Original Article

Iraqi National Journal of Medicine. January 2026, Volume 8, Issue 1

Platelet Count Pitfalls Between Routine and Advanced Techniques

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ABSTRACT

Background: Precise quantification of platelet counts is a fundamental aspect of clinical hematology, pivotal in diagnosing and managing conditions such as thrombocytopenia and thrombocytosis. However, inconsistencies in platelet measurements across various automated hematology analyzers present significant challenges, potentially compromising the reliability of results. This variability is especially critical when platelet counts inform urgent clinical interventions, including the administration of platelet transfusions. **Aim**: The present study evaluated the accuracy of Sysmex XN-350 and Mindray in comparison to flow cytometry, the gold standard for platelet counting. **Methods**: 120 blood samples were categorized into thrombocytopenic, thrombocytosis, and normal groups. Platelet counts were measured using Sysmex XN-350, Mindray BC-720, and flow cytometry. Statistical analyses, including correlation coefficients, Bland-Altman plots, and repeated measures ANOVA, were employed to assess agreement and differences among the methods. **Results**: The study revealed significant discrepancies in platelet counts among the devices. Sysmex XN-350 consistently overestimated platelet counts compared to flow cytometry, particularly at higher counts, with a mean difference of 176.76 ± 358.51. Mindray BC-720 demonstrated greater agreement with flow cytometry, with a mean difference of 60.062 ± 119.67 and a stronger correlation (r = 0.972). Bland-Altman analysis showed that Sysmex exhibited substantial overestimation at higher platelet counts, while Mindray maintained consistency within clinically relevant ranges. **Conclusions**: Mindray BC-720 outperformed Sysmex XN-350 in terms of agreement with flow cytometry, especially in the thrombocytopenic and normal ranges. These findings highlight the importance of validating automated hematology analyzers against advanced techniques like flow cytometry to ensure precision in platelet enumeration.

Keywords: Platelet enumeration, automated hematology analyzers, flow cytometry validation.

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Disclaimer: The authors have no conflicts of interest.

DOI: https://doi.org/10.37319/iqnjm.8.1.13

Received: 6 MAY 2025 Accepted: 2 AUG 2025 Published online: 15 JAN 2026

INTRODUCTION

Platelets are the smallest blood cells, disc-shaped and anucleate, measuring 2–4 µm in diameter and 0.5 µm in thickness. Originating from bone marrow megakaryocytes, platelets are indispensable for maintaining hemostasis by initiating and supporting blood clot formation following vascular injury. Normal platelet count ranges from 150–400 × 10^3/µl, with a mean volume of 7.7–11.2 fL and a lifespan of about 10 days. Approximately 30% are sequestered in the spleen at rest.[1] Thrombocytopenia occurs in conditions such as

purpura, aplastic anemia, and leukemia, while elevated counts are seen in thrombocythemia, polycythemia vera, and chronic myelogenous leukemia.[2] The Italian pathologist Giulio Bizzozero first identified platelets as distinct corpuscles and recognized their role in coagulation and thrombosis in 1882.[3] Accurate platelet count measurement is vital in clinical hematology, as low counts can lead to bleeding complications. It is particularly recommended for monitoring treatments that may cause thrombocytopenia, such as chemotherapy and heparin.[4] Variations in platelet count are associated not only with hemostatic and thrombotic disorders but also with cancer and chronic inflammatory diseases. Consequently, platelet count has emerged as a potential biomarker and prognostic indicator in various clinical conditions, including colorectal cancer, vasculitis, and viral infections. This underscores the critical importance of accurate and consistent platelet measurement for effective disease monitoring and risk stratification.[5,6] Despite advancements in automated hematology analyzers, pre-analytical and analytical pitfalls still impact platelet count accuracy. Pre-analytical issues include sample collection, handling, and choice of anticoagulant. Inadequate sample storage or delays in processing can result in platelet activation or degradation, potentially leading to inaccurate measurements and compromising the integrity of test results. Advanced techniques also face standardization and interpretation challenges, requiring robust quality control measures to ensure consistency and accuracy.[7] Analytical pitfalls include EDTA-induced pseudo-thrombocytopenia, platelet clumping, macro and giant platelets, and platelet satellitism.[8] Users must be aware of the technology's limitations to ensure accurate results. Several automated methods are available for platelet count determination, primarily in controlled laboratory settings, each employing different technologies.[9] Common techniques include manual counting with a hemocytometer and automated electrical impedance, both valued for simplicity and cost-effectiveness. Manual counting depends heavily on technician skill and is prone to errors from poor sample preparation, inadequate mixing, and fatigue.[10,11] The impedance method, pioneered by Beckman Coulter, quantifies cells by measuring changes in electrical resistance as they traverse a small aperture. While widely used, this technique is susceptible to misclassification, as it may erroneously count small particles, cell fragments, or microcytic red blood cells as platelets—particularly in samples containing significant debris or abnormal cell populations. Optical methods—such as light diffraction and fluorescence used by analyzers like Sysmex and Mindray—offer improved accuracy by better distinguishing platelets from similar-sized particles.[12] Advanced optical light scattering provides more accurate counts and additional parameters like mean platelet volume (MPV) and platelet distribution width (PDW), though accuracy may be affected by sample turbidity, large platelets, or clumping.[13] Immunofluorescence techniques, such as flow cytometry using monoclonal antibodies against platelet surface glycoproteins, offer high specificity and detailed characterization but are costly, time-consuming, and require specialized expertise, limiting routine use in smaller laboratories.[14] While routine platelet counting techniques are accessible and cost-effective, they are susceptible to various pitfalls that can compromise accuracy. Advanced techniques like optical light scattering and flow cytometry offer enhanced precision and additional diagnostic information but come with higher costs and operational complexities. Addressing the strengths and limitations of each method is important to choose the appropriate technique based on clinical needs and available resources, ensuring accurate and reliable platelet count results. This study aimed to evaluate and compare the platelet counts determined by various automated hematology analyzers (focusing on the Sysmex XN-350 and Mindray BC-720) with those determined by flow cytometry.

MATERIALS AND METHODS

This experimental study was conducted from March to December 2024 in the medical laboratories of Al-Sayyab Hospital and Basra Children's Specialty Hospital, Basra, Iraq. A total of 120 EDTA-anticoagulated blood samples were collected from pediatric patients across inpatient and outpatient departments, encompassing hematology, oncology, and general pediatric wards. Samples were selected to represent a broad spectrum of platelet counts, including thrombocytopenia, normal counts, and thrombocytosis. Every fourth sample was randomly chosen for flow cytometric analysis, resulting in 30 samples categorized as follows: 13 thrombocytopenic, 6 with normal platelet counts, and 11 thrombocytotic. All ethylenediaminetetra acetic acid-anticoagulated blood samples submitted for hematological evaluation during the study period were included in the analysis. Samples

were excluded if they exhibited platelet clumping (as indicated by analyzer flags or peripheral smear), had insufficient volume, or were otherwise unsuitable for analysis. Post-routine analysis, residual EDTA samples were gently mixed on a roller mixer for 5 minutes before being analyzed on both the Sysmex XN-350 and Mindray BC-720 hematology analyzers. Selected samples for flow cytometry were promptly transferred to the flow cytometry unit. All analyses were completed within 6 hours of sample collection to ensure result integrity. Key instruments included the Sysmex XN-350 (Sysmex Corporation, Japan), Mindray BC-720 (Mindray Bio-Medical Electronics Co., China), and BD FACS Lyric flow cytometer (BD Biosciences, USA). To corroborate automated results, peripheral blood smear examinations were performed, assessing for platelet clumps, microaggregates, and size variability. Sysmex XN-350: This analyzer employs impedance technology (PLT-I) for platelet counting, where diluted blood passes through an aperture, and changes in electrical resistance are measured as cells traverse the aperture. Each change corresponds to a cell, allowing for counting and sizing of platelets. While effective, this method can be influenced by the presence of small red blood cells or other particles, potentially leading to inaccuracies in certain samples. The XN-350 operates in open mode with a 25 µL aspiration volume and includes integrated quality control features. Mindray BC-720*:* This analyzer utilizes both optical and impedance techniques, incorporating the PLT-H parameter, which offers enhanced accuracy by reducing interference from platelet clumps and microcytic red blood cells. The BC-720 also features automated rerun and reflex mechanisms to ensure result reliability. Flow Cytometry*:* Platelets were identified using forward and side scatter properties and specific fluorescent markers (CD42b and CD61). The International Reference Method (IRM) was employed, calculating platelet counts based on the ratio of platelet to red blood cell events, with red blood cell counts obtained from the Mindray BC-720. Informed consent was obtained from all participants prior to participation. Ethical approval was obtained from the Iraqi Board for Medical Specializations and the Basrah Health Directorate. All procedures adhered to aseptic techniques to ensure patient safety and data integrity.

Data analysis was conducted using SPSS version 25.0. An independent t-test was applied for dichotomous numerical variables, one-way ANOVA for multichotomous numerical variables, and the Chi-square test for qualitative data. Spearman correlation assessed relationships between variables. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 3.1 shows that Sysmex XN-350 and Mindray BC-720 reported higher mean platelet counts (342 ± 446.79 and 352.04 ± 321.1) than flow cytometry (280.43 ± 242.63). The mean difference was greater for Sysmex (176.76 ± 358.51) than for Mindray (60.06 ± 119.67). While overall platelet counts differed significantly between methods (p = 0.03), differences from flow cytometry were not statistically significant (p = 0.092), indicating variability among techniques.

Table 1: Platelet counts by different techniques in comparison to flow cytometry

Method	Platelet count (n=30)	The mean difference of platelet counts from flow cytometry (n=30)
Sysmex XN-350 (Mean ± SD) Median	342 ± 446.79 314	176.76 ± 358.51 28.4
Mindray BC-720 (Mean ± SD) Median	352.04 ± 321.1 271	60.062 ± 119.67 12.4
Flow Cytometry (Mean ± SD) Median	280.43 ± 242.63 266	-
p-value	0.03*	0.092**

*Repeated measures ANOVA, **Paired-Samples T Test

The correlation analysis (Fig. 1) demonstrates a positive correlation between the platelet counts measured by Sysmex XN-350 and Mindray BC-720 devices with flow cytometry. Mindray's correlation with flow cytometry (r = 0.945) is the strongest, while Sysmex XN-350's correlation with flow cytometry was (r = 0.350). The results indicate superior agreement of Mindray BC-720 with flow cytometry compared to Sysmex.

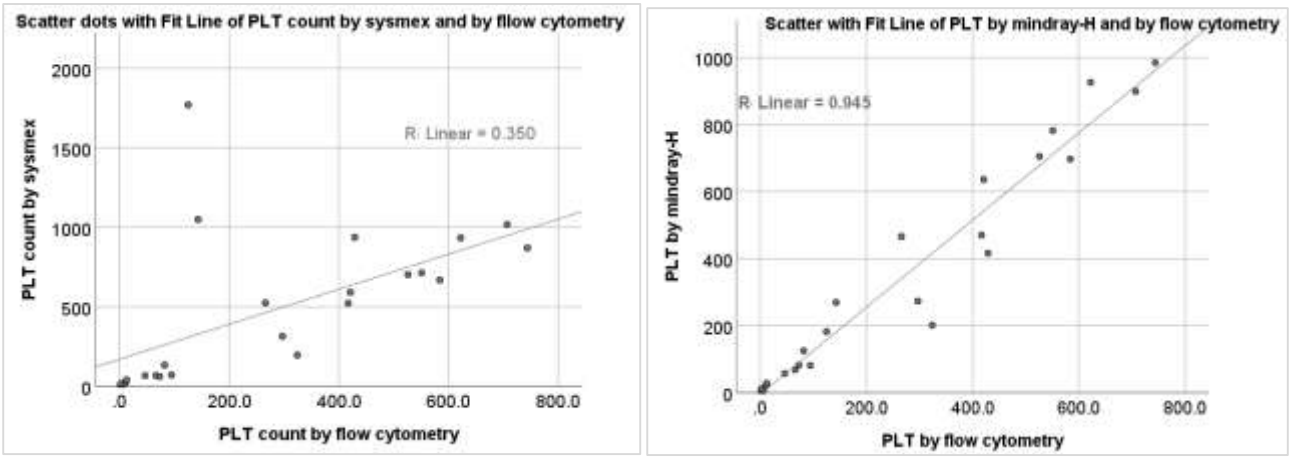

Figure 1: The (left) scatter plot (Sysmex vs. flow cytometry) shows a weak correlation (R = 0.350) with significant data dispersion, indicating poor agreement and unreliable platelet (PLT) counts compared to the reference method. In contrast, the (right) plot (Mindray-H vs. flow cytometry) demonstrates a strong correlation (R = 0.945) with tightly clustered data points, reflecting good agreement and accuracy.

Table 2 reveals significant differences in platelet count measurements among Sysmex, Mindray-I, and Mindray-H analyzers, particularly in the high platelet count group, where Sysmex showed the highest mean (878.29 ± 480.09) compared to Mindray-H (769.96 ± 420.42) and Mindray-I (745.15 ± 354.57), with a significant p-value (<0.001), suggesting Sysmex may overestimate counts in thrombocytosis. No significant differences were found in the normal (p = 0.33) and low (p = 0.17) platelet count groups. However, the overall mean platelet counts differed significantly (p = 0.021), with Sysmex having the highest median (132) and Mindray-H the lowest (118), indicating variability across analyzers, especially at extreme platelet levels.

The Bland-Altman analysis highlights the agreement between each device and flow cytometry. The Sysmex device shows good agreement at lower platelet counts (up to 420), but overestimates more significantly at higher counts, with deviations reaching around 1800. In contrast, the Mindray device stays closer to flow cytometry results, especially in the 80 to 750 platelet count range. While it also tends to overestimate, the extent of deviation is less pronounced than with Sysmex. The level of agreement plot compares the Sysmex and Mindray devices across a range of values. The X-axis represents the mean of measurements from both devices, and the Y-axis shows the differences between them. The central horizontal line indicates the mean difference (bias), which is close to zero, suggesting no consistent overestimation or underestimation between the two devices. The upper and lower horizontal lines represent the limits of agreement (LOA), defining the range within which most differences lie (±1.96× standard deviation of the differences). While most data points fall within these limits, a few outliers appear at higher measurement ranges, indicating occasional discrepancies. Overall, the plot shows reasonable agreement, with variability increasing as measured values rise.

Table 2: Comparison of platelet counts and differences across Sysmex, Mindray-I, and Mindray-H analyzers according to the platelet count level

Device	Platelet count status (Mean±SD) (n=120)				
	High	Normal	Low	Overall mean	Overall median
Sysmex (n=120)	878.29 ± 480.09	259.06 ± 52.13	51.02 ± 40.63	344.2 ± 459.7	132
Mindray-I (n=120)	745.15 ± 354.57	257.2 ± 52.65	51.53 ± 40.92	278.5 ± 353.9	133
Mindray-H (n=120)	769.96 ± 420.42	250.63 ± 61.27	59.38 ± 44.79	296.01 ± 380.9	118
p-value	<0.001	0.33	0.17	0.021	0.001

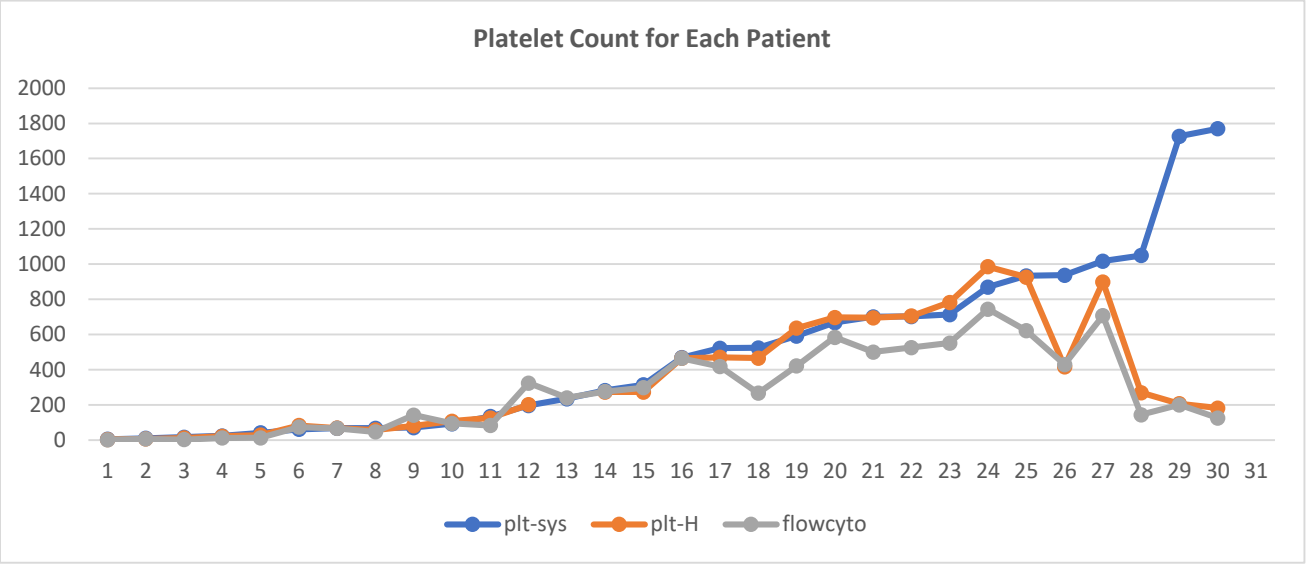

Figure 2: Bland-Altman Plot for the three devices' readings of platelets.

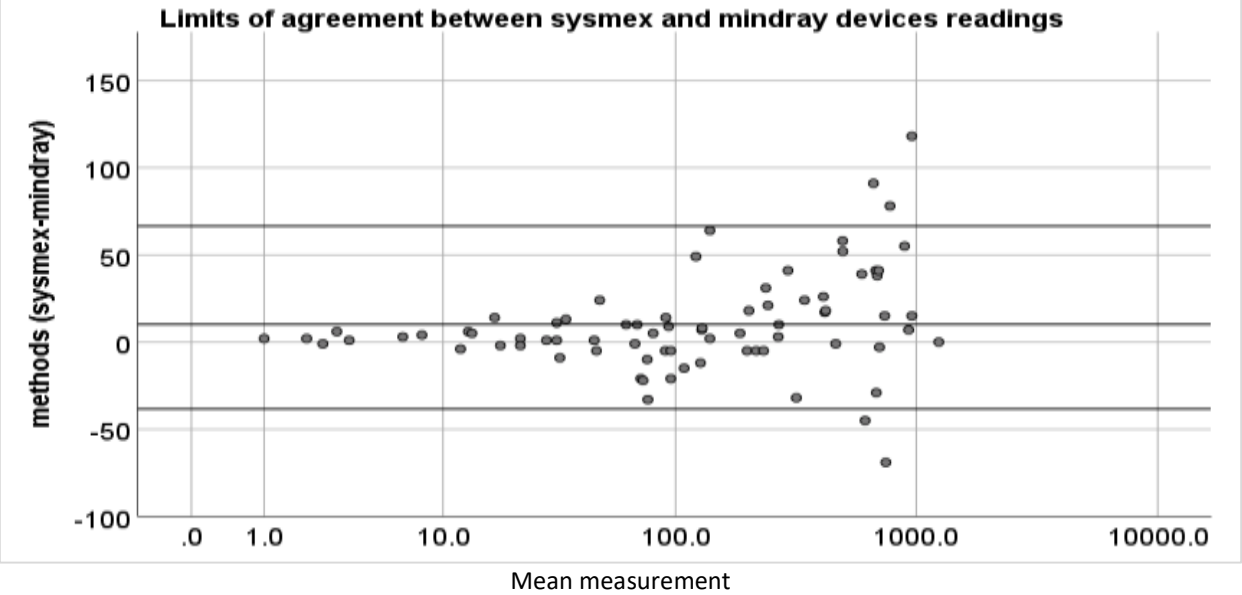

Figure 3: The level of agreement between Sysmex and Mindray devices.

DISCUSSION

Advancements in medical laboratory technology have led to the widespread use of modern diagnostic instruments, significantly improving testing efficiency and accuracy. In Iraq, commonly used hematology analyzers include the Chinese Mindray and Japanese Sysmex systems.[15] which differ in methodology, internal design, reagents, and calibrators. These differences can cause result discrepancies, potentially impacting clinical decisions. Therefore, comparing instruments is essential to ensure consistency when measuring the same parameters.[16] This study's findings demonstrated significant variations among the devices, with Sysmex showing a higher mean platelet count and mean difference compared to Mindray-H, while Mindray-H exhibited greater agreement with flow cytometry. Notably, the results of Mindray-I are very close to Sysmex. The overestimation of platelet counts by Sysmex and Mindray-H compared to flow cytometry aligns with prior studies identifying systematic biases in automated analyzers. Kaklar et al. reported that automated analyzers often overestimate platelet counts due to interference from microcytic red blood cells and platelet clumping.[17] This is reflected in the current study, where Sysmex showed significant bias at higher platelet counts, especially in patients with microcytosis or hemoglobinopathies (83.4% of microcytosis cases were in the thrombocytosis group, overestimated compared to flow cytometry). This is particularly relevant in populations with a high prevalence of iron deficiency anemia or thalassemia. Relying solely on automated analyzers in such cases may yield inaccurate results. The impedance method for platelet counting is unreliable at low MCV values, often causing falsely elevated counts, which can impact clinical decisions such as platelet transfusion requirements.[18] Pan et al. reported overestimation of platelet counts in microcytic samples analyzed using the XE 2100™ automated analyzer (Sysmex Corp).[19] These observations underscore the importance of pathologists exercising caution when interpreting high platelet counts reported by automated analyzers, particularly in cases of microcytosis. Several studies, including those by Gulati et al.[20] and Balakrishnan et al.[21] have documented automated analyzers falsely reporting low platelet counts, later corrected by manual estimation. However, false overestimation of platelet counts is less commonly reported. This discrepancy highlights the limitations of automated technologies and emphasizes the importance of peripheral blood smear examinations to verify complete blood count results. In the present study, both Mindray-H and Sysmex showed a positive correlation with flow cytometry and with each other. Similarly, Wang et al., in their study about the analytical comparison between two hematological analyzer systems: Mindray BC-5180 vs. Sysmex XN-1000, found a linear correlation between the results of the two instruments.[22] The closer agreement of Mindray-H with flow cytometry, especially in normal and low platelet ranges, suggests it uses algorithms or calibration methods that reduce discrepancies in platelet counts. This aligns with previous studies reporting that both BC-6800P and XN analyzers met acceptable precision standards for thrombocytopenic samples.[23,24] The significant differences in platelet counts across devices highlight the need for standardization and cross-validation in hematology labs. While Sysmex may be less accurate at higher counts, it remains useful for rapid, high-throughput settings. In contrast, Mindray-H's closer alignment with flow cytometry suggests it may be more suitable where precision is critical, such as in managing thrombocytopenia or guiding platelet transfusions. This study is limited by a relatively small sample size (n = 120), which may not reflect the full variability in platelet counts across broader populations. Additionally, using only the Sysmex XN-350 and Mindray BC-720 restricts the generalizability of the results to other models or manufacturers. In conclusion, the study reveals significant variations in platelet counts between Sysmex and Mindray analyzers, with Mindray-H showing better agreement with flow cytometry than Sysmex. These results emphasize the importance of validating automated hematology devices to ensure accurate and reliable platelet enumeration.

CONCLUSIONS

Mindray BC-720 outperformed Sysmex XN-350 in terms of agreement with flow cytometry, especially in the thrombocytopenic and normal ranges. These findings highlight the importance of validating automated hematology analyzers against advanced techniques like flow cytometry to ensure precision in platelet enumeration.

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