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Accuracy of Automated Sysmex XN-1000 Haematology Analyzer to Diagnose Malaria Keeping Microscopy as Gold Standard

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ABSTRACT

Objective: To assess the diagnostic accuracy of the Sysmex XN-1000 haematology analyser for malaria detection, using peripheral blood smear microscopy as the reference standard. **Methods:** A cross-sectional diagnostic accuracy study that included 185 blood samples obtained from patients undergoing routine complete blood count testing. Samples were taken by using non-probability consecutive sampling at the Haematology Department of PGMI/Hayatabad Medical Complex, Peshawar for the duration of three months from March 21, 2025 to June 20, 2025. Each sample was evaluated by using the Sysmex XN-1000 analyser with particular assessment of malaria-associated scattergram abnormalities. Paired peripheral blood smears were prepared and independently examined by a consultant haematologist who was blinded to analyser results. Direct comparisons with microscopic findings were used to compute diagnostic indices. **Results:** 68 out of 185 samples confirmed malarial parasites in microscopy, suggesting a prevalence of 36.8%. The Sysmex XN-1000 analyser showed a 92.65% sensitivity and 89.74% specificity. The 95.45% negative predictive value, indicates a strong ability to exclude malaria when analyser flags were absent. The overall diagnostic accuracy was 90.81%. **Conclusion:** As a screening tool for malaria, the Sysmex XN-1000 haematology analyzer demonstrates a strong diagnostic accuracy and high sensitivity. In regions where malaria is endemic, its regular application may help identify suspected cases promptly. It further expedites the confirmation tests and starts the management on time, even though it does not substitute for microscopy.

INTRODUCTION

Malaria is a serious global public health concern. Tropical and resource-limited regions are most severely affected. The World Health Organization (WHO) reports that there are approximately 228 million cases and 405,000 fatalities every year (1). Plasmodium species are the cause of this protozoan infection, and it continues to be a major contributor to febrile morbidity and mortality(2). While control techniques have improved over recent years, increasing resistance and inadequacies in healthcare delivery remain major barriers to malaria elimination(2).

Pakistan is among the seven countries in the WHO Eastern Mediterranean Region that account for nearly 98% of reported malaria cases, which emphasizes its status as a high-burden endemic country (3). Clinically, dengue, influenza, and typhoid, and other febrile illnesses share the symptoms with malaria. For a precise diagnosis and prompt treatment, laboratory confirmation is essential. (4). Giemsa-stained blood smears evaluated under the microscope continue to be the gold standard for malaria diagnosis, since they provide direct parasite visualization, species identification, and parasite load estimation (5). However, its diagnostic accuracy is operator dependent and may be compromised in cases of low parasitaemia or during periods of heavy laboratory workload(6).

Rapid diagnostic tests (RDTs) provide a simpler alternative, the only drawback being their low sensitivity when there is low parasite density, as they do not quantify parasitemia(7). These limitations have encouraged the use of automated haematology analyzers as supporting screening tools for malaria. Sysmex XN-series analyzers use fluorescent flow cytometry and advanced software to generate scattergrams that detect structural and nucleic acid changes in malaria-infected erythrocytes. Key indicative patterns include a rightward shift in the RBC ghost area, double neutrophil or eosinophil clusters, greying of the WBC scattergram, and pseudo-eosinophilia(8). Previous work has shown that these analysers can detect such abnormalities with high diagnostic utility(9, 10).

Given the public health importance of timely malaria diagnosis and the widespread use of Sysmex XN-1000 in routine complete blood count analysis, this study aimed to evaluate the diagnostic accuracy of Sysmex XN-1000

scattergram abnormalities for malaria detection, using microscopy as the reference standard.

MATERIAL AND METHODS

This cross-sectional diagnostic accuracy study was conducted at the Haematology Department of PGMI/Hayatabad Medical Complex, Peshawar. Ethical approval was obtained from the institutional review, and the total duration of the study was three months from March 21, 2025 to June 20, 2025. The total sample size was 185, and a non-probability consecutive sampling technique was used. The sample size was calculated using a standard formula with a 95% confidence level, 6% precision and expected sensitivity and specificity derived from previous studies(10). The inclusion criteria for this study were adult patients aged 18 to 60 years whose blood samples were sent for a complete blood count. The exclusion criteria included a history of malignancy, chemotherapy, radiotherapy and aplastic anaemia. Two 5 mL blood samples were collected from each patient after receiving informed consent. For each patient, the initial blood sample was evaluated using the Sysmex XN-1000 analyser. During this process, particular attention was given to detecting the presence or absence of specific abnormal scattergram patterns that are recognized as markers for malaria infection. These included a rightward shift in the RBC ghost region and the appearance of double neutrophil clusters. The second 5 ml blood sample was prepared into a peripheral smear which was examined independently by a consultant haematologist who was blinded to analyser findings. Microscopy was taken as the gold standard.

All data was collected on a structured proforma. Statistical analysis was performed using SPSS Version 26. A 2x2 contingency table was constructed to calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy of the automated analyser.

RESULTS

In this study, a total of 185 blood samples were analyzed to evaluate the diagnostic performance of the Sysmex XN-1000 in detecting malaria. The mean age was 35.4 ± 11.2 years, and 51.2% of the participants were male (Table 1).

Table 1

Baseline Characteristics of Study Participants

Characteristic		Value
Age (Years)	Mean ± Standard Deviation	35.4 ± 11.2
	Range	18 - 60
Gender, n (%)	Male	95 (51.2%)
	Female	90 (48.8%)

A total of 142 samples were positive for malaria on microscopy (prevalence 36.9%). Against this, the automated analyser identified 75 samples as malaria suspects from their scattergram abnormalities. Compared with microscopy, the Sysmex XN-1000 correctly identified 63 true positives and 105 true negatives, as well as 12 false positives and 5 false negatives (Table 2).

Table 2

2x2 Table Comparing Sysmex XN-1000 Findings with Microscopy

	Microscopy Positive	Microscopy Negative	Total
Sysmex Positive	63 (True Positive)	12 (False Positive)	75
Sysmex Negative	5 (False Negative)	105 (True Negative)	110
Total	68	117	185

The analyser had demonstrated a sensitivity of 92.65% and a specificity of 89.74%. The positive predictive value was 84%, and the negative predictive value was 95.45% (Table 3). The overall diagnostic accuracy was 90.81%. Among the true positive samples, the most common analyser trigger was a rightward shift in the RBC ghost region.

Table 3

Diagnostic Accuracy of Sysmex XN-1000 for Malaria Detection

Diagnostic Metric	Formula	Value (%)
Sensitivity	(TP / [TP+FN]) x 100	(63 / 68) x 100 = 92.65%
Specificity	(TN / [TN+FP]) x 100	(105 / 117)x100 = 89.74%
Positive Predictive Value (PPV)	(TP / [TP+FP]) x 100	(63 / 75) x 100 = 84%
Negative Predictive Value (NPV)	(TN / [TN+FN]) x 100	(105 / 110)x100 = 95.45%
Accuracy	([TP+TN]/Total)x100	(168 / 185)x100 = 90.81%

DISCUSSION

This cross sectional diagnostic accuracy study shows that the Sysmex XN-1000 haematology analyser functions as a reliable screening tool for malaria, with a sensitivity and specificity of 92.65% and 89.74% respectively. These results are therapeutically significant in malaria endemic regions, such as Pakistan, where rapid diagnosis and treatment depend on early laboratory support (1, 3). Malaria presents with non-specific clinical features that overlap with other febrile illnesses, thus making laboratory testing a necessity(5, 11). Though peripheral blood smear microscopy remains the diagnostic gold standard, automated analyzer may assist as useful adjunct within daily laboratory workup.

This study's diagnostic accuracy is in accordance with recent regional and international literature. The sensitivity of 92.65% is closely comparable to the 93.16% reported by Qamar et al. (2023) (12). Such consistency across different settings supports the reproducibility of scattergram-based screening using Sysmex analyzers.

Furthermore , a latest systematic review and meta-analysis by Mulatie et al. (2024) shows that Sysmex analyzers established a high pooled sensitivity and specificity to detect malaria(13). This evidence further supports the current study's outcomes and highlights the increasing use of automated haematology analyzers as supplementary diagnostic tool rather than standalone examination.

The study's high sensitivity is particularly significant, as it reduces the possibility to miss true malaria cases during the initial automated screening phase, thus potentially reducing delays in diagnosis and treatment. The high negative predictive value (95.45%), which demonstrates

that samples not flagged by the analyzer are not likely to be malaria positive, is equally important.

The high Negative Predictive Value (NPV) has important clinical implications. In practical terms, a non-flagged sample on the Sysmex XN-1000 strongly suggests the absence of malaria, allows clinicians to consider alternative causes of acute undifferentiated fever, such as dengue fever, bacterial infections, or viral illnesses(14)(15).This "rule-out" feature could help with diagnostic stewardship and better use of lab resources.

Malaria induced hematological changes may account for the diagnostic performance of the Sysmex XN-1000 analyser. A rightward shift in the RBC ghost region is the most often observed abnormality, which indicates structural and nucleic acid alterations within parasitized erythrocytes detected by fluorescent flow cytometry(16). Additional changes, including haemozoin-related effects on leukocytes, may produce greying of scattergrams and abnormal cell clustering(17). Laboratory personnel must have adequate training and experience in order to accurately analyze these patterns.

The Sysmex XN-1000 has significant limitations despite its advantages. The existence of false-positive flags implies that scattergram abnormalities might be regarded as screening alerts instead of confirmatory findings. Analogues analyzer patterns may exhibit by conditions which includes severe bacterial infections and haemolytic anaemias, leading to diagnostic perplexity(14, 15). Therefore, confirmatory microscopic analysis is needed for all analyser-flagged samples. Likewise, the possibility of missed cases is highlighted by false-negative results, particularly in samples with extremely low parasitemia that fall below analyser detection thresholds(14).For this reason, clinical judgment should always take priority, and microscopy should always be performed when clinical suspicion of malaria persists in spite of negative automated findings.

CONCLUSION

This study demonstrates that the Sysmex XN-1000 haematology analyser performs reliably as a frontline screening tool for malaria in routine laboratory practice. While it cannot substitute microscopic examination, its ability to promptly flag suspicious samples allows for more efficient triage and prioritization for confirmatory microscopy. Incorporating this analyzer into the routine evaluation of patients presenting with febrile illness may reduce the likelihood of overlooked infections and support earlier clinical intervention. Future efforts should focus on optimizing analyzer software algorithms to minimize false-positive alerts and further improve diagnostic precision. In addition, targeted training of laboratory personnel in scattergram interpretation is essential to maximize the clinical utility of this technology. With these refinements, automated heamtology analyzers can play an increasingly valuable role in strengthening malaria diagnostic pathways.

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