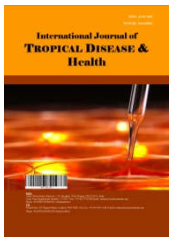

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Malaria Infection and Efficacy of Antimalarials among Persons Patronizing Drugstores for Malaria Treatment in Port Harcourt

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Authors' contributions

This work was carried out in collaboration among all authors. Authors ELAD and AEA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AEA and ELAD managed the analyses of the study. Author EOO managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Monitoring of malaria infection and antimalarial drug efficacy is necessary for effective case management, detection of resistance and control of the disease.
Objective: The aim of this study was to assess malaria infection and the efficacy of antimalarials among persons patronizing drugstores for malaria treatment in Port Harcourt and its environs, Rivers State, Nigeria.
Materials and Methods: Whole blood was randomly collected from individuals visiting 24 drug stores for malaria treatment in three different locations in Port Harcourt and analysed using both microscopy and rapid diagnostic techniques.
Results: The overall prevalence of 22.8% was recorded out of 633 participants for (*P. falciparum*)

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malaria. Infection was highest in Mile IV (Rumueme) 30.8% followed by Rumuosi, 23.1% and the least was D/Line area, 14.5% out of 221 participants per location respectively. The incidence of malaria in the study area was significantly different (X2 = 16.69; p = 0.001). There was no significant difference in the intensity of malaria parasite infection in the study areas. Seven types of drugs were purchased to treat perceived malaria. 177 (26.7%) participants purchased coatem, 187 (28.3%) purchased Lonart. The others were Lumartem 133 (20.1%), P.alaxin 83 (12.5%), Amarla by 19 (2.9%) and artesunate by 57 (8.6%). All the antimalarial were purchased by those that tested positive. The most purchased drug was Lonart 11 (34.37%), Lumartem 25 (36.8%) and Malareich 19 (31.3%) in D/Line, Mile IV and Rumuosi cluster areas respectively. There was a significant difference in the antimalarials purchased. Result of Follow up test shows that only 59.6% returned to be tested and they all tested negative.

Conclusion: Malaria preponderance was high among studied subjects, ACT was topmost among antimalarials regularly purchased by the individuals. Conformity to the use of ACT could be said to be impressive though not yet 100%. People who are treated for malaria should be encouraged to undergo a test after treatment for effective case management and detection of resistance.

Keywords: Malaria infections; antimalarials; efficacy; drugstores.

1. INTRODUCTION

Malaria is an acute febrile illness caused by plasmodium parasites. According to the World malaria report, released by WHO in 2019, there were 228 million cases of malaria in 2018 compared to 231 million cases in 2017. The estimated number of malaria deaths stood at 405 000 in 2018, compared with 416 000 deaths in 2017 [1]. Though this report showed a slight decrease from the previous year in cases and death, Malaria still remain a major public health challenge especially in the African region. In 2018, 6 countries which accounted for more than half of all malaria cases worldwide are all in Africa: Nigeria (25%), the Democratic Republic of the Congo (12%), Uganda (5%) and Côte d'Ivoire, Mozambique and Niger (4% each).

The global malaria control strategy has used Insecticide-treated net (ITN), Indoor residual spraying (IRS) with insecticides and Antimalarial medicines to prevent malaria. Monitoring the efficacy of antimalarial medicines is a key component of malaria control [2]. Routine monitoring of antimalarial drug efficacy is necessary for effective case management and detection of resistance [2]. Artemisinin Combination Therapy (ACTs) has been an integral part of the remarkable recent success in global malaria control, and there is broad consensus that protecting the efficacy of these combination medicines is an urgent priority [2]. WHO recommended artemisinin-based combination therapies (ACTs) as the current first- and second-line treatment for *Plasmodium falciparum* malaria which is the most prevalent in Nigeria.

A visit to the drugstore results in the consumption of all kinds of antimalarial [3]. These drugs might not be the WHO recommended Artemisinin Combination Therapy (ACT). The efficacy of these unprescribed antimalarials is not known. Even where testing is done and the right drug administered, ACT purchased and consumed, tracking is not done [4]. This is observed even in most public health institutions in Nigeria [5]. Efforts aimed at controlling malaria, have employed an integrated management approach. This approach has yielded some positive result, with global incidence falling by 37% and death rate by 60% from the year 2000 [6,7]. In Nigeria, a decrease in the incidence was also observed [8]. To sustain this effort, a new strategy, comprising of a fifteen year road map was developed. This is captured in the Sustainable Development Goals (SDGs).This strategy is aimed at reducing the incidence of malaria and death due to malaria world wide by 90% by the year 2030 [9].

Majority of the people taking antimalarial reside in rural areas of the world [10]. These rural areas do not have good roads to their health centres, equipped laboratories and adequate drugs for the treatment of malaria. Hence, they take medications bought from drug sellers without visiting any professionals. Even in their health care centres, the staffs are not formally trained [11].

Medicine sellers in Nigeria are very important in the treatment of uncomplicated malaria [12] and are found in general stores, drug stores, kiosks and market stalls [13]. They are preferred even when more convenient and less expensive

alternatives exist, such as village health workers [14]. Their levels of education vary and they do not give professional consultation [13]. Majority of them have little or no formal training in pharmacy or medicine, though some may be trained or untrained as medical assistants or as nurses [15]. This has hampered effective implementation of the policy of using ACT as the first line drug for uncomplicated malaria. A policy adopted by Nigeria as far back as the year 2005 [16,17].

Studies on malaria burden and efficacies of antimalarials are key factors in the designing, implementation and monitoring of malaria prevention and control programmes. However in Nigeria, these studies are mostly carried out in the formal health sector [17]. This study is aimed at assessing malaria infection and efficacy of antimalarials among persons patronizing drugstores for malaria treatment in Port Harcourt.

2. MATERIALS AND METHODS

2.1 Study Area

The study was conducted in three areas of Port Harcourt (Rivers State, Nigeria) and its environs. These were D/line, a major business and medium densely populated residential area, Mile IV (Rumueme), a highly densely populated residential area and Rumuosi, a farming community, in a semi-urban setting. All located within 4°55'30" N and 7°0'0"E.

Port Harcourt is a metropolitan city. It is the capital of Rivers State in the south-south geopolitical zone of Nigeria. It lies along the Bonny River and has many creeks. It is host to many major companies, and is the centre of Nigerian economy. Port Harcourt is one of the largest cities in Nigeria with an estimated population of 1, 865, 000 inhabitants [18]. It is found in the forest bet of Nigeria with a lengthy and heavy wet climate. It has a very short dry season and the average temperature is between 25°C and 28°C.

2.2 Study Design

The design was a clustered randomized one.

2.3 Study Population

The participants were individuals reporting to participating drugstores and requesting for antimalarial for treatment of perceived malaria for themselves. Eligibility for the study was based on both inclusion and Exclusion criteria.

2.3.1 Inclusion criteria

People that procured antimalarial to treat alleged malaria for themselves from partaking drugstores in the study area that gave permission to participate in the study.

2.3.2 Exclusion criteria

Individuals who purchase antimalarial for malaria management for others not present.

All those Persons that procured antimalarial for treatment of malaria for themselves from participating drugstores but not inhabitants of the study area were excluded.

Those who purchased antimalarial from participating drugstores but did not give permission to the study were also excluded.

2.4 Sampling Method

Sample size was 663 (221 per cluster). It was determined using the formula by Gaur [19].

Drugstores were randomly selected. 24 (8 per cluster) drugstores whose owners gave written were randomly enrolled for the study. Clients patronizing participating drugstores for antimalarial to treat perceived malaria were approached for oral permission to participate in the study. They were informed that they will be offered a free malaria test before drug administration. If the first test is positive, another free test, a follow up test will be offered after drug treatment. A free glucose test was also offered as incentive to the participants for the follow up test.

Samples were collected in the evening of every other day except Sundays. Two days were chosen for each area in a week and two drugstores randomly chosen for a day. A time convenient in the evening of the day after completion of dosage (Day 4) was chosen for follow up participants.

Names of antimalarial purchased and the phone numbers of those who tested positive before commencement of treatment were documented. This was to remind them of their follow up test. They were informed that information obtained will be confidential.

2.5 Sample Collection

Whole blood samples were collected from participants by venipuncture, using established practice. The samples were put in a clean well labeled sample bottle, containing anticoagulant (EDTA). Rapid diagnostic test (RDT) was conducted immediately. The samples were then put into a box and transported to the laboratory. Thick and thin blood film preparation for Giemsa staining technique was performed on all RDT positive samples for parasite identification and quantification.

2.5.1 Rapid diagnostic test (RDT)

RDT was performed on the samples immediately after collection using a standard RDT kit (Aria, manufactured by CTK Biotech, Inc., San Diego, CA 92121, USA) following standard methods as recommended by the producer.

2.6 Microscopy

Thick and thin blood films were prepared, stained using Giesma staining technique and examined.

2.7 Thick Blood Film Preparation, Staining and Examination

A clean grease- free glass slide was properly labeled with the participants' identification number. To one end of the slide was placed a drop of blood, which was evenly spread to moderate thickness, allowing one to see a print through it. It was then kept horizontally to dry, protected from dust and flies.

The thick blood film was allowed to air dry and transferred to a staining rack. It was then flooded with a freshly prepared Giemsa working solution for 30 minutes.

The slide was flushed with water allowed to dry, and examined with x100 objective of the microscope for the presence of *Plasmodium* parasite and the estimation of parasite density (parasitaemia).

Parasite density was estimated by counting asexual forms of the parasite against 200 WBCs and against 500 WBCs where less than nine (9) parasites were counted. The number of parasite counted divided by the number of WBC's multiplied by 8000 gave the number of parasite per µl of blood.

2.8 Data Analysis and Presentation

The data was analysed using the latest version of Statistical Package for the Social Sciences (SPSS version 22).

3. RESULTS

Out of the 633 participants, 151(22.78%) tested positive for malaria. *P. falciparum* was found to be responsible for all the positive cases.

Mile IV (Rumueme) had the highest infection 68(30.8%) followed by Rumuosi 51(23.1%) and the least was D/Line area, 32 (14.5) out of 221 participants respectively. The incidence of malaria in the study area was significantly different (X^2 = 16.69; p = 0.001) as shown on Table 1.

There was no significant difference in the intensity of malaria parasite infection in the study areas as out of the 151 positive cases, 134 (88.0%) had an intensity level of $\leq$ 1,000 parasites/µl, 16 (10.6%) had 1000-9999 parasites/µl and only 1(0.71%) had an intensity level of $\geq 10,000$ parasites/µl (X^2 = 2.58; P = 0.275) as shown in Table 2.

Seven types of drugs were purchased to treat perceived malaria (Table 3). 177 (26.7%) participants purchased coatem, 187 (28.3%) purchased Lonart. The others were Lumartem 133 (20.1%), *P. alaxin* 83 (12.5%), Amarla by 19 (2.9%) and artesunate by 57 (8.6%). All the antimalarial were purchased by those that tested positive. The breakdown according to the clusters (Table 4) shows that in D/Line area, Lonart was the most purchased drug 11 (34.37%), followed by Coartem 5 (15.6%) and Lumertem 2 (6.3%). In Mile IV, Lumartem 25 (36.8%) was the highest drug purchased followed by Coartem 13 (19.1%) and Lonart 12 (17.7%). While in Rumuosi, Malareich 19 (31.3%) was highest followed by coartem 12 (23.5%) and Lonart 10 (19.6%). There was a significant difference in the antimalarials purchased (D/Line X^2 = 50; P=0.001; Mile IV X^2 = 46.29; P = 0.001 Rumuosi X^2 = 42.82; P = 0.001).

Result of Follow up test shows that only 90 (59.6%) returned to be tested and they all tested negative (Table 5).

Table 1. Incidence of malaria among persons patronizing drugstores for malaria treatment in Port Harcourt (Rivers State, Nigeria) and its environs

Study area	Total no. tested	Number positive	Percentage (%) positive	*P. falciparium*	*P. vivax*	Chi-square (χ2) (*p-value)*
D Line	221	32	14.48	32	0	
MILE IV	221	68	30.77	68	0	16.69 (*0.001*)*
RUMUOSI	221	51	23.08	51	0	
Total	663	151	22.78	151	0	

**Statistically significant (p<0.05)*

Table 2. Malaria parasitaemia among persons patronizing drugstores for malaria treatment in Port Harcourt (Rivers State, Nigeria) and its environs

Study area	Total no. tested	Intensity of malaria parasitaemia number (%)			Chi-square (χ2) (*p-value)*
		<1000 Parasites/µl	<1000-9999 Parasites/µl	$\geq 10,000$ Parasites/µl	
D LINE	32	31 (97.0)	1 (3.0)	NIL	2.58 (*0.275*)
Mile IV	68	60 (88.0)	8 (12.0)	NIL	
RUMUOSI	51	43 (84.0)	7 (14.0)	1	
Total	151	134 (88.0)	16 (10.6)	1 (0.7)	

Statistically significant (p<0.05)

Table 3.Types of antimalarials purchased from drugstores for treatment of perceived malaria by persons patronizing drugstores for malaria treatment in Port Harcourt (Rivers State, Nigeria) and its environs

Anti malarials	Study area				
	D Line	Mile IV (Rumueme)	Rumuosi	Total	Percentage (%)
Coartem (ACT)	67	61	49	177	26.7
Lonart (ACT)	68	68	51	187	28.3
Lumartem (ACT)	38	53	42	133	20.1
P.Alaxin (ACT)	35	18	30	83	12.5
Amarla (Sulphadoxine/ Pyrimethamine)	5	6	8	19	2.9
Malareich (Sulphadoxine/Pyrimethamine)	1	3	3	7	1.1
Artesunate (Monotherapy)	7	12	38	57	8.6
Total	221	221	221	663	100

Table 4. Antimalarials purchased by persons patronizing drugstores for malaria treatment in Port Harcourt (Rivers State, Nigeria) and its environs

Anti malarials purchased	Study area		
	D/Line (%)	Mile IV (Rumueme) (%)	Rumuosi (%)
Coartem (ACT)	5 (15.63)	13 (19.12)	12 (23.53)
Lonart (ACT)	11 (34.38)	12 (17.65)	10 (19.61)
Lumartem (ACT)	2 (6.25)	25 (36.76)	3 (5.88)
Amarla (Sulphadoxine/	0 (0.00)	0 (0.00)	4 (7.84)
Pyrimethamine)	11 (34.37)	6 (8.82)	3 (5.88)
P. Alaxin (ACT)	0 (0.00)	6 (8.82)	0 (0.00)
Malareich (Sulphadoxine/	0 (0.00)	6 (8.82)	19 (37.25)
Pyrimethamine)			
Total	32 (100)	68 (100)	51 (100)
Chi-square (χ2) (*p-value)*	51.60 (*0.001*)*	46.29 (*0.001*)*	42.82 (*0.001*)*

**Statistically significant (p<0.05)*

Table 5. Result of follow up test for persons patronizing drugstores for malaria treatment in Port Harcourt (Rivers State, Nigeria) and its environs

Study Area	Number that tested positive before treatment (%)	Number that shown up for test after treatment (%)	Number that did not show up for test after treatment (%)	Number that tested positively after treatment (%)
D/ Line	32(100)	28(87.5)	4(12.5)	0(0)
Mile iv (Rumeme)	68(100)	43(63.2)	25(36.8)	0(0)
Rumuosi	51(100)	19(37.3)	32(62.7)	0(0)
Total	151((100)	90(59.6)	61(40.4)	0(0)

4. DISCUSSION

In this study, we recorded 22.8% preponderance of malaria infection and the incidence was significantly different in the study area. We still consider this result to be high bearing in mind the global decrease in malaria cases though Port Harcourt and Environs has favourable climatic condition such as high rainfall, temperature and humidity all of which combine to affect the number and survival of the malaria vector. Similar high preponderance has been reported among different target groups in Port Harcourt and its environment; Long distance truck drivers [20], Blood donors [21], Different socio-economic groups [22], and Prison inmates [23].

In terms of parasite intensity, it was observed that 88% of persons who tested positive for malaria had a parasitaemia of <1000 parasites/µl. This agrees with the observation of Okeke [24] and Isiguzo et al. [12] that most of those patronizing drugstores for malaria treatment do not have severe malaria.

Present study shows that out of the seven antimalarials regularly purchased, four were ACTs with 87.6% purchased, two were sulphadoxine/ pyrimethamine based drugs and one, Artesunate, a montherapy antimalarial with 8.6% purchased. The reason for this may be likely due to ACTs' effectiveness and policy of government to provide the drug at an affordable price. This finding is contrary to the study of Omole and Onademuren [25] in Abeokuta, who reported that Sulphadoxine/Pyrimethamine (SP) combinations such as Amalar™ and Fansidar™ are frequently purchased antimalarial drugs followed by chloroquine and that Artesunate monotherapy is the most frequently purchased of the artemisinin derivatives. However, the finding is in agreement with Tola et al. [26], who in their study of Antimalarial medicine preference and usage in rural and peri-urban communities in Lagos and Osun states in southwestern Nigeria reported that the most common drug used by the respondents for the treatment of malaria was ACT where about 50% treated malaria with ACT, 11.9% with SP and 23.8% claimed they did nothing about the infection. Conformity to the use of ACT could be said to be impressive. This is higher than the 73.9% recorded in the study of compliance to drug policies among persons patronizing drugstores for malaria treatment [5]. It is however lower than the 95% compliance recorded at two health facilities in Anambra State [11]. The impressive usage of ACT recorded in the study only substantiates WHOs' assertion that ACTs have been an integral part of the remarkable recent success in global malaria control [2]. However, not recording 100% in the use of ACT does not auger well for malaria control. It has been over 10 years since this policy was adopted. Not implementing it fully could lead to wastage of resources, treatment failure and risk of drug resistance. The better compliance observed by persons patronizing health facilities could be as a result of more enlightenment. These campaigns are focused in the formal health sectors.

This study shows that only 59.6% (90) of the persons that tested positive for malaria show up for the follow up test. This is the first of such studies in these neighbourhoods. A similar study was a phone follow up survey in Oyo state where 97.9% of persons reached said that they felt better after treatment with antimalarial [12]. Not showing up for follow-up test means that the WHO policy of tracking for all cases of malaria is not adhered to, thus drug efficacies are not monitored. This might have been due to the assumption that it is a waste of time, since they were already feeling better, it is however forgotten that parasite clearance might not be complete. This could lead to mutation and drug resistance as *P. falciparum* resistance to ACT has been observed in the Greater Mekong sub region of Cambodia, the Lao's people's Democratic republic Myanmar, Thailand and

Vietnam. A molecular marker for resistance to artemisinin has been identified, though not widespread [27,28]. This has been considered a major treat to malaria prevention and control efforts.

We observed and reported that all the persons that showed up for the follow-up test, tested negative. This means that the molecular marker for the resistance to artemisinin, which has been identified though not widespread, might not have spread to Nigeria. This finding agrees with observation of Olasehinde et al. [29].

5. CONCLUSION

Malaria preponderance was high among studied subjects, ACT was topmost among antimalarials regularly purchased by the individuals. Conformity to the use of ACT could be said to be impressive though not yet 100%. Only 59.6% of the persons that tested positive for malaria showed up for the follow-up test and all the persons that showed up for the follow-up test, tested negative signifying that the antimalarials are effective. People who are treated for malaria should be encouraged to undergo a test after treatment for effective case management and detection of resistance.

CONSENT AND ETHICAL APPROVAL

The study protocol was approved by the Research Ethics committee of the University of Port Harcourt (UPH/ CEREMAD/REC/04) and a written consent was obtained from owners of drugstores and participating individuals.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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