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Platelet indices and Platelet-To-Lymphocyte ratio in iron deficiency anemia: Insights for clinical interpretation from a comparative study

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Abstract

Iron Deficiency Anemia (IDA) is conventionally defined by reduced hemoglobin concentration; however, iron deficiency also influences non-erythroid hematopoietic lineages, particularly platelet biology. This cross-sectional comparative study evaluated platelet indices and the platelet-to-lymphocyte ratio (PLR) in 500 adults with IDA and 150 healthy controls to explore their potential hematologic significance. Platelet count, Mean Platelet Volume (MPV), plateletcrit (PCT), and PLR were compared between groups, and their discriminatory performance for IDA was assessed using receiver operating characteristic analysis. Individuals with IDA demonstrated significantly higher platelet count, increased PCT, and elevated PLR compared with healthy controls, whereas MPV did not differ significantly between groups and showed limited discriminatory value. Receiver operating characteristic analysis revealed modest but consistent discrimination for platelet count, PCT, and PLR, while MPV contributed minimally. These findings indicate that iron deficiency is associated with a distinct platelet-related phenotype extending beyond hemoglobin reduction alone. Although these indices are not diagnostic for IDA, their routine availability may provide useful adjunctive information, enhancing interpretation of complete blood count results and supporting clinical assessment of iron-deficient states, particularly when iron studies are unavailable or delayed.

Keywords: Iron deficiency anemia, Platelet indices, Platelet-To-Lymphocyte ratio, Plateletcrit, Mean platelet volume, Complete blood count

1. Introduction

Iron Deficiency Anemia (IDA) is the most prevalent form of anemia worldwide and remains a major public health challenge, particularly in resource-limited settings across diverse global populations (Stoltzfus, 2001). While iron deficiency anemia is traditionally defined by reduced hemoglobin concentration and impaired erythropoiesis, iron deficiency also exerts important effects on other hematopoietic lineages, which in clinical practice are frequently reflected by reactive changes in platelet production, including thrombocytosis, that may accompany iron-deficient states in affected adult patients (Song et al., 2020; Li et al., 2022).

Beyond absolute platelet count, composite hematologic markers derived from routine complete blood counts, such as the Platelet-To-Lymphocyte Ratio (PLR), have attracted increasing clinical interest. PLR integrates platelet and lymphocyte dynamics and may reflect the balance between reactive thrombopoiesis and immune cell alterations. Several studies have reported higher PLR values in patients with IDA compared with healthy individuals, indicating altered platelet-to-lymphocyte balance in iron-deficient states (Hegde & Puranik, 2020). Reduced lymphocyte counts observed in iron-deficient states may further contribute to PLR elevation by lowering the denominator of the ratio (AlRajeh et al., 2022). Importantly, normalization of iron status following treatment has been shown to reverse PLR elevation, supporting a close association between PLR and iron-deficient states (Uz et al., 2016).

Platelet indices, including Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and plateletcrit (PCT), provide indirect insight into platelet size, production, and activation processes (Liu et al., 2024). Given the established role of iron in hematopoiesis, alterations in platelet parameters such as platelet count, plateletcrit (PCT), and Platelet Distribution Width (PDW) have been frequently reported in patients with IDA worldwide (Chalise et al., 2019). However, findings regarding MPV and PDW remain inconsistent, and their clinical interpretation in iron deficiency is not yet fully established (Beguin, 1999).

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From a clinical perspective, understanding these hematologic changes is relevant because platelet indices and PLR are automatically generated, inexpensive parameters that require no additional laboratory testing. Despite this practical advantage, relatively few adult studies have evaluated platelet indices and PLR within a comparative framework that includes healthy controls, limiting clinicians' ability to interpret these parameters in everyday practice. Clarifying whether such markers differ meaningfully between iron-deficient and non-anemic states may enhance clinicians' awareness of the broader hematologic manifestations of IDA and support more informed interpretation of routine complete blood count results.

Therefore, the present study aimed to evaluate platelet indices and the platelet-to-lymphocyte ratio in adults with iron deficiency anemia and to compare these parameters with those of healthy controls. In addition, this study provides data from the Kurdistan Region of Iraq, where regional evidence on these hematologic patterns remains limited.

2. Methods

2.1 Study design and setting

This cross-sectional comparative study was conducted at the Duhok Specialized Laboratory Center, Duhok Province, Kurdistan Region of Iraq, over a 12-month period from November 2024 to October 2025. The study was designed to compare platelet indices and the platelet-to-lymphocyte ratio (PLR) between adults with iron deficiency anemia (IDA) and healthy non-anemic controls using routinely collected laboratory data.

2.2 Study population

A total of 650 adults aged 18–65 years were included in the analysis. The study population comprised 500 patients diagnosed with iron deficiency anemia and 150 apparently healthy controls.

2.2.1 Iron deficiency anemia group

Iron deficiency anemia was defined by the presence of low serum ferritin levels (<15 µg/L) in conjunction with reduced hemoglobin concentration (<13.0 g/dL in men and <12.0 g/dL in women).

2.2.2 Healthy control group

Healthy controls were defined as individuals with normal hemoglobin concentrations and normal serum ferritin levels (≥15 µg/L), with no laboratory or clinical evidence of anemia.

2.2.3 Exclusion criteria

Exclusion criteria for both groups included known hemoglobinopathies, hemolytic anemia, acute blood loss, pregnancy, and vitamin B12 or folate deficiency. Individuals with active infection, chronic inflammatory or autoimmune diseases, or malignancy were also excluded. These conditions were assessed through medical history, physical examination, and review of medical records, supported by the absence of laboratory evidence of systemic inflammation at the time of blood sampling, as indicated by normal erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) levels, in order to minimize potential confounding effects on hematologic parameters among all enrolled study participants.

2.3 Hematological and biochemical measurements

Venous blood samples were obtained using standard aseptic techniques under routine laboratory conditions. Complete Blood Counts (CBC) were performed on Ethylenediaminetetraacetic Acid (EDTA)–anticoagulated blood samples using an automated hematology analyzer, in accordance with routine laboratory procedures.

2.3.1 Complete blood count parameters

The platelet parameters evaluated included platelet count (PLT, $\times 10^3/\mu L$), mean platelet volume (MPV, fL), and plateletcrit (PCT, %) as routinely reported parameters. Hemoglobin concentration and absolute lymphocyte count were also obtained from the CBC results for each study participant.

2.3.2 Calculation of platelet-to-lymphocyte ratio

The Platelet-To-Lymphocyte Ratio (PLR) was calculated for each participant by dividing the platelet count by the absolute lymphocyte count for subsequent comparative statistical evaluation.

2.4 Definitions of iron deficiency anemia and platelet parameters

Iron deficiency anemia was defined by low serum ferritin (<15 μg/L) together with reduced hemoglobin concentration (<13.0 g/dL in men and <12.0 g/dL in women). Healthy controls were defined by normal hemoglobin and ferritin values. Platelet parameters were analyzed as continuous variables for comparative assessment between the iron deficiency anemia and healthy control groups. Platelet count values were additionally interpreted according to conventional clinical reference ranges.

3. Statistical analysis

Statistical analyses were performed using standard statistical software. Continuous variables were assessed for normality using visual inspection and distributional characteristics. Data are presented as mean ± Standard Deviation (SD) for approximately normally distributed variables and as median with Interquartile Range (IQR) for non-normally distributed variables. Categorical variables are summarized as frequencies and percentages.

Comparisons between adults with Iron Deficiency Anemia (IDA) and healthy controls were performed using the independent-samples t test or Welch's t test, as appropriate, for continuous variables. The χ^2 test was used to compare categorical variables. All tests were two-tailed.

To quantify the magnitude of between-group differences, effect sizes were calculated using Hedges' g, with values of approximately 0.2, 0.5, and 0.8 interpreted as small, moderate, and large effects, respectively.

The discriminatory performance of platelet indices and the Platelet-To-Lymphocyte Ratio (PLR) for differentiating IDA from non-anemic states was evaluated using Receiver Operating Characteristic (ROC) curve analysis. The Area Under the Roc Curve (AUC) was calculated with corresponding 95% confidence intervals, estimated using bootstrap resampling. Optimal cutoff values were determined using the Youden index, and associated sensitivity and specificity were reported. All statistical tests were considered significant at a p-value < 0.05.

4. Results

4.1 Study population

A total of 650 adults were included in the analysis, comprising 500 patients with iron deficiency anemia (IDA) and 150 healthy controls. Participants in both groups were aged between 18 and 65 years. The mean age was comparable between the two groups (IDA: 33.9 ± 10.6 years; controls: 32.7 ± 8.7 years; p = 0.17). As expected, hemoglobin concentration was significantly lower in the IDA group compared with healthy controls (10.4 ± 1.4 vs 14.3 ± 1.0 g/dL; p < 0.001).

In the IDA group, 200 participants (40.0%) were male and 300 (60.0%) were female, while the healthy control group included 75 males (50.0%) and 75 females (50.0%) (Table 1).

Table 1. Baseline demographic and hematologic characteristics of adults with iron deficiency anemia and healthy controls

Variable		IDA (n = 500)	Healthy Controls (n = 150)	*p* value
Age (years)		33.9 ± 10.6	32.7 ± 8.7	0.17
Sex, n (%)	Male	200 (40.0)	75 (50.0)	0.031
	Female	300 (60.0)	75 (50.0)	
Hemoglobin (g/dL)		10.4 ± 1.4	14.3 ± 1.0	<0.001
Platelet count (×10^3/μL)		300.9 ± 85.0	251.1 ± 45.1	<0.001
Mean platelet volume (fL)		9.84 ± 1.29	9.70 ± 0.81	0.12
Plateletcrit (%)		0.30 ± 0.09	0.25 ± 0.05	<0.001
Platelet-to-lymphocyte ratio		157.1 ± 61.7	125.8 ± 43.5	<0.001

Notes: Data are presented as mean ± standard deviation or number (percentage), as appropriate. Comparisons between groups were performed using Welch's independent-samples t test for continuous variables and the χ^2 test for categorical variables. The p value for sex distribution refers to the overall comparison between groups. IDA: iron deficiency anemia

4.2 Comparison of platelet indices and PLR between IDA and healthy controls

Platelet-related parameters differed significantly between adults with IDA and healthy controls (Table 2).

Patients with IDA demonstrated a significantly higher platelet count compared with controls (300.9 ± 85.0 vs 251.1 ± 45.1 $\times 10^3/\mu L$; $p < 0.001$), with a moderate effect size (Hedges' g = 0.64). Similarly, plateletcrit (PCT) was significantly increased in the IDA group (0.30 ± 0.09% vs 0.25 ± 0.05%; $p < 0.001$; Hedges' g = 0.58).

The platelet-to-lymphocyte ratio (PLR) was also significantly higher in individuals with IDA than in healthy controls (157.1 ± 61.7 vs 125.8 ± 43.5; $p < 0.001$), corresponding to a moderate standardized difference (Hedges' g = 0.54). In contrast, mean platelet volume (MPV) did not differ significantly between groups (9.84 ± 1.29 vs 9.70 ± 0.81 fL; p = 0.12), and the associated effect size was small.

Boxplot visualizations illustrate these findings (Figure 1), showing a clear upward shift and greater dispersion of platelet count, PCT, and PLR in the IDA group, whereas MPV distributions largely overlapped between IDA patients and healthy controls.

Table 2. Comparison of platelet indices and platelet-To-Lymphocyte ratio between iron deficiency anemia and healthy controls

Parameter	IDA (n = 500)	Healthy Controls (n = 150)	*p* value	Effect size (Hedges' *g*)
Platelet count ($\times 10^3/\mu L$)	300.9 ± 85.0	251.1 ± 45.1	<0.001	0.64
Mean platelet volume (fL)	9.84 ± 1.29	9.70 ± 0.81	0.12	0.11
Plateletcrit (%)	0.30 ± 0.09	0.25 ± 0.05	<0.001	0.58
Platelet-to-lymphocyte ratio	157.1 ± 61.7	125.8 ± 43.5	<0.001	0.54

Notes: Data are presented as mean ± standard deviation. Between-group comparisons were performed using Welch's independent-samples t test. Effect sizes were calculated using Hedges' g, with values of approximately 0.2, 0.5, and 0.8 representing small, moderate, and large effects, respectively. IDA: iron deficiency anemia.

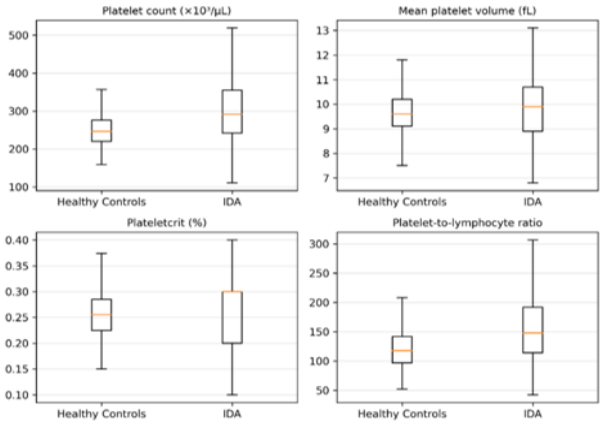

Figure 1. xplots of platelet count, Mean Platelet Volume (MPV), plateletcrit (PCT), and Platelet-To-Lymphocyte Ratio (PLR) in adults with iron deficiency anemia and healthy controls.

4.3 Discriminatory performance of platelet indices and PLR :

Receiver Operating Characteristic (ROC) curve analysis was performed to assess the ability of platelet indices and PLR to differentiate IDA from non-anemic states (Table 3, Figure 2).

Platelet count showed the highest discriminatory performance, with an AUC of 0.69 (95% bootstrap CI: 0.65–0.73). A Youden-derived cutoff of approximately 277 $\times 10^3/\mu L$ yielded a sensitivity of 59.6% and specificity of 76.7%. Plateletcrit (PCT) demonstrated comparable performance (AUC = 0.68, 95% CI: 0.63–0.72), with relatively high specificity (83.3%). PLR showed modest but significant discrimination between IDA and healthy controls (AUC = 0.67, 95% CI: 0.62–0.71).

Table 3. Receiver Operating Characteristic (ROC) analysis of platelet indices and platelet-to-lymphocyte ratio for discrimination of iron deficiency anemia.

Marker	AUC	95% Confidence Interval	Optimal cutoff†	Sensitivity (%)	Specificity (%)
Platelet count (×10^3/μL)	0.69	0.65–0.73	277	59.6	76.7
Plateletcrit (%)	0.68	0.63–0.72	0.30	70.6	83.3
Platelet-to-lymphocyte ratio	0.67	0.62–0.71	143.7	54.6	76.0
Mean platelet volume (fL)	0.53	0.49–0.58	10.7	25.6	89.3

Notes: AUC area under the receiver operating characteristic curve. Confidence intervals were estimated using bootstrap resampling. †Optimal cutoff values were determined using the Youden index. Sensitivity and specificity are reported at the optimal cutoff. IDA: iron deficiency anemia.

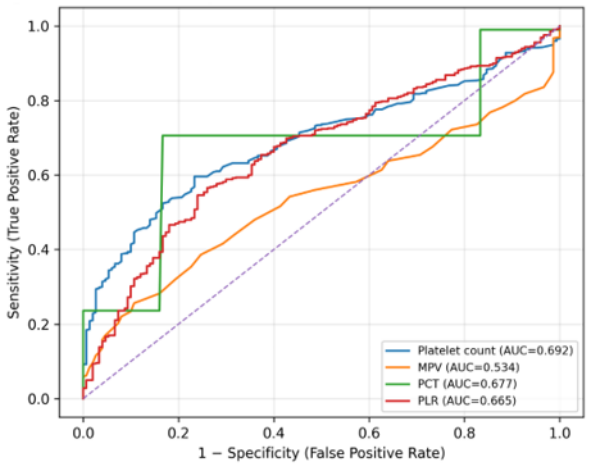

Figure 2. ROC curves for platelet count, mean platelet volume (MPV), plateletcrit (PCT), and platelet-to-lymphocyte ratio (PLR) differentiating iron deficiency anemia from non-anemic states

In contrast, MPV exhibited limited discriminatory value (AUC = 0.53), consistent with the absence of a significant between-group difference.

The combined ROC curves (Figure 2) illustrate that platelet count, PCT, and PLR provide moderate but consistent discrimination, whereas MPV contributes minimally to differentiating iron-deficient from non-anemic states.

4.4 Summary of key findings

Compared with healthy adults, individuals with IDA exhibited higher platelet count, increased plateletcrit, and elevated platelet-to-lymphocyte ratio, with moderate effect sizes. These findings indicate that iron deficiency is associated with recognizable and consistent alterations in platelet-related parameters beyond hemoglobin reduction alone. Recognizing these routinely available CBC-derived changes may enhance clinicians' interpretation of hematologic profiles and support more informed assessment of iron-deficient versus non-anemic states.

5. Discussion

The present comparative analysis demonstrates that IDA is associated with consistent and clinically recognizable alterations in platelet-related parameters, including increased platelet count, elevated plateletcrit (PCT), and higher platelet-to-lymphocyte ratio (PLR), when compared with healthy non-anemic adults. These findings reinforce the concept that iron deficiency affects multiple hematopoietic lineages and that its laboratory manifestations extend beyond hemoglobin reduction alone (Song et al., 2020; Li et al., 2022).

Reactive thrombocytosis is a well-documented feature of iron deficiency anemia and may reflect altered platelet production and maturation in iron-restricted states (Li et al., 2022; Faraj et al., 2021). Recent clinical observations further demonstrate that platelet counts often decrease following iron repletion in patients with IDA, reflecting resolution of reactive thrombocytosis after treatment. Talamo et al. (2025) reported significant reductions in platelet counts and thrombocytosis prevalence after iron replacement therapy, supporting the dynamic nature of platelet responses in IDA (Talamo et al., 2025).

In this study, platelet count showed a significant increase in patients with iron deficiency anemia, with a moderate effect size and the highest discriminatory performance among the evaluated indices. This observation is consistent with previous reports

indicating that iron deficiency may stimulate platelet production and may involve shared regulatory pathways between erythropoietin and thrombopoietin signaling (Chalise et al., 2019; Beguin, 1999). The concomitant elevation in plateletcrit (PCT) suggests an increase in total circulating platelet mass rather than isolated changes in platelet size.

In contrast, mean platelet volume (MPV) did not differ significantly between patients with iron deficiency anemia and healthy controls and demonstrated limited discriminatory value. Previous studies examining MPV in IDA have reported inconsistent findings, with decreased, increased, or unchanged values across different populations and study settings (Liu et al., 2024; Chalise et al., 2019). Further, emerging work has investigated novel composite indices such as the mean platelet volume/platelet count ratio (MPR), with Kandangwa et al. (2025) reporting significant sex-related differences in MPR among patients with iron deficiency anemia, suggesting that sex-specific hematological responses may influence platelet index interpretation (Kandangwa et al., 2025). Consistent with our finding of limited MPV discrimination, previous work has shown that MPV levels may remain unchanged despite improvements in other platelet indices following iron therapy, underscoring the variable behavior of MPV in iron deficiency anemia (Kurt & Demirkiran, 2023). Such variability may be attributable to differences in study populations, disease stage, analytical platforms, and the dynamic balance between platelet production and peripheral consumption, thereby limiting the clinical utility of MPV as a standalone marker in iron-deficient states.

PLR integrates platelet and lymphocyte counts into a single composite index and may reflect the combined effects of reactive thrombopoiesis and immune cell alterations. In the present study, PLR was significantly higher in adults with iron deficiency anemia than in healthy controls, with a moderate effect size and modest discriminatory capacity. These findings are consistent with previous reports demonstrating elevated PLR values in iron-deficient individuals and a reduction following iron replacement therapy (Hegde & Puranik, 2020; Uz et al., 2016).

Although PLR did not outperform platelet count alone in discriminating IDA from non-anemic states, its consistent elevation suggests that it captures a broader hematologic response to iron deficiency rather than serving as a purely inflammatory marker. From a clinical perspective, an elevated PLR in the context of anemia may provide additional interpretive context and support suspicion of iron deficiency when assessed alongside conventional hematologic and biochemical parameters.

ROC curve analysis demonstrated that platelet count, plateletcrit, and platelet-to-lymphocyte ratio provided moderate discrimination between iron-deficient and non-anemic states, whereas mean platelet volume contributed minimally. The low sensitivity observed at the optimal MPV cutoff further limits its clinical utility as a discriminatory marker for IDA. These findings suggest that platelet-related indices should not be considered diagnostic tests for IDA but may serve as adjunctive markers complementing established laboratory evaluation, in line with previous observations of iron-dependent changes in platelet parameters (Hasan et al., 2022; Prajapati, 2025).

The clinical value of these indices lies in their availability and cost-effectiveness. Platelet indices and PLR are automatically generated as part of routine complete blood counts and require no additional testing or financial burden. Awareness of the characteristic behavior of platelet-related indices in IDA may assist clinicians in interpreting complete blood count results more comprehensively, particularly in resource-limited settings or when iron studies are unavailable or delayed.

Hemoglobin concentration remains central to the diagnosis of anemia and assessment of its severity; however, it does not fully capture the systemic hematologic effects of iron deficiency. The present findings highlight that IDA is associated with a recognizable platelet phenotype characterized by increased platelet mass and elevated PLR. Recognizing these characteristic patterns may enhance clinicians' understanding of iron-deficient states, aid in distinguishing IDA from non-anemic conditions, and improve interpretation of routine hematologic profiles in everyday clinical practice.

The strengths of this study include its comparative design, relatively large sample size, and simultaneous evaluation of multiple platelet indices and PLR in adults. Nonetheless, several limitations should be acknowledged. The cross-sectional design precludes causal inference, and platelet parameters may be influenced by unmeasured clinical factors or analytical variability. Future prospective studies incorporating longitudinal follow-up and treatment response would help clarify the temporal relationship between iron repletion and normalization of platelet-related indices.

6. Conclusion

In summary, IDA is associated with higher platelet count, increased plateletcrit, and elevated platelet-to-lymphocyte ratio compared with healthy non-anemic adults. Although these parameters demonstrate only moderate discriminatory ability, their consistent alteration underscores the broader hematologic impact of iron deficiency. As routinely available and low-cost indices, platelet parameters and PLR may serve as useful adjuncts to conventional laboratory assessment, aiding clinicians in the interpretation of complete blood count results in patients with suspected or confirmed IDA.

Ethical considerations

The study protocol was reviewed and approved by the Research Ethics Committee of the Duhok Directorate General of Health (Approval No. 30102024-9-46). Prior to enrollment, all participants provided written informed consent, and all research procedures adhered to national and institutional ethical standards.

Declaration of conflict of interest

The authors declare that they have no conflict of interest

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