Pre-Hospital Use of Antimalarial Drug and Associated Factors among Children with Febrile Illnesses Presenting to a Tertiary Health Facility

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mortality. The initiation of treatment with antimalarial drug within 24 hours of fever onset at home and before presentation to the hospital is one of the recommended strategies to reduce mortality from malaria in sub-Saharan Africa. **Objective:** To determine the pattern of use of antimalarial drug prior to hospital presentation among

Background: Malaria is still a major public health problem in Nigeria and it is a leading cause of infant and childhood

Objective: To determine the pattern of use of antimalarial drug prior to hospital presentation among febrile children presenting to a tertiary health facility in southwestern Nigeria.

Methods: This was a cross-sectional, descriptive study. All consecutive febrile children who presented in the Children Emergency Room of Olabisi Onabanjo University Teaching Hospital during the study period were recruited. Data on socio-demographics, treatments given at home, history of present illness and outcome of blood smear testing for malaria parasite were collected and analysed.

Results: A total of 50 children aged one month to 13 years who had documented fever were studied. Three-quarters of the febrile children had duration of fever of more than one day (77.5%) and four-fifths had negative blood smear for malaria parasite (82.2%). Only four (8.0%) of the febrile children received antimalarial drug prior to hospital presentation. Twelve of the febrile children (24.0%) had a presenting temperature of ≥38.5oC. All the four febrile children who received anti-malarial drug prior to hospital presentation had a negative blood smear for malaria parasite and duration of fever of greater than two days

Conclusion: This study showed that pre-hospital home treatment with antimalarial drug was inappropriate among the enrollees. Health education on appropriate antimalarial drug use for febrile children should be intensified.

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INTRODUCTION

Malaria is a leading cause of morbidity and mortality among children in tropical countries (1). According to a national survey, the percentage of under-five children who tested positive for malaria parasite by microscopy decreased from 42% in 2010 to 22% in 2021 (2). Some of the essential and tested strategies to reduce mortality attributable to malaria included: prompt evaluation of all febrile

illnesses, case-recognition and use of appropriate antimalarial therapy (Orimadegun et al., 2008).

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Fever is a key symptom of malaria and other acute infections seen in children. It is also an important entry point into case management for malaria. The overall prevalence of fever among under-five children was 37% in a national survey conducted by the Federal Ministry of Health in 2021 (National Malaria Elimination Programme, 2021). The 2021 national survey documented that the prevalence of fever among children under the age of five years was 39% in rural areas, as compared with 31% in urban areas (National Malaria Elimination Programme, 2021). However, in developing countries such as Nigeria that is endemic for malaria, caregivers usually recognize fever in children as being synonymous with malaria (O'Dempsey et al., 1993; Olaleye et al, 1998). Likewise, in the clinical diagnosis and empirical treatment of malaria by healthcare workers, using fever as the major symptom has historically been the most widely used approach (Nankabirwa et al., 2009; O'Boyle et al., 2020).

It has been reported that over 50 - 75% of febrile illnesses are managed at home (McCombie, 2002; Ajayi & Falade, 2006). This approach aligns with the recommendation by the revised National Guidelines for the Diagnosis, Treatment, and Prevention of Malaria of prompt presentation of fever cases as well as prompt and effective treatment to prevent malaria morbidity and mortality (National Malaria Elimination Programme, 2021). These empirical treatments initiated at home may often be inappropriate9 and may have very low diagnostic accuracy given the fact that the symptom of malaria overlaps with those of many other tropical diseases (O'Dempsey et al., 1993; Hamer et al., 2007; O'Boyle et al., 2020).

The advent of malaria Rapid Diagnostic Test (RDT) kits has made the test-and-treat approach of malaria a lot easier even at community level (Mubi et al., 2011; Chanda et al., 2011) and at privatelyowned healthcare facilities (Maloney et al., 2017; Visser et al., 2017). In spite of this ease of using RDT kits; the adherence to the test-and-treat protocol still remains a challenge. Some group of researchers reported that 30% of febrile patients whose RDT results were negative in rural Uganda received antimalarial drug and that febrile underfive children were three times more likely to receive antimalarial medications without testing compared to older children (Kyabayinze et al., 2010). The use of antimalarial medications among febrile patients whose RDT results were negative may be tantamount to wastage of antimalarial drug, patients' exposure to the side-effects of inappropriate treatment, and the emergence of drug resistance (Kyabayinze et al., 2010). Some authors (English et al., 2009) have argued in the defence of empirical treatment despite the wide availability of RDTs and available evidence that it is safe to withhold antimalarial treatment for febrile patients pending laboratory confirmation for malaria across all age group (Njama-Meya et al., 2007).

This study aimed to determine the pattern of use of antimalarial drugs prior to hospital presentation among febrile children presenting to a tertiary health facility in southwestern Nigeria in light of the current antimalarial treatment guidelines and to determine the factors associated with these practices. It is expected that the data generated will provide an assessment tool for the initiation of antimalarial drug within 24 hours of fever onset at home and before presentation to the hospital as a strategy to reduce childhood mortality from malaria in sub-Saharan Africa.

SUBJECTS AND METHODS

Study Area- The study was conducted at the Children Emergency Room (CHER) of Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Nigeria, a referral centre for health facilities within Ogun State and in the contiguous parts of the neighbouring Lagos, Ondo and Edo States. The CHER is the first port of call for seriously ill children and it provides 24-hour emergency paediatric healthcare services.

Study Subjects: All children with history of fever who presented to the Children Emergency Room whose parents/caregivers consented to the study were the study participants

Study Design This was a cross-sectional descriptive study conducted from 1st August to 30th October, 2019 to determine the pattern of prehospital use of antimalarial drugs among febrile children. Data was collected with the use of a pretested questionnaire administered by the researcher. Three respondents used for the pretest of the study questionnaire were subsequently excluded from the actual study. Confidentiality was maintained throughout the study. The information obtained from each subject included: socio-demographic data, types of treatments received at home, history of present illness and outcome of blood smear testing for malaria parasite.

Sampling technique: Average of five to ten children and their parents/caregivers respectively attended the CHER of OOUTH on each day. All the eligible caregiver-child pair who presented at CHER during the study period was conveniently recruited, except those who did not give consent.

Inclusion and Exclusion Criteria: All febrile patients who presented to the Children Emergency Room of OOUTH and their parents/caregivers consented to participate in the study

Sample size: The sample size was determined using the standard statistical formula for sample size estimation in a study of proportions in a single population (Balogun et al.,2019) $n = (z^2pq)/d^2$ where, n = Minimum sample size, z = Standardnormal deviate set at 1.645, which corresponds to the 90% confidence interval. p = 16.2% (0.162) being the prevalence of malaria in South West Nigeria from a national survey (2), q = 1 - p (1 - p)0.162) = 0.838, d = degree of accuracy desired = 0.1. Substituting these figures into the formula the calculated sample size was 37, an additional 25% of the calculated sample size (9 subjects) was added adjusting for drop-off participants to bring the calculated minimum study sample size to 46. Ethical Considerations: All recruited caregivers gave voluntary consent for their participation in the study which was based on the protocol approved by the Department of Paediatrics of OOUTH. A detailed explanation of what the study entails was given to the caregivers before they gave their voluntary consent. The study was carried out following the basic principle of research ethics as outline with the Helsinki declaration.

Data analysis: Social classification was done using Oyedeji (1985) proposed scheme based on the parents' occupational and educational levels into five classes (I – V) in descending order of privilege. Classes I and II were grouped together as upper

social strata, class III was considered middle strata while classes IV and V were grouped together as lower social strata. A rural area is defined as an open swath of land that has few homes or other buildings, and population density is very low (Rural Area., 2023). The collected data were entered into Microsoft Excel and Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 17.0. The mean, median, standard deviation and proportion were used for data summarization. The Chi-Square test was used to test relationship between categorical variables. P values < 0.05 were considered significant.

RESULTS

Characteristics of the study population

During the study period, a total of 50 children were studied. The children had a median age of 26.5 months (IQR 1.0 – 156.0). Majority of the recruited febrile children (62.0%) belonged to the age category 0 – 5 years. Almost three-quarters (72.0%) of the children were males. The majority of the caregivers were parents (94.0%). The mean age of the fathers and mothers were 40.7 (±9.3) years and 34.1 (±8.0) years respectively, with a range of 27.0 to 78.0 years and 20.0 to 52.0 years respectively. The parental socioeconomic strata were upper, middle and lower for 17 (34.0%), 24 (48%) and 9 (18.0%) of the febrile children respectively (Table 1). About three-quarters (74.0%) lived within an urban community.

Table 1: Characteristics of the study population

Characteristics	Variable	N	%
Age Group of Child (years)			
	0 - 5	31	62.0
	>5 - 10	9	18.0
	>10	10	20.0
Gender of Child			
	Male	36	72.0
	Female	14	28.0
Caregiver's Relationship to Child			
,	Parent	47	94.0
	Aunt	1	2.0
	Grandparent	2	4.0
Parental Socioeconomic Strata	·		
	Upper	17	34.0
	Middle	24	48.0
	Lower	9	18.0
Place of Residence			
	Urban	37	74.0
	Rural	13	26.0

Clinical characteristics of the study population

Table 2 shows the clinical characteristics of the study population. There-quarters of the febrile

children had duration of fever of more than one day (77.5%) and four-fifths had negative blood smear for malaria parasite (82.2%). Only four (8.0%) of the febrile children received an antimalarial drug before presentation at OOUTH. Twelve of the febrile children (24.0%) had a presenting temperature of \geq 38.5°C. The mean presenting temperature was 37.8 (\pm 1.2) °C with range of 35.5 to 41.0°C.

Antimalarial drug use among study population
The distribution of febrile children with and without antimalarial drug use by clinical and socio-economic characteristics is as shown in Table 3. Four (8.0%) of the 50 children with febrile illnesses had received antimalarial drug prior to presentation to the hospital. Three and one of the febrile children who used antimalarial drug before hospital presentation belonged_to middle and upper social strata respectively. Three of the four febrile children who used antimalarial drug before

five years or less. The parent was the primary caregivers and the presenting temperature was <38.5 °C for the four febrile children who received antimalarial drug prior to presentation to the hospital. All the four febrile children who received antimalarial drug prior to presentation to the hospital had a negative blood smear for malaria parasites and a duration of fever greater than two days prior to presentation to the hospital. Three of the four febrile children who received antimalarial drug before hospital presentation resided in urban community.

The antimalarial drug used by all the four febrile children before hospital presentation was artemether-lumefantrine. The drugs were obtained by: over-the counter purchases. The other medications used included: paracetamol (41.2%), antibiotics (29.4%). teething mixtures (11.8%), ibuprofen (2.9%), herbal concoction (5.9%) and cough mixtures (8.8%).

Table 2: Clinical characteristics of the study population

hospital presentation belonged to age category

Characteristics	Variable	N	%
Duration of fever before presentation at OOUTH (days) (n = 40)	1	9	22.5
	2 – 4	15	37.5
	5-9	13	32.5
	≥10	3	7.5
Use of antimalarial drug before presentation at OOUTH by febrile patients (n = 50)	Yes No	4 46	8.0 92.0
Malaria blood film result (n = 45)	Positive Negative	8 37	17.8 82.2
Presenting temperature (°C)	<38.5 ≥38.5	38 12	76.0 24.0

Table 3 Antimalarial drug use among study population

Characteristics	Variable	Used Antimalarial drug (n = 4)	Did not use Antimalarial drug (n = 46)	p- value
Age Group of Child (years)	0 – 5 >5	3 (9.7) 1 (11.1)	28 (90.3) 8 (88.9)	0.900
Gender of Child	Male	2 (5.6)	34 (94.4)	0.659
Caregiver's Relationship to Child	Female Parent	2 (14.3) 4 (8.5)	12 (85.7) 43 (91.5)	0.761
Parental Socioeconomic Strata	Others Upper	0 (0.0) 1 (5.9)	1 (100.0) 16 (94.1)	o.866
	Others	3 (12.5)	21 (87.5)	
Place of Residence	Urban Rural	3 (8.1) 1 (7.7)	34 (91.9) 12 (92.3)	0.962
Malaria parasitaemia (n = 45)	Positive Negative	o (o.o) 4 (10.8)	8 (100.0) 33 (89.2)	0.772
Duration of fever before presentation at OOUTH (days)	≤2	0 (0.0)	13 (100.0)	0.368
(n = 40)	>2	4 (14.8)	23 (85.2)	
Presenting temperature (°C)	<38.5 ≥38.5	4 (10.5) 0 (0.0)	34 (89.5) 12 (100.0)	0.575

DISCUSSION

Pre-hospital drug utilization in sick children is of great concern globally (Oshikoya et al., 2007)). Previous authors (21) have shown various problems ranging from misuse and abuse of prescribed drugs, as well as errors of medications. The first response by most families to their sick children during illnesses was the use of non-prescribed drugs (Oshikoya et al., 2007). The conditions for which the drugs were used include fever, diarrhoea, vomiting, cough and upper respiratory tract infection (Oshikoya et al., 2007)).

The overall rate of pre-hospital use of antimalarial in the present study was 8% of the recruited febrile children. The reported rate of pre-hospital use of antimalarial from the present study is lower than 47% and 83.2% reported by Hamel *et al* (2001) and Senbanjo *et al* (2006) among children with fever in Kenya and Ile-Ife Southwestern Nigeria. This implies that self-medication is less popular among our study participants. The Kenyan and Southwestern Nigeria studies were conducted more than two decades ago when relatively cheaper and more affordable chloroquine was the first line of antimalarial drug.

During the acute phase, fever is the most apparent clinical manifestation of Plasmodium falciparum infection (24). The data from the current study demonstrated that all the four febrile children who received antimalarial drug prior to presentation to the hospital had a negative blood smear for malaria parasite. This implies that the mother's presumptive diagnosis of malaria in sick children with fever and subsequent administration of an antimalarial drug might promote early emergence of resistant malaria to the novel antimalarial drug. This finding corroborates the observation of previous authors that empirical treatments initiated at home may often be inappropriate (Tumukunde et al., 2017), with very low diagnostic accuracy (O'Dempsey et al., 1993; Hamer et al., 2007; O'Boyle et al., 2020). It is therefore, attractive to suggest that the test - and - treat approach to management of malaria still remains the way to prevent resistant to the commonly used antimalarial drugs. The introduction of the malaria Rapid Diagnostic Test (RDT) kits which can be used by caregivers at home has made the test-and-treat approach of malaria possible at community level (Mubi et al., 2011; Chanda et al., 2011).

Previous studies have shown that the pattern of self-medication differs from one population to another depending on their socio-demographic factors including: age, gender, income, educational level and medical knowledge (Abdelwahed et al., 2023). It was observed in the

present study that three out of the four febrile children who received antimalarial medications prior to presentation to the hospital were older than five years, resided in urban settings and had parental socioeconomic status below the upper strata. This finding may be anecdotal as the figures obtained were too small for meaningful statistical analysis. This further emphasizes the need for a larger, collaborative study in order to clarify the situation.

The current study revealed that all the four febrile children who received antimalarial drugs prior to presentation to the hospital had duration of fever of greater than two days prior to presentation to the hospital. This finding suggested that the caregivers brought these children to the hospital due to the persistence of the fever. The explanation for the persistence of the fever is not far-fetched. All these four patients had a negative blood smear for malaria parasite suggesting other febrile illnesses aside malaria and thus, making the administration of antimalarial drug inappropriate in them.

In the present study, the use of artemetherlumefantrine by all the four febrile children before hospital presentation as observed was probably due to malaria treatment guidelines which recommends artesunate combination therapy (ACT) as the first line antimalarial drug and probably because some brands of artemetherlumefantrine are quite cheap in the market. A descriptive cross-sectional study conducted by Mbah et al (2020) reported that the most sold antimalarial drug is artemether-lumefantrine. There are no current reports of in vivo resistance to artemether-lumefantrine in Nigeria (Aiavi & Ukwaja, 2013), therefore, if the practice of its inappropriate use as documented in this study is not checkmated, the likelihood of developing resistance to the drug is imminent.

It is easy to purchase prescribed and non-prescribed drugs with or without medical prescriptions from a wide variety of sources in Nigeria (21). These drugs, if not completely used, may be kept for future use by the parents (Oshikoya et al., 2007). It was observed that the sources of the antimalarial drugs used by the studied febrile children were obtained through the over-the counter purchases which represent self-medication and improper antimalarial use.

CONCLUSION

In conclusion, this study has shown that prehospital use of antimalarial does occur but its practice is less popular among our study participants and this action may be generally inappropriate. There is need for more emphasis in the area of public enlightenment to further educate the people on the proper use of common antimalarial. This would guide against breeding strains of the malaria parasite that would be resistant to artemether-lumefantrine.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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