78%, and 94%, respectively; this difference in result can be explained by the difference in the age group of participants in Gulati's study [20].

L. Norrasethada et al. (2019) concluded that when using a cutoff value of 8.8 fl, the sensitivity, specificity, PPV, and NPV were 77%, 89%, 89%, and 77%, respectively, with 86% accuracy in the differentiation between the two pathogenesis of thrombocytopenia. This difference in MPV cutoff point due to greater variety in over destructive causes including TTP& DIC and underlying BM defects including AML and ALL [2].

The current study reported also that patients with a plastic anemia have a significantly higher frequency of current bleeding (74% *vs.* 38.3%; p < 0.001) and transfusion dependency (94% *vs.* 37%; p < 0.001) in comparison to those with ITP; this makes sense according to the nature of the two different diseases.

This study showed that all platelets' indices had insignificant value in the prediction of bleeding in ITP (p > 0.05). This was not discussed before in similar studies, but limited studies linked high MPV and chronic ITP as in K. Heitink-Pollé et al. (2014) who reported in their meta-analysis that a significantly higher platelet count at diagnosis was found in patients who developed chronic ITP. Two studies analyzed MPV at diagnosis of ITP. Both found a significantly higher MPV in patients who developed chronic ITP. One study found a significantly higher mean MPV of 9.2 fl in patients developing chronic ITP compared with a mean of 8.1 fl in patients with recovered ITP (p 5.04). Another study found significantly more patients with an MPV 8.0 fl in the chronic ITP group (*OR* 15.4, 95% *CI* 4.1–56.9) [21].

R. Xu et al. (2013) reported that MPV and PDW do not have suitable predictive reliability for the diagnosis of BMF in thrombocytopenic patients [22].

This study regards the accuracy of platelet indices in the prediction of transfusion dependency in the ITP (Table 6). It was found that all platelets' indices had insignificant values in the prediction of transfusion dependency in ITP (p > 0.05). But PDW had the highest accuracy which was 54%, and this result was not reported before.

The same as regard AA, all platelets' indices had insignificant value in the prediction of transfusion dependency.

#### Study strengths

These are easy simple affordable test, study impact on prognosis and outcome, very low or no risk on participants, assessment of the value of PIs in more than one type of thrombocytopenia, and an evaluation of a new novel idea about the prognostic value of PIs.

#### **Study limitations**

Missing data on the medical records of some patients as the study included patients' medical records since 2016.

#### Conclusion

For diagnosis of ITP, it was found that PDW has the best diagnostic accuracy (85%) at a cutoff point of 14.9% with an area under the curve which was 0.866 followed by MPV at a cutoff point of 9.4 fl with an area under the curve which was 0.626 with 77% overall accuracy. While

for diagnosis of aplastic anemia, it was found that PDW has the best diagnostic accuracy (91.9%) at a cutoff point of 17.2% with an area under the curve which was 0.765 followed by MPV at a cutoff point of 9.4 fl with an area under the curve which was 0.862 with 89.3% overall accuracy. Meanwhile, PLCR had insignificant accuracy in the diagnosis of ITP or aplastic anemia. Also, it was found that all platelets' indices had insignificant value in the prediction of bleeding or transfusion dependency in ITP or AA (p > 0.05).

#### **Recommendations and future work**

- For the health care system
  - Platelet indices in particular PWD and MPV can help in the diagnosis of ITP from hypo-productive thrombocytopenia.
- For family physicians
- Provide attention to platelet indices included in complete blood count analysis of thrombocytopenic patients.
- ♦ For future research
  - Future studies should be directed toward the value of the use of platelet indices on the diagnosis of more types of hyper-destructive thrombocytopenia which may enable us to use these indices for broader patient groups.
  - Do multicentric studies on the diagnostic and prognostic value of PIs in thrombocytopenia.

#### Abbreviations

- AA Aplastic anemia
- MDS Myelodysplastic syndrome
- ITP Immune thrombocytopenia DIC Disseminated intravascular coard
- DIC Disseminated intravascular coagulopathy TTP Thrombotic thrombocytopenic purpura
- ICH Intracerebral hemorrhage
- BMFS Bone marrow failure syndrome
- Pls Platelet indices
- MPV Mean platelet volume
- P-LCR Platelet large cell ratio
- PDW Platelet distribution width

#### **Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s43162-024-00338-0.

Additional file 1: Supplementary Fig. 1: Accuracy of platelet indices in the diagnosis of Aplastic anemia. Supplementary Fig. 2: Correlation between baseline platelet count and MPV in patients with ITP at the clinical hematology unit. Supplementary Table S1: Baseline and follow-up laboratory data and platelets indices in the ITP group at the clinical hematology unit. Supplementary Table S2: Correlation between platelets count and platelets indices at baseline among the study participants in clinical hematology unit. Supplementary Table S3: Correlation between platelets count and platelets indices at follow-up in thrombocytopenic patients at clinical hematology unit.

#### Acknowledgements

Not applicable.

#### Authors' contributions

SK and DM proposed and designed the study. MA and MZ followed the patients, collected the clinical data, and analyzed the results. All authors contributed in writing and revising the manuscript.

#### Funding

No funding.

#### Availability of data and materials

The data sets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Declarations

#### Ethics approval and consent to participate

Ethical approval number: IRB No.: 17101645. The study adhered to the regulations of Assiut University's Ethical Committee and approved by the committee with approval number IRB No.:17101645.

#### **Consent for publication**

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

Received: 11 June 2024 Accepted: 19 July 2024 Published online: 19 September 2024

#### References

- Negash M, Tsegaye A, Medhin AG (2016) Diagnostic predictive value of platelet indices for discriminating hypo productive versus immune thrombocytopenia purpura in patients attending a tertiary care teaching hospital in Addis Ababa, Ethiopia. BMC Hematol 16(1):18. https://doi.org/ 10.1186/s12878-016-0057-5
- Norrasethada L, Khumpoo W, Rattarittamrong E, Rattanathammethee T, Chai-Adisaksopha C, Tantiworawit A (2019) The use of mean platelet volume for distinguishing the causes of thrombocytopenia in adult patients. Hematol Rep 11(1):23–27. https://doi.org/10.4081/hr.2019.7732
- Wu F, Li C, Mao J, Zhu J, Wang Y, Wen C (2023) Knowledge mapping of immune thrombocytopenia: a bibliometric study. Front Immunol 14(May):1–10. https://doi.org/10.3389/fimmu.2023.1160048
- Hato T et al (2020) Risk factors for skin, mucosal, and organ bleeding in adults with primary ITP: a nationwide study in Japan. Blood Adv 4(8):1648–1655. https://doi.org/10.1182/bloodadvances.2020001446
- Clucas DB et al (2019) Revisiting acquired aplastic anemia: current concepts in diagnosis and management. Intern Med J 49(2):152–159. https:// doi.org/10.1111/imj.14140
- S.-Ż M, Pogorzelska K, Krętowska A, Krawczuk-Rybak M (2020) Characteristics of platelet indices and their prognostic significance in selected medical condition – a systematic review. Adv Med Sci 65(2):310–315. https://doi.org/10.1016/j.advms.2020.05.002
- Khaled S. A. A, Mahmoud H. F. F (2021) Platelet indices parameters in the new disease activity score of rheumatoid arthritis with ankle involvement: a comparative analytic study. PLoS One 16(9):1–12. https://doi.org/ 10.1371/journal.pone.0257200
- Khaled SAA, Eldin EN, Makarem YS, Mahmoud HFF (2020) Value of platelet distribution width and mean platelet volume in disease activity score of rheumatoid arthritis. J Inflamm Res 13:595–606. https://doi.org/10.2147/ JIR.S265811
- 9. Hamed Altaf Mali AK, Ronad Girish, Senior (2021) Role of platelet indices in the evaluation of thrombocytopenia. Int. J. Heal. Clin. Res 4(11):174–178

- Elsewefy D, Farweez B, Ibrahim R (2014) Platelet indices: consideration in thrombocytopenia. Egypt J Haematol 39(3):134. https://doi.org/10.4103/ 1110-1067.148240
- 11. Arshad A, Mukry SN, Shamsi TS (2021) Clinical relevance of extended platelet indices in the diagnosis of immune thrombocytopenia. Acta Clin Croat 60(4):665–674. https://doi.org/10.20471/acc.2021.60.04.14
- 12. Al-Musawi Z, Al-Kabi M, Alnoor M (2017) The utility of platelet indices in differentiating between hyper-productive and hypo-productive thrombocytopenia in children. Kerbala J Med 10(1):2650–2655
- Khaleel KJ, Ahmed AA, Alwash M, Anwar A (2014) Platelet indices and their relations to platelet count in hypo-productive and hyper-destructive thrombocytopenia. Karbala J Med 7(2):1952–1958
- Khan A, Masood A, Bari F, Tabassum N (2019) Role of mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLCR) in the diagnosis of hyper destructive thrombocytopenia. Prof Med J 26(8):1266–1271. https://doi.org/10.29309/tpmj/2019.26.08.3867
- Nayak J, Behera B, Mohanty SR, Patro MK, Singh K, Meher LK (2023) "A cross-sectional study evaluation of diagnostic implications of platelet indices in thrombocytopenia. Student's J Health Res Africa. 4(6):1–9
- Ramalakshmi R, Reddy R, Phansalkar M (2018) Mean platelet volume(MPV) in thrombocytopenia. J. Egypt. Women's Dermatologic Soc 15(2):80–87. https://doi.org/10.1097/01.ewx.0000532719.31339.7c
- Shreya RK, Sen Deepshikha R, Shreya S, Renuka V, Sunita S (2019) The role of platelet indices as predictive markers of immune thrombocytopenic purpura (ITP) in bone marrow aspirate a study in a tertiary care center. Int. J. Curr. Med. Pharm. Res 5(10):4282–4586
- Bali IK, Singh Y, Nagger S, Sharma U (2019) Role of platelets indices in various causes of thrombocytopenia amongst rural population : a tertiary care hospital study. IOSR J Dent Med Sci 18(5):37–41. https://doi.org/10. 9790/0853-1805063741
- Al-Sharifi LMM (2018) Value of platelet indices in diagnosing etiology of thrombocytopenia. J Univ Babylon Pure Appl Sci. 26(3):153–162
- Gulati I, Kumar H, Sheth J, Dey I (2017) Diagnostic implication of mean platelet volume in thrombocytopenia. Med J Dr DY Patil Univ. 10(4):370– 375. https://doi.org/10.4103/MJDRDYPU.MJDRDYPU\_306\_16
- Heitink-Pollé KMJ, Nijsten J, Boonacker CWB, De Haas M, Bruin MCA (2014) Clinical and laboratory predictors of chronic immune thrombocytopenia in children: a systematic review and meta-analysis. Blood 124(22):3295–3307. https://doi.org/10.1182/blood-2014-04-570127
- Xu RL, Zheng ZJ, Ma YJ, Hu YP, Zhuang SH (2013) Platelet volume indices have low diagnostic efficiency for predicting bone marrow failure in thrombocytopenic patients. Exp Ther Med 5(1):209–214. https://doi.org/ 10.3892/etm.2012.799

#### Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.