PLATELETS ABNORMALITIES IN CHILDREN WITH IRON DEFICIENCY ANEMIA

By

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ABSTRACT

Background: *Iron deficiency anemia (IDA) is the most frequent type of anemia in young children worldwide. In IDA, platelet behavior is often unpredictable and complicated. It may lead to reactive thrombocytosis and rarely thrombocytopenia.*

Objective: *To assess the association between iron deficiency anemia and platelet alterations.*

Methods: *This case-control study included 130 children under 18 years old diagnosed with IDA at Al-Hussein University Hospital's pediatric outpatient clinics during the period from August 2021 to August 2022. Moreover, 70 apparently healthy age and sex-matched children were selected as a control group. All patients and controls were subjected to meticulous history taking, thoroughly full clinical assessment, and Laboratory investigations, including complete blood count (CBC) with a peripheral blood smear as well as Serum iron, total iron-binding capacity (TIBC), and Ferritin.*

Results: *Most platelet indices were significantly lower in children with IDA, except platelet count and plateletcrit (PCT) were statistically significantly higher than in the control group. In particular, mean platelet volume (MPV) had the greatest area under curve (AUC was 0.828), indicating a better predictive capacity, sensitivity, and specificity in discriminating the children with IDA, followed by platelets large cell count (PLCC), platelet large cell ratio (PLCR), and Platelet distribution width (PDW). After adjusting for confounding variables, Multivariate regression analysis showed that MPV at <10.55fl. (AOR (95%CI):5.9(2.9-12.5)) and PLCC at <89.4fl. (AOR(95%CI):3.2(1.54-6.56)) were significant independent predictors of anemia among children.*

Conclusions: *Reactive thrombocytosis is the most common platelet abnormality associated with IDA. MPV can be considered as a marker helping diagnose IDA and follow-up. So, physicians should pay attention to thinking about IDA as a diagnosis.*

Keywords: *Iron, platelet abnormalities, thrombocytopenia, thrombocytosis.*

INTRODUCTION

Iron deficiency (ID) is the most prevalent micronutrient deficiency worldwide, and nearly two billion individuals have anemia **(Abdel-Aaty et al., 2015)**. Moreover, ID is a condition when the body lacks sufficient iron to maintain normal physiological functions. It is defined as decreased total body iron or, in some cases, serum ferritin level <12 mg/l in children up to 5 years and <15 mg/l in children 5 years and older **(Özdemir, 2015)**. Since anemia is the most crucial indicator of iron shortage, the terms ID and IDA are commonly utilized reciprocally.

IDA has reached epidemic proportions in developing countries and has become a major global public health problem, affecting mainly 0–5-year-old children and young women of childbearing age, especially during pregnancy. In Egypt, IDA was found to be the most common cause of anemia among infants 6 to 24 months of low socioeconomic standard affecting 43% of them **(Elalfy et al., 2012)**. In Qena governorate, the prevalence of IDA was 12% among children aged 6–11 years **(Mansour et al., 2004)**. Recent studies have shown that ID may be associated with both hematologic and nonhematologic adverse effects, which may be irreversible. The prevalence of IDA among primary school children was 25.6% **(Abdel-Aaty et al., 2015)**. Iron deficiency can lead to life-threatening loss of red blood cells, muscle function, and energy production. Therefore, the pathogenic features associated with IDA are weakness and impaired growth, motor, and cognitive performance **(Chaparro & Suchdev, 2019)**.

The main principles of treatment include investigation and elimination of the underlying cause, iron supplementation, improvement of nutrition, and education of the patient and family. Oral iron supplements are desirable as first-line therapy. Follow-up is very important to confirm the diagnosis and to ensure that anemia is adequately treated **(Jimenez et al., 2021)**.

IDA can also affect the platelet count. Most patients with IDA will have normal or elevated platelet counts, some higher than 1,000 × 10*9/L at diagnosis; thrombocytopenia in association with ID is relatively rare **(Ibrahim et al., 2012)**. The association of IDA with thrombosis is also increasingly being recognized. A previous study on thrombocytosis in children showed IDA as an etiological factor for reactive thrombocytosis **(Ray et al., 2019)**.

Moderate IDA usually shows thrombocytosis (RT) while thrombocytopenia is usually found in severe IDA suggesting a biphasic mechanism **(Huscenot et al., 2018)**. Thrombocytopenia is more common in severe iron-deficiency anemia. Thrombocytosis is present when there is associated bleeding.

Several changes in platelets indices (PI) have been reported in patients with IDA. Mean platelet volume (MPV) has been reported to be decreased in the case of IDA **(Miri-Aliabad et al., 2021)**. So, the association between iron deficiency anemia and platelet alterations should be considered.

Ethical consideration:

1. Patients were enrolled in the study after taking informed oral and written consent from their parents.
2. Ethical approval was obtained from the ethics committee of the Pediatrics department at the faculty of medicine at Al-Azhar University, with registration number: 1Ped. _161Med.Research_Platelets Abnormalities Child. Iron Deficiency Anemia. _0000161. Patient data confidentiality was preserved during all study procedures.
3. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.
4. All the data of patients and results of the study are confidential and the patient have the right to keep it.
5. The patient has the right to withdraw from the study at any time.
6. The researcher explained to the patient the aim of the study.

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Sample size:

The sample size estimation was done using the Epi info7 program for sample size calculation, setting the confidence level at 95% and margins of error at 10% and based on the work done by **Sobeih et al (2020)**, a total of 130 patients was estimated to be sufficient sample size.

Inclusion criteria:

Both sex under the age of 18 years who were newly diagnosed with IDA based on:

1. Red cell distribution width (RDW)> 14.

2. Red blood cells (RBC): low.
3. Hemoglobin (Hb), Hematocrit (Hct) and mean corpuscular volume (MCV) are low according to age and gender.
4. Patients with Mean Corpuscular hemoglobin (MCH) <27pg.
5. Mean Corpuscular Hb concentration (MCHC) <30%.
6. Low total body iron or, in certain cases.
7. Serum ferritin levels at <12 μg /L in children less than 5 years and at <15 μg/L in children 5 years and older **(Özdemir, 2015)**.

Exclusion criteria:

1. Children who received a blood transfusion or hematinic.
2. Children who were critically ill.
3. Children who suffered from hematological disorders other than IDA.

Study procedure:

This is a case-control study that was conducted between August 2021 and August 2022 at pediatric outpatient clinics of Al-Hussein University Hospital in Egypt on 130 randomly selected children with suspected IDA; in addition, 70 apparently healthy age and sex-matched children were selected as a control group.

The principal aim was to assess the association between iron deficiency anemia and platelet alterations.

All included patients were subjected to thorough:

1. History taking, including personal data, family, medical and nutritional history, Anorexia and fatigue.
2. General examination: with stress on signs of anemia.
3. Systemic examination was done with emphasis on signs of anemia.
4. Laboratory investigations: including:
   A. The CBC and peripheral blood smear were studied using Sysmex XN330 hematology autoanalyzer.
   B. Serum iron profile to confirm IDA, including serum iron, total iron-binding capacity (TIBC), transferrin saturation, and serum ferritin were studied using COBAS c311.

METHODS

Six ml of venous blood was drawn from all participants and then separated into two parts: 2 ml

were placed in a vacutainer tube containing an ethylenediaminetetraacetic acid (EDTA) for CBC and blood smear measurement, and 4 ml were placed in a serum (plain) tube and centrifuged for 10 minutes after clotting the samples. CBC was done using a Sysmex XN330 hematology autoanalyzer, while the blood smear was done by Leishman stain. On the other hand, the separated serum was divided into two parts; one was used for measuring serum iron and TIBC by COBAS c311 chemistry autoanalyzer system, and the other was kept at -20 in the freezer to determine serum ferritin by COBAS e411, ROCHE diagnostics.

Statistical analysis:

All analyses were performed using Statistical Package for the Social Sciences (SPSS) software (Version 26 for Windows; SPSS Inc., Armonk, NY: IBM Corp). Categorical variables were represented as numbers (n) and percentages (%). Continuous variables were expressed as means ± standard deviation (SD). Independent t-test was used to compare the two groups. The correlation between continuous data was analyzed by Pearson correlation test. The receiver operating characteristics (ROC) curve was used to assess the sensitivity and specificity at various cut-off points. Univariate logistic analysis predicted the most significant variables, and the results of the univariate analysis were input into a multivariate logistic regression model. A P-value<0.05 was considered to be statistically significant.

RESULTS

Our results will be demonstrated in the following tables and figures:

Table (1): Sociodemographic data among the studied groups

Variables	Patients group (n=130)	Control group (n=70)	Test of significance	P-value
Age (years) Mean ± SD Min-Max	 5.89±3.20 1.0-14.0	 6.60±2.37 2.0-16.0	 t=1.62	 0.106
Gender, N (%) Male Female	 73 (56.20%) 57 (43.8%)	 38 (54.3%) 32 (45.7%)	 χ^2 =0.064	 0.800
Residence, N (%) Urban Rural	 130(100%) 0(0.0%)	 70(100%) 0(0.0%)	 -	 -
Family Income, N (%) Low High	 124(95.4%) 6(4.6%)	 55(78.6%) 15(21.4%)	 13.687	 <0.001*
Maternal Education, N (%) Illiterate Primary preparatory secondary high schools	 106(81.5%) 8(6.1%) 6(4.6%) 4(3%) 6(4.6%)	 50(71.5%) 3(4.2%) 5(7.1%) 7(10%) 5(7.1%)	 2.710	 0.100

This table shows highly significant difference between patient and control regarding family income.

Table (2): Clinical manifestation among our studied groups

Variables	Outcome (n=130)
Symptoms of IDA, N (%)	
Anorexia	104 (80.0%)
Decreased gaining weight	40 (30.8%)
Easy fatigability	26(20%)
Decreased mental activity	20(15.4%)
Pica	13 (10%)
Sign of IDA, N (%)	
Pallor	30 (23%)
Atrophic glossitis	17 (13.1%)
Nail ridges	11(8.5%)
Angular stomatitis	5(3.8%)

This table shows that the most common symptoms in our cases were anorexia and decrease weight gain and the most common signs was pallor followed by atrophic glossitis.

Table (3): Comparison of CBC parameters between IDA patients and control groups

Variables	Patients group (n=130)	Control group (n=70)	Test of significance	P-value
Hb (g/dl)	10.40±0.73	13.15±0.71	t=25.56	<0.001*
Erythrocytes ($x10^6$/ µl)	4.68±0.32	4.63±0.27	t=1.16	0.250
HCT (%)	35.15±2.34	39.68±2.48	t=12.77	<0.001*
MCV (fl.)	74.89±5.69	85.72±3.24	t=14.69	<0.001*
MCH (pg)	22.21±1.81	28.35±1.13	t=25.72	<0.001*
MCHC (g/dl)	29.61±1.87	33.10±1.32	t=13.87	<0.001*
RDWCV (%)	14.75±1.64	15.36±2.03	t=2.32	0.021*
WBCs ($x10^3$/ µl)	10.79±3.94	10.02±3.17	t=1.41	0.160

This table shows highly significant difference between patient and control regarding HB, HCT, MCV, MCH, MCHC and RDWCV.

Table (4): Comparison of platelets measures between IDA patients and control groups

Variables	Patients group (n=130)	Control group (n=70)	Test of significance	P-value
PLT count ($x10^3$/µL)	329.25±109.67	285.00±68.87	t=3.06	0.002*
MPV (fl.)	9.29±9.29	11.06±1.74	t=8.95	<0.001*
PCT (%)	0.29±0.09	0.261±0.07	t=2.24	0.026*
PDW (%)	12.59±2.09	13.49±2.58	t=2.67	0.008*
PLCC (fl.)	75.83±21.65	94.85±30.47	t=5.12	<0.001*
PLCR (%)	25.73±6.94	29.88±8.72	t=3.68	<0.001*

This table shows highly significant difference between patient and control regarding all platelet parameters.

Table (5): Comparison of serum iron profile between IDA patients and control groups

Variables	Patients group (n=130)	Control group (n=70)	Test of significance	P-value
Total serum iron (µg/dL)	47.11±16.24	84.17±20.15	t=14.12	<0.001*
TIBC (µ/dL)	435.08±48.29	384.10±51.92	t=6.93	<0.001*
Transferrin Saturation (%)	10.79±3.50	22.09±5.06	t=18.52	<0.001*
Serum ferritin (µg/L)	9.42±2.96	44.16±21.12	t=18.47	<0.001*

This table shows highly significant difference between patient and control regarding all iron profile parameters.

Table (6): Correlation between platelet measures and other variables in children with IDA

Variables	PLT count ($x10^3$/µL)	PDW (%)	MPV (fl.)	PCT (%)
Hb(g/dl)	**-0.339****	**0.368****	**0.174***	**-0.222***
Erythrocytes ($x10^6$/ µl)	-0.016	0.151	**0.207***	0.028
HCT (%)	**-0.253***	**0.199***	0.185	-0.135
MCV (fl.)	**-0.285****	0.008	**0.206***	**-0.185***
MCH (pg)	**-0.216***	0.119	0.009	-0.167
MCHC(g/dl)	0.081	0.076	**0.260***	0.041
RDWCV (%)	0.134	0.122	-0.071	**0.226***
MPV (fl.)	**-0.353****	**0.650****	1	-0.006
PCT (%)	**0.856****	0.126	-0.006	1
PDW (%)	-0.115	1	**0.650****	0.126
PLCC (fl.)	**-0.374****	**0.204***	**0.228***	0.486
PLCR (%)	**-0.349****	**0.586****	**0.680****	-0.161
Total serum iron (µg/dL)	**-0.311****	**0.182***	**0.286****	**-0.175***
TIBC(µ/dL)	-0.062	-0.102	**-0.213***	-0.074
Tfsat (%)	-0.152	-0.170	**-0.181***	**-0.179***
Serum ferritin (µg/L)	**-0.217***	**0.221***	**0.234***	-0.139

Table 6 showed that the PLT negatively correlated with Hb, HCT, MCV, MCH, MPV, PLCC, PLCR, total serum iron, and Ferritin level. On the other hand, platelet count was significantly positively associated with PCT.

Also, PDW was moderately significant positive correlated with Hb, PLCC, PLCR, total serum iron, and Ferritin level,

whereas a significantly strong positive correlation with MPV.

The MPV significantly correlated with Hb level, erythrocytes, MCV, MCHC, PLCC, PDW, PLCR, total serum iron, and ferritin level. However, there was a statistically significant negative correlation between MPV, TIBC, and Transferrin Saturation.

Table (7): Logistic regression analysis model of independent variables for anemic children

Independent variables	Univariate model				Multivariate model		
	Constant	β	P-value	OR (95%CI)	β	P-value	AOR (95%CI)
PLT count >296 x10^3/µL	0.388	0.451	0.131	1.6 (0.9-2.9)	-	-	-
PCT> 0.275%	0.575	0.088	0.767	1.1 (0.6-1.9)	-	-	-
MPV <10.55 fl.	-0.693	1.885	**<0.001***	6.6 (3.3-13)	1.791	**<0.001***	5.9 (2.9-12.5)
PDW <12.85%	0.258	0.613	**0.043***	1.8 (1.02-3.3)	0.077	0.860	1.1 (0.46-2.54)
PLCC <89.4 fl.	-0.182	1.261	**<0.001***	3.5 (1.9-6.6)	1.156	**0.002***	3.2 (1.54-6.56)
PLCR <29.45%	0.001	1.017	**0.001***	2.8 (1.5-5.1)	0.278	0.544	1.3 (0.54-3.24)

In univariate regression analysis, MPV <10.55 fl. (OR=6.6, 95% CI: 3.3 – 13), PLCC <89.4 fl. (OR=3.5, 95% CI: 1.9 -6.6), PLCR <29.45 % (OR=2.8, 95% CI: 1.5 - 5.1) and PDW <12.85 % (OR=1.8, 95% CI: 1.02 - 3.3) were significant predicted factors for anemia.

However, after adjusting for confounding variables, MPV <10.55 fl. and PLCC <89.4 fl. were the only independent predictors of anemia, where MPV <10.55 fl. increased the risk of IDA by 5.9-fold, and PLCC <89.4 fl. increased the risk by 3.2-fold.

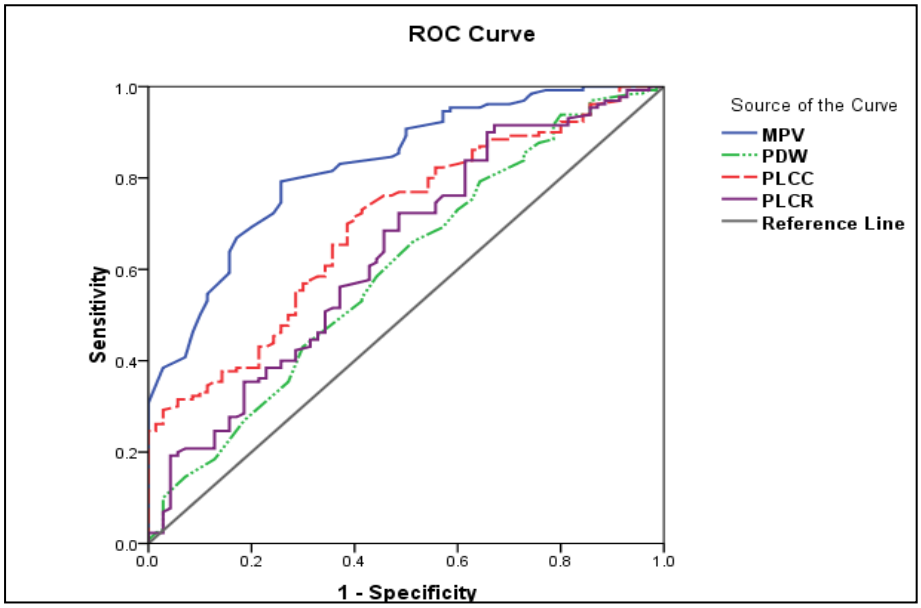

Figure (1): ROC curve for prediction of anemic children by MPV, PDW, PLCC and PLCR

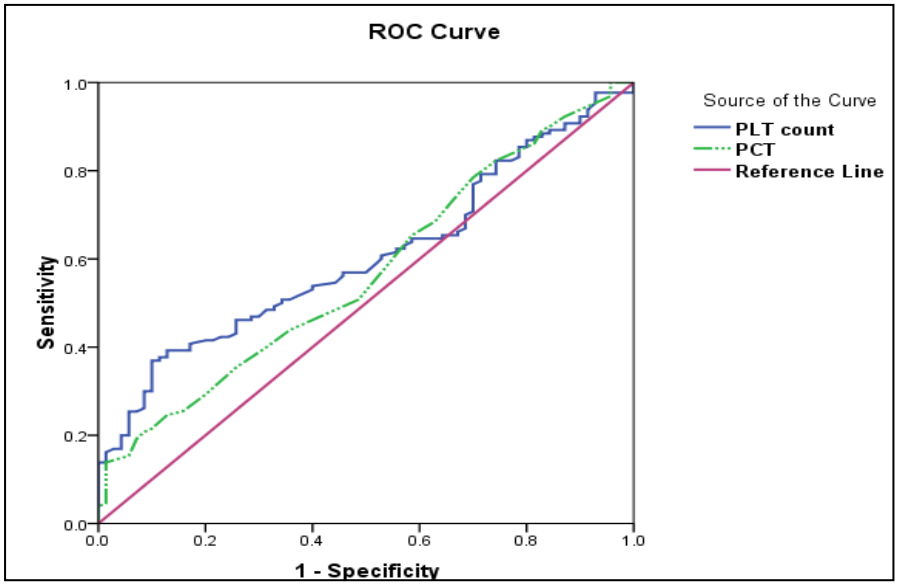

Figure (2): ROC curve for prediction of anemic children by platelet count and PTC

DISCUSSION

The present study showed that the mean age among anemic children was 5.89 years compared to 6.6 years in the control group, with no statistically significant difference. In addition, the predominance of males over females in both groups. Similarly, Fahim et al. found that 71.3% of patients were males and 28.7% were females **(Fahim et al., 2022)**.

In addition, most of our participant had Anorexia. In a similar result, Fahim et al. found that the most common symptoms in among patients with IDA were anorexia (87.8%), followed by lack of attention span, irritability, decreased gaining weight, easy fatigability, pica, recurrent infections, and decreased school performance **(Fahim et al., 2022)**.

Regarding sign, Atrophic glossitis, Nail ridges, and Angular stomatitis were detected. On the other hand Malnutrition, Signs of vitamins deficiency, Angular stomatitis, Glossitis, Nail changes, Nail striations, Spooning of the nail (Koilonychias), Brittle nails were noticed among patients with IDA **(Fahim et al., 2022)**.

The current study detected a significantly lower Hb, HCT, MCV, MCH, MCHC, and RDWCV among children with IDA compared to the control group. At the same time, anemic children had slightly higher erythrocytes and WBCs but did not achieve significant differences from the control group. This finding is consistent with Deshmukh et al. **(Deshmukh et al., 2021)** and Fahim et al. **(Fahim et al., 2022)**, except concerning erythrocytes, which reported lower RBCs in IDA patients than in the control group. This may be due to patients having another medical condition. Iron deficiency causes Hb synthesis defect resulting in RBC microcytic RBCs and decreased Hb synthesis **(Faraj et al., 2020)**.

Regarding platelet measures, IDA patients had significantly higher mean PLT and PCT than the control group. Our findings agreed with previous studies **(Deshmukh et al., 2021**; **Mohammed Mujib et al., 2014)**. Fahim et al. also observed that the mean PLT and PCT were significantly increased in IDA than in controls.

IDA children also had lower MPV, PDW, PLCC, and PLCR than the control group. PLCC and PLCR are simple and straightforward methods of an indirect assessment of platelet stimulation and activity **(Kalantar-Zadeh et al., 2004)**

(Desai et al., 2013). **Fahim et al. (2022)** revealed that IDA patients had lower MPV, PDW, PLCC, and PLCR than controls. In patients with IDA, the bone marrow produces more platelets but with a smaller volume of platelets under normal circumstances. Therefore, MPV and PDW decrease among cases of IDA. Additionally, platelets are usually relatively young and contain intracellular granules; consequently, they are more reactive and vice versa. Thus, in cases of IDA, the reactivity of platelets decreases as platelet volume decreases **(Desai et al., 2013)**.

In this study, anemic children had significantly lower mean serum iron, Transferrin Saturation, and ferritin levels than the control group. However, the TIBC levels were significantly higher in the anemic children than in the control group. In consistency with our results, Latif et al. and Mohammed et al. observed that serum iron, Transferrin Saturation, and ferritin levels were significantly lower in anemic patients than in the control group, while TIBC was higher in IDA children than the non-anemic children with a statistically significant difference **(Latif et al., 2017**; **Mohammed et al., 2020)**.

In our findings, PLT was significantly correlated negatively with Hb, HCT, MCV, MCH, MPV, PLCC, PLCR, total serum iron, and ferritin level but positively with PCT. Likewise, a previous study found a negative correlation between PLT and Hb, HCT, MCV, MCH, MCHC, MPV, PDW, and serum iron **(Kuku et al., 2009)**. PLT was positively correlated with RDW, PCT, and iron binding. However, no significant correlation was found between platelet and platelet counts and RBC and ferritin, which is consistent with previous studies **(Ayan et al., 2015) (Kumar, 2017) (Rafieemehr et al., 2017)**. In contrast, Kadikoyluet al., reported a positive correlation between PLT and serum ferritin **(Kadikoylu et al., 2006)**, while Lotfy et al. revealed a positive correlation between PLT and MPV **(Lotfy et al., 2021)**.

A significant negative correlations were noticed between PLT and each of MPV, PLCR, Hb, HCT, MCHC, MCV, serum iron, and serum ferritin; significant positive correlations were noticed with each of PCT, RDW, and TIBC **(Fahim et al., 2022)**. Patel & Prajapati suggested that decreased serum iron and Transferrin Saturation, increasing TIBC, may enhance

megakaryopoiesis in IDA **(Patel & Prajapati, 2022)**.

MPV correlated positively with Hb level, erythrocytes, MCV, MCHC, PDW, PLCC, PLCR, total serum iron, and ferritin and negatively with TIBC and Transferrin Saturation. Similarly, Elsewefy et al., Ayan et al. and Fahim et al. demonstrated that MPV correlated positively with Hb, PLCR, HCT, RBCs, MCHC, MCV, serum iron, and serum ferritin and negatively with TIBC **(Ayan et al., 2015**; **Elsewefy et al., 2014**; **Fahim et al., 2022)**. Suggesting that platelet size could reflect platelet activity, reducing platelet activity **(Arslan et al., 2017**; **Zareifar et al., 2014)**. However, Chalise et al. observed no association between MPV and iron parameters **(Chalise et al., 2019)**.

Moreover, PCT significantly negatively correlated with Hb, MCV, total serum iron, and Transferrin Saturation. However, PCT was significantly positively correlated with RDWCV. Likewise, Park et al., and Han et al. demonstrated that PCT negatively correlated with Hb level, MCV, serum iron, and Transferrin Saturation in patients with IDA **(Han et al., 2018**; **Park et al., 2013)**. In contrast, Kadikoylu et al. found no association between PCT and iron parameters in IDA patients.

Our ROC analysis showed that MPV was the best predictor of anemic patients (AUC was 0.828, with the optimal MPV cut-off value for predicting anemic children being 10.55 fl.). According to a previous study evaluated the MPV/platelet ratio in patients in the IDA group, the ROC curve analysis of the MPV/platelet count ratio revealed 73% sensitivity and 80% specificity at a cut-off point of 0.0318 **(Cho et al., 2013)**. Also, another study showed that the platelet /MPV ratio at level 0.015 could help the pediatrician have a high suspicion index to diagnose IDA (AUC was 0.68) **(Ghali et al., 2022)**.

From the multivariate regression analysis, MPV <10.55 and PLCC <89.4 were the only independent anemic predictors. Also, Cho et al. showed the MPV/platelet count ratio outstanding performance in differentiating patients with IDA from other types of anemia **(Cho et al., 2013)**. In line with the results of our study, it is likely to be used as a panel along with traditional biochemical indicators, including TIBC, Transferrin Saturation, and serum iron.

LIMITATIONS OF THE STUDY

The main limitations of this analysis are the small sample size and the non-longitudinal assessment of causes and complications.

CONCLUSIONS

We conclude that reactive thrombocytosis is the most common IDA-related platelet abnormality. Platelet activity can be determined indirectly using platelet volume indicators, including MPV, PLCC, and PLCR). The most significant predictors for anemic patients were MPV, PLCC, and PLCR based on the ROC curve. Moreover, the only independent predictors for anemia were MPV and PLCC. So, MPV can be considered a marker that helps diagnose IDA and follow-up, and physicians should pay attention to thinking about IDA as a diagnosis.

RECOMMENDATION

The present study provided evidence of the usefulness of a newly diagnosed MPV as a convenient and sensitive biomarker for predicting IDA patients.

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REFERENCES

1. **Abdel-Aaty, N., Abdel-Rasoul, G., El Bahnasy, R., El Shazly, H., & Gabr, H. (2015):** Epidemiology of iron-deficiency anemia among primary school children (6-11 years), Menoufia governorate, Egypt. Menoufia Medical Journal, 0(0), 0. https://doi.org/10.4103/1110-2098.165127.
2. **Arslan, H. H., Guzel, M., Meral, Y., Dalgin, D., Gokalp, G., & Ozcan, U. (2017):** A New Approach to Blood Parameters in Dogs with Hemorrhagic Enteritis. Acta Scientiae Veterinariae, 45(1), 6. https://doi.org/10.22456/1679-9216.80180.
3. **Ayan, N. N., Savas, Z., Bireroglu, N., Keles, A., Aksoy, N., & Serin, N. O. (2015):** The Comparison of Platelet Counts between the before and after Treatments of Women with Iron Deficiency Anemia. Journal of Academic Research in Medicine, 5(3), 94–96.

https://doi.org/10.5152/jarem.2015.712.

4. **Chalise, S., Acharya, N., & Pradhan, S. B. (2019):** Correlation between Iron Parameters and Platelet Parameters in Iron Deficiency Anemia. Journal of Institute of Medicine Nepal, 41(3), 35–38. https://doi.org/10.3126/jiom.v41i3.37362.

5. **Chaparro, C. M., & Suchdev, P. S. (2019):** Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. Annals of the New York Academy of Sciences, 1450(1), nyas.14092. https://doi.org/10.1111/nyas.14092.

6. **Cho, S. Y., Yang, J. J., Suh, J., Lee, W., & Lee, H. J. (2013):** Mean platelet volume / platelet count ratio in anemia. 7104(May 2012), 2012–2014. https://doi.org/10.3109/09537104.2012.684734.

7. **Demirin, H., Ozhan, H., Ucgun, T., Celer, A., Bulur, S., Cil, H., Gunes, C., & Yildirim, H. A. (2011):** Normal range of mean platelet volume in healthy subjects: Insight from a large epidemiologic study. Thrombosis Research, 128(4), 358–360. https://doi.org/10.1016/j.thromres.2011.05.007.

8. **Desai, K. N., Patel, K., Shah, M., Ranapurwala, M., Chaudhari, S., Shah, M., & Shah, M. (2013):** A study of platelet volume indices (PVI) in patients of coronary artery disease and acute myocardial infarction in tertiary care hospital. Int. J. Adv. Res, 1(1), 185–91.

9. **Deshmukh, A., Konsam, V., Gupta, A., & Gangane, N. (2021):** Significance of platelet parameters in cases of iron deficiency anemia with reference to thromboembolic complications - A study in central India. Saudi Journal for Health Sciences, 10(3), 165. https://doi.org/10.4103/sjhs.sjhs_132_21.

10. **Elalfy, M. S., Hamdy, M., & RABBAbdel Maksoud, S. (2012):** Pattern of milk feeding and family size as

risk factors for iron deficiency anemia among poor Egyptian infants 6 to 24 months old. Nutr Res, 32, 93–99.

11. **Elsewefy, D., Farweez, B., & Ibrahim, R. (2014):** Platelet indices: consideration in thrombocytopenia. The Egyptian Journal of Haematology, 39(3), 134. https://doi.org/10.4103/1110-1067.148240.

12. **Fahim, F. M., Helal, S. R., Fathalla, E., Saeed, A. N., & Galal, S. M. (2022):** Platelets abnormalities in children with iron deficiency anemia. Journal of Current Medical Research and Practice, 7(1), 22. https://doi.org/10.4103/JCMRP.JCMRP.

13. **Faraj, S. A., AL-Rubae, A. M., & Ansaf, A. I. (2020):** Evaluation of mean platelet volume before and after iron deficiency anemia treatment. International Journal of Pharmaceutical Research, 13(01). https://doi.org/10.31838/ijpr/2021.13.01.081.

14. **Ghali, H. H., Neamah, A. M., Abbood, M. A., & Faraj, S. A. (2022):** Evaluation of mean platelet volume / platelet count ratio before and after Iron deficiency anemia treatment. 11(2), 54–59. https://doi.org/10.9790/1959.

15. **Giovanetti, T. V., Nascimento, A. J. do, & Paula, J. P. de. (2011):** Platelet indices: laboratory and clinical applications Thayse. Revista Brasileira de Hematologia e Hemoterapia, 33(2), 164–165. https://doi.org/10.5581/1516-8484.20110040.

16. **Han, D.-D., Ma, C., Zhao, L., Gao, Y.-J., & Su, Y.-H. (2018):** [Relationship between Iron Metabolism and Platelet Parameters in Patients with Iron Deficiency Anemia]. Zhongguo Shi Yan Xue Ye Xue Za Zhi, 26(6), 1738–1741. https://doi.org/10.7534/j.issn.1009-2137.2018.06.026.

17. **Huscenot, T., Luc, D., Wagner Ballon, O., Valentine, L., Gobert, D., Le cann, M., Morbieu, C., & Michel, M. (2018):** Iron

Deficiency Anemia, a Rare and Potentially Underestimated Cause of Thrombocytopenia and a Differential Diagnosis of Immune Thrombocytopenia (ITP): Results from a Retrospective Case-Controlled Study. Blood, 132(Supplement 1), 4984–4984. https://doi.org/10.1182/blood-2018-99-118532.

18. **Ibrahim, R., Khan, A., Raza, S., Kafeel, M., Dabas, R., Haynes, E., Gandhi, A., Majumder, O. L., & Zaman, M. (2012):** Triad of Iron Deficiency Anemia, Severe Thrombocytopenia and Menorrhagia–-A Case Report and Literature Review. Clinical Medicine Insights: Case Reports, 5, CCRep.S9329. https://doi.org/10.4137/CCRep.S9329.

19. **Jimenez, K., Leitner, F., Leitner, A., Scharbert, G., Schwabl, P., Kramer, A. M., Krnjic, A., Friske, J., Helbich, T., Evstatiev, R., Khare, V., & Gasche, C. (2021):** Iron deficiency-induced thrombocytosis increases thrombotic tendency in rats. Haematologica, 106(3), 782–794. https://doi.org/10.3324/haematol.2019.245092.

20. **Kadikoylu, G., Yavasoglu, I., Bolaman, Z., & Senturk, T. (2006):** Platelet parameters in women with iron deficiency anemia. Journal of the National Medical Association, 98(3), 398–402. https://doi.org/16573304.

21. **Kalantar-Zadeh, K., Rodriguez, R. A., & Humphreys, M. H. (2004):** Association between serum ferritin and measures of inflammation, nutrition and iron in haemodialysis patients. Nephrology Dialysis Transplantation, 19(1), 141–149. https://doi.org/10.1093/ndt/gfg493.

22. **Kuku, I., Kaya, E., Yologlu, S., Gokdeniz, R., & Baydin, A. (2009):** Platelet counts in adults with iron deficiency anemia. Platelets, 20(6), 401–405. https://doi.org/10.1080/09537100903137306.

23. Kumar, D. (2017): Erythrocytes and Platelets: A Critical Analysis of their Ontogenic Relationship through Automated Parameters. JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH, May1;11(5). https://doi.org/10.7860/JCDR/2017/25153.9807.

24. Latif, A., Alam, M. R., Khanam, A., Hoque, F., Rahim, M. A., & Islam, R. N. (2017): Role of Serum Transferrin Receptor in Diagnosing and Differentiating Iron Deficiency Anemia from Anemia of Chronic Disease in Patients with Chronic Kidney Disease. BIRDEM Medical Journal, 7(2), 132–137. https://doi.org/10.3329/birdem.v7i2.32451.

25. Lotfy, A. E. R. M., Ahmed, A. Z. E. S., & Fahmy, E. M. (2021): Thrombocytosis in children: Clinical and heamatological study in pediatric department, sohag university hospital. Egyptian Journal of Hospital Medicine, 84(1), 2435–2441. https://doi.org/10.21608/ejhm.2021.184663.

26. Mansour, P., Barduagni, A. S., & Ahmed, F. (2004): Anemia among schoolchildren in Qena Governorate. Upper Egypt East Mediterr Health J, 10, 916–920.

27. Miri-Aliabad, G., Teimouri, A., Hossein, S., & Mousavi, S. (2021): Platelet Parameters in Children with Iron Deficiency Anemia before and After Treatment. Int J Pediatr, 9(87), 13249–13256. https://doi.org/10.22038/ijp.2020.53642.4251.

28. Mohammed Mujib, A. S., Mohammad Mahmud, A. S., Halder, M., & Monirul Hasan, C. M. (2014): Study of Hematological Parameters in Children Suffering from Iron Deficiency Anaemia in Chattagram Maa-o-Shishu General Hospital, Chittagong, Bangladesh. Anemia, 2014, 1–10. https://doi.org/10.1155/2014/503981.

29. Mohammed, S., Mousa, A., & Hashim, A. (2020): Role of Hypochromia and

Microcytosis in theprediction of iron deficiency anemia. Minia Journal of Medical Research, 31(3), 262–268. https://doi.org/10.21608/mjmr.2022.220289.

30. **Nah, E., Kim, S., Cho, S., & Cho, H. (2018):** Complete Blood Count Reference Intervals and Patterns of Changes Across Pediatric, Adult, and Geriatric Ages in Korea. Annals of Laboratory Medicine, 38(6), 503–511. https://doi.org/10.3343/alm.2018.38.6.503.

31. **Özdemir, N. (2015):** Iron deficiency anemia from diagnosis to treatment in children. Turk Pediatri Arsivi, 50(1), 11–19. https://doi.org/10.5152/tpa.2015.2337.

32. **Park, M. J., Park, P. W., Seo, Y. H., Kim, K. H., Park, S. H., Jeong, J. H., & Ahn, J. Y. (2013):** The relationship between iron parameters and platelet parameters in women with iron deficiency anemia and thrombocytosis. Platelets, 24(5), 348–351. https://doi.org/10.3109/09537104.2012.699641.

33. **Patel, G. R., & Prajapati, G. R. (2022):** Platelet Count in Adults with Iron Deficiency Anemia and Its Correlation with Serum Iron Parameters: An Observational Study at a Tertiary Care Center in Northwestern India. Scholars Journal of Applied Medical Sciences, 10(6), 910–916. https://doi.org/10.36347/sjams.2022.v10i06.009.

34. **Rafieemehr, H., Rafiee, M., Mahmoodi, M., & Abbasi Oshaghi, E. (2017):** Survey of Correlation Between Serum Transferrin Saturation and Platelet Indices in High School Female Students in the Northwest Iran. International Journal of School Health, In Press(In Press). https://doi.org/10.5812/intjsh.13666.

35. **Ray, S., Chandra, J., & Sharma, S. (2019):** Clinico-hematological study of abnormalities of platelet count in children with iron deficiency anemia. International Journal of

Contemporary Pediatrics, 6(4), 1519. https://doi.org/10.18203/2349-3291.ijcp20192748.

36. **Sobeih A, Sakr M&Abolmaaty R. (2020):** assessment of cardiac diastolic function in infants of diabetic mothers using tissue doppler echocardiography. Egypt pediatric association Gaz., 68, 10 http://doi.org/10.1186/s43054-020-00021-3.

37. **Zareifar, S., Farahmand Far, M. R., Golfeshan, F., & Cohan, N. (2014):** Changes in Platelet Count and Mean Platelet Volume During Infectious and Inflammatory Disease and Their Correlation with ESR and CRP. Journal of Clinical Laboratory Analysis, 28(3), 245–248. https://doi.org/10.1002/jcla.21673.