

Comparative assessment, awareness and perception of community pharmacists on use of malaria rapid diagnostic test in Lagos state

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ABSTRACT

Background: Presumptive treatment of malaria has led to over diagnosis and over use of antimalarial leading to development of resistance to antimalarial medications. The gold standard for the detection of malaria is microscopic examination. However, the development of RDTs made it possible to get reliable diagnostic testing at all times where previously only clinical diagnosis was available. Method: A cross sectional study which involved 223 Patients and 321 Community Pharmacists in Lagos state, a south western part of Nigeria. Patients, who presented to the Pharmacy with symptoms such as chills, loss of appetite and other symptoms suggestive of malaria were recruited, and tested using RDT kit, and laboratory microscopic evaluation. An open and closed ended administered Questionnaires was used to assess the awareness and perception of Pharmacists on the use of RDT. Results: RDT had a sensitivity of 14.29% and a specificity of 100%. The negative predictive value gotten from the study was 11.33% and a positive predictive value of 100%. The Community Pharmacists indicated high awareness, and were also of the opinion that RDTs were unreliable. Conclusion: From this study, it was shown that RDT kit is not an efficient diagnostic tool for detecting malaria, as the result obtained showed low sensitivity as compared to microscopy. The study also explains why, community Pharmacists are aware of the use of RDT, but lack the willingness to use it. Hence, microscopy still remains a better and more reliable tool for detecting presence of malaria parasite.

1. Introduction

In 2020, nearly half of the world's population was at risk of malaria. However, some population groups, are at a far higher risk of contracting malaria and suffering severe sickness. Infants, children under the age of five, pregnant women, HIV/AIDS patients, and those with low immunity who go to locations where malaria is prevalent.^[1]

According to the most recent global malaria data, there were 241 million malaria cases in 2020, up from 227 million cases in 2019. In 2020, about 627000 fatalities were registered, representing a 69000 rise in the death rate over

the previous year. ^{[1].} The worldwide malaria load has consistently been high in the African region. In 2020, the region accounted for about 95% of all malaria cases, with 96 percent of malaria-related deaths. In the Region, children under the age of five years account for about 80% of all malaria deaths, with Nigeria accounting for 31.9 percent of all malaria deaths worldwide.^[1]

The gold standard for the detection of malaria is microscopic examination^[2] but microscopy has so many limitations which includes the need for skilled professionals to operate appropriately especially in rural areas where the transmission is more, including irregular supply of reagents that will be used for staining, which may not be readily available in endemic countries ^{[3].} The development of rapid diagnostic test (RDT) made it possible to get reliable diagnostic testing at all times where previously only clinical diagnosis was available ^[4] The RDT kit's simplicity of use, as well as its ability to generate results in the shortest amount of time possible, are some of its advantages over microscopy^[5], In addition to detecting *P.Falciparum's* specific histidine-rich protein 2 (HRP-2^{),[6]}

Private retail Pharmacies play a major role in promoting access to basic health services in sub- Saharan Africa as they are the most accessible health facility for the management of commonly occurring diseases ^[7,8,9,10]. This is evident in countries such as Ghana, South-Africa, as well as Nigeria.^[8,9] In Nigeria, about 60% of People seek treatment in the private health sector which consists of community Pharmacy and patent medicine dealers^[11]. To ensure rational use of antimalarial in community Pharmacies, introduction of RDT will make it easier for dispensers in community Pharmacies to give a more definite diagnosis and therefore treat confirmed cases of malaria. Patients would also benefit by saving cost and reduction in waiting time as opposed to visiting a public health facility, which is an important value the Pharmacists, adds in improving the health of clients through the use of RDT^[12]. The objectives of this study were to access the awareness and perception of community Pharmacists in Lagos state on the use of malaria rapid diagnostic test, as well as to compare the efficacy of RDTs and microscopy in the detection of malaria parasite.

2. Method

The study was a cross-sectional survey among community Pharmacies in Lagos State (6.5227'N, 3.6218'E), which is located in the south-western part of Nigeria. Two hundred and twenty-three persons were recruited to participate in this research for the comparative assessment of rapid diagnostic test kit and microscopic evaluation of malaria parasite. None of the Patients used in this research had, used any antimalarial at least 3 weeks before the test was done. Samples were obtained from patients who randomly walk into the community pharmacy to purchase antimalarial as a result of symptoms they are experiencing such as fever, chills, vomiting, and body pain.

2.1 Rapid Diagnostic Test

SDBioline by Codix brand of RDT was used in conducting the tests. Instructions available in the kit were adopted in carrying out this Test. The RDT cassette was well labelled with the patients name and number assigned according to the label, the patient's blood sample was collected and with the capillary pipette provided, whole blood was collected up to the black line on the pipette, this was transferred into the round specimen well, 4 drops of assay diluent was dispensed into the specimen well. The result was read after 25 minutes.

RDT KIT – SDBioline Manufacturer : Codix Pharma Limited Production date : 11/2018 Expiry Date ; 10/2021

2.2 Microscopic Evaluation

Using the same patients, who were tested with RDT kit, a pipette was used to collect the blood sample which was dropped on a greaseless slide and a drop of the finger pricked blood was dropped on a greaseless slide to prepare a thick blood film, stained with Giemsa stain and left to dry, to be examined under a microscope using x 100 immersion oil.

Two independent laboratory scientists each blinded to the reading of each other were used to score the thick film as either positive or negative. Further steps was to be taken if there were any disagreements with results viewed by the scientist

The Sensitivity, specificity, Negative predictive value (NPV) and Positive predictive value (PPV) were calculated respectively for both RDT and Microscopy.

Formula used in determining specificity, sensitivity and NPV are shown below (Equation 1-4)

Sensitivity = $\frac{TP}{TP + FN}$ Equation 1	
Specificity = $\frac{TN}{TN + FP}$	Equation 2
Positive Predictive value (PPV) $=\frac{TP}{TP+FP}$.Equation 3
Negative predictive Value (NPV) $=\frac{TN}{TN+FP}$	Equation 4
WHERE;	

- i. TP = Number of true positives
- ii. FN = Number of false negatives
- iii. FP = Number of false negatives
- iv. TN = Number of true negatives

Assessment of Awareness and Perception Among Community Pharmacists

Community Pharmacists, who are registered and licensed to practice by the Pharmacists council of Nigeria, were recruited for this survey. Questionnaires were distributed to 321 community Pharmacists to assess their awareness and perception on the use of malaria RDT. 137 Male Pharmacists and 184 Female Pharmacists were recruited for this study. With their years of Practice ranging from 1 to >10 years.

2.4 Statistical analysis

Paired T-test was used for this study to compare the means of rapid diagnostic test kits and microscopic tests and the hypothesis was stated based on the result that was obtained.

Sensitivity, specificity, Negative and Positive predictive values were calculated using the appropriate formula

Chi-square (X2) compares the categorical variable, which was used in checking the association between community pharmacist's perception and the use of RDTs

2.5 Inclusion Criteria: This involved patients would had a temperature above 37.5°C at the point of recruitment or who has had a fever within 24 hours of recruitment. Also included are patients who had more than one symptom which included fever, chills, headache, and abdominal discomfort. Patients who are not on any malaria treatment and Community Pharmacists who use malaria rapid diagnostic test kit in their practice for point of care test.

2.6 Exclusion Criteria: Patients with either confirmed severe or chronic malaria or with sepsis as concomitant infection Community pharmacists who do not use rapid diagnostic test kits.

2.7 Ethical Approval

Ethical approval was sought and obtained from the Health Research and Ethics Committee, Lagos university teaching hospital (HREC, LUTH), Nigeria. Approval number is (ADM/DCST/HREC/APP/3252)

1. Results

Two hundred and twenty-three Patients who visited the Pharmacy on account of fever, headaches, and bodily discomfort were tested using thick-film microscopy and RDT, and the results were compared to assess the specificity and sensitivity. Microscopy yielded a positive result in 200 patients (89.7%), while RDT yielded a positive result in 30 patients (13.5%). As may be seen in **Table 2.** RDT exhibited an overall sensitivity of 14.29 %, with a specificity of 100 %, a positive predictive value of 100 %, and a negative predictive value of 11.33 %. Microscopy, on the other hand, recorded a 100% for sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Microscopy, also revealed a 94.5 % overall prevalence of malaria, which was much higher than the RDT result (13.4 percent). RDT sensitivity increased considerably, with an increase in *P. falciparum*, which was the parasite detected in all positive cases. Chi square analysis showed significance at P<0.05.

Age (years)	Female (N)	Percent (%)	Male (N)	Percent (%)
1-6	12	6.72	8	3.59
7-12	30	13.45	20	8.96
13-18	13	5.83	22	22.42
Above 19	68	30.49	50	22.42
Total	123		100	

Table 1: Age and Sex Distribution of Study Population for the Microscopy and RDT Evaluation

	Positive	(N %)	Negative	(N %)	Total	(N %)
Microscopy	200	89.7	23	10.3	223	100
RDT	30	13.5	193	86.5	223	100

 Table 2: Comparison Between Microscopic Tests and RDT Results

 Table 3: Assessment on Awareness of Community Pharmacists on RDT

	Frequency	Percent (%)
Ever heard about RDT kit for Malaria		
	82	25.55
Rarely	39	12.15
Sometimes	64	19.94
Often	33	10.28
Always	103	32.09
Total	321	100
Have you used RDT kit for malaria test		
Never	104	32.40
Rarely	39	12.15
Sometimes	91	28.35
Often	48	14.95
Always	39	12.15
Total	321	100
What Brand of RDT	57	33.5
	65	38.2
GREG	48	28.2
SD BIOLINE	170	100
SD, GREG		
Total		

	Frequency	y Percent (%)
Was it easy to use		
Very difficult	13	5.99
Difficult	25	11.52
Neutral	34	15.67
Easy	91	11.94
Very easy	54	24.88
Total	217	100
Is it time efficient		
Never	19	8.76
Rarely	52	23.96
Sometimes	28	12.90
Often	52	23.96
Always	66	30.41
Total	217	100
Is it convenient to use		
Never	12	5.53
Rarely	32	14.75
Sometimes	33	15.21
Often	67	30.88
Always	73	33.64
Total	217	100
Is it comfortable for the Patient		
Rarely	51	20.99
Sometimes	40	16.46
Often	51	20.99
Always	101	41.56
Total	243	100
Do you think RDT are reliable for malaria to	est	
No	206	64.17
Yes	115	35.83
Total	321	100
Would you recommend the use of malaria R	DT	
No	121	37.69
	200	62.31
Yes	200	02.51

 Table 4 : Assessment of Perception of Community Pharmacists on the Use of RDT

4. Discussion

The results from this study shows the sensitivity of the RDT kit to the malaria parasite, and also measures the awareness and perception of the community Pharmacists on the reliability of the kit. The recommended sensitivity, for malaria RDTS as stated by the world health Organization (WHO) is 95%^[13]. However, the sensitivity gotten from this study was 14.29%, which indicates a low sensitivity when compared with the standard recommendation. This could be disastrous, as most cases of malaria could be left untreated in locations where RDT is their only source of reliable test. Microscopy was positive in 200 (89.7%) and negative in 23(10.3%) patients, while RDT was positive in 30(13.5%) and negative in 193 (86.5%) patients.

Certain studies have shown that parasite density play a role in the sensitivity of RDT^[14]. A study reported a sensitivity of 88.8% sensitivity for *P.falciparum*, which increased to 94.3% and 99.3% at parasite densities above 100 and 1000/ul respectively [14]. In a study carried out in Gusau, Nigeria, a sensitivity of 9.09% was reported for RDT, while a specificity of 92.06% was reported. Microscopy also gave more positive result (46.61%), when compared to RDT (8.47%)^[15]. Certain studies have shown relatively high sensitivity for both RDT and microscopy. Studies reported in Countries, such as Thailand, Zanzibar and Zambia, have reported good sensitivities [16,17]. In a study carried out in Uganda, RDT showed a sensitivity of 61.6%, the study also emphasized the reduction in waiting time experienced by these patients, which is an advantage to encourage its use in endemic regions^[18].

A specificity of 100% was recorded by this study for both RDT and microscopy, which was similar to that recorded in a study carried out in Cameroon. ^[18] But higher than that which was done in Ijebu-Ode, a western part of Nigeria in which a specificity of 87.1% was recorded. ^[19].

Though, the specificity for RDT and microscopy were similar, the advantage of microscopy over RDT is its ability to quantify Parasitaemia. This study showed no false positive result for RDT. Hence, the absence of a false positive showed that the study is a good one. Thus, accurate diagnosis of malaria is the basis for disease control and delay in spread of antimalarial drug resistance.

From the results measuring the awareness and perception of community Pharmacists on the use of RDT, it was observed that, majority of community Pharmacists are aware of the RDT kits, and the popular brands that have been used from this study were SDBioline by Codix and Dr Greg. However, they do not regard it as a good diagnostic test kit. They were of the opinion that most times, RDTs gives negative results even when the symptoms of the patient is evident of malaria, thus, they go ahead and treat the patient with antimalaria disregarding the result from the RDT. However, a few Pharmacists said, they would send patients for further tests, while some were of the opinion that RDT were very unreliable and didn't show willingness to use.

Obi *et al*, 2019^[20], studied the perception of RDT among health workers, and reported that there was a poor perception of RDTs which led to prescribing of medications despite a negative result^[20] Prescriber perception of malaria RDT was found to be a substantial predictor of antimalaria prescriptions for patients with negative results when compared to those with favorable perception. This is comparable to the findings of this study, in which the majority of community pharmacists would still treat a patient for malaria , despite obtaining a negative RDT result.

5. Conclusion

A reluctance to shift from a presumptive therapy, which could be as a result of huge negative results obtained from RDT. Although, RDTs are simple and easy to use, they should not be regarded as a first line diagnostic tool for detecting malaria. The study also explains why community Pharmacists, are aware of the use of RDT, but lack the willingness to use it. Hence, microscopy still remains a better and more reliable tool for detecting presence of malaria parasite.

6. Recommendation

It is recommended that the marketers or distributors of RDT kits should maintain the appropriate storage temperature as recommended by the manufacturers as this may lower the incidence of low sensitivity reported frequently from its use.

In addition, adequate and proper quality control measures should be put in place to ensure the RDT is in good condition prior to use for diagnostic test, as well as regular validation.

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