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Presumptive Diagnosis and Treatment of Malaria in Febrile Children in Parts of South Eastern Nigeria

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Abstract

Background: Malaria treatment in Nigeria and other Sub-Saharan Africa is largely based on presumptive diagnosis leading to poor management of non-malaria febrile illness and abuse of antimalarial drugs.

Objectives: To evaluate malaria treatments based on presumptive diagnosis and describe the actual density of uncomplicated malaria among febrile children in South Eastern Nigeria.

Methods: Parasitological diagnosis using microscopy was done among 560 febrile children, 0-12 years attending Paediatric Clinics in a tertiary health facility in the study area. Their blood samples were collected prior to malaria treatment using IMCI guidelines and standard routine clinical practice. These children were grouped into under 5 years and 5-12 years. Data was analysed using SPSS.

Results: Out of 560 children (0-12 years) enrolled in this study, 156(27.9%) were positive for malaria parasites, while 404(72.1%) were negative. Children's age was significantly related to the prevalence of uncomplicated malaria (p<0.05) and a high determinant in explaining 6.4% of the variance in the prevalence of uncomplicated malaria (F=37.915 and p<0.05). Children 5-12 years (51.9%) had higher parasite density (40,678.2 P/μl) compared to those less than 5. The negative result of 72.1% indicated possibility of overtreatment with antimalarial.

Conclusion: The findings highlight the need for the scaling-up of parasitological confirmation of all malaria suspected cases before treatment with the artemesinin-based combination therapies. Improving the diagnostic system for effective health care delivery in endemic areas will not only provide a good platform for malaria treatment/ monitoring but also reduce rapid onset of drug resistance.

Keywords: Presumptive diagnosis; Malaria; Febrile children; Artemesinin-based combination therapy; South Eastern Nigeria

Introduction

Malaria remains an important public health problem and a principal cause of childhood mortality [1]. It is estimated that at least 10 percent of all childhood deaths are due to malaria [2]. The clinical presentation of malaria is highly variable and overlaps with that of a number of other common illnesses, including pneumonia, which is associated with significant morbidity and mortality [3-5]. Mortality is highest among children under five years of age who do not receive prompt/ appropriate treatment [2].

Despite the fact that the main strategy for reducing childhood mortality and morbidity is presumptive treatment of all fevers in children with antimalarial drugs [6], the greatest challenge of malaria treatment still occurs during treatment as many children with malaria are treated at home [7].

The policy of presumptive treatment of malaria for all febrile illnesses has been widely advocated in sub-Saharan Africa, especially in young children [8,9]. One of the reasons for presumptive treatment is the fear of rapid mortality of untreated malaria, especially in young children. Until recently, the diagnosis of malaria in children in most African settings was on the clinical basis of fever and other malaria related symptoms that are, however, not specific to malaria alone. In a recent trial, clinicians prescribed antimalarials only in patients with a negative test as often with rapid diagnostic tests (RDTs) as with microscopy [10]. The underlying problem appears to be that clinicians are often unsure of what to do when clinical features are compatible with malaria, but the malaria diagnostic test (one of the few tests often available) is negative

A history of fever and positive blood smear on light microscopy is the standard for malaria diagnosis and basis of treatment, but in practice this is not often adhered to. Microscopy is often not used even when it is available [11]. The most important consequence of treating only for malaria when no parasitemia exists is failure to address other life-threatening conditions.

Malaria control measures have been scaled up in malaria endemic countries and there is growing evidence of overtreatment of malaria as fewer cases of fever or suspected cases of malaria are likely to be

malaria upon confirmation [10-12]. Over-prescription of ACT may result in substantial unnecessary use of this class of drugs and the risk of developing resistance [13]. In addition, blind treatment of malaria without parasitological confirmation of the parasite deviates from best practices There is increasing reports of the decrease in incidence of malaria [14-16] and with almost universal introduction of artemisinin-based combination therapy (ACT), it is imperative that parasite-based confirmation of malaria be scaled up even in the under-fives, given the proclivity to overtreatment of malaria due to clinical over diagnosis.

Emphasis on prompt treatment and distribution of pre-packaged antimalarial drugs are strengths of the Home Management of Malaria [17], a strategy proposed by the World Health Organization in an effort to improve prompt access to treatment. This is predicated on the observation that the majority of fevers in that age group in Sub-Saharan Africa are due to malaria [18]. The need to reduce malaria morbidity and mortality through the improvement of home treatment of childhood fevers has led to a number of community-based initiatives, including the training of mothers, community health workers, or shopkeepers in diagnosis, appropriate antimalarial use, and referral [19].

This study is intended to describe the prevalence of uncomplicated malaria among febrile children attending PHC clinic and hospitals in Imo State, Nigeria and make inferences towards improving treatment protocols.

Materials and Methods

Study setting

This study was conducted at the Federal Medical Center Owerri, a Tertiary Health Facility in Imo State, Southeastern Nigeria. This center receives patients from primary and secondary health facilities in the state on referral and its location contributes immensely to large patient turnout.

Patients recruitment

A total of 560 children aged 0–12 years, who presented with fever or history of fever in the last 24 hours at the Outpatient's Department (OPD) were recruited for this study. The children were enrolled if they met the following inclusion criteria: 0 to 12 years, documented fever at presentation or history of fever in the last 24 hours, absence of danger signs of complicated/severe malaria and known serious chronic disease, and willingness of the parent/guardian to provide written assent and consent. Those that presented with signs of complicated malaria namely convulsions/coma, prostration, severe vomiting, and so forth were excluded and these were managed accordingly. The case report form (CRF) that included documented axillary body temperature, history of fever, and other presenting symptoms was completed for each patient before making a finger prick for malaria blood smear preparation.

Variables	Frequency	Percentage (%)
Gender		
Male	299	53.4
Female	261	46.6
Age distribution		
Less than 5 years		67.1
5-12 years		32.9
Presence of *Plasmodium falciparum*		
Positive	156	27.9
Negative	404	72.1

Table 1: Study participation.

Determination of malaria parasiteamia by microscopy

Blood was collected from the finger tip of each child who had been presumptively diagnosed of having malaria. Good laboratory practice was adhered to during sample collection, smear preparation and staining. Two slides were made from the fingertip blood of each child. The first slide was the read "(R)" slide (that is the slide that was read), while the other slide was archived "(A)" slide. This is for quality assurance purposes. The thin films were fixed with methanol and left to dry. The prepared smears were stained with 10% Giemsa at a pH of 7.2 for 10 minutes. The staining process was quality controlled to ensure that the morphology of the malaria parasites in positive slides were distinct and clear.

The parasite density was computed as the number of parasites per 500 white blood cells on a thick film and reported as parasites per microlitre of blood assuming an average white blood-cell count of 8000 per L [20]. Stained slides were examined under the light microscope using 100X objective lens (immersion oil). A slide was considered negative after 100 high power fields (HPF) have been examined. Another Microscopist, the second reader, was made to re-read each slide. Parasite counts of >20% discordance between two readers were reread by a third reader, who served as the tie breaker. However, parasite counts of less than 20% discordance between the first and second readers was accepted and the mean parasite count taken to compute the parasite density or parasitaemia for each child. The Microscopists that read the slides were prequalified before the study through a rigorous process. Each child that was confirmed to have malaria parasites was treated with antimalarial combination therapy.

Ethical approval

The study was approved by the Federal Medical center Owerri Nigeria Ethical/Research Committee. Consent was obtained from the children and their parents/guardian/caregiver before they were enrolled. All patients studied received the appropriate standard of care.

Data analysis

Result was analyzed using IBM SPSS version 20 and presented in tables and charts. Chi square and regression was used to make inference about variables.

Density and Intensity falciparum			
Variables	**Positive**	**Parasitaemia Range (P/µl)**	**Mean Parasitaemia (P/µl)**
Less than 5 years	75(48.1)	15 – 698, 269	39,903.6
5-12 years	81(51.9)	16 – 432, 077	40,678.2

Table 2: Density and intensity of *Plasmodium falciparum* in the different age group.

Presence of Plasmodium falciparum			
Variables	**Positive**	**Negative**	**Total**
Less than 5 years	75(19.9)	301(80.1)	376(100)
5-12 years	81(44.0)	103(56.0)	184(100)
χ^2= 35.630, df=1, p=0.000			

Table 3: Age group and presence of *Plasmodium falciparum*.

Model Summary					Change Statistics		Sig. F Change
Model	**R**	**R Square**	**Adjusted R Square**	**Std. Error of the Estimate**	**R Square Change**	**F Change**	
1	0.252a	0.064	0.062	0.43458	0.064	37.915	0. 000
Predictors: (Constant), Age group, Dependent variable: Presence of *Plasmodium falciparum*							

Table 4: Age and presence of *Plasmodium falciparum* Regression.

Coefficients							
Model			**Unstandardized Coefficients**		**Standardized Coefficients**	**T**	**Sig.**
		B	**Std. Error**		**Beta**		
1	(Constant)	2.041	0.055			37.050	0.000
	Age group	-0.241	0.039		-0.252	-6.158	0.000

Table 5: Age and presence of *Plasmodium falciparum* coefficients.

Results

A total of 560 children participated in the study comprising 53.4% males and 46.6% females. Only 27.9% of the children whose blood films were examined microscopically was positive for malaria parasites, while 72.1% of the slides were negative (Table 1).

Table 2 shows the density and intensity of *P. falciparum* among the different age brackets studied who were positive. Those below 5 years had parasitaemia ranging 15-698,269 P/µl with a mean parasitaemia of 39,903.6 P/µl whereas those 5 years and above had parasitaemia ranging 16-432,077 P/µl with mean parasitaemia of 40,678.2 P/µl (Table 2).

About 19.9% of the 376 children of age<5 years and 44% of the 184 children of age 5-12 years were respectively positive for *P. falciparum*. Also 80.1% of children <5 years and 56% of those 5-12 years were over diagnosed and treated following IMCI guideline and standard routine practice of the clinic. There was a significant relationship between the age of the children and the presence of *Plasmodium falciparum* predominantly in those aged 5-years and above instead of the high risk group (<5years).

Tables 3-5 shows the regression analysis to investigate the relationship between age and presence/prevalence of *Plasmodium falciparum*. Children's age was significantly related to the prevalence of uncomplicated malaria (p=0.000) and a high determinant in explaining 6.4% of the variance in the prevalence of uncomplicated malaria (F=37.915 and p=0.000).

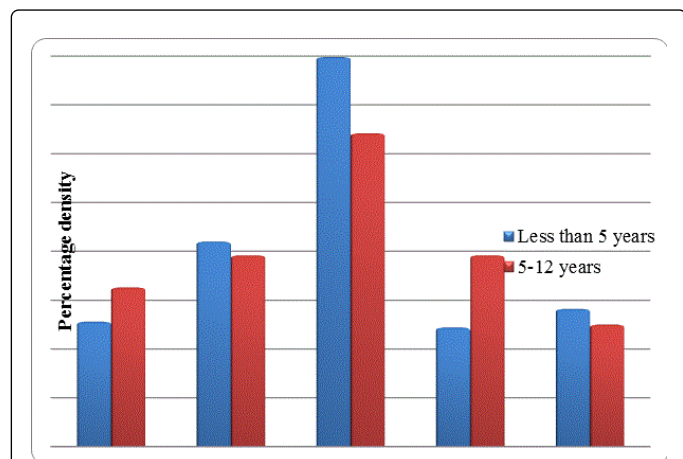**Figure 1:** Distribution of parasitaemia in age group (<5 years and 5-12 years).
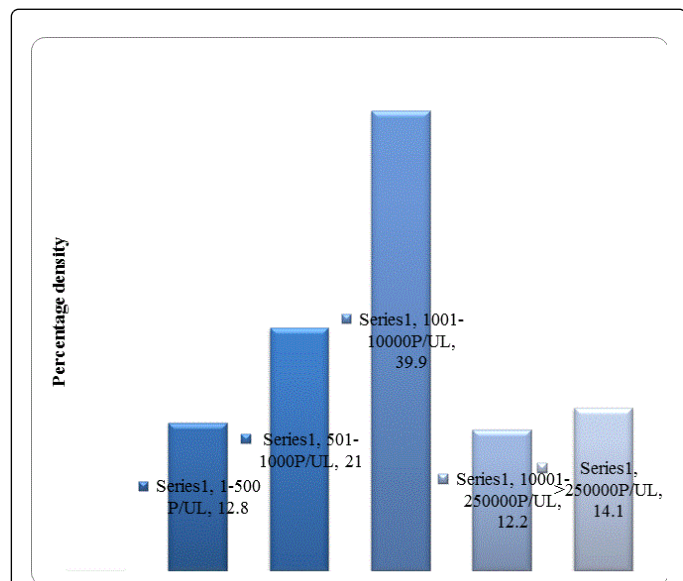

Figure 2: Density Distribution in age group 0-12 years.

Figure 1 shows the distribution of parasitaemia among the study children. The highest level of parasitaemia (1001–10,000 P/μl) was observed for those less than 5 years (35%) and those 5-12 years (>30%) respectively.

Generally, 39.9% of the children had parasite density of 1001-10,000 P/μl while about 12.2% recorded between 10,001-250,000 P/μl (Figure 2).

Figure 3 depicts the symptomatic presentations of the children. About 84.4% of those who were positive for malaria had fever and

while 92.6% of those who had fever were malaria slide negative. Those positive also presented symptoms like chills (53.4%), cough (44.8%), convulsion (1.8%), diarrhoea (46.6%), headache (32.8%) and loss of appetite (50%).
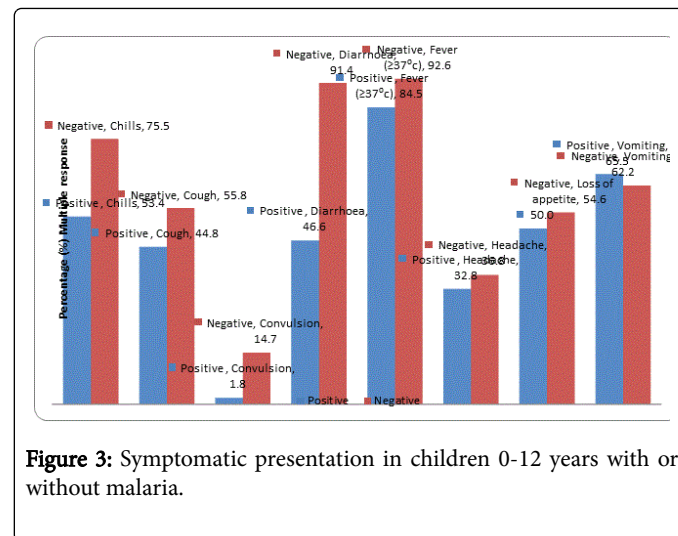

Figure 3: Symptomatic presentation in children 0-12 years with or without malaria.

Discussion

Traditionally, malaria has been regarded as the most common and important febrile illness in sub-Saharan Africa [21]. The malaria burden is indeed a threat to life and a drain in the economy of the already impoverished people of the sub-Saharan Africa [22].

Early diagnosis, prompt and effective therapy are the pivots of the global malaria control strategy aimed at reducing unnecessary use of antimalarials and also reducing the mortality and morbidity associated with the illness [23]. We observed that 53.4% and 46.6% of the male and female children respectively who were febrile were on antimalarial treatment based on presumptive diagnosis. However only 27.9% among them were actually malaria slide positive when examined microscopically. A majority (72.1%) were slide negative. This may corroborate indications that malaria prevalence may be decreasing in several areas of sub-Saharan Africa in recent years [24], and so most patients seen with febrile illness in these areas might not apparently have malaria infection.

Although 84.4% of the febrile children actually had malaria with high parasite density, the number who also presented with fever but were misdiagnosed for malaria and then treated with antimalarials may have important consequences. This will include mismanagement of other febrile illnesses and vulnerability of the patient to worsening of the underlying true cause of fever [25]. An unnecessary anti-malarial treatment of non-malarial fevers with the generally recommended artemisinin-based combination therapy (ACT) [26], leading to wastage of antimalarials is also implied. It can result in abuse of antimalarials which are mostly obtained over the counter [27] or left over drugs from previous treatments [28]. Furthermore, there is likely spread of resistance towards these compounds, by exposing infecting parasites to sub-therapeutic doses of the long-acting partner drug during a considerable period of time [29-31].

Malaria can be suspected presumptively from the signs and symptoms such as we observed in our study and consistent with those previously reported [32]. However, since most mothers usually take

action when fever is recognized [33], it is necessary that a definitive diagnosis is encouraged using tests demonstrating the parasite or its components [34]. This must be in line with the 2010, WHO recommendation of parasitological confirmation before anti-malarial treatment [35,36]. It will no doubt be a gateway to effective and sustained malaria treatment protocol. An improved awareness and capability of mothers and caregivers to control the difficulties associated with complexity and dynamism of factors influencing their decisions in managing childhood illnesses at home is also important34. This will generally bring about a substantial improvement in integrated management of childhood illnesses.

Conclusion

Malaria is a problematic health issue in children but frequently over diagnosed. Our results indicate a lower proportion of the febrile children actually having malaria. Presumptive malaria diagnosis a lot of times may lead to over diagnosis and therefore mismanagement of other febrile illnesses e.g. pneumonia, meningitis, enteric fever etc. Antimalarial treatment to all that presents with fever without due confirmation means; Waste of resources by the poor, failure to treat/look for other potential life threatening illnesses, and Increase risk of emergence of resistance to ACT.

There is need to improve diagnostic systems for fever and to understand that proper diagnosis precedes adequate treatment.

Parasitological diagnosis in all health care systems should be scaled up through strategic awareness creation/promotion and behavioural change communication for health workers.

In addition, there should be increased awareness and use of rapid diagnostic test (RDT) in rural communities where malaria microscopy is not readily available. In such places and other endemic areas, community distribution points where these RDTs can be easily accessed by the inhabitants should be set up. Patent medicine dealers (PMDs) who are the first contact of most rural dwellers [28] can as well be used to ensure adequate diagnosis before treatment by making them stock RDTs constantly and also use them when necessary to rapidly diagnose malaria before treating their clients who present with fever.

Acknowledgement

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