Prescription of Anti-Malarial Drugs to Patients with Negative Malarial Rapid Diagnostic Test (mRDT) Result by Health Care Workers in Kano, Nigeria

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Abstract

The World Health Organization and the National Malaria Treatment Guideline recommend parasite-based malaria diagnosis by light microscopy or Rapid Diagnostic Tests (RDTs). Positive result is the only indication for anti-malarial treatment whereas negative cases should be reassessed for other common causes of fever. However, contrary to this and for reasons not to be cleared, health workers (HWs) still prescribe antimalarial to patients with negative malarial rapid diagnostic test (mRDT) results of antimalarial drug resistance. To explore the possible reasons for this practice, we assessed compliance with the guidelines among healthcare workers and identified factors associated with the prescription of antimalarial drugs to patients with negative mRDT results. Data on socio-demographic characteristics, years of professional experience, choice, and compliance to mRDT results, and management of fever were generated using a questionnaire. We tested associations between these variables and the prescription of antimalarial drugs to patients with negative mRDT results using Chi-square at P< 0.05 adopted as the level of significance. The study revealed that higher proportion of doctors and nurses (79.4% and 52.5%, p 0.001) and HWs with less than five years of clinical practice (60.8%, P<0.024), prescribed antimalarial to patients with negative mRDT results. Our results demonstrated a significant lack of adherence to National health policy on the treatment of malaria among young healthcare workers. The practice would presumably promote drug overuse and accelerate the emergency visit of antimalarial drug resistance. We recommend the supervision and guidance of junior and early career healthcare workers by their seniors to ensure compliance with test results and good healthcare practices.

INTRODUCTION

Malaria, though preventable and treatable, continues to cause unacceptably high levels of disease and death throughout the world (WHO, 2021; WHO, 2022). According to the World Health Organization (WHO), globally, there were an estimated 247 million malaria cases in 2021 in 84 malaria-endemic countries (WHO, 2021; WHO, 2022). Between 2019 and 2021, an estimated additional 13.4 million cases were attributed to disruptions during the COVID-19 pandemic. Twenty-nine countries accounted for 96% of the global malaria cases, and four countries, Nigeria (27%), the Democratic Republic of the Congo (12%), Uganda (5%) and Mozambique (4%) accounted for almost half of all cases (WHO, 2022). The national malaria treatment guideline in the malaria-endemic countries of the WHO African region recommended parasite-based malaria diagnosis by light microscopy or RDTs (FMOH, 2020). Positive result is the only indication for anti-malarial treatment whereas negative cases should be reassessed for other common causes of fever.

In Nigeria, the case management of malaria is hinged on two important components, these are testing using microscopy and RDTs for parasitological confirmation and prompt treatment using Artemisinin-based Combination Therapy (ACT) for uncomplicated malaria (Anjorin *et al.*, 2023). With the availability of parasite-antigen-based rapid test kits, it is now imperative that cases of suspected malaria should have parasitological confirmation before treatment. This allows for targeted treatment, accurate estimation of true malaria cases, and rational use of antimalarial drugs. However, it has been demonstrated that some patients receive malaria treatment without parasitological confirmation (FMOH, 2020).

Between 2010 and 2020, manufacturers sold 3.1 billion rapid diagnostic tests (RDTs) for malaria, with sub-Saharan African nations accounting for about 81% of total sales (Goodman et al., 2023). National malaria programs (NMPs) dispersed 2.2 billion RDTs during the same period, with 88% of those doses going to sub-Saharan Africa (WHO, 2021). Despite the wide availability of mRDT in African countries, many studies (Bilial *et al.*, 2015., Singlovic *et al.*, 2016., Zongo *et al.*, 2016, Rakotonandrasana *et al.*, 2018., Bruxvoot *et al.*, 2013) have shown that healthcare workers continue to prescribe anti-malarial drugs despite negative results. A study conducted in Enugu state Nigeria reported that 32% of the health workers prescribe ACT to their patients despite negative mRDT results (Mokulu *et al.*, 2018). Similar practice was reported in Ebony State Nigeria, which showed that up to 37.6% of healthcare facility workers had a poor perception of mRDT, and 50.8% prescribed anti-malarial drugs to patients with negative mRDT results. The authors further reported that the likelihood of prescribing ACTs to patients with negative mRDT results was higher among healthcare workers in public health facilities (95%) than those in private (Obi *et al.*, 2019). Another study in Oyo state Nigeria reported that 26.0% of the HW prescribed antimalarial to mRDT-negative patients, a lower rate compared to previous studies (Akinyode *et al.*, 2018).

Nevertheless, there is a paucity of data to assess the knowledge and awareness of healthcare workers on Artemisinin drug resistance and the factors associated with noncompliance with results of RDT as recommended by WHO and the national guideline on malaria diagnosis and treatment. We therefore conducting this study with a view to closing gap by assessing the compliance of health care workers in Kano state to mRDT results.

MATERIALS AND METHODS

Study area

The study was conducted across four general hospitals in Kano state. These are Murtala Muhammad Specialist Hospital ($11^0 59' 56''$N $8^0 31' 19''$E), Waziri Gidado ($12^0 00' 7.9''$N $8^0 35' 3.1''$E), Sir Sunusi ($8^0 31' 0.19''$E $12^0 00' 0.43''$N), and Wudil General Hospitals ($11^0 8.0,'93''$N $8^0 84' 34''$ E). Kano is one of the seven states that make up the North-West geopolitical zone of Nigeria. It shares borders with Katsina to the Northwest, Jigawa to the Northeast, Bauchi to the Southeast, and Kaduna to the Southwest. The state capital is Kano. Kano State lies at latitude 11° 30' North and longitude 8° 30' East. Kano state is one of the most populous states in Nigeria, with a population of approximately 15.9 million people according to the 2021 projection by the National Population Commission of Nigeria. Accordingly, the male population of Kano state was estimated to be 51.4%, while the female population was estimated to be 48.6% as of 2021. The median age of Kano state is approximately 18 years old, with about 68% of the population being under the age of 30 (NPC, 2018). The major ethnic group is the Hausa-Fulani, accounting for about 90% of the population, with other minority ethnic groups including Kanuri, Tiv, Igbo, Yoruba, and others. Islam is the predominant religion in Kano state, with over 95% of the population being Muslims. Christianity and traditional religions are also practiced by small minority groups (NIS, 2020). According to the 2018 Nigeria Health Facility Census, there are 2,818 health facilities in Kano state. These facilities include hospitals, health centres, clinics, dispensaries, and maternity homes. The state maternal mortality is 576/100,000 (NDHIS 2013) and the child mortality rate is 103/1000 live births (FMOH, 2023). Within Nigeria, Northwest has the highest prevalence of malaria diagnosed by RDT (51.6%) in the country. Within the northwest, Kano state had a prevalence of 54.0% by diagnosis RDT, the fourth in the zone after Kebbi, Zamfara, and Jigawa state consecutively (NMIS, 2021).

Malaria treatment is free for children below 5 years and pregnant women. The treatment guideline indicates ACT as the first drug of choice for the treatment of uncomplicated malaria. Preventive measures such as long-lasting insecticidal nets and indoor residual spray are deployed in the state. The State Malaria Elimination Program is responsible for malaria control activities. Similarly, Local Government Areas (LGAs) Roll Back Malaria focal persons are responsible for their respective LGAs (Lourenco *et al.*, 2019; Visa *et al.*, 2013)

Ethical Approval

Ethical approval was obtained from the Research and Ethical Committee of the Kano State Ministry of Health before the commencement of the study (References number: NHREC/17/03/2018, date: - 19th April 2023). An informed consent was sought and signed. The confidentiality and anonymity of all information were guaranteed.

Study design and population

The study was a descriptive, quantitative and cross-sectional conducted from 30th April to 31st August 2023 at Murtala Muhammad Specialist Hospital, Waziri Gidado, Sir Sunusi, and Wudil General Hospitals Kano. The study population comprised Doctors, Nurses, Midwives, Community Health officers (CHOs) and Community Health Extension Workers (CHEW) working in these hospitals whose job description in the facility included diagnosis

and treatment of malaria. Among these health workers, those who were not available at the time of the study were excluded.

Sample size estimation:
A minimum sample size of 381, required was calculated using the formula.

$$n = \frac{1.96^2 P(1-P)}{d^2}$$

Where the proportion of health workers prescribing antimalarial to mRDT-negative patients of (p) of 26% (Akinyode *et al.*, 2018) and a level of precision (d) of 5%.

Sampling procedure
We selected the health workers using a multistage sampling technique. In the first stage, four (4) of the LGAs in Kano state were selected by simple random sampling. In the second stage, from each of the LGAs one General hospital was selected using simple random sampling. In the third stage, we selected health workers from the selected facilities by proportional allocation. The sample size was allotted to each of the facilities proportionately to the number of health workers in the facility. Health workers were then selected from the list of the health workers in each facility by balloting to fill the quota allotted to the facility.

Data collection
A questionnaire was designed and validated by experts for correctness and suitability to address the objectives of the study. A pretest was conducted among health workers in an LGA that was not selected for the study. The questionnaires were administered by a nurse in each hospital and the interview was done in a secluded area of the clinic.

Data analysis
Data errors related to inconsistency were checked and corrected during data cleaning. The data was entered and analysed using IBM SPSS version 25.0.1 Windows. The main outcome of this study was prescribing antimalarial medicine to mRDT-negative patients. The independent variables included age, professional cadre, duration of professional practice of health workers, and health workers knowledge of causes of resistance. Association between the prescription of antimalarial medicine to mRDT-negative patients and each independent variable was assessed using the Chi-square test at a p-value of 0.05 and predictors of antimalarial use in mRDT-negative patients were ascertained.

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RESULTS
Socio-demographic Characteristics of respondents

Data was collected from 340 participants, 210 females (61.8%) and 130 males (38.2%), who volunteered to participate in the study. The mean age of health workers was 31 ± 8.0 years of age. And mean years of professional practice was 7 ± 6.6, and the Majority (69.4%) are Hausa by tribe (Table 1).

Table 1: Socio-demographic Characteristics of respondents

Variables	Frequency	Percentage
Years of professional practice		
≤ 5	189	55.6
6 – 10	101	29.7
11 – 15	20	5.9
16 – 20	15	4.4
>20	15	4.4
Mean ± SD	7 ± 6.6	
Age group		
≤20	08	2.4
21 – 30	203	59.7
31 – 40	90	26.5
41 – 50	24	7.1
>50	15	4.4
Mean ± SD	31 ± 8.0	
Gender		
Female	210	61.8
Male	130	38.2
Tribe		
Yoruba	39	11.5
Hausa	236	69.4
Igbo	06	1.8
Fulani	27	7.9
Others (Edo, Nupe, Zuru, Ebira)	32	9.4
Marital status		
Divorced	1	0.3
Married	187	55.0
Single	152	44.7

Test preference, compliance with malarial rapid diagnostic test results, and awareness of antimalarial drug resistance

More than half (52.6%) of the respondents preferred to use mDRT to diagnose malaria, among which 30.6% would not wait for the outcome before prescribing antimalarial drugs. 55.6% of healthcare works prescribed antimalarial medications to patients with negative mDRT results mainly because they suspected the result might not be accurate. 52.9% of these patients come back with a relapsing fever after 3 days of treatment with antimalarial drugs and the majority (65.0%) responded to such situation by retesting and treating in compliance with the test result. 3.5% of healthcare workers are aware of emerging antimalarial drug resistance and the majority (77.9%) suspected at it's as a result of non-compliance to treatment dosage by patients (Table 2).

Table 2: Test preference, compliance with malarial rapid diagnostic test results, and awareness of antimalarial drug resistance

Response	Frequency	Percentage
Respondent requests for mRDT		
No	38	11.2
Yes	302	88.8
Respondent waits for mRDT result before prescribing antimalarial drugs		
No	104	30.6
Yes	236	69.4
Reasons for not waiting		*(multiple responses)*
No time	31	9.1
Absolutely sure of the diagnosis	65	19.1
Lack of differential diagnosis	27	7.9
Fear of wrong diagnosis	38	11.2
Patient's influence	23	6.8
Lack of supervision and guidance	8	2.4
Lack of training on mRDT	20	5.9
Others (Collegue's influence, lack of mRDT strip, preferring microscopy)	5	1.5
Test respondent prefers to request for patients		
Microscopy	161	47.4
mRDT	179	52.6
Respondent often prescribes anti-malarial drugs to patients with negative mRDT		
No	151	44.4
Yes	189	55.6
Reason for prescribing anti-malarial drugs to patients with negative mRDT		*(multiple responses)*
The patient requested for the drug to be prescribed	16	4.7
Respondent trusts his/her clinical judgment	80	23.5
Patient will benefit from the drug even if the test result is negative	66	19.4
Result takes too long	14	4.1
Result may not be accurate	112	32.9
Others (RDT is not a sensitive test, species may not be Plasmodium falciparum)	06	1.8
Some of the respondent's patients come back with the same complaints after 3 days of treatment with anti-malarial drugs		
No	160	47.1
Yes	180	52.9
Method of treatment given to such patients		*(multiple responses)*
Respondent tests for malaria parasite again and treat	221	65.0
Consider another diagnosis	134	39.4
Treat with other brands of anti-malaria	150	55.9
Refer patient to another health facility	19	5.6
Respondent is aware of emerging anti-malarial resistance		
Never heard of it	46	13.5
No	44	12.9
Yes	250	73.5
Possible factors that can contribute to anti-malarial drug resistance		*(multiple responses)*
Non-compliance to treatment dosage	265	77.9
Poor adherence to treatment guidelines	177	52.1
Parasite mutation	66	19.4
Parasite load	46	13.5
Indiscriminate use of anti-malarial drugs	156	45.9
Fake drugs	174	51.2

Association between the request for mRDT, socio-demographic characteristics, and prescription of antimalarial for patients with negative mRDT results.

There is a significant statistical association between a request for mDRT for malaria diagnosis in outpatient and years of professional practice (P<0.007). It also shows a significant association between prescription of antimalarial medication and professional cadre as well as years of professional practice (P<0.001) and P(<0.024). It also demonstrates that younger healthcare workers are more likely to request mRDT for malaria diagnosis (P< 0.001). (Table 3).

Table 3: Association between the request for mRDT, socio-demographic characteristics, and prescription of antimalarial for patients with negative mRDT results.

Variables	Request for mRDT		χ^2	p-value	Prescription of antimalarial for patients with negative mRDT result		χ^2	p-value
	No (%)	Yes (%)			No (%)	Yes (%)		
Professional cadre			1.557	0.669			25.453	**0.001**
CHEW	7 (14.0)	43 (86.0)			32 (64.0)	18 (36.0)		
Doctor	9 (13.2)	59 (86.8)			14 (20.6)	54 (79.4)		
Midwife	0 (0.0)	5 (100.0)			1 (20.0)	4 (80.0)		
Nurse	22 (10.1)	195 (89.9)			103 (47.5)	114 (52.5)		
Years of professional practice			13.990	**0.007**			11.208	**0.024**
≤ 5	17 (90)	172 (91.0)			74 (39.2)	115 (60.8)		
6 – 10	10 (9.9)	91 (90.1)			56 (55.4)	45 (44.6)		
11 – 15	3 (15.0)	17 (85.0)			7 (35.0)	13 (65.0)		
16 – 20	2 (13.3)	13 (86.7)			9 (60.0)	6 (40.0)		
> 20	6 (40.0)	9 (60.0)			11 (73.3)	4 (26.7)		
Age group			23.086	**0.001**			4.067	0.397
≤ 20	1 (12.5)	7 (87.5)			5 (62.5)	3 (37.5)		
21 – 30	16 (7.9)	187 (92.1)			90 (44.3)	113 (55.7)		
31 – 40	8 (8.9)	82 (91.1)			38 (42.2)	52 (57.8)		
41 – 50	7 (29.2)	17 (70.8)			13 (54.2)	11 (45.8)		
>50	6 (40.0)	9 (60.0)			4 (26.7)	11 (733)		

DISCUSSION

The findings from this study demonstrated that most healthcare workers in Kano state (88.8%) request mRDT to diagnose malaria in outpatients, and the majority (52.6%) prefer to request mRDT over microscopy. It also showed that younger healthcare workers are more likely to request for mRDT for malaria diagnosis (P<0.001). This is much higher compared to what was reported from Papua New Guinea where 40.2% of health workers do not request any test before treating malaria, mainly due to the absence of fever at the time of diagnosis (Bell *et al.*, 2017). The study also showed that 30.6% of these healthcare workers do not wait for the result before proceeding to prescribe antimalarial to their patients, mainly because they trusted their clinical judgment (19.1%). This is comparable to a study in Ebonyi state Nigeria, where 19.1% of healthcare workers believe that clinical signs and symptoms are enough to diagnose malaria (Obi *et al.*, 2019). Our study also showed that 55.6% of healthcare workers in Kano state prescribed antimalarial medication to patients with negative mRDT results. The major factor shown to be driving the prescription of antimalarial medication to patients with negative mRDT results was a lack of trust in rapid diagnostic test results (32.9%) seconded by trust in the accuracy of clinical judgment (23.5%). A significant association between prescription of antimalarial medication and professional cadre as well as years of professional practice (P<0.001 and P< 0.024) has been observed. Midwives and doctors with more than 20

years in practice are more likely to prescribe antimalarial drugs to patients with negative mRDT. This may be attributed to a lack of continuous education on up-to-date protocols for managing malaria. This high percentage will lead to excessive use of antimalarial medication which would have health and economic implications as majority of patients pay out of pocket. More importantly, it can contribute to the development of resistance. Findings from another study in Uganda also demonstrate that the limited ability to identify alternative causes of fever was one of the identified drivers of antimalarial prescription to mRDT-negative patients which is contrary to what we found in Kano (Bell *et al.*, 2017). However, lower prevalence has also been reported in some other studies but within and outside Nigeria (Akinyode *et al.*, 2018., Pulford *et al.*, 2016).

A similar study conducted in Oyo state of Nigeria reported that about 24.3% percentage of healthcare workers prescribed antimalarial medication to patients with negative mRDT results. This is similar to another study in the country but among private hospitals, which showed 26.0% on compliance with negative mRDT results (Mokuolu *et al.*, 2016). Another study from Papua New Guinea reported that 23.7% of healthcare workers prescribed antimalarial drugs to patients with negative mRDT results and associated with the most common reason reported was to confirm a clinical diagnosis of malaria and patient request (Pulford *et al.*, 2016). A qualitative study from Uganda reported that only 4.1% of patients diagnosed malaria-negative with mRDT were given antimalarial drugs. This is comparable with what was reported by a study in Burkina Faso which showed that 14.0% of children with negative mRDT and 47.04% of patients with negative microscopy results were prescribed antimalarial medications (Bonko *et al.*, 2019). A study that assessed compliance of community healthcare workers to mRDT results across three malaria-endemic countries in sub-Saharan Africa found that 6.8% of the workers prescribed antimalarial medication to patients with negative mRDT results (Singlovic *et al.*, 2016).

Most of these studies focussed on the patient receiving antimalarial with negative mRDT in this study which focussed on the healthcare workers prescribing antimalarial to patients with mRDT. Like what we obtained in our study, several studies from many parts of the continent reported high prescriptions of antimalarial medication to patients with negative mRDT results by healthcare workers. This can be seen in a study conducted in Mozambique, which reported that antimalarial medication was prescribed to 72.0 % of patients with negative mRDT by healthcare workers. The study also demonstrated variation in the rate of prescription of antimalarial medication between the northern and southern parts, compared to the central region of the country (Salomao *et al.*, 2015). This correlated to a higher rate of what we observed compared to the lower rate reported in Nigeria where our research reported a higher rate compared to the lower rate reported in studies done in the southern part of the country (Obi *et al.*, 2019., Akinyode *et al.*, 2018).

A study that assessed adherence to mRDT results by healthcare workers working at four health facilities in Malawi showed that 58% of patients with a negative mRDT result were treated with an anti-malarial (Chinkhumba *et al.*, 2010), which is similar to what we detected in this study. We also showed that fever persisted for more than three days in 52.9% of patients prescribed antimalarial despite negative mRDT results and in such situations, the majority (65.0%) of healthcare workers retested for malarial using both mRDT and microscopy and treated as appropriate to the results.

Our study similarly discovered that 73.5% of healthcare workers in the state are aware of the emerging antimalarial drug resistance and that the majority (77.9%) tend to associate the

resistance with non-compliance to treatment dosage by patients. Other possible reasons outlined by the healthcare workers included poor adherence to treatment guidelines (52.1%), indiscriminate use of anti-malarial drugs (45.9%), and fake antimalarial medications (51.2%). Doctors and nurses showed more awareness of the emergence of antimalarial resistance as well as healthcare workers aged more than 40 years and above (P< 0.005 and P<0.027).

CONCLUSION

Health worker compliance with mRDT test results is high, however, a large proportion of healthcare workers across Kano state (55.6%) prescribed antimalarial medication to patients with negative mRDT results. The main reason reported to be driving the prescription of antimalarial medication to patients with negative mRDT results was lack of trust in rapid diagnostic test results (32.9%). This can negatively affect the patients and healthcare system by overstretching it beyond its limit.

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