RESEARCH BRIEF

Evaluation of three LDH-based malaria rapid diagnostic tests in Senegal

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Background

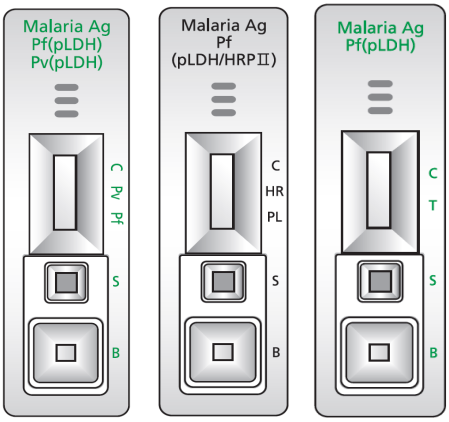
Accurate and timely malaria diagnosis is essential for effectively treating patients and advancing control and elimination efforts. Lateral flow immunochromatographic rapid diagnostic tests (RDTs) for malaria are widely used in endemic areas because they are simple, are low cost, require minimal infrastructure, and provide rapid results. The vast majority of RDTs targeting *Plasmodium falciparum* (Pf)—the malaria species that contributes to the greatest burden in Africa—detect the histidine-rich protein 2 (HRP2) antigen. While HRP2-based Pf RDTs have been historically preferred over RDTs targeting lactate dehydrogenase (LDH) due to higher clinical sensitivity and heat stability, they do have limitations, including the persistence of the HRP2 antigen in the peripheral bloodstream for multiple weeks following parasite clearance, and—most importantly—increasing reports of parasites with deleted *hrp2/hrp3* genes. To address these limitations, improvements in PfLDH-based RDTs are needed to minimize trade-offs in sensitivity for countries considering a switch to these tests.

Rapigen (Republic of Korea) has developed three novel malaria RDTs (Figure 1) with improved limits of detection (LODs) for PfLDH:

- The BIOCREDIT Malaria Ag Pf (pLDH/HRPII) RDT, with one test line for HRP2 and a separate line for PfLDH.
- The BIOCREDIT Malaria Ag Pf/Pv (pLDH/pLDH) RDT, with one test line for PfLDH and a separate line for *Plasmodium vivax*–specific LDH.
- The BIOCREDIT Malaria Ag Pf (pLDH) RDT, with one test line for PfLDH.

This study aimed to evaluate the clinical performance of these three RDTs among a febrile population in Kédougou, Senegal, compared with a reference polymerase chain reaction (PCR) assay and antigen concentration quantification. The study also evaluated the performance of microscopy and an existing HRP2-based RDT, the SD Bioline™ Malaria Ag Pf (#05FK50), in the same population to support informed decisions about recommending new, highly sensitive point-of-care malaria diagnostic tools.

Figure 1. Rapigen BIOCREDIT RDTs.



Abbreviations: Ag, antigen; HRPII, histidine-rich protein 2; Pf, *Plasmodium falciparum*; pLDH, *Plasmodium* lactate dehydrogenase; Pv, *Plasmodium vivax*; RDT, rapid diagnostic test.

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Methods

Figure 2. Map of the Kédougou region of Senegal.

Source: Institut Pasteur de Dakar/Babacar Souleymane Sambe.

The Institut Pasteur de Dakar and PATH partnered to conduct a cross-sectional diagnostic accuracy study to evaluate the clinical performance of the three BIOCREDIT RDTs in Kédougou, Senegal (Figure 2). The study was conducted between November 2021 and February 2022. Febrile patients aged 6 months and older were recruited from five health facilities in Kédougou. Capillary blood was tested using the three investigational (BIOCREDIT) and standard of care (SD Bioline) RDTs. Venous blood was collected to repeat the investigational BIOCREDIT RDTs and prepare microscopy slides. Venous specimens were then frozen and tested with a reference PCR and quantitative antigen concentration assays at the PATH laboratory (Seattle, Washington). A usability study was also conducted with end users of malaria RDTs in Senegal, focusing on the two Pf-only BIOCREDIT tests.

Results

Two hundred and twenty participants were included in the analysis. Of these, 154 (70 percent) were Pf-positive by PCR. No *Plasmodium vivax*–positive specimens were observed on any of the assays. Only one suspected *hrp2/hrp3* deletion case was identified from a participant who was Pf-positive by PCR, with HRP2-negative and PfLDH-positive antigen concentration results.

Table 1 summarizes the diagnostic performance of investigational and comparator tests compared to the PCR reference assay. Microscopy had the lowest overall performance with a sensitivity of 53 percent. The BIOCREDIT Malaria Ag Pf (pLDH/HRPII) test had the highest sensitivity of all evaluated RDTs; however, the improved sensitivity of the test was driven by the HRP2 line. The specificity of this test was lowest, at 89 percent. The two BIOCREDIT PfLDH-only tests, as well as the PfLDH line alone on the BIOCREDIT Malaria Ag Pf (pLDH/HRPII) test, had the lowest sensitivity, which was notably lower than that of the comparator (SD Bioline) HRP2-based RDT. Additionally, all RDTs performed better against quantitative antigen concentration results than against PCR results (data not shown).

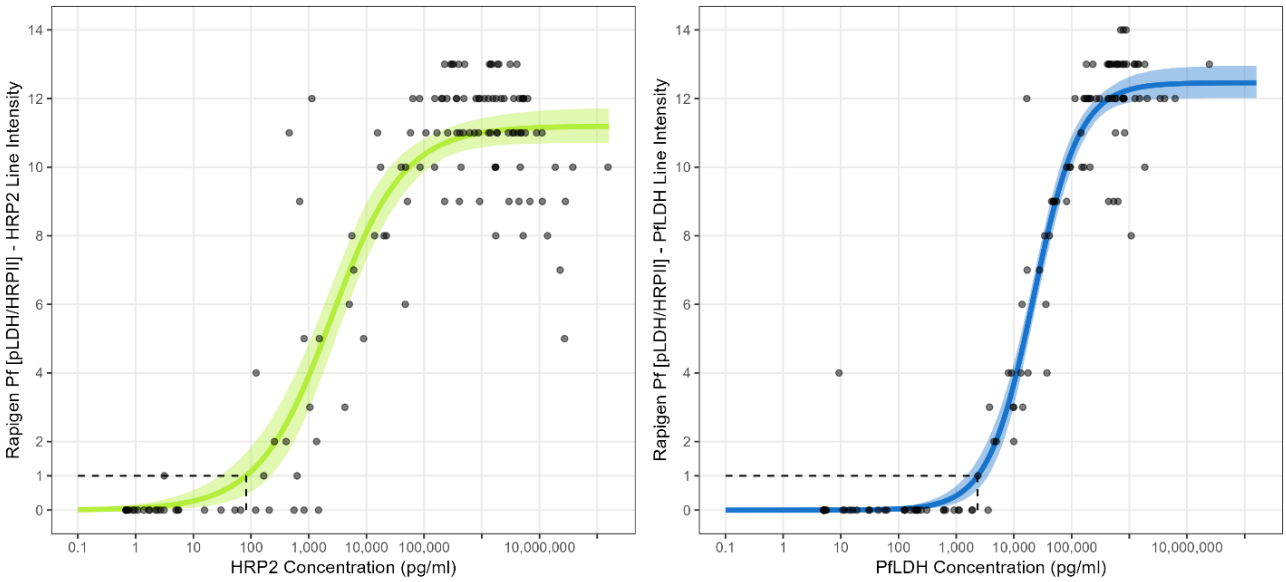
For the BIOCREDIT Malaria Ag Pf (pLDH/HRPII) test, further analysis found that RDT line intensity correlated with the quantitative antigen concentrations, with an antigen-dependent increase in visible intensity between approximately 0.1 ng/mL and 100 ng/mL (100–100,000 pg/mL) for HRP2 and 2 ng/mL and 100 ng/mL (2,000–100,000 pg/mL) for PfLDH (Figure 3). Additionally, the laboratory-derived LOD of the BIOCREDIT Malaria Ag Pf (pLDH/HRPII) test was combined with the distribution of antigen concentrations and reference PCR results from the study population to estimate the predicted performance of the RDT, which was then compared to the observed performance from this study (Table 2). Predicted and observed performance were found to be comparable.

Table 1. Diagnostic performance of investigational and comparator tests against reference PCR for detection of Pf.

Test	Target	Specimen type	N	Sensitivity (95% CI)	Specificity (95% CI)
SD Bioline Ag Pf (#05FK50)	PfHRP2	Capillary	220	0.714 (0.636–0.784)	0.939 (0.852–0.983)
BIOCREDIT Pf (pLDH/HRPII)	Pf (HRP2 and/or PfLDH positive)	Capillary	218	0.783 (0.709–0.846)	0.894 (0.794–0.956)
	PfHRP2 Only	Capillary	218	0.776 (0.702–0.840)	0.924 (0.832–0.975)
	PfLDH Only	Capillary	218	0.618 (0.536–0.696)	0.955 (0.873–0.991)
BIOCREDIT Pf/Pv (pLDH/pLDH)	PfLDH	Capillary	218	0.645 (0.563–0.721)	0.955 (0.873–0.991)
BIOCREDIT Pf (pLDH)	PfLDH	Capillary	217	0.642 (0.560–0.719)	0.955 (0.873–0.991)
Microscopy	Parasites	Venous	183	0.534 (0.445–0.622)	0.981 (0.897–1.000)

Abbreviations: Ag, antigen; CI, confidence interval; HRPII/2, histidine-rich protein 2; N, number; PCR, polymerase chain reaction; Pf, *Plasmodium falciparum*; PfHRP2, *Plasmodium falciparum*–specific histidine-rich protein 2; PfLDH, *Plasmodium falciparum*–specific lactate dehydrogenase; pLDH, *Plasmodium* lactate dehydrogenase; Pv, *Plasmodium vivax*.

Figure 3. Correlation between antigen concentration and BIOCREDIT Pf (pLDH/HRPII) RDT line intensity.



Abbreviations: HRPII/2, histidine-rich protein 2; mL, milliliter; Pf, *Plasmodium falciparum*; PfLDH, *Plasmodium falciparum*–specific lactate dehydrogenase; pg, picogram; pLDH, *Plasmodium* lactate dehydrogenase; RDT, rapid diagnostic test.

In total, 26 health care workers evaluated the usability of the two Pf-only RDTs. Health care workers were able to successfully conduct the tests, comprehend key elements of the product labels, and correctly interpret test results, with minimal errors. Participants reported slightly higher ease of use for the single-line Pf test, as compared to the test with two separate Pf test lines.

Table 2. Performance of the Rapigen BIOCREDIT Pf (pLDH/HRPII) RDT.

Test line	Quantitative antigen assay reference		PCR reference			
	Sensitivity (95% CI)		Sensitivity (95% CI)		Specificity (95% CI)	
	Predicted	Observed	Predicted	Observed	Predicted	Observed
HRP2 line	0.844 (0.769–0.902)	0.876 (0.806–0.927)	0.775 (0.697–0.842)	0.812 (0.741–0.870)	0.984 (0.912–1.000)	0.958 (0.881–0.991)
PfLDH line	0.920 (0.848–0.965)	0.911 (0.838–0.958)	0.667 (0.581–0.745)	0.662 (0.582–0.736)	1.000 (0.941–1.000)	0.990 (0.945–1.000)
HRP2 and/or PfLDH lines	0.838 (0.764–0.897)	0.893 (0.827–0.940)	0.783 (0.704–0.848)	0.818 (0.748–0.876)	0.984 (0.912–1.000)	0.971 (0.899–0.996)

Abbreviations: CI, confidence interval; HRPII/2, histidine-rich protein 2; PCR, polymerase chain reaction; Pf, *Plasmodium falciparum*; PfLDH, *Plasmodium falciparum*–specific lactate dehydrogenase; pLDH, *Plasmodium* lactate dehydrogenase; RDT, rapid diagnostic test.

Conclusions

In summary, this study confirms that despite the higher analytical sensitivity of the BIOCREDIT tests' LDH line compared to other currently World Health Organization–prequalified RDTs, the HRP2 line primarily drives the sensitivity of RDTs in this high-burden setting with negligible suspected *hrp2/hrp3* deletions. An RDT that performs equally to support clinical diagnosis of Pf malaria, regardless of the underlying prevalence of *hrp2/hrp3* deletions, should detect both HRP2 and LDH, possibly on the same line to simplify interpretation. Additionally, we also found that RDT analytical LODs can be used to predict performance in populations with known antigen concentrations, which is a valuable tool for assessing the impact of new tests in diverse contexts of use.

For more information

Please see the full publication from this study:

> Sambe, B.S., Zobrist, S., Sheahan, W. *et al.* Performance and usability evaluation of three LDH-based malaria rapid diagnostic tests in Kédougou, Senegal. *Parasites Vectors* **18**, 280 (2025). https://doi.org/10.1186/s13071-025-06914-9

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