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Management of fever among under-fives and utility of malaria rapid diagnostic test under reduced malaria burden in Rufiji District, Southeastern Tanzania

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ABSTRACT

Objective: To investigate case management of fever among under-fives, performance and utility of malaria rapid diagnostic test (mRDT) under reduced malaria burden in Rufiji District, Southeastern Tanzania.

Methods: A quantitative cross sectional study was conducted at primary health facilities in Rufiji District from April to May 2012. Information on socio-demographic characteristics, history and duration of fever, fever measurement, clinical diagnosis and drugs prescribed were recorded. Parasitological malaria confirmation was done by mRDT and microscopy. Performance of mRDT and utility of mRDT results to guide on the management of malarial and non-malarial fevers were assessed.

Results: Of the 466 under-fives with fever, 111 (23.8%) were mRDT positive and 100 (21.5%) were microscopically positive for malaria. Sensitivity and specificity of mRDT were 90% [95% confidence interval (*CI*): 82.6%–94.5%] and 94.3% (95% *CI*: 91.4%–96.2%) respectively; overall diagnostic accuracy was 93.3% (95% *CI*: 91.1%–95.6%). A total of 130 (28.5%) under-fives received an antimalarial. Among them, 109 (83.8%) were mRDT positive while 21 (16.2%) were negative. Of the 100 under-fives with microscopic parasitaemia, 34 had counts > 200 000/μL an indication for quinine but only 5/34 (14.7%) received quinine prescription. Five under-fives with parasitaemia > 200 000/μL had negative mRDT results. Being mRDT negative was significantly associated with receipt of an antibiotic prescription ($\chi^2 = 162.2$, $P < 0.001$).

Conclusions: Use of mRDT reduced unnecessary antimalarial use by 71.5%. However, this had the potential for over prescribing an antibiotic for non-malarial fevers. The diagnostic performance of mRDT was still high despite decline in malaria burden.

1. Introduction

Malaria resulting from *Plasmodium falciparum* (*P. falciparum*) is a disease which presents with fever. Fever has thus been used as a marker of malaria for both clinical and epidemiological settings[1]. However, even in areas of high transmission, not all fever cases are due to malaria[2]. Thus, treatment based on fever alone results in a high rate of over treatment with antimalarials because of the non-specificity. The non-specificity of fever makes it a poor marker of malaria and critically depends on the prevalence of both asymptomatic malaria infection and the overall prevalence of fever[3]. Recent WHO guideline recommends that all persons of all ages in all epidemiological settings with suspected malaria should receive a parasitological confirmation of malaria[4]. Microscopic examination of Giemsastained blood smears remains the gold standard for malaria diagnosis despite its technical challenges and demand for trained personnel. However, most peripheral health facilities in malaria endemic countries lack the capacity to carry out parasitological confirmation of malaria by microscopy[5-7]. Malaria rapid diagnostic test (mRDT) has been recommended for use in health facilities where microscopy cannot be performed, as the test is accurate in detecting malaria infections and easy to use[8].

There is a growing evidence documenting a substantial decline in malaria transmission, morbidity, and mortality in more than 13 African countries where malaria control interventions have been massively deployed leading to a decline of *P. falciparum* prevalence in children aged 2–10 years from 37% before the year 2000 to 17% after 2000[9,10].

In Tanzania, available data show that malaria incidence and

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prevalence are declining in most parts of the country as shown in the national survey of 2007-8 whereby the overall prevalence of malaria among under-fives was 18.1% while in the 2011-12 survey the overall prevalence was 9.7% by mRDT and 4.2% by microscopy[11,12]. The decline was observed in all geographical zones and in both surveys; the Lake, Southern and Western zones had the highest prevalence while the Northern and Southern high land zones had the lowest prevalence. The decline has also been demonstrated by area specific studies in some parts of the country[13].

The decline in malaria burden poses challenges for the routine use of mRDT in the management of malarial and non-malarial fevers[14]. Since malaria-related fevers have significantly declined in endemic areas[15], emphasis should now be put on the management of non-malarial fevers by prescribing antimalarials to only laboratory confirmed cases[4]. However, prescribers do not always adhere to guidelines either as a result of fear to miss malaria or due to pressure to conform with perceived patient preferences[16]. Furthermore, in face of the decline in malaria burden, most patients would maintain low parasitaemia which may not be detectable by the currently available mRDTs known to have a low sensitivity when used in individuals with low parasitaemia[17,18]. Despite the universal adoption of mRDT for malaria confirmation before antimalarial prescription[19], it is unclear that to what extent this guides the management of malarial and non-malarial fevers under reduced malaria burden. It is not known that to what extent the decline in malaria burden would have changed the performance of mRDT. The changing malaria epidemiology with a decline in prevalence of malaria cases would conceivably lower the specificity and predictive value of fever for the clinical diagnosis of malaria. Decrease in malaria prevalence would influence the predictive values positive and negative of mRDT such that the test will pick up more false positives, true negatives and indices which would change the diagnostic performance of the mRDT[20]. Here we report a study on fever management among under-fives and the utility of mRDT for the management of malarial and non-malarial fevers at primary health facilities in Rufiji District, Tanzania.

2. Materials and methods

A quantitative facility based cross sectional study was conducted from April to May 2012 in Rufiji, one of the districts in Pwani region, others in Bagamoyo, Kibaha, Kisarawe, Mafia, and Mkuranga in Southeastern Tanzania. A prominent feature of the district is the Rufiji River with its large flood plain and delta, the most extensive in the country. This condition makes the district have intensive perennial malaria transmission[21]. Primary health care facilities which included eight dispensaries and two health centres were included in the study. The study participants comprised of under-fives attending in the facilities during the day time; those who fulfilled the inclusion criteria: age $\leqslant$ 59 months, febrile (axillary temperature $\geqslant$ 37.5˚C) or history of fever in the last 48 h; and caregivers giving consent for their participation were recruited into the study.

The sample size was calculated for three different categories namely, proportions of under-fives with a history of fever who received temperature measurement and found to have high temperature at the health facility, accuracy of mRDT in routine practices for confirmation of malaria in febrile under-fives and extent of antimalarial prescription in under-fives presenting with history of fever. The needed sample size in each category was estimated by using the formula for cross sectional surveys:

$N = (1.96/d)^{2p}(1-p)$

where, N is sample size, d is the desired precision for the parameter to be estimated [measured as half the width of the expected 95% confidence interval (CI)], p is proportion reported in the previous studies.

Sample size I: d = 6%, p = 25.3% proportion of children with history of fever and found to have fever in Mwanza, Tanzania[22]; $N = (1.96/6)^2 25.3(100-25.3) = 202$.

Sample size II: For sensitivity, p = 91% sensitivity of mRDT in patients with fever in field practices at Blantyre, Malawi[23]; d = 4%, $N = (1.96/4)^2 91(100-91) = 197$.

For specificity, p = 68% specificity of mRDT in patients with fever in field practices at Blantyre, Malawi[23]; d = 6%, $N = (1.96/6)^2 68(100-68) = 233$.

The sum of sample for sensitivity and specificity gave the total sample size required to determine performance of mRDTs. Thus, total sample size required = 197 + 233 = 430.

Sample size III: d = 5%, p = 36% proportion of patients who receive antimalarials despite negative mRDT results in primary health facilities in Zambia[24]; $N = (1.96/5)^2 236(100-36) = 355$.

The sample size used in this study was 480 (highest sample size of the three above plus 10% missing data).

Eight dispensaries and two health centers that qualified for the study were involved. The sample of under-fives obtained from each health centers were twice as much compared to each dispensary as the health centers usually served twice the population than the dispensaries. Under-fives who fulfilled the inclusion criteria were consecutively enrolled in each facility until the required sample per facility was met (Figure 1).

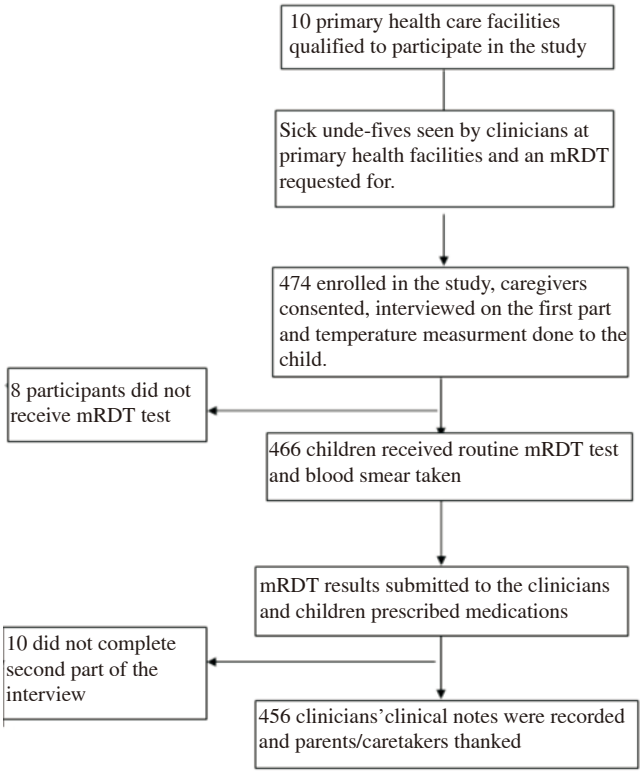

Figure 1. Flow chart showing selected health facilities and enrollment of under-fives with fever in the study.

Structured Swahili questionnaire was used to collect information for the under-fives on their socio-demographic characteristics, history and duration of fever, body temperature measurement by the health facility staffs, investigation done and drugs prescribed. The study used digital thermometer to measure axillary temperature of each recruited under-five. Two thick and thin blood smears were taken from each participant receiving mRDT testing. These were stained with 4% Giemsa for 20 min. One of the blood smears was read in the field by microscopist who was blind to the results of clinical diagnosis and mRDT results, while the other was sent to the Parasitology Laboratory at Muhimbili University of Health and Allied Sciences (MUHAS) for another microscopic examination by two expert laboratory technologist who were blind to the results of clinical diagnosis and mRDT results. Each smear required approximately 20 min for reading. Parasite species was identified in the thin film and count was made on the thick film. A minimum of 200 consecutive fields were counted in the thick blood film before a slide was declared negative. Parasites in thick blood films were counted against 200 white blood cells, and the parasite density was estimated assuming 8 000 white blood cells/μL of blood.

2.1. mRDT kits

The SD BIO LINE Malaria Antigen P.f/Pan mRDT manufactured by Standard Diagnostics, Inc. Korea and supplied by the Medical Store department were in use during the study. All the studied facilities last received the kits on January 2012. The manufactured dates noted at the bottom of the boxes of kits were between February and May 2011 and the earliest expiry date noted was March 2013 while the furthest was August 2013. The kits were stored in the boxes in laboratories at health centers and in injection rooms/dispensing rooms at dispensaries. In all facilities the kits were stored at room temperature, the mean diurnal temperature of all facilities was 32 ˚C.

2.2. Availability of thermometers

All the studied facilities were noted to have clinical thermometers. However, three facilities (Jaribu-Mpakani, Kimbuga and Kibiti) had digital clinical thermometers while other facilities had mercury clinical thermometers.

2.3. Quality control

Two expert laboratory technicians at MUHAS Parasitology Laboratory unaware of the mRDT results independently read the blood slides to provide results that were used for the determination of diagnostic accuracy of mRDT results. A third technician was sought in case the two had contrasting results or they had a difference of more than 1 000 malaria parasite counted in a microlitre of blood.

2.4. Data entry and analysis

Data were cleaned, entered and processed by using SPSS computer software version 13. Analysis was carried out by using SPSS version 13 and Epi Info 2000. Descriptive analysis was done by using frequencies and proportions to estimate magnitude of the outcomes of interest. Bivariate analysis was done by 2 × 2 tables and *Chi*-square and Z-tests were performed to test differences in distributions and compare proportions respectively. The performance of mRDT for parasitological malaria confirmation was computed against microscopy as the gold standard. Multiple logistics regression analysis was used to assess the factors that predict the performance of mRDT for parasitological malaria confirmation; adjusted odds ratios and their 95% *CI* were estimated and associations were drawn.

2.5. Ethical considerations

Informed written consent was obtained from each parent/guardian on behalf of the under-fives by reading the consent statements from the consent form using the local language (Swahili). The study protocol was approved by the MUHAS ethical review board. Administrative permission to carry out the study was obtained from the Regional Medical Officer and District Medical Officer.

3. Results

A total of 474 under-fives who were eligible for mRDT testing were recruited in the study; eight did not receive mRDT testing and were excluded in the analysis. Ten under-fives whose blood samples had been taken did not complete the second part of the interview. However, they were included in the analysis with some missing information. Participation rate in this study was 96.2%; 297 (62.7%) of under-fives were recruited from eight dispensaries and 177 (37.3%) from two health centers.

3.1. Characteristics of the study population

The socio-demographic and clinical characteristics of the study population are shown in Table 1. One third (33.3%) of the study population was below one year of age. The mean age (SE) was found to be 23 (0.71) months and the median (inter quartile range) was 20 (10-33.5) months. The study population had almost equal gender distribution. Caregivers of 454 (97.4%) children gave history of fever as the chief complaint when bringing their children at the health facility for care whereas 12 (2.6%) did not report fever but were found to have high body temperature at the health facility. Out of 466 children studied, 244 (52.4%) children had elevated body temperature equal or above 37.5 ˚C as shown in Table 1.

Table 1
Socio-demographic and clinical characteristics of the study population.

Characteristics of children (*N* = 466)		Amount	Percentages
Age groups(months)	3-12	155	33.3
	13-24	136	29.2
	25-36	86	18.4
	>36	89	19.1
Sex	Male	246	52.8
	Female	220	47.2
History of fever	Yes	454	97.4
	No	12	2.6
Measured body temperature (study)	<37.5	222	47.6
	37.5	244	52.4

The mean (SE) and median (inter quartile range) duration of fever were found to be 60 (1.3) hours and 48 (48-72) hours respectively. Out of 454 under-fives with a history fever, only in 55 (12.1%) did the caregivers reported presence of fever within 24 hours before recruitment into the study, while in 398 (87.9%) the caregivers reported presence of fever of more than 24 hours prior to attending the facility. Of the 454 children with fever or history of fever, 235 (53.8%) had body temperature taken at the facility and completed the

interview. Among the 235 children who had body temperature taken, 145 (61.7%) were found to have elevated body temperature above normal.

3.2. Factors influencing health workers temperature measurement in under-fives

As Table 2 shows, the duration of fever in children was not associated with body temperature measurement in the facilities. About half of the children in the age groups ≤ 24 months (53.5%) and > 24 months (48.3%) had temperature measurements at the facilities. There was no significant difference on temperature measurement between different age groups. Likewise, there was no significant difference on body temperature measurement between dispensaries (51.8%) and health centres (51.4%). Clinical officers were more likely to do temperature measurement as compared to assistant medical officers. Furthermore, facilities using digital thermometers were highly likely to measure body temperature as compared to the facilities using mercury thermometers.

Table 2

Factors influencing health workers' temperature measurement in under-fives.

Factor		Temperature taken [*n* (%)]	Temperature not taken [*n* (%)]	χ^2	*P*-value
Duration of fever (hours)	48	118 (53.2)	104 (46.8)		
	> 48	130 (58.8)	91(41.2)	1.4	0.2
Age categories (months)	≤ 24	152 (53.5)	132 (46.5)		
	> 24	83 (48.3)	89 (51.7)	1.2	0.29
Facility type	Health center	85 (51.8)	79 (48.2)		
	Dispensary	150 (51.4)	142 (48.6)	0.009	0.5
Staff type	Clinical officer	147 (60.2)	97 (39.8)		
	AMO	88 (41.5)	124 (58.5)	15.9	< 0.001
Thermometer type	Digital	120 (80.5)	29 (19.5)		
	Mercury	115 (37.5)	192 (62.5)	74.5	< 0.001

AMO: Assistant medical officers.

3.3. Relationship of clinical malaria diagnosis with mRDT findings among febrile under-fives

Of the 466 under-fives with a presumptive malaria diagnosis who received mRDT testing, 111 (23.8%) and 100 (21.5%) were found to be positive for malaria by mRDT and microscopy respectively; thus using microscopy as the gold standard, the prevalence of malaria parasitaemia was 21.5% (95% *CI*: 17.9%–25.5%). Of the 100 under-fives with microscopic parasitaemia, 35 had parasite counts > 200 000/ μL of blood, of which 5 were negative by mRDT. The mRDT still had high diagnostic performance indices (Table 3), with a sensitivity and specificity of 90% (95% *CI*: 82.4%–95.1%) and 94.3% (95% *CI*: 91.4%–96.4%) respectively and an overall diagnostic accuracy of 93.3% (95% *CI*: 91.1%–95.6%).

Table 3

Diagnostic performance of mRDT for malaria in under-fives (*N* = 466).

Performance of mRDT	Microscopy
True positives (a)	90
False negatives (b)	10
False positives (c)	21
True negatives (d)	345
Sensitivity [a/(a+b)]	90.0% (95% *CI*: 82.4-95.1)
Specificity [d/(c+d)]	94.3% (95% *CI*: 91.4-96.4)
Predictive value positive [a/(a+c)]	81.1% (95% *CI*: 72.8-87.3)
Predictive value negative [d/(b+d]	97.2% (95% *CI*: 94.7-98.6)
Overall diagnostic accuracy [(a+d)/N]	93.3% (95% *CI*: 91.1-95.6)

3.4. Factors affecting diagnostic performance of mRDT

Both bivariate and multivariate logistic regression showed that clinical officers or nurse assistants were more likely to get accurate mRDT results as compared to expert laboratory technicians as shown in Table 4.

Likewise, age of the under-fives, duration of fever, measured body temperature, history of antimalarials used in the past two weeks and malaria parasitaemia level (< 5 000 or > 5 000/μL of blood) did not affect the accuracy of mRDT. However, of the 35 under-fives with parasite counts > 200 000/μL of blood, 5 had negative mRDT results indicating that at such high parasite density false negative results may occur in histidine rich protein II based on mRDT such as the one used in the study and may decrease the diagnostic accuracy.

Table 4

Bivariate and multivariate analysis of the factors that predict the performance of mRDT for malaria confirmation among febrile under-fives in Rufiji District.

Factor		Children with blood slide positive (*N* = 100)	True positive for mRDT (*N* = 90) sensitivity [*n* (%)]	Unadjusted odds ratio (95% *CI*)	Adjusted odds ratio (95% *CI*)
Age (months)	≤ 24	41	37 (90.2)	1	1
	> 24	59	53 (89.8)	1.0 (0.3-3.6)	1.3 (0.3-5.9)
Duration of fever (h)	≤ 48	44	39 (88.6)	1	1
	> 48	56	51 (91.1)	1.3 (0.4-4.8)	1.4 (0.3-5.0)
Measured body temperature	< 37.5 ˚C	31	26 (83.9)	1	1
	≥ 37.5 ˚C	69	64 (92.8)	2.5 (0.7-9.3)	2.4 (0.6-10.2)
Antimalarials past two weeks	Yes	7	6 (85.7)	1	1
	No	93	84 (90.3)	1.6 (0.2-14.5)	1.9 (0.2-21.3)
mRDT performer	Lab tech	55	46 (83.6)	1	1
	CO/NA	45	44 (97.8)	8.6 (1.0-71.4)	8.5 (1.0-71.6)
MPs intensity/μL	< 5 000	15	13 (86.7)	1	1
	≥ 5 000	85	77 (90.6)	1.5 (0.3-7.8)	0.9 (0.2-5.7)

CO: Clinical officers; NA: Nurse assistants; MPs: Malaria parasitaemia.

3.5. Guidance of mRDT results for the management of malarial and non-malarial fevers

Among the 456 under-fives completing the second part of the interview, 130 (28.5%) received an antimalarial; of these, 109 (83.8%) were mRDT positive while 21 (16.2%) were mRDT negative. Among 100 under-fives microscopically positive for malaria, ten were negative by mRDT and would therefore not receive antimalarial if there is strict adherence to mRDT results. Six of the 66 under-fives with parasitaemia ≤ 200 000/μL did not receive antimalarial, while 4 of 34 under-fives with parasitaemia > 200 000/μL, an indication for management as a case of severe malaria, did not receive an antimalarial.

Among the 456 under-fives, 313 (68.6%) were judged to have non-malarial fever and therefore received an antibiotic prescription; among them, 292 (84.1%) had negative mRDT results indicating that 21 (15.9%) were judged to have both malarial and non-malarial fevers and therefore received treatments for both. A significant difference was found in antibiotics prescription among under-fives who were mRDT negative as compared to those who were mRDT positive ($\chi^2 = 162.2$, $P < 0.001$) indicating that mRDT results guided prescribers to think of other possible non-malaria causes of fever which might include bacterial infections hence the decision to give an antibiotic prescription.

4. Discussion

This study was carried out during rainy season from April to May 2012 when malaria transmission was at peak in the study area to examine the diagnostic performance of mRDT for the parasitological confirmation of malaria among febrile under-fives and the guidance of mRDT results for the management of malarial and non-malarial fevers under the recorded declined malaria prevalence.

4.1. Response to fever by caregivers and health workers

The present findings reaffirm that fever is the entry point for the presumptive diagnosis of malaria[2]. Thus, the large majority (97.4%) of the under-fives had a history of fever, of whom 235 (53.8%) had body temperature taken by health workers at the facility. Among them, 145 (61.7%) were found to have raised body temperature (≥ 37.5 ˚C). Though guidelines provide that every child suspected to have malaria must be confirmed by mRDT[4], not all under-fives with fever were suspected to be due to malaria got parasitological confirmation by mRDT, as only 36.5% (19/52) of the primary health facilities had mRDT kits available at the time of the study. Consequently, the facilities (63.5%) without mRDT kits would presumptively manage under-fives with fever as malaria resulting in overuse of antimalarial drugs and mismanagement of non-malarial fevers. The WHO observation that less than 20% of children with fever suspected to be malaria receive parasitological confirmation in health facilities is a result of the unavailability of mRDT kits[25]. Similar findings were reported in Zambia whereby only 27% of patients with history of fever received parasitological diagnosis at health facilities[24]. District health authorities in liaison with the National Malaria Control Programme should ensure constant availability of mRDT kits by strengthening the supply chain so as to meet the WHO advocated universal access to malaria diagnostic testing[19]. A diagnosis based on clinical symptoms alone has very low specificity, with the result that the number of false-positive results can be considerable and other diseases may be overlooked and not treated in a timely manner. This would contribute to an increase of non-malaria morbidity and mortality, the misuse of antimalarial drugs, the development of parasite drug resistance, increased costs to the health services and patient dissatisfaction.

Temperature measurement at health facilities was found to be in only 51.5% of the children. This was tremendously low in comparison to the observations in Ghana whereby 91% of febrile children had temperature measurement taken at the facilities[26]. This unexpected finding may be associated with the tendency of clinicians to estimate body temperature by facial palpation.

4.2. Performance of mRDT for parasitological malaria confirmation of malarial fevers among under-fives

The main purpose of parasitological confirmation of malaria in this era is to improve management of febrile under-fives and reduce unnecessary use of artemisinin-based combination therapies (ACTs) used as 1st line antimalarial drugs. Early accurate diagnosis and treatment with an ACT antimalarial are very important aspects of malaria control as they will reduce the parasite load in the community and reduce malaria transmission. The performance of mRDT was assessed against microscopic findings of blood smears as a gold standard. The sensitivity (90%) and specificity (94.3%) of mRDT in children with fever were obtained in this study and were within the range found in previous studies[18,27-29]. The overall diagnostic accuracy (93.3%) was also very high indicating that the recorded decline in malaria prevalence has not affected the diagnostic performance of the mRDT[20]. However, the sensitivity and specificity were slightly below 95% as previously recommended[30]. An accurate and correct laboratory diagnosis is essential as false negatives can result in untreated malaria patients and potentially severe consequences, including death. False negatives can also significantly undermine both clinical confidence in laboratory results and credibility in the community. False positive results are equally problematic as patients presenting with fever but not caused by malaria may be misdiagnosed and the true cause of their fever may be not treated, which can also have severe consequences, including death.

The finding that 5 out of the 35 under-fives with parasite counts > 200 000/μL of blood had negative mRDT results contrasts with the observation by Bisoffi *et al*. in 2010 in which false negative results occurred at the lowest parasite counts[29]; while Murray *et al*.[30] in 2008 argued that at high level of parasite density the sensitivity of mRDT is 100.0%. In those with parasite counts > 200 000/μL, an excess of *P. falciparum* antigens in the mRDT antigen-antibody reactions, would lead to the prozone effect[31]. The mRDT kits used in Rufiji District were from the SD BIO LINE Malaria Antigen P.f/Pan manufactured by Standard Diagnostics Inc. Korea that detects histidine rich protein II specific to *P. falciparum* and is affected by prozone[32].

The cadre of health worker was found to affect the accuracy of mRDT results. Thus, clinical officers and nurses who had few days of training on performing mRDT obtained accurate results than the certified laboratory technicians. It was difficult to explain this result, but it might be related to the fact that the laboratory technicians had many other laboratory procedures to do and did not read the test at the required interval of time.

4.3. Guidance of mRDT findings for the management of malarial fevers

Before the introduction of mRDTs, all under-fives with fever attended at primary health facilities would receive an antimalarial as previously advocated in the integrated management of childhood illnesses (IMCI). This would inevitably lead to an over-prescription of antimalarials given that fever is not specific for malaria[2,3]. Findings from this study show that, irrespective of mRDT results, 28.5% of febrile under-fives received an antimalarial indicating that there was about a two thirds (71.5%) reduction in antimalarial prescription. In this study, less than a quarter (23.9%) of the under-fives with fever was found to be mRDT positive. If there was a 100.0% adherence to mRDT results, prescription of antimalarial would have been reduced by more than three quarters (76.1%). Studies conducted in other parts of the country have shown that the correct use of mRDTs and adherence to test results by health workers reduced prescription of antimalarial drugs by more than 60%[18,33].

In this study, 16.2% of under-fives who received an antimalarial had negative mRDT results. Similar findings were also recorded in Zambia and Ghana[24,34]. It has been shown that clinicians

are unlikely to adhere with the new guidelines of mRDT-directed antimalarial treatment due to their strong preference for a diagnosis of malaria as a result of their notion that malaria is easier to diagnose than alternative diseases; that malaria is a more acceptable diagnosis; and that missing malaria is indefensible[16,35], and therefore tendency to ignore parasitological results as a guide for giving an antimalarial prescription appears[36]. The aim of laboratory testing for malaria is not just to confirm the presence of malaria parasites but to decide on the right treatment. A positive mRDT result is an indication for giving an antimalarial prescription, and a negative result should prompt the clinicians to look for and treat the alternative non-malaria causes of fever. The benefit of testing is lost if clinicians decide not to use test result as a basis for the clinical decision making on the type of treatment to give.

It was found that 34 under-fives had parasite counts > 200 000/μL which formed one of the laboratory indices for severe malaria in which case quinine should be prescribed[37]. However, only 5/34 (14.7%) received a quinine prescription. Since mRDT is a qualitative test and cannot quantify parasite count, it is likely that under-fives with counts > 200 000/μL parasites would wrongly receive ACT instead of quinine and in the absence of monitoring, they may get into complicated malaria[38].

4.4. Guidance of mRDT findings for the management of non-malarial fevers

Negative mRDT results poses a new challenge of what would be the other treatable causes of non-malarial fevers. Prescribers oriented to the IMCI strategy would prescribe an antibiotic which was as shown in this study. Antibiotic prescription was highly influenced by mRDT results, thus under-fives with negative mRDT results were highly likely to receive an antibiotic prescription as compared to those with positive mRDT results. Studies have shown that a decrease in antimalarial use among mRDT negative fever cases is accompanied by an increase in antibiotic use[33,36]. However, giving an antibiotic to all fever cases with negative mRDT results may not be justifiable. In a recent study which used advanced diagnostic techniques (microbiological testing of blood, nasal and throat swabs by rapid testing and culture; serology and molecular analysis as well as chest radiology), it was shown that most under-fives with fever probably have a viral disease that does not require an antibiotic[39]. In the absence of severe clinical signs which is defined by the WHO[40], the children could reasonably be sent home without antibiotic treatment[41,42]. Routine antibiotic treatment for febrile under-fives with negative mRDT results could potentially expose them to unnecessary adverse events, drug pressure in the community and development of microbial resistance to the drugs.

Use of mRDT guided management of malarial and non-malarial fevers reduced unnecessary antimalarial use by 71.5%. The diagnostic performance of mRDT was still high despite the reported decline in malaria burden. Since the mRDT is qualitative and may be affected by prozone, there is a likelihood of missing hyper parasitaemia cases which should be treated as severe malaria. Further studies are required to determine the frequency of prozone, and the health outcome of under-fives with counts > 200 000/μL parasites deserving treatment for severe malaria but not receiving the right treatment as well as the safety of withholding antibiotic treatment for negative mRDT cases without severe clinical manifestations.

Conflict of interest statement

We declare that we have no conflict of interest.

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