Treatment failure among patients on self medication for malaria seen at a teaching hospital

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Abstract

Background: Claims of treatment failure for malaria may be due to over diagnosis. We report the outcome of a follow-up study conducted to investigate the claim of treatment failure.
Methods: One hundred and four patients who said they were not cured after home management of malaria were studied. Giemsa stained blood smears were examined qualitatively and quantitatively using thin and thick films to confirm specie and determine parasite density. Nine symptoms (fever, headache, loss of appetite, nausea, vomiting, body pain, joint pain, cold sores and diarrhoea) were assessed based on the patients' perception and classified as present or absent.
Results:Only 85 (81.7%) patients were confirmed for *Plasmodium falciparum* malaria parasite. Of the 85 confirmed cases. There were 19 (22.4%) symptoms-less infections. Seven symptoms present during assessment were scored according to frequency of occurrence. The most frequent symptoms were body pain (47.1%), nausea (38%), fever (38%) and headache (36%). Fever and headaches were present among those that were not confirmed and had been treated with antimalarial and reported as cases of failed home management of malaria.
Conclusion: Claims of treatment failure after home management of malaria should be reported to the clinic promptly for proper investigation and care in order to prevent over treatment of malaria and its associated risks of neglecting other illnesses which may require urgent attention.

Keywords: Antimalarial, Malaria, Failure, Self-treatment

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Introduction

Home management is a very common practice in the treatment of malaria and other febrile illnesses[1]. Self-medication for malaria is widely practiced around the world[2]. However, most countries have switched from single to artemisinin-based chemotherapy (ACT) as first line treatment for uncomplicated malaria[3]. The reason why unprescribed antimalarial drugs are used include: Lack of access to health facilities, cost of treatment in health facilities and social distance of health workers from patients[4]. Home treatment of perceived malaria in Benin City is similar to other areas within high malaria transmission zones[5].

There is no previous documentation of descriptive cross-sectional study of cases of treatment failure for the management of malaria at home in Edo State, Nigeria. Although many home treatment episodes are successful, the risk of under or over dosing is always present[2].
Our result of adescriptive cross-sectional study of cases of treatment failure of home management of malaria is discussed and our suggestions could be useful in malaria control strategies.

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Materials and Methods

Study area and population

This study was conducted between June 2011 and December 2012 at the University of Benin Teaching Hospital (UBTH) Benin City, Nigeria. Benin City lies within the rainforest vegetation with high humidity, annual rainfall of between 300 – 900mm and most of the rainfall is between the months of March through to November. The average temperature is 32°C and malaria transmission occurs all year round. We studied 104 patients who were booked for follow-up after claims of treatment failure based on self/family perceived malaria.

Blood collection and laboratory diagnosis of malaria

A base line questionnaire was administered to all patients at enrollment to obtain clinical, socio-economic and demographic data.Blood samples were collected from all patients into EDTA labeled bottles for microscopic examination. Stained Blood slides were examined microscopically using the oil immersion objective for malaria parasite species and identified based on morphological characteristics (Cheesbrough)[6]. Parasite densities were stratified based on quantitative study of thick blood smears under the oil immersion objective as ≤ 100 parasites in 100 fields (roughly

corresponding to 1– 300 parasites/µl of blood), and >100 parasites in 100 fields (>300 parasites/µl of blood[5]).

Clinical assessment

Symptoms associated with malaria were assessed clinically according to the patient's perception and recorded using a structured questionnaire addressing the following reported symptoms (fever, headache, loss of appetite, nausea, vomiting, body pain, joint pain, cold sores and diarrhoea). According to the patient's perception each clinical manifestation was considered absent or present. Confirmed and unconfirmed participants were matched according to presence and absence of symptom, age, sex, qualitative and quantitative blood studies.

Statistical analysis

The proportion of patients who were microscopically confirmed to have malaria was compared to the proportion of an earlier self/family perceived malaria. Intergroup comparisons were based on age, gender and clinical manifestation. The severities of symptoms were compared in patients with low and moderate to high parasitaemia. Differences in proportion were compared for significance using Chi-square test and p-value of < 0.05 was considered significant.

Ethical clearance

Approval of the study protocol was obtained from the Ethical Review Board (ERB) of the UBTH. All study participants provided informed consent. In the cases of children, consent was obtained from parent/guardian.

Treatment of malaria cases

After microscopic investigation of blood samples all malaria cases that were confirmed during this follow-up cases were treated with antimalarials using Arthemesimin –based chemotherapy: Artemether plus Lumefantrine fixed combination tablets containing: 20mg artemether, 120mg Lumefantrine. For adult dosage: 4tablets stat, 8hours later 4tablets. On the second and third day, 4tablets twice daily. For children: 5-14kg (one tablet), 15-24kg (2 tables), 25-34kg (3 tablets), ≤35kg or ≤12years (4 tablets). Proof of cure was done after treatment with satisfactory outcome.

Results

One hundred and four patients who complained of treatment failure for malaria were booked for this study. There were significant differences between the confirmed and unconfirmed cases. Eighty-five (81.7%) and 19 (18.3%) were confirmed and unconfirmed respectively following qualitative studies of blood slides which revealed *Plasmodium falciparum* malaria parasites. There were also significant differences for fever, loss of appetite and body pain ($p<0.05$).

Table 1. Confirmed and Unconfirmed malaria cases matched with symptoms present

Symptoms*	Confirmed n (%)	Not Confirmed n (%)	P - Value
Fever	38 (36.5)	2 (1.9)	< 0.05
Headache	36 (34.6)	10 (9.6)	NS
Loss of appetite	30 (28.8)	5 (4.8)	< 0.05
vomiting	30 (28.8)	0 (0.00)	-
Nausea	38 (36.5)	0 (0.00)	-
Body pain	40 (47.0)	2 (10.5)	< 0.05
Joint pain	2 (1.9)	7 (6.7)	NS
Cold Sores	0 (0.00)	0 (0.00)	-
Diarrhea	0 (0.00)	0 (0.00)	-

Percentages are in parentheses; *Multiple responses reported.

The following symptoms occurred more frequently (fever 36.5%, headache 34.6%, loss of appetite 28.8%, vomiting 28.8%, nausea 36.5%, body pain 38.5%, joint pain 1.9%) among those confirmed compared to fever 1.9%, headache 9.6%, Loss of appetite 4.8%, body pain 1.9%, joint pain 6.7%) among those not confirmed. Contrary to the perceived symptoms used by the patients for self-diagnosis, clinical assessment showed that diarrhea and cold sores were absent.

Table 2. Quantitative and qualitative blood analysis of followed population 104 confirmed cases

Variables	Symptomatic n = 66 (77.6)	Asymptomatic n = 19 (22.4)
Qualitative		
*Trophozoites	61(71.8)	24 (28.2)
Gametocytes	5(4.8)	8(9.4)
Quantitative	56(53.9)	19(22.4)
1 -300 parasites/µl of blood	56 (65.9)	19 (22.4)
>300 parasites/µl of blood	10(9.6)	0 (0.0)

*Trophozoites and or gametocytes reportable in the same sample. Percentages are shown in parenthesis.

Microscopic blood analysis

Qualitative analysis of 85 blood samples among those confirmed shows that 66(77.6%) and 19(22.4%) were symptomatic and asymptomatic respectively. Trophozoites were seen in 61(71.8%) and 24(28.2%) blood samples among those symptomatic and asymptomatic respectively. Among those that were

symptomatic 5(5.9%) had gametocytes in their blood while 8(9.4%) of the asymptomatic subjects had gametocytes. Parasite burden showed that 56(65.9%) symptomatic and 19(22.4%) asymptomatic subjects had 1 – 300 parasite/μl of blood. While only symptomatic 10(11.8%) subjects had parasite load of > 300 parasites/μl of blood.

Table 3. Prevalence of malaria among followed-up patients (n=104) according to presence or absence of symptom and age at the UBTH, Benin City, Nigeria

Age group (yrs)	No followed	No positive	No Negative	No. symptomatic	No. Asymptomatic
≤ 10	12 (11.5)	12 (11.5)	0 (0.0)	12 (11.5)	0 (0.0)
11 - 19	12(11.5)	2(1.9)	10(9.6)	8(7.7)	4(3.8)
≥ 20	80 (76.9)	71(68.3)	9(8.5)	46(44.2)	15(14.2)
Total	104(100)	85(81.7)	19(18.3)	66(63.5)	19(18.3)

Of the 104 patients studied, 85 (81.7%) and 19(18.3%) were found to be slide positive and negative respectively after microscopic examination. Participants aged ≤ 10 years were all slide positive and were all symptomatic, while 71(68.3%) and 9(8.6%) were symptomatic and asymptomatic respectively among those aged 11-19 years. Among those aged ≤ 20, 2(1.9%) were slide positive for malaria and 10(9.6%) were negative, 8(7.7%) were symptomatic and 4(3.8%) asymptomatic.

Discussion

In areas of stable malaria, asymptomatic and symptomatic illness with the characteristic febrile paroxysm is the spectrum of malaria[8,9]. We report findings of a descriptive cross-sectional study which compared the outcome of a population after claims of treatment failure of home management of malaria in Benin City, Nigeria. Of the 104 patients that were booked for this study, 61(71.8%) were symptomatic while 24(28.2%) were asymptomatic. The factors which modulate the clinical expression of malaria include naturally acquired immunity, parasite load and age of the host[10].

This study demonstrates that only 85 (81.7%) participants of the total 104 were confirmed to have malaria suggesting that the remaining 19(18.3%) were due to febrile illnesses rather than due to malaria; and contrary to the patient's claim, cold sores and diarrhoea were absent at time of this study. However, among those not confirmed the following symptoms: vomiting, nausea, cold sore and diarrhea were absent. The differences in the presenting symptoms between confirmed and unconfirmed ($P<0.05$) suggests that such symptoms may not be due to malaria. Among those not confirmed, fever, headache, body pain and joint pain were present during our clinical assessment suggesting that some symptoms which may be characteristic of malaria need proper clinical assessment after treatment failure in order to avoid overdosing with antimalarials. Although often considered a predominantly rural disease in Africa, malaria represents a leading cause of morbidity and mortality among many urban African populations[11]. Our finding that some symptoms perceived to be due to malaria may not be correct has been similarly reported. The differences in prevalence and frequency of symptoms among those confirmed and unconfirmed would need to be assessed independently in other populations.

Brinkmann and Brinkman[12] reviewed the literature on malaria in Africa and found rates for self-treatment ranging from a low of 19% in Guinea to a high of 94% in rural Ghana[12]. Since self-medication for malaria is widely practiced[2], it is necessary to review periodically in different locations the association between prevalence or perceived intensity of symptoms that would be useful for the diagnosis of malaria.

Policies regarding prevention and control of malaria should be matched with reality, for instance self-treatment for malaria should be addressed during campaign programmes aimed at enlightening the masses.Forster[2] observed that most treatment manuals for antimalarials assume that no self-treatment has occurred and yet it is well known that this is not true in most cases. Clearer guidance on asking about previous treatment ought to be included in treatment guidelines if serious mistakes and overdosing are to be minimized[2]. Other causes of treatment failure include under-dosing, incomplete treatment, poor drug quality and resistance.

The presenting symptoms of malaria whether present or absent appear to correspond to parasite load; all 10 (11.8%) cases with parasite load > 300 parasites/μl of blood were symptomatic while those that were asymptomatic 19 (22.4%) had parasite load 1 – 300 parasite/μl of blood.

There were no asymptomatic malaria episodes among those aged ≤10 years, suggesting that they were more susceptible to manifestations (Table 3).

We were faced with the problem of inability to recruit large number of willing participants for this study. This may have some effects on the outcome of this study.

Claims of treatment failure after home management of malaria should be reported to the clinic promptly for proper investigation and care in order to prevent over treatment of malaria and its associated risks of neglecting other illnesses which may require urgent attention.

Conflict of Interest

None declared in this work.

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