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Preplanned Studies

Evaluation of Malaria Standard Microscopy and Rapid Diagnostic Tests for Screening — Southern Tanzania, 2018–2019

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Summary

What is already known about this topic?

Microscopy is the gold standard for parasitological confirmation, but the accuracy of microscopic diagnosis is influenced by the skill of the technicians. An alternative is the immunologic-based malaria rapid diagnostic tests (mRDTs).

What is added by this report?

Our study evaluated standard microscopy in health system (SMHS) and mRDTs for focused screening and treatment of malaria (FSAT) in Southern Tanzania. We showed that mRDTs were more sensitive than local SMHS for diagnosing malaria infection.

What are the implications for public health practices?

Malaria rapid diagnostic tests can be useful as an alternative to SMHS for FSAT in the local context of Tanzania.

Focused screening and treatment for malaria (FSAT) is an epidemiological technique to identify and treat cases of malaria in a targeted geographic area. FSAT has been identified as a key approach for reducing the burden of malaria in southern Tanzania. The two main diagnostic tools in FSAT are local standard health system microscopy (SHSM) and malaria rapid diagnostic tests (mRDTs). However, performance and operating characteristics of SHSM and mRDTs in local practice conditions are not completely determined. To address this knowledge gap, we analysed paired mRDTs and SHSM results from individuals screened in FSAT during 2018–2019 by re-examining blood slides using the World Health Organization's (WHO) Level 1 Qualification for Malaria Microscopy as reference standard. We measured local SHSM and mRDTs operating characteristics of sensitivity, specificity, and concordance. We showed that in a low economic situation with a shortage of microscopy technicians and insufficient SMHS equipment in local health

facilities, mRDTs can be useful as an alternative to standard microscopy in health system (SMHS) for FSAT in the local context of Tanzania.

Malaria remains one of the most serious vector-borne diseases impairing human health worldwide (1). In 2020, over 241 million cases of malaria were reported globally, 95% of which were in Africa. In Tanzania, as in many other countries in sub-Saharan Africa, national malaria prevalence decreased — from 18.1% in 2008 to 9.3% in 2017 (2). The “China-UK-Tanzania Pilot Project on Malaria Control” (the Pilot Project) was implemented in Southern Tanzania to explore a new model for reducing the malaria burden and for scaling up locally tailored approaches in similar areas in Africa and to share China's experiences of malaria control and elimination. The Pilot Project was initiated in 2015 in Rufiji District, Tanzania.

Microscopy is a convenient and direct diagnostic method for parasitological detection of *Plasmodium* species (*Plasmodium* spp.) and is the gold standard for parasitological confirmation. However, the accuracy of microscopic diagnosis is largely dependent on skills of the technicians. Microscopy tests only 50–100/μL blood for the presence of *Plasmodium* spp. and has a low rate of detection of asymptomatic carriers with their low-density infections (3). Use of anti-malarial drugs reduces *Plasmodium* spp. density and causes morphological changes in the parasite, both of which challenge parasite detection and species differentiation, leading to errors in microscopic detection (4).

mRDT is an immunological method for detecting specific antigens of *Plasmodium* spp. using peripheral blood. It has advantages of high sensitivity, simple operation, and rapid results, and requires only short-term training of local health staff. mRDTs are potentially ideal routine screening tools for detecting malaria in highly endemic countries with limited access to microscopy.

Progress of the Pilot Project highlighted the importance of evaluating performances of microscopy and mRDTs in Rufiji District, Tanzania. Our study

aimed to analyze performance characteristics of SMHS and mRDTs to identify their relative suitability for malaria diagnosis in local settings.

We selected 1,497 blood slides from a FSAT that was implemented between 2018 and 2019 in seven villages in Ikwiriri that were classified as low transmission areas (LTA) (n=679 slides, 45.36% of the sample) and seven villages in Muhoro that were classified as high transmission areas (HTA) (n=818, 54.64%). Blood slide preparation and microscopy were done by local health staff.

Blood samples were collected from people with and without fever, and slides were prepared at field focal points. Samples were collected on clean, grease-free microscope slides. After staining films with 10% Giemsa solution for 10 minutes, slides were air-dried and then examined using light microscopy with an oil-immersion objective lens. A slide was declared negative only if 100 microscopic fields were examined and no parasites were observed. For each specimen, thick films were first examined for malaria parasite detection and then parasite species were differentiated in thin films. Results were recorded as positive when two microscopists recorded positivity for the same slides. Discrepancies were resolved by a third microscopist (5).

Re-examination of microscopy was considered the gold standard in our study. Following WHO guidelines, selected slides were re-examined by two experts from China with WHO Level 1 Qualification for malaria microscopy. The two expert microscopists re-examined each blood sample independently under double-blind conditions and recorded their results. Discrepancies were resolved by a third microscopist.

Chi-square tests (χ^2 test) were used for pairwise

comparisons of diagnostic accuracy and concordance rates of the two methods (SMHS and mRDT) with a significance level of $\alpha=0.05$. SMHS and mRDT results were evaluated for accuracy and reliability using the gold standard modality, described above, as the reference standard (6). Operating characteristics evaluated included sensitivity and specificity, where sensitivity=true positives/(true positives+false negatives) $\times 100\%$ and specificity=true negatives/(true negatives+false positives) $\times 100\%$. Statistical analyses were performed using SAS software (version 9.3, Statistical Analysis System, NC, USA).

Of the 1,497 slides, 244 (16.30%), 382 (25.45%), and 309 (20.64%) were positive by SMHS, mRDTs, and the gold standard, respectively (Table 1).

mRDTs were more sensitive than SMHS in both HTAs and LTAs ($\chi^2=7.54$, $P=0.0105$; $\chi^2=20.48$, $P<0.001$). The difference in the sensitivity between mRDTs and SMHS was smaller in HTAs (87.10% vs. 76.88%) than in LTAs (86.99% vs. 65.04%). SMHS was more specific than mRDTs in both HTAs ($\chi^2=41.95$, $P<0.001$) and LTAs ($\chi^2=21.76$, $P<0.001$). The difference in specificity between mRDTs and SMHS was significantly greater in HTAs (87.83% vs. 98.38%) than in LTAs (92.52% vs. 98.13%) ($P<0.05$) (Table 2).

DISCUSSION

Our study showed that mRDTs were more accurate and reliable as a screening tool for malaria than SMHS, and were more sensitive in both HTAs and LTAs. The sensitivity gap between mRDTs and SMHS was smaller in HTAs than in LTAs, suggesting that mRDTs were more efficient in LTAs. The false

TABLE 1. Comparison of positive rates of three diagnostic modalities in Rufiji District of Tanzania during 2018–2019.

Ward	Diagnostic tools	Number of positive slides	Positive rate (%)
Ikwiriri (LTAs)	SMHS	93	11.37
	mRDTs	159	19.44
	Gold standard	123	15.04
Muhoro (HTAs)	SMHS	151	22.24
	mRDTs	222	32.70
	Gold standard	186	27.39
Both	SMHS	244	16.30
	mRDTs	382	25.45
	Gold standard	309	20.64

Notes: Ward is an administrative unit larger in area than a village and smaller than a county.

Abbreviations: LTAs=low transmission areas; HTAs=high transmission areas; SMHS=standard microscopy in health system; mRDTs=malaria rapid diagnostic tests.

TABLE 2. Comparison of performance of SMHS and mRDT in Rufiji District, Tanzania during 2018–2019.

Ward	Diagnostic tool	Sensitivity (%)	False negative rate (%)	Specificity (%)	False positive rate (%)
Ikwiriri (LTAs)	SMHS	65.04 (56.10–73.17)	34.96 (26.83–43.9)	98.13 (96.98–98.9)	1.87 (1.1–3.02)
	mRDTs	86.99 (80.49–92.68)	13.01 (7.32–19.51)	92.52 (90.5–94.39)	7.48 (5.61–9.5)
Muhoro (HTAs)	SMHS	76.88 (70.43–82.8)	23.12 (17.2–29.57)	98.38 (96.98–98.99)	1.62 (1.01–3.02)
	mRDTs	87.1 (82.26–91.94)	12.90 (8.06–17.74)	87.83 (84.99–90.67)	12.17 (9.33–15.01)
Both	SMHS	72.17 (67.31–77.02)	27.83 (22.98–32.69)	98.23 (97.47–98.91)	1.77 (1.09–2.53)
	mRDTs	87.06 (83.17–90.61)	12.94 (9.39–16.83)	90.57 (88.89–92.26)	9.43 (7.40–11.11)

Abbreviations: SMHS=standard microscopy in health system; mRDTs=malaria rapid diagnostic tests; LTAs=low transmission areas; HTAs=high transmission areas.

negative rates of mRDTs in LTAs (12.90%) and HTAs (13.01%) were less than respective SMHS false negative rates (23.12% and 34.96%). Together, these findings indicate that mRDTs demonstrated superior performance for identifying malaria infections in this Tanzania setting.

Our findings are consistent with those of Shakeley and colleagues who reported that mRDTs enhance performance for detecting malaria infections compared with microscopy, favouring their use in community cross-sectional malaria surveys, where microscopy expertise is difficult to find (7). Judith Kahama-Maró and colleagues proposed that microscopy should be replaced by mRDTs as the first-line diagnostic tool for malaria in all medical institutions because of poor quality of routine malaria microscopic examinations at different levels of the health system in Tanzania (8). The main findings from our study were similar to those of other studies. Fançony and colleagues used polymerase chain reaction (PCR) as the gold standard and compared screening performance of microscopy and mRDTs in Angola (9). They concluded that mRDTs were more sensitive than microscopy. Harchut and colleagues evaluated the cost efficiency of microscopy and mRDTs for malaria diagnosis in Southern Tanzania and found that use of mRDTs reduced government expenditure and facilitated rapid diagnosis of malaria (10).

Our study had some limitations. Samples were not tested by PCR. Hence, some patients with low-density parasitemia, particularly individuals with asymptomatic infection, may have been missed. The sample size was relatively small. If the sample size could be expanded, results could be more representative. However, the strategy of initial screening using mRDTs in HTAs followed by malaria microscopy confirmation should be a good strategy for improving the efficiency of local malaria detection.

In conclusion, mRDTs could be a useful alternative to SMHS for FSAT in local health facilities in

Tanzania that, due to poor economic conditions, have a shortage of certified microscopy technicians and lack some equipment necessary for conducting SMHS.

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