

Adherence to test, treat and track policy for malaria control as reported by a rural district in Ghana: a five-year retrospective data review

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Abstract

Background: The WHO in 2012 recommended the T3 (Test, Treat and Track) policy in endemic countries to aid in achieving universal coverage with diagnostic testing, antimalarial treatment and malaria surveillance systems strengthening. This study, therefore, analyzed reported malaria data in the DHIMS2 database to assess the adherence of the 'Test', 'Treat' and 'Track' strategy in a rural district. **Method:** This was a retrospective cross-sectional descriptive analysis of reported OPD malaria secondary data from January 2016 to December 2020 to evaluate adherence to T3 policy in a district in Ghana. Reported DHIMS2 data by eight health facilities were extracted and analyzed to ascertain the test and treat component whilst an observational checklist was used to assess the track component of the policy. The analysis outcomes were presented on frequency tables and a chart. **Findings:** The overall testing rates for all ages, children under five years and pregnant women were 79.1%, 79.7% and 97.1% respectively. Presumptuous treatment among children under five years and pregnant women was 29.5% and 6.2%. Over 11% of clients were prescribed antimalarial though malaria test results proved they were negative. There was no documented evidence of malaria surveillance, though malaria data were duly reported in DHIMS2. **Conclusion:** Adherence to the 'Test' policy was consistently encouraging especially among children under five years and pregnant women. The facilities compliance with the 'Treat' policy was marginally low with a poor tracking malaria surveillance system.

Keywords: Malaria, Test, Treat, Track, Adherence to T3, Antimalarial, DHIMS2, Offinso North, Secondary data

INTRODUCTION

Globally, malaria remains a major cause of health menace creating a substantial level of threats by causing most morbidities and mortalities in endemic countries especially among children under five years and pregnant women [1].

The World Health Organization (WHO) African Region continues to carry a disproportionately high share of the global malaria burden. In 2020, the Region contributed to about 95% of all malaria cases and 96% of deaths of the global burden. However, the scale-up of interventions has resulted in some reduction in malaria burden even in the high transmission countries of sub-Saharan Africa [3]. Even though a substantial decrease has been realized in the menace of malaria over the past years, the Malaria Millennium Development Goal of a 90% reduction in worldwide malaria occurrence and mortality by 2030 is far to be attained [4].

In Ghana, data suggest that the proportion of deaths attributed to malaria per 1 00,000 population has decreased from 1 0.8/1 00,000 in 2012 to 1 .1 /1 00,000 in 2019. Notwithstanding, half of the world still lives at risk of malaria. About 80% of all malaria deaths in the African Region were recorded among children under five years of age [2]. Ghana remains part of the top countries, which contributes to the global malaria burden [5]. Consequently, the nation has made some remarkable accomplishments by reducing malaria-related deaths from 88% of 2,799 in 2012 to 333 in 2019. In 2012, Ghana documented about eight malaria mortalities daily but was abridged to only a single incidence of malaria mortality daily in 2019. All inpatient malaria-related cases were abridged by 8% from 2012 to 2019, while the percentage of malaria parasites amongst children under five years decreased from 21 in 2016 to 14 in 2019. Furthermore, the decrease indicates a 32% reduction in the prevalence of malaria from 2016 to 2019. The percentage of Out-Patients Department (OPD) malaria morbidities, tested by microscopy has gradually improved from 40 in 2012 to 94 in 2019 [6].

Malaria continues to be the first on the list of top ten morbidities in Offinso North district's annual report since the inception of the district in 2008. The district recorded 27.6%, 25.6% and 21.5% OPD malaria cases for 2018, 2019 and 2020 respectively. As anticipated, children less than five years accounted for 35.3%, 35.2% and 35.9% of the total OPD malaria cases reported for 2018, 2019 and 2020 respectively. Pregnant women subsequently accounted for 2.2%, 1.7% and 2.4% of the total reported OPD malaria morbidities in the district in 2018, 2019 and 2020 respectively.

Since Ghana accepted the Roll Back Malaria Initiative in 1998/1999, the country has been employing a blend of preventive and curative interventions as delineated in the Malaria Control strategies in Ghana. Ghana continuously implements policies that are

considered to enhance the attainment of the set goals. Not confirming malaria before prescribing Artemisinin-based Combination Therapy (ACTs) is likely to result in misdiagnosis especially in children, as well as the inappropriate use of exceedingly expensive ACTs. [7]. The WHO in their quest to curb malaria launched a new initiative called “T3: Test, Treat and Track” in 2012 as a framework for malaria-endemic countries in their efforts to achieve universal coverage with diagnostic testing and antimalarial treatment, and also ensure effective malaria surveillance systems [8]. In 2013, Ghana adopted the Test, Treat and Track strategy which is directed at ensuring; that every assumed malaria morbidity is tested, that every case tested positive is treated with the recommended quality-assured anti-malarial medicine. Additionally, the policy demands that all malaria morbidities and mortalities be traced through timely and precise reporting to guide policy and operational decisions. These processes if strictly adhered to, will enhance accurate profiling of the malaria menace and significantly contribute to appropriately managing other causes of febrile ailments. It will additionally reduce the unnecessary exposure of patients to anti-malaria medicines, reduce consumption of ACTs and thus eliminate pressure on the medicines. The adopted policy paved way for the subsequent revision of malaria control guidelines. This important guidelines revision was a great sign of a positive shift from the past when fever was invariably equated with malaria to testing every suspected case of malaria before treatment [9].

The T3 initiative has been the other of the day for malaria control in every district in Ghana after its adoption in 2013. Offinso North district since the introduction of T3 has made an interminable effort to implement this policy as mandated by Ghana Health Service. Notwithstanding, at the center of this important implementation of the T3 is data management for effective decision-making. Routine collection and analysis of malaria data are very beneficial for making informed decisions towards allocation of resources to improve the disease burden and hence the need for a national database for routine data collection. The District Health Information Management System (DHIMS2) is a web-based database for the routine collection of morbidity and mortality health data in Ghana. DHIMS2 helps in tracking malaria cases from the district to the national level [7]. This study, therefore, sought to review reported OPD malaria morbidity data in DHIMS2 to assess the adherence to the T3 (test, treat and track) policy for malaria control in a rural district of Ghana.

MATERIALS AND METHODS

Study site description

This review was conducted for all eight health facilities in Offinso North District. The district is one of the 43 districts in the Ashanti region of Ghana and has a projected population of 71,410. Children under five years and expected pregnancy account for an estimated projection of 14,282 and 2,856 respectively as projected for the year 2020. The district has five health demarcated sub-districts and about Eighty-Six communities. The district has two hospitals, one clinic, one maternity home, one CHPS compound and three health centres.

Study design

A retrospective cross-sectional descriptive analysis of reported OPD malaria secondary data from January 2016 to December 2020 to assess adherence to T3 policy was conducted in the Offinso North district.

Sampling method

All eight (8)-health facilities in the district were purposively included in the data review to assess T3 adherence.

Data collection procedure

Aggregated reported OPD malaria data for children under five years, pregnant women and all ages for 2016 to 2020 by Offinso North district were extracted from DHIMS2. The data extracted included variables such as total uncomplicated malaria cases: suspected, suspected tested, tested positive, not tested but treated as malaria, tested negative but treated as malaria and treated with anti-malarial. A checklist was used to collect primary data on the availability and utilization of malaria statistics for surveillance purposes at all eight health facilities used for the review.

Data analysis

The extracted data were exported to Microsoft Excel 2016 where descriptive analysis was performed. Absolute and relative frequencies were generated for the selected variables and the final outputs were presented in tables and a chart. The analysis was performed using the three dimensions of the T3 (test, treat and track) policy as described by WHO. The first T (Test) according to WHO is to ensure that all suspected malaria cases are tested. To measure this dimension, all suspected uncomplicated malaria cases referred for testing using either Rapid Diagnostic Test (RDT) or microscopy were divided by the total number of uncomplicated malaria suspected to attain the proportion of uncomplicated malaria suspected tested. The second T (Treat) is to ensure that every confirmed malaria case should be treated with a quality-assured anti-malarial medicine. To assess this dimension, total uncomplicated malaria cases tested positive and treated with anti-malarial were divided by total uncomplicated malaria treated with antimalarial (confirmed and clinical). The third T (Track) according to WHO, is to ensure that every malaria case is tracked in a surveillance system. To assess this dimension, a total number of aggregated malaria reports (monthly OPD morbidity returns and monthly malaria data returns on anti-malarial) transmitted into DHMS2 by all health facilities were tracked against the total expected reports for the years under review. Additionally, the availability and use of malaria statistics for surveillance purposes were also tracked in all health facilities used for this review. Expectations for the malaria statistics included: periodic trends of malaria cases and deaths with an emphasis on person, place and time.

RESULTS

The outcome of this review has been described under the various components of the T3 (Test, Treat and Track) policy.

Test

The proportion of uncompleted malaria suspected tested has seen an appreciable continuous upsurge from 2016 to 2020 for all ages and most especially among children under five years. Most test done for suspected uncompleted malaria cases for the years under review was reported among pregnant women. The testing rate among this group has been inconsistently stagnant. The overall testing rate for the years under review was 79.1%, 79.7% and 96.9% for all ages, children under five years and pregnant women respectively as depicted in Table 1.

Table 1. Reported OPD suspected uncomplicated malaria cases tested in a rural district in Ghana, 2016 to 2020

Period	All Ages		Children under 5yrs		Malaria in Pregnancy	
	^{A1} Total Uncomplicated Malaria suspected Cases	N1 (% Tested) ^B	^{A2} Total Uncomplicated Malaria suspected Cases	N2 (% Tested) ^C	^{A3} Total Uncomplicated Malaria suspected Cases	N3 (% Tested) ^D
2016	27,282	15,776 (57.8)	10,523	6,279 (59.1)	590	569 (96.4)
2017	17,097	12,862 (75.2)	6,603	5,008 (75.8)	530	523 (98.7)
2018	23,200	17,492 (75.4)	8,077	6,116 (75.7)	446	434 (97.3)
2019	32,682	29,062 (88.9)	10,733	9,752 (90.9)	538	525 (97.6)
2020	29,313	27,287 (93.1)	10,034	9,501 (94.7)	647	614 (94.9)
Total	129,574	102,479 (79.1)	45,970	36,656 (79.7)	2751	2,665 (96.9)

^{A1,A2,A3}total uncomplicated malaria suspected cases; **N1**=total uncomplicated malaria suspected cases tested for all ages; **N2**=total uncomplicated malaria suspected cases tested for children under five years; **N3**=total uncomplicated malaria suspected cases tested for pregnant women; ^Bproportion of uncomplicated malaria suspected cases tested for all ages= $N1/A1$; ^Cproportion of uncomplicated malaria suspected cases tested for children under five years= $N2/A2$; ^Dproportion of uncomplicated malaria in pregnant suspected tested= $N3/A3$.

Treat

The antimalarial treatment rate for uncomplicated malaria tested positive increased from; 52.3% in 2016 to 78.3% in 2020 for all ages assessed, 57.8% in 2016 to 78.8% for children under five years, and 90.6% in 2016 to 93.8% among pregnant women. Overall anti-malarial treatment rate for confirmed uncompleted malaria cases for the five years assessed stood at 68.9%, 70.5% and 93.8% for all ages, children under five years and pregnant women respectively as illustrated in Table 2.

Table 1. Reported OPD malaria cases not tested but treated as malaria in a rural district in Ghana, 2016 to 2020

Period	All Ages		Children Under 5 years		Pregnant women	
	^{M1} Total OPD malaria cases treated (confirmed +clinical)	^{M2} Uncomplicated Malaria confirmed cases treated with antimalarial (%) ^A	^{M3} Total OPD malaria cases treated (confirmed +clinical)	^{M4} Uncomplicated Malaria confirmed cases treated with antimalarial (%) ^B	^{M5} Total OPD malaria cases treated (confirmed +clinical)	^{M6} Uncomplicated Malaria confirmed cases treated with antimalarial (%) ^C
2016	15,455	8,076 (52.3)	5840	3377 (57.8)	672	609 (90.6)
2017	12,191	7,138 (58.6)	4708	2963 (62.9)	513	499 (97.3)
2018	17,130	10,814 (63.1)	6398	4194 (65.6)	389	370 (95.1)
2019	26,246	20,649 (78.7)	9232	7207 (78.1)	436	401 (92.0)
2020	23,673	18,533 (78.3)	8502	6699 (78.8)	563	535 (95.0)
Total	94,695	65,210 (68.9)	34680	24440 (70.5)	2573	2414 (93.8)

^Aproportion of uncomplicated malaria confirmed cases treated with antimalarial for all age= $M2/M1$; ^Bproportion of uncomplicated malaria confirmed cases treated with antimalarial, children under five years= $M4/M3$; ^Cproportion of uncomplicated malaria in pregnancy confirmed cases treated with antimalarial = $M6/M5$

There has been an upsurge of 11.4% in the treatment of clients with negative test results for uncomplicated malaria from 2017 to 2020.

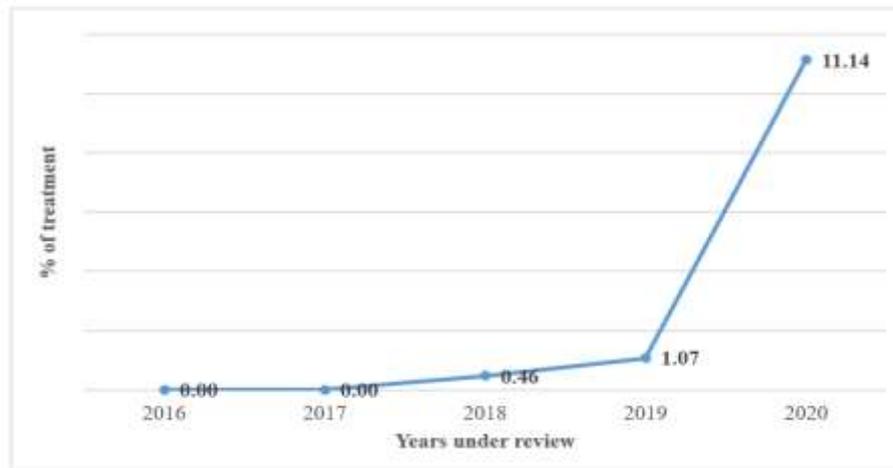


Figure 1. Reported trend of Malaria tested negative but treated as malaria in a rural district in Ghana, 2016 to 2020

Track

The district achieved a 100% reporting rate for DHIMS2 submission of monthly OPD morbidity returns and monthly malaria data returns on anti-malarial for 2017 after submitting only 89.4% of its expected total malaria data returns three years within the implementation of the T3 policy in Ghana. However, there has been a significant increase in malaria data returns since 2018 as shown in Table 3.

Table 2. Reported aggregated malaria returns submission in a rural district in Ghana, 2016 to 2020

Period	Malaria aggregated Report Submission		
	Expected submission	Actual submission	% submission
2016	192	172	89.4
2017	192	192	100
2018	192	164	85.3
2019	192	167	87.0
2020	192	179	93.1
Total	960	873	90.9

Table 4 expounds availability of malaria statistics and its usage level. Overall none of the facilities assessed had readily available and monitored documented malaria statistics as proof for malaria surveillance.

Table 4. Availability and utilization of malaria statistics for surveillance purposes

Facility	Availability of malaria statistics for surveillance readily available		Malaria statistics Monitored?	
	Yes (%)	No (%)	Yes (%)	No (%)
Facility A	0 (0%)	1 (100%)	0 (0%)	1 (100%)
Facility B	0 (0%)	1 (100%)	0 (0%)	1 (100%)
Facility C	0 (0%)	1 (100%)	0 (0%)	1 (100%)
Facility D	0 (0%)	1 (100%)	0 (0%)	1 (100%)
Facility E	0 (0%)	1 (100%)	0 (0%)	1 (100%)
Facility F	0 (0%)	1 (100%)	0 (0%)	1 (100%)
Facility G	0 (0%)	1 (100%)	0 (0%)	1 (100%)
Facility H	0 (0%)	1 (100%)	0 (0%)	1 (100%)
Total	0 (0%)	1 (100%)	0 (0%)	1 (100%)

DISCUSSION

Adherence to Test policy

Preceding the introduction of the T3 policy by WHO in 2012, fever was predominantly equated with malaria and treated as such mostly without testing, especially in endemic countries. Testing of uncomplicated malaria suspected cases before treatment reduces the rate of misdiagnosis among high transmission areas of Africa [10].

In this study, the proportion of uncomplicated malaria suspected cases tested continuously increased over the five years reviewed. Uncomplicated malaria suspected cases tested for all ages increased from 57.8% in 2016 to 79.1% in 2020. This finding in our study contradicts a descriptive secondary data analysis conducted to assess adherence to malaria T3 strategy in Bosomtwi District in the Ashanti Region of Ghana which documented a decline of the overall testing rate of malaria from 84.4% in 2015 to 76.8% in 2016 [7]. This continuous increment of suspected uncomplicated malaria cases tested for all ages identified in this present study could largely be associated with the constant availability and supply of high-quality and inexpensive RDTs to the district from the regional health administration since the inception of the implementation of the T3 in Ghana. It can be observed in this study that, uncomplicated malaria tests done for children under five years increased from 59.1% in 2016 to 94.7% in 2020. Despite being among the vulnerable group for malaria infection, about 80% of suspected malaria cases among children under five years were tested for the years under review in this current study. This present finding is lower compared to findings in similar studies conducted by [7] and [11] which documented about 89.1% and 91.2 % of uncomplicated malaria testing rates respectively in their descriptive cross-sectional studies conducted to assess adherence to WHO T3. The malaria rate among pregnant women has been constantly encouraging, recording more than 90% testing rate consecutively in all years reviewed. This achievement could be linked to the fact that pregnant women are among the most vulnerable group and as part of the documented guidelines for their well-being, no stone was left unturned to get them tested when they present with fever at the health facilities. Among all the suspected uncomplicated malaria cases recorded among pregnant women for the years under review, 97.1% were tested. A similar finding was documented in a retrospective data review conducted somewhere in Ghana [7]. This current study further revealed that 79.1% of all suspected uncomplicated malaria cases reported for the years under review were tested before commencing antimalarial treatment. A similar result was documented in a retrospective data review conducted in Kenya which recorded about 72% malaria testing rate among all ages surveyed [3]. The overall malaria testing rate realized in this present study further conforms to the finding recorded in a mixed-method study conducted in selected countries in sub-Saharan Africa [12]. However, the malaria testing rate for all ages in our current study was lower compared to the result (100%) recorded in the Jirapa district but was higher than the testing rate (56%) ascertained in the West Mamprusi district as stated in a study conducted in selected districts to assess the implementation of the Test, Treat and Track policy for malaria control [8]. A cross-sectional study carried out to assess clinicians' adherence to implementation of the Test, Treat and Track strategy for malaria control in Ghana documented a 58.5% overall testing rate which is lower than the testing rate revealed in this current study [13].

The present study revealed workload, inadequate staff and time constraints as reasons for not adhering fully to the Test policy in the various health facilities. All facilities assessed, however, confirmed the consistent availability of adequate RDTs for adhering to the test policy. This reason gathered in this present study is not in line with another study conducted elsewhere which documented RDT stock-out and non-availability of the laboratory as reasons for health care providers not adhering to the test policy [11].

Adherence to Treat policy

The second dimension in the T3 policy implementation is the "Treat" which mandates Prescribers to treat every confirmed uncomplicated malaria case with a quality-assured antimalarial medicine. Prompt and appropriate treatment of uncomplicated malaria is critical to preventing progression to severe disease, as well as reducing the overall parasite reservoir in a community. WHO recommends ACTs as the first-line treatment for uncomplicated malaria cases caused by *P. falciparum*.

The present study depicts a continuous decrease of non-adherence to the "Test" and "Treat" policy especially among all ages and children under five years. This confirms the assertion made by [7] that a decrease in presumptive treatment inversely increases adherence to the "Treat" policy. Though the decrease is a good indication of gradual adherence to the "Treat" policy, it is alarming to observe that consecutively more than 20% of suspected uncomplicated malaria cases reported for the said age categories were treated with antimalarial without testing for the years reviewed. The alarming presumptive treatment identified in this study could be as a result of workload on the part of Prescribers. Non-adherence to the "Test" and "Treat" policy was quite low (less than 10%) per the data reviewed about pregnant women for the years under review. As discussed under the "Test" policy above, pregnant women are among the vulnerable groups for malaria transmission. This reason notably warranted the high (more than 90%) proportion of adherence to testing before treatment.

In this current study, the non-adherence to the "Treat" policy among all ages for the period under review stood at 31.1%. Our finding is relatively lower compared to a study conducted in selected districts in Ghana which documented that about 45% of surveyed clients were treated without being tested [8]. The overall treatment adherence rate revealed in this study conforms to a cross-sectional study conducted in Kenya to assess T3 adherence which opined that about 30% of malaria cases assessed were treated based on clinical judgement [3]. A study in Ghana reported that 52.0% of fever cases reported were treated with ACT based on clinical judgement. This finding by [13] is higher than the rates revealed in this present study.

Ghana Health Service in its quest to improve the malaria testing rate ordered its facilities to test all clients who present with a fever above the normal body temperature at the vitals section using RDT before clients are ushered to the consulting room. They further urged Prescribers to refer all suspected uncomplicated malaria cases to the laboratory if available or use RDT for testing. Out of the eight facilities used in this study, only three are equipped with laboratories thus most of the uncomplicated malaria cases tested are done using RDTs. Despite this eminent policy, most Prescribers normally ignore the negative test results especially with RDT and treat clients with antimalarial ignoring the harm it can cause.

This was evidenced in this present study, where uncomplicated malaria cases tested negative but treated with antimalarial increased from 0% to 11% for the years under review. This is comparably lower than a study conducted in Ghana to assess T3 policy which documented that about 29% of cases for all age groups, were treated with antimalarial even though their malaria test results were negative [13]. This current finding conforms to a cross-sectional study conducted in selected sub-Saharan African countries which reported that 10% of clients with uncomplicated malaria had negative results yet they were prescribed antimalarial drugs [12].

Adherence to Track policy

The third dimension in the T3 policy implementation is the “Track”. The WHO mandates malaria-endemic areas to improve surveillance for malaria morbidities and mortalities. Malaria data management becomes of much essence in the tracking of malaria cases for an effective decision on measures and policies to reduce the public health menace born out of malaria infection. In this study, tracking of malaria data for surveillance purposes and subsequent decision making was observed under two main categories; aggregated malaria report transmission and use of information realized from such data to inform the decision on malaria control in the district.

Our study shows that all aggregated malaria reports transmitted into the DHIMS2 database were below the expected 100% score except in 2017. However, there was a recurrent increase in the proportion of submission of the said aggregated malaria reports from 85.3% in 2018 to 93.1% in 2020. This upsurge realized in this study confirms the outcome documented by another study conducted in Kenya which reported an increase from 89% to 95% in facilities’ aggregated malaria reporting rate over their study period [3]. This consistent increase was attributed to the periodic Onsite Training and Supportive Supervision (OTSS) planned and implemented quarterly by the District Health Directorate which is aimed at giving the needed onsite support to health service personnel about malaria case management and malaria data management. The overall aggregated malaria reports submission rate revealed in this present study was 90.9%. This is below the recommended figure of 100% by WHO. This underachievement of malaria report submission could be linked to the erratic report submission by a private-own health facility as a result of staff redundancy born out of low patronage of the facility.

Analysis of service data goes a long way to inform policymakers and local health managers on proper allocation and use of the ever scarce resources to make the needed impact. This current study revealed the non-existence of malaria statistics which is readily accessible to enhance immediate interpretation and monitoring of malaria cases and deaths to inform a decision on interventions in all eight health facilities assessed. However, upon request of malaria statistics showing a trend of cases and deaths, all eight facilities confirmed having such surveillance write-up incorporated in their half and yearly performance reports for the years under study. Surprisingly, in all facilities assessed, the said malaria statistics were only filed or archived and ready to be retrieved upon request. This revelation confirms a documented finding in a cross-sectional data analysis conducted in the Bosomtwe district in Ghana. In their study, they emphasized that there was no malaria monitoring chart readily available to track malaria trends even though malaria cases and deaths were duly reported [7].

Limitations

This study assessed retrospective secondary data entered into the DHIMS2 database to ascertain the WHO T3 adherence thus, data inconsistencies could affect the overall analysis. Additionally, there was scarce literature on the assessment of WHO T3 using secondary data, hence there was little comparison with other studies done.

Strength

This study reveals a broader view of how malaria data are not utilized to inform decision making at the local level. This we believe will add up to other literature on malaria data utilization to inform policy and interventions to curb non-usage of reported malaria data.

Conclusions

The adherence to the test policy was consistently encouraging especially among children under five years and pregnant women. However, measures should be outlined to discourage presumptuous diagnosis of suspected malaria cases. Compliance with the treat policy is conspicuously low with about a quarter of clients treated presumptuously. The adherence to the track policy was very poor resulting in low malaria surveillance practices.

Recommendation

- The District Health Management Team should lobby for more Prescribers from the Regional Health Directorate to augment existing staff to aid in workload reduction.
- The District Health Management Team should strengthen the existing practices which mandate all clients with a fever above the normal cut-off point to be tested for malaria using RDT before meeting the prescriber.
- The District Health Management Team should prioritize orientation on malaria case management to build staff capacity on the T3 policy.
- The District Health Management Team should assist the lower level in prioritizing malaria data reporting and usage to improve tracking of malaria activities to enhance surveillance of malaria in the district.

Ethics approval and consent to participate

Permission was sought from the District Health Management Team and an approval letter was issued to commence the study. The Approval letter was used to seek the concern of all eight facilities assessed.

List of abbreviations

WHO	-	World Health Organization
DHIMS2	-	District Health Information System 2
OPD	-	Out Patient Department
ACT	-	Artemisinin-based Combination Therapy
CHPS	-	Community-based Health Planning and Services
RDT	-	Rapid Diagnostic Test
OTSS	-	Onsite Training and Supportive Supervision

Data Availability

The data used for this study will be available upon request.

Conflicts of Interest

The authors declare no competing interest.

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The authors had no external funding.

Authors' contributions

RBN, DN, NAA, SA and SAD conceived the study, RBN, JAB, GLN and DN performed the data analysis. RBN, SA, JAB and RA drafted the methodology section. RBN, JAB, SA, NAA and DN reviewed the literature. RBN, DN, SAD, JAB, GLN and RA draft the initial manuscript. All authors reviewed and approved the final version of the manuscript.

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