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PREVALENCE AND PATTERN OF ANTIBIOTIC USE IN MALARIA TREATMENT IN A SECONDARY HEALTHCARE FACILITY

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ABSTRACT

Introduction: Malaria remains one of the most common and widely treated infections in tropical countries including Nigeria. Treatment of malaria is complicated in the presence of typhoid fever which requires the use of antibiotics. Proper diagnosis is usually needed to exclude typhoid fever and the subsequent use of antibiotics with malaria therapy, since inappropriate use contributes to antimicrobial resistance. **Objectives:** This study aims to determine the prevalence of the co-administration of antibiotics in malarial treatment and the most commonly prescribed antibiotics. **Methods:** This is a descriptive cross-sectional study conducted at the General Outpatient Pharmacy Department (GOPD) of Central Hospital, Benin city, Edo state, Nigeria. Structured interview questionnaire was used for data collection and analyzed using Statistical Package for Social Sciences [SPSS] version 22. Descriptive statistics was carried out on all variables. **Results:** A total of 276 respondents participated in the study. About 97(35.1%) conducted a malaria test on current hospital visit. 117(42.4%) said antibiotics were prescribed alongside their antimalarials the last time they treated malaria before their current hospital visit. About 185(67%) of respondents used artemisinin-based combination therapies the last time they treated malaria. 151(54.7%) of current prescription for malaria treatment had an antibiotic. The most prescribed antibiotic is Amoxicillin clavulanic acid 38(13.7%). **Conclusion:** The findings from this study indicate that more than half of the prescriptions for treatment of malaria had an antibiotic majority of which do not have a laboratory basis for it. This suggests that most prescribers practice presumptive treatment with antibiotics which is a culprit for antimicrobial resistance.

KEYWORDS: Malaria, Antimalarial drugs, Pharmacists, Patients, Antibiotics.

INTRODUCTION

Malaria is an infectious life-threatening disease caused by plasmodium parasites that are transmitted to people through the bites of infected female anopheles mosquito. Malaria remains an important public health concern in countries where transmission occurs. It is a major problem with hundreds of millions of casualties per year, without treatment in a non-immune patient; it could progress to severe disease in days characterized by multi-organ dysfunction and mortality even with adequate malaria treatment. The disease is widespread in the tropical and subtropical regions that exist in a broad band around the equator. This includes much of Sub-Saharan Africa, Asia, and Latin America (WHO, 2014). In 2016, there were 216 million cases of malaria worldwide resulting in an estimated 445,000 to 731,000 deaths (WHO, 2017). Approximately 90% of both cases and deaths occurred in Africa. Rates of disease have decreased from 2000 to 2015 by 37%, but increased from 2014, during which there were 198 million cases. Malaria is commonly associated with poverty and has a major negative effect on economic development (Gollin and Zimmermann, 2007). In Africa, it is estimated to result in losses of 12 billion dollars a year due to increased healthcare costs, decreased ability to work, and negative effects on tourism (Greenwood et al, 2005).

Typhoid fever is believed to be endemic and prevalent in Nigeria (Ohanu et al., 2003). Patients who do not respond or respond poorly to malaria treatment are usually suspected to have typhoid fever. Especially at the onset of typhoid fever, the symptoms are similar with that of malaria (Nsutebu et al., 2001). As a result of the non-specific nature of Widal agglutination test, which is the common diagnostic test for typhoid fever in Nigeria, co-infection with malaria and typhoid is believed to be quite common. Consequently, the simultaneous treatment of both fevers is rampant (Mbuh et al., 2003).

In a study carried out at Ibadan, Southwest Nigeria, on the prevalence of the co infection of malaria and typhoid fever, discovered that one-third of patients presenting with fever have neither malaria or typhoid. However, there is an increased prescription of antibiotics with

antimalarials during malaria therapy with the goal of treating typhoid, though there may be other comorbidities requiring the use of antibiotics. They concluded that empirical treatment of typho-malaria symptoms should be discouraged (Igbeneghu et al., 2009). The implications of irrational use of antibiotics as combination in treating malaria includes threat of antibiotic resistance which is gradually turning into a global menace, patients likely suffering from adverse effects from antibiotics and unnecessary cost incurred from use of antibiotics (Pokharel et al 2019).

This study aims to determine the prevalence of the co-administration of antibiotics in malarial treatment and the most commonly prescribed antibiotics.

METHODS

Study design and setting

This is a descriptive cross-sectional study conducted at the General Outpatient Pharmacy Department (GOPD) of Central Hospital, Benin city, Edo state, Nigeria. It is a state government hospital located at Sapele Road, few kilometres from City Centre in Oredo local government area, Edo state.

Study population

The study population included both male and female respondents aged 18 and above being treated for malaria and those who expressed willingness to participate in the study. Pediatric patients and patients being managed for disease conditions other than malaria were excluded.

Data Collection

Data was collected using a self-administered structured questionnaire. The questionnaire consisted of three sections; section A, B and C. Section A was based on the respondent's demographics which include age, sex, religion, marital status and social status. Section B was used to collect respondent's information about their frequency of malaria treatment in a year, their use of antimalarials and antibiotics in the treatment of malaria, the class of antimalarials and antibiotics they had used in the past, use of laboratory results, their use of mosquito nets, adherence and also their perception of the effectiveness of antimalarials. Section C included the collection of data based on the current prescription such as the tests carried out, antimalarial, type and number of antibiotics prescribed for each respondent through assessment of the patient case file.

Data Analysis

Data obtained from the study were collected, organized, entered into Microsoft Excel and sorted. Data was then transported to Statistical Package for Social Sciences (SPSS) version 22 for analysis. Descriptive statistics was carried out on all variables.

Ethical Consideration

Ethical clearance was obtained from the ethical and review committee of Hospitals Management Board, Benin City. Informed consent was obtained from participants before administration of questionnaires and all information obtained were kept confidential.

RESULTS

A total of 276 respondents participated in the study. Table 1 shows the social demographics of the study population of which about half were of either gender. The majority of the respondents were within 18-29 years with a frequency of 120(43.4%).

Table 1: Social demographics of Respondents.

Variables	Frequency (N)	Percentage (%)
Age		
18 – 29	120	43.4
30 – 39	40	14.5
40 – 49	31	11.3
50 – 58	35	12.5
60 – 69	30	10.9
70 – 87	20	7.4
Sex		
Male	133	48.2
Female	143	51.8
Education		
No formal education	22	8.0
Primary	23	8.3
Secondary	45	16.3
Tertiary	186	67.4
Occupation		
Civil servant	48	17.4
Private sector	22	8.0
Self employed	71	25.7
Unemployed	21	7.6
Student	97	35.1

Retired	17	6.2

Table 2 shows results obtained from participants responses about previous and current malaria treatment. One hundred and forty eight (53.6%) of them do not usually conduct a test before treating malaria, while only about ninety-seven (35.1%) conducted a malaria test on current hospital visits. 42.4% said antibiotics were prescribed alongside their antimalarials the last time they treated malaria before their recent hospital visit.

Table 2: Responses obtained from patients about previous and current malaria treatment.

Variable	Yes (N/%)	No (N/%)	Sometimes (N/%)	Cannot remember (N/%)
Do you usually conduct tests to confirm malaria before treatment?	46(16.7)	148(53.6)	82(29.7)	
Was a test conducted the last time you treated malaria?	75(27.2)	178(64.5)		23(8.3)
Do you always complete the drugs prescribed to treat malaria?	220(79.7)	21(7.6)	35(12.7)	
Was antibiotics added to the drugs for the previous treatment of malaria?	117(42.4)	101(36.6)		56(20.3)
Did you complete the antibiotics added to your antimalarial?	99(35.9)	38(13.8)		35(12.7)
On this visit, did you conduct a malaria test?	97(35.1)	179(64.5)		
On this visit, did you conduct a typhoid test?	54(19.6)	222(80.4)		
Do you react to any antimalarial drug?	33(12)	243(88)		
Do you add herbal preparations to antimalarial drugs?	36(13)	203(73.6)	37(13.4)	

Table 3 shows that about 67% of respondents used artemisinin-based combination therapies the last time they treated malaria. About 60% of the respondents reported treating malaria twice or more in the past year, while 72(26.1%) said they treated malaria about a month before.

Table 3: Frequency of previous malaria treatment and antimalarial prescribed.

Variable	Frequency (N)	Percentage (%)
Number of times patients had been treated for malaria in the past year		
Once	57	20.7
Twice	59	21.4
Three times	50	18.1
Four or more	60	21.7
None	22	8
Cannot remember	28	10.1
The last time patients treated malaria		
1 month ago	72	26.1
2 months ago	47	17.0
3 months ago	44	15.9
4 or more months ago	57	20.7
Cannot remember	56	20.7
Antimalarial patients used the last time they treated malaria		
Artemisinin-based combination therapy	185	67.0
Others	26	9.4
Cannot remember	35	12.7
Don't know	30	10.9

Table 4 shows the most prescribed antibiotics alongside antimalarials in previous treatment were amoxicillin and ciprofloxacin with 44(15.9%) and 26 (9.4%) respectively while more than half of the respondents 165(59.8%) got their antimalarial medications from a pharmacy. 170 (61.6%) of the respondents consulted either a doctor or a pharmacist before prescribing, but 59 (21.4%) self-medicated with antibiotics.

Table 4: Antibiotics used in the previous treatment and drug prescribers.

Variable	Frequency (N)	Percentage (%)
Antibiotic used alongside previous treatment of antimalarial		
Amoxicillin Clavulanate	19	6.9
Amoxicillin	44	15.9
Ampiclox	9	3.3
Ciprofloxacin	26	9.4
Ofloxacin	1	0.4
Drug prescriber last time patients treated malaria		
Doctor	90	32.6
Pharmacist	80	29.0
Nurse	23	8.3
Chemist	24	8.7
Self-medication/family/friend	59	21.4
Place where patients purchased their drugs last time of treatment		
Pharmacy	165	59.8
Chemist	49	17.8
Hospital	57	20.7
Leftover drug	5	1.8

The most frequently prescribed antimalarial from current prescription was artemisinin-based combination therapies with a percentage frequency of 97%, with artemether-lumefantrine having a percentage of about 68.1%. (See Table 5).

Table 5: Antimalarials Prescribed on current prescription.

Variable	Frequency (N)	Percentage (%)
Name of the antimalarial prescribed		
Arthemether Lumefantrine	188	68.1
Arteether injection	5	1.8
Artequin	15	5.4
Artesunate	6	2.2
Camosunate	7	2.5
Dihydroartemisinin piperaquine phosphate	44	15.9
Emal injection	3	1.1
Quinine	6	2.2
Sulphadoxine pyrimethamine	1	0.4
Arterolane maleate + Piperaquine	1	0.4

Table 6 depicts 54.7% of prescriptions had an antibiotic present and the most frequently prescribed was amoxicillin and clavulanate. Also, about half (45.7%) of the prescriptions had only one antibiotic co-prescribed.

Table 6: Presence of an antibiotic on current prescription.

Variable	Frequency (N)	Percentage (%)
Presence of antibiotics in the prescription		
Yes	151	54.7
No	125	45.3
Name of antibiotic prescribed		
Amoxicillin clavulanate	38	13.7
Amoxicillin	27	9.8
Apriflox	1	0.4
Nitrofurantoin	9	3.2
Azithromycin	17	6.2
Cefuroxime	3	1.1
Ciprofloxacin	36	13.0
Clarithromycin	2	0.7
Doxycycline	1	0.4

Erythromycin	5	1.8
Flagyl	21	7.6
Levofloxacin	8	2.9
Number of antibiotics prescribed		
1	126	45.7
2	25	9.1

Table 7: Tests conducted and results for malaria and typhoid Tests conducted

Variable	Frequency (N)	Percentage (%)
Microscopy	19	6.9
Microscopy + Widal	26	9.4
Rapid diagnostic test	31	11.2
Rapid diagnostic test + Widal	20	7.2
Widal	5	1.8

Tests results

Variable	Frequency (Number/Percentage)	
	Positive	Negative
Malaria test	95(34.4%)	0
Widal test	24(8.7%)	35(12.7%)

DISCUSSION

The study was carried out to evaluate antimalarial prescriptions and from the results obtained, 54.7% of malaria prescriptions had an antibiotic co-prescribed which is less compared to studies carried out in Kano, which had 65% prescriptions of malaria containing an antibiotic, and near about 80% drugs were prescribed from essential drug list (Chedi BAZ et al., 2010). In other studies conducted, 43% of prescriptions had antibiotics co-prescribed, out of which 16.3% was doxycycline which has an anti-malarial effect itself (Pratyay et al., 2016). However, only about 0.4% of prescriptions in this study had doxycycline co-prescribed. Studies conducted in Tanzania indicates that antibiotics were co-prescribed for 20% of encounter (Mustafa et al., 2013), while co-prescription of 30.8% was observed in Ghana (Dodoo et al., 2009). Also, about 45.7% of prescriptions containing an antibiotic had only one antibiotic prescribed.

In comparison, 9.1% had two antibiotics co-prescribed and this is low compared to studies carried out in Zambia, where out of the 872 patients with suspected malaria, 470(53.9%) were prescribed at least one antibiotic. Among these, 446(94.9%) were prescribed a single antibiotic, 23(4.9%) two antibiotics and 1(0.2%) received three antibiotics. Penicillin (amoxicillin), cotrimoxazole and erythromycin were commonly used, being prescribed to 279 (57.9%), 98 (21.3%) and 35 (9.3%) patients, respectively. The rest included metronidazole, doxycycline, gentamicin, chloramphenicol, quinolones and cephalosporins (cephalexin, cefuroxime and ceftriaxone), together accounting for slightly over 10% (Micky et al., 2015). Therefore, the prevalence of antimalarials and antibiotics co-prescription was relatively high but low compared to other studies. Although co-prescription could be a result of co-infection with malaria or due to routine practice of the prescribers, it could also be due to the use of antibiotics for the treatment of malaria. It is possible that some of the antibiotics co-prescribed may be appropriate for suspected bacterial infections. Still, the odds that some might be irrationally for malaria is high as about one in two prescriptions have an antibiotic. In line with previous studies, irrational administration of antibiotics to patients was obvious. From the study, only 22 patients tested positive to a widal test and were given an antibiotic, while about 6 of them were negative but were also given an antibiotic. Those who tested positive to the typhoid test may have been given an antibiotic to take care of typhoid. Therefore, most patients were given an antibiotic alongside antimalarial, even in the absence of typhoid infection.

About half of the prescriptions (54.7%) had at least one antibiotic in them and the most commonly prescribed antibiotics were amoxicillin, amoxicillin-clavulanate, ciprofloxacin, azithromycin and flagyl (metronidazole). These antibiotics could have been prescribed as a result of co-infections, routine practice of the prescriber, or as a medication for use alongside antimalarials in treating malaria.

Antibiotics known to have antimalarial properties include the tetracyclines, the macrolides, and their derivatives, including cotrimoxazole, and quinolones (Tiphaine et al., 2016). But, they are not used alone in malaria treatment. The Word Health Organization malaria treatment guideline only recommends doxycycline, tetracycline, or clindamycin with the antimalarial quinine(WHO 2015; Dahl et al., 2007). From this study, it is apparent that the antibiotics used alongside antimalarials were mainly for empirically suspected co-infections.

The percentage frequency of participants who conducted a test before receiving treatment was about 35.1% and 64.5% for those who did not conduct any test. Less than 20% of respondents had a rapid diagnostic test, while 18.4% conducted a microscopy test to confirm malaria. Also, more than half of the participants do not usually conduct tests before treating malaria, and 64.4% of them did not also conduct any test the last time they treated malaria. The findings corroborate previous studies in Nigeria and other African countries, which have reported widespread limited use of laboratory diagnosis even with diagnostic tools. A study by Meremikwu et al. in 2007 reported a laboratory test rate of 45%, while Uzochukwu et al. (2010) reported a rate of 51.1%. Similar results were obtained in another study conducted in two public health facilities in Nigeria, which showed that 49% of the patients were sent to conduct a laboratory test, mostly microscopy.

In contrast, the other 51% were treated presumptively (Charles et al., 2014). Following the results obtained, it was observed that prescribers in the hospital were not adherent to the Test Treat and Track initiative of WHO. Therefore, presumptive treatment is still very much the practice in the hospital. A high level of presumptive treatment indicates the high incidence of overdiagnosis and overuse of antimalarial drugs due to the degree of inaccuracy associated with presumptive treatment. Also, it could result in missed diagnosis of other illnesses and increased risk of morbidity. Therefore, there is the need to intensify efforts to promote diagnostic approaches to malaria treatment in health facilities through regular education programs for health workers. The low use of diagnostic tests could be a result of high patient load in the hospital, lack of trained laboratory personnel, insufficient materials for diagnosis, patients' lack of finance for tests, and also because malaria is endemic in Nigeria; therefore, prescribers' suspicion rate is high. Therefore, there is the need for an increased number of trained healthcare professionals and the availability of funds to purchase items needed to carry out tests to reduce the financial burden on patients who may not be able to afford laboratory investigations (Moyo K et al., 2015).

The pattern of prescription in the study showed a clear preference for artemisinin-based combinations as 97% of drugs prescribed were ACTs, with artemether-lumefantrine having a percentage of 68.1%, indicating that it was the most prescribed. Similar findings were observed in a study by Charles et al. (2014), as 95% of drugs prescribed in public health facilities were ACTs. This indicated high conformity of prescribers to the WHO policy recommendation of artemisinin-based combination therapy as first-line drugs in treating uncomplicated malaria. The study's findings present a clear understanding of the prescribing practices at the hospital. However, there were a few limitations. Comprehensive diagnostic information was not collected, which could have better informed the use of the antibiotics in the prescription. While the study may be limited in terms of the number of facilities used as only Central hospital was used and this may influence the generalization of results. On the other hand, data were collected from patients visiting the hospital for malaria treatment. Hence the data collected were current, which is strength of this study.

CONCLUSION

Prescription of antibiotics in patients with malaria is high and antibiotic use could depend on prescribers' behavior, its use in the treatment of typhoid and its use in malaria treatment. The findings from this study indicate that although most prescribers conform to the treatment policy of artemisinin-based combination therapy, they do not adhere to the use of laboratory diagnostic tests. Presumptive treatment is still very much prevalent in the hospital and therefore it is important to ensure adequate training and education of healthcare professionals on the need to adhere to treatment guidelines in order to avoid the development of resistant parasites, treatment failure and prevent unnecessary treatment cost.

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