



Science

PRESUMPTIVE DIAGNOSIS OF MALARIA IN FEBRILE CHILDREN; IS IT JUSTIFIED?

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Abstract

Background: Malaria is deadly and a major disease burden in Africa especially among the under-5s. Due to the high death rate from malaria in endemic region, World Health Organization previous recommendation was presumptive treatment of malaria.

Aim: This study aimed to evaluate if presumptive diagnosis of malaria in our region is still justified, and increase the awareness for proper evaluation for other causes of fever in febrile children.

Methods: Apart of a single blinded prospective interventional study carried out between March and May 2016, at the children outpatient unit of Lagos State University Teaching Hospital, Ikeja, Nigeria. Consecutive children aged 6 months to 12 years with temperature of 37.50C and above at presentation without prior antimalaria treatment were recruited. Clinical and laboratory evaluation for malaria were done in these subjects. Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0. Test of statistical significant was set at <0.05.

Results: Eighty-eight (88) children were recruited. The mean age of studied subjects was 43±46.5 months with a median of 25 months. Male to female ratio was 1.1:1. The axillary temperature range of studied subjects ranged between 37.50C to 390C. The mean temperature of subjects was 37.8±0.370C. Out of 88 children recruited for the study, 51 (58%) had microscopic malaria test being positive. Up to 37 (42%) febrile children tested negative for malaria.

Conclusion: Malaria infection in children is still high in our environment, but presumption treatment of malaria is no longer justified. There is a need to scale up provision of diagnostic tools for malaria so that overtreatment can be curtailed.

Keywords: Malaria; Fever; Presumptive Treatment; Nigeria.

Cite This Article: Animasahun Adeola B, Adekunle Motunrayo O, Afadapa Maria A, and Salisu Mohammed A. (2017). "PRESUMPTIVE DIAGNOSIS OF MALARIA IN FEBRILE CHILDREN; IS IT JUSTIFIED?." *International Journal of Research - Granthaalayah*, 5(12), 291-297. <https://doi.org/10.5281/zenodo.1134797>.

1. Introduction

Malaria is a deadly disease; it is a major disease burden in Africa especially among the under-5s [1] the burden of malaria infection and its causal effect is concentrated in the sub-Saharan countries where over 88% of the cases occur with 90% death occurrence in this region. [1]

In Nigeria, the burden of malaria is high as 97% among the population at risk. [2] It account for over 60% of public hospital visit. [2] Malaria is the commonest cause of morbidity and mortality in Nigerian children accounting for 20% of mortality in under-5s.[2] Despite this data, there was appreciable decline in the occurrence of malaria by 18% in the year 2015 in Nigeria.[3]

Due to the high death rate from malaria in endemic region, World Health Organization previous recommendation was presumptive treatment of malaria. [4] However, the availability of rapid diagnostic test has led the recommendation of parasitological diagnosis before treatment. [5] Reasons for the new guideline are the recorded successes of decline in malaria transmission in sub-Saharan Africa and the availability of rapid diagnostic test. [5] However, there is a conflicting opinion by Graz et al. [6] where the cost effectiveness of parasitological diagnosis before treatment of malaria infection especially in regions yet to attain a decline in infection rate was questioned.

The benefits of testing before treatment of malaria have been highlighted by World Health Organization; [5] this will prevent unnecessary use of antimalaria and will reduce the frequency of adverse effect especially in those that do not need the drug. Also, test before treatment will improve malaria case detection and reporting.

In five primary health centers in Jos, Nigeria, Ikeh and co-researchers [7] found a prevalence of malaria of 56.9% among 260 under-five children with fever. The prevalence of malaria in subjects that have not had antimalaria prior to presentation was 56.8% and a slightly higher prevalence of 57% was reported in subjects that had antimalaria commenced before presentation. Prevalence of malaria in febrile children presumptively diagnosed with malaria was 54% in a study done in Zamfara, Nigeria by Abdulkadir et al. [8] However, in this study, 57% of the subjects already had one form of antimalaria treatment.

There is need for further review of the routine presumptive malaria diagnosis which currently is still being practiced in most centers in Nigeria. This will provide knowledge on the need for further review of malaria protocols and guidelines and also provide additional data on the effectiveness of measures instituted in the eradication of malaria. This study aimed to evaluate the rightfulness of presumptive diagnosis of malaria in our region and increase the awareness for proper evaluation for other causes of fever in febrile children.

2. Subjects and Methods

This was part of a single blinded prospective interventional study carried out between March and May 2016 at the outpatient unit of Lagos State University Teaching Hospital, Ikeja, Nigeria (LASUTH). It is a center that receives patients from both public and private clinics within Lagos State and its environs. The Paediatric outpatient department of LASUTH attends to averagely 80 children per day.

Inclusion criteria for the study was children aged 6 months to twelve years with fever of temperature of 37.5°C and above at presentation who have not had any antimalaria treatment in the current illness. Informed and written consent was obtained from the caregiver and assent was obtained from children seven years and above before recruitment into the study. Clinical and laboratory evaluation for malaria was done in all the children with febrile illness: Throat, ear and other systemic examinations were done for the identification of the cause of the fever. As required, further investigations done were chest radiograph and swab analysis for microscopy culture and sensitivity in cases with suppurative otitis media. Microscopy test for malaria was done in children that met the inclusion criteria. Microscopy test for malaria was done in children that met the inclusion criteria. Examination for the presence of malaria parasite density and specie was determined using the thick film and the thin blood film respectively. The thin film was fixed in methanol. Staining of the film using a Giemsa stain and visual examination using a microscope was done. The red blood cells were examined for intracellular parasites. Semi quantitative count of parasitized red blood cell using the plus system was done. The presence of 1 to 10 and 11 to 100 asexual parasites per 100 thick field was classified as one plus (+) and 2 pluses (++) respectively. 1 to 10 and 11 to 100 asexual parasites per one thick field was classified as 3 (+++) and 4 (+++++) pluses respectively. Thorough examination of at least 100 microscopic field of thick film was examined before a result was concluded as negative result. The thin films were examined for different morphologic features of the different species of malaria parasite. [9] Complete blood count was also done. Antimalaria medication was given to children that tested positive for malaria and a repeat microscopy malaria test was done one week after completion of the antimalaria to ensure parasitic clearance.

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0. Patients' demographics were represented as frequency and percentages. Continuous variables were presented as mean \pm standard deviation for parametric data. Test of statistical significant was set at <0.05 .

3. Results

A total number of 88 children had fever at presentation during the study period. The mean age of studied subjects was 43 ± 46.5 months with a median value of 25 months. The median age was 25 months with the highest number of subjects being 12 months of age. Male subjects seen were 53% and female accounted for 47% of the studied subjects. The axillary temperature range of studied subjects was 37.5°C to 39°C . The mean temperature of subjects was $37.8\pm 0.37^{\circ}\text{C}$ and the median temperature was 37.7°C

Out of 88 children recruited for the study, 51 had microscopic malaria test being positive (58%) and 42% febrile children tested negative for malaria. Malaria infection was highest within the age range of 6 months and five years which accounted for 71% of positively malaria tested subjects. Only four subjects (7.8%) with positive result were between six and twelve months.

Table 1: Demographic Characteristics of Subjects

Sex Distribution of Subjects	Male	47(53%)
	Female	41(47%)
Age Distribution of Subjects with Malaria	Less than 1 year	4(7.8%)
	Years	34(66.7%)
	>5 years	13(25.5%)

All children that had parasitological diagnosis for malaria had *Plasmodium falciparum* as the causative parasite and they all had one plus of malaria parasite (+) which is 1 to 10 parasitized red cells per 100 thick fields. They all had artemisinin combination therapy for three days and a repeat microscopic test done in 40 out of 51 children. Eleven children treated for malaria infection were lost to follow-up. Repeat parasitological test in 40 that presented for follow up showed total clearance of parasite in the blood film.

Result of full blood count in four children treated for malaria showed co-bacterial infection evidenced by leukocytosis and neutrophilia. The mean packed cell volume of subjects with malaria was $31.7 \pm 4.9\%$.

In children with negative result for malaria parasite, 54% had upper respiratory tract infection and 3 case of uncomplicated bronchopneumonia were seen. A five years old boy had diagnosis of mumps following subsequent development of jaw swelling. Other causes of fever diagnosed were acute suppurative otitis media, diarrhea disease, tonsillitis, urinary tract infection and bronchiolitis.

Table 2: Diagnosis in Subjects

Disease Conditions	No of Cases (%)
Malaria	51(58%)
URTI	20(22.7%)
Uncomplicated Bronchopneumonia	3(3.4%)
Suppurative Otitis Media	2(2.3%)
Bronchiolitis	2(2.3%)
Furunculosis	2(2.3%)
Diarrhea	1(1.1%)
Mumps	1(1.1%)
Tonsillitis	1(1.1%)
Urinary Tract Infection	1(1.1%)
Sepsis	1(1.1%)
Unspecified	3(3.4%)

4. Discussion

The prevalence of malaria infection in febrile children aged 6 months to 12 years in the current study is 58%. This is similar to the findings by Ikeh et al. [7] and Abdulkadir et al. [8] with result of 54% and 56.3% respectively. A similar finding was also seen in the study done between October 2008 and June 2009 in Sokoto, Nigeria by Singh et al. [10] where the prevalence of malaria in 800 febrile children was 56%. However, the prevalence in the current study is higher than a prevalence of 20.7% reported by Oladosu and Oyibo [11] in a primary health center in Lagos. Inclusion of children without fever at presentation could account for a lower prevalence in their study. The prevalence in this present study and other Nigerian studies reviewed above are high compared to a prevalence of 12% seen by Mazigo et al. [12] in Tanzania. This disparity is alarming despite both regions with holo-endemicity for malaria. The immediate reason for this disparity is not clear.

Presumptive diagnosis of malaria in febrile children is commonly done in malaria endemic region. In this present study, 42% of the subjects would have been wrongly diagnosed and treated for malaria. This is lower than the finding by Okoro et al. [13] in Imo State, Nigeria where 92.6% of subjects that had fever had negative blood film for malaria parasite. The inclusion of children without fever at presentation but within its 24 hour could have falsely increased the number of children with fever. Children recruited in this study were those with fever at presentation. This is because tactile assessment of fever is often practiced in our environment which has been studied to overestimate fever by over 24%. [14]

Presumptive diagnosis of malaria in febrile children is high in our environment. This has led to unnecessary treatment with antimalaria with manifestations of adverse effect. Omission of life threatening causes or complications of other causes of fever in children can occur if children are presumptively treated as having malaria. Clinical diagnosis of malaria has a low specificity and overtreatment of cases often occur. [5] Though the need for proper evaluation of every child for other causes of fever is the standard practice, in region where children are presumptively treated for malaria, this is often neglected. [13]

The existence of rapid diagnostic testing for malaria has made quick and universal laboratory screening and diagnosis of malaria a possibility. Rapid diagnostic test has a high sensitivity for the detection of malaria parasites. The confirmation of infection in those with possible falsely negative result can then be confirmed by microscopic testing. [8]

Malaria was commonest in subjects five years and below. This is not surprising because there is deficient immunity for malaria parasite in this age group. This finding is similar to that reported by other researchers in Nigeria. However, this finding has not been consistent; Umaru and co-researchers [15] had the highest prevalence of malaria in children five to fifteen years. No immediate explanation can be given for this conflicting result.

Subjects with positive malaria test in infancy were only 7.8% of the subjects. The explanation for this is the protection from malaria due to the presence of passive immunity acquired from the mother. This finding was also seen in the studies by Mbanugo et al. [16] and Nwaorgu et al. [17]

No significant difference was seen in the prevalence of malaria between male and female subjects with a disparity of slightly higher percentage in male subjects. This is similar to the result reported by Nmadu et al. [18] where there was a slight male preponderance.

Plasmodium falciparum was the causative parasite of malaria in all subjects in this current study. This finding is an additional report to previously documented findings of *Plasmodium falciparum* as the commonest Plasmodium specie that causes malaria with a high predominance in Africa. [7,16,19] The predominance of *P. falciparum* parasite, the deadliest specie in Nigeria emphasizes the need for drastic measures for eradication of malaria.

Artemisinin combination therapy is the WHO recommended choice of drug for uncomplicated antimalaria. [5] In this present study there was 100% clearance of parasite in the blood following the use of the combination therapy.

The second commonest cause of fever in this current study is upper respiratory tract infection. Subjects with this diagnosis had mainly coryza and mild fever. The explanation for this is possible because the study was done in rainy season when respiratory tract infection occurrence is high. TemiyeEdamisan [20] identified malaria and respiratory infection as the commonest illnesses in the rainy period. Increase in the breeding sites of mosquito occurs at this period, and the tendency for closure of windows at this period with inadequate ventilation increases the spread of germs that causes respiratory infection.

5. Conclusion

Malaria infection in children is still high in our environment. *Plasmodium Falciparum* is still the predominant cause. Presumptive treatment of malaria can no longer be justified and requires urgent attention. There is need for a scale up in provision and accessibility of diagnostic tools for malaria so that overtreatment can be curtailed. The need for more preventive measures in control of malaria infection cannot be overemphasized.

6. Ethical disclosures

Ethical clearance for the study was obtained. Informed consent was obtained from the parent.

Acknowledgement

We gratefully acknowledge the subjects who participated in this study, their parents, caregivers and other healthcare workers involved in their care.

Disclosures

No Conflict of interest among the authors

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