

Full Length Research Paper

Patterns of acute febrile illness in children in a tertiary health institution in the Niger Delta Region of Nigeria

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Abstract

Differentiating between causes of febrile illness is difficult in malaria-endemic regions where presumptive treatment of all fevers as malaria is practised. To ascertain the proportion of febrile illnesses attributable to malaria and non-malaria causes among children in a tertiary health institution in a malaria-endemic area, blood, ear swab, throat swab and urine samples were obtained from 190 children with febrile illness. Giemsa-stained thick and thin blood films were examined for malaria parasite, while the swabs and urine samples were inoculated on appropriate media and cultured. Standard techniques were used to identify micro-organisms. The proportion of fevers attributable to malaria only was 48.42% (95% CI: 41.32 - 55.52), whilst the proportion of fevers attributable to bacterial infection only was 12.63% (95% CI: 7.93 - 17.33). The cause of fever could not be detected in 62 patients (32.63%: 95% CI: 25.97 - 39.29). There were no significant differences in white blood cell counts between the patients. Our study highlights the importance of other causes of fever outside malaria in malaria-endemic regions, as just over half of the fevers could be linked to malaria. Diagnostic facilities should be strengthened physicians educated on other causes of fever.

Keywords: Fever, malaria, endemic, children, bacterial infection, white blood cell.

INTRODUCTION

Infectious diseases are the major causes of morbidity and mortality in most parts of the developing world, and acute febrile illness is a common cause of hospital admission and death in Africa (Bryce et al., 2005). Malaria is a major cause of morbidity and mortality in children in sub-Saharan Africa (Black et al., 2010). In these malaria-endemic regions of sub-Saharan Africa, a diagnostic dilemma confronts physicians attending to children with fevers, as malaria, bacterial and viral infections in children have overlapping manifestations, making differentiation difficult. This difficulty contributes to missed diagnosis, delayed intervention and inappropriate

treatment. In Nigeria, the presumptive treatment of all fevers as malaria has been the adopted strategy as recommended by the Integrated Management of Childhood Illnesses (Gove, 1997; Federal Ministry of Health 2005; World Health Organization 2005). Generally, febrile children on presentation are assessed and then treated for malaria. If the child doesn't get better, it is assumed that the fever was caused by a resistant malaria strain and stronger or second line anti-malarial agents are then used. Lack of adequate facilities and affordability of tests have meant that most patients would be treated for malaria without any parasitological diagnosis. The accuracy of clinical diagnosis of malaria and the appropriateness of treatment has not been well studied (Reyburn et al., 2004). Studies have shown that bacterial infections are responsible for a sizeable proportion of deaths among children in sub-Saharan

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Africa (Kinney et al., 2010). However, most physicians ask for only malaria parasite tests and full blood counts when febrile children present at the hospital. Clearly defined guidelines on the management of other causes of febrile illnesses in children outside malaria are either lacking or not adhered to in most parts of the country. The 2010 World malaria report noted the low usage of both microscopic diagnostic and rapid diagnostic testing in the diagnosis of malaria in public and private health facilities in Nigeria (World Health Organization, 2010).

The causes and patterns of febrile illnesses in children are not well characterized in the Niger Delta region of Nigeria. With the diagnostic dilemma of children presenting with fever in mind, this study was designed to ascertain the proportion of febrile illnesses attributable to malaria and other bacterial causes in Bayelsa State of Nigeria.

MATERIALS AND METHODS

Study design

This was a prospective cross-sectional study carried out over a 6 months period spanning from October 2011 to March 2012. 190 children between aged between 6 months and 11 years presenting with a fever to the Paediatric Unit of the Niger Delta University Teaching Hospital (NDUTH), Okolobiri, were recruited for the study.

Study Area

The study was carried out at the NDUTH situated in Okolobiri community, a semi-urban community in the Yenagoa Local Government Area of Bayelsa State, in the Niger Delta region of Nigeria. This region lies in the tropical rainforest belt that is endemic for malaria, with all year round transmission of malaria. The NDUTH is a tertiary hospital that serves the entire Bayelsa State and neighbouring communities in Delta and Rivers States of Nigeria. The hospital serves different socio-economic strata of the society - mostly the lower and middle socio-economic groups.

Exclusion/Inclusion criteria

Fever was defined as a having a measured axillary temperature $\geq 37.5^{\circ}\text{C}$. Children whose parents gave a history of fever in the past two weeks were recruited for the study. Children with fever who had received treatment with anti-malarials or antibiotics within two weeks of the study, those with fever of more than two weeks duration, and those whose parents did not give consent were excluded.

After obtaining a full medical history, a full general

medical examination was carried out on each subject. The temperature was recorded.

Ethical Clearance

Ethical approval for the study was obtained from the Ethics Review Board of the NDUTH. Informed consent was obtained from the parents/guardians of the children recruited into the study.

Sample collection and processing

Malaria parasite and full blood count

5ml of blood was obtained by venepuncture from each subject into sterile bottles containing dipotassium EDTA anti-coagulant.

A full blood count, white blood cell and differentials were done for each sample. Full blood count was analyzed using the Biocode Hycel 9000 Analyzer® (Biocode-Hycel, Belgium). The analyzer was calibrated daily as part of internal quality control measures.

Thick and thin blood films were done for each sample for malaria parasite count and to identify parasite species respectively. Thin and thick smears were prepared by placing a drop or 3 drops of blood respectively, onto clean slides, which were then Giemsa-stained (World Health Organization 2010). All slides were read twice independently by two experienced microscopists for concordance. Any discordant slide was re-read by a third microscopist. Thick films were examined using a X100 oil-immersion lens. A thick smear was declared negative if no parasites were seen after examination of at least 100 high power-fields.

Parasite densities were determined by counting the number of asexual parasites per 200 white blood cells (WBCs). The densities were converted to number of parasites per microlitre assuming each subject as having 8000 WBCs per microlitre of blood as recommended by WHO (World Health Organization 2010):

$$\frac{\text{Number of parasites counted} \times 8000}{\text{Number of leukocytes}} = \text{parasites per microlitre}$$

Microscopy, culture and sensitivity for urine sample, ear and throat swabs

A clean-catch urine sample, throat and ear swab samples were obtained from each subject. Smears from the swab samples and a calibrated loopful of urine, were inoculated on the following media: cystine lactose electrolyte-deficient (CLED) agar, blood agar, chocolate agar and Macconkey agar. Cultures were incubated aerobically at 37°C for 24 to 48 hours. Gram-staining and standard

Table 1. Age and gender distribution of the study subjects.

Age (years)	Male	Female	Total
<1	24	18	42
1 to 2	47	33	80
3 to 4	18	11	29
5 to 6	15	8	23
7 to 8	1	3	4
9 to 10	3	3	6
11	4	2	6
Total	112	78	190

Table 2. Frequency of malaria parasitaemia by age and gender

Age (years)	Malaria parasitaemia		
	Male	Female	Total
<1	8	2	10
1 to 2	36	22	58
3 to 4	8	6	14
5 to 6	8	4	12
7 to 8	1	3	4
9 to 10	0	2	2
11	2	2	4
Total	63	41	104

biochemical tests were performed for identification and classification of bacterial isolates. A positive culture was defined as pure growth of a single pathogenic micro-organism and expressed as colony forming units.

Statistical analysis

Statistical analysis was performed with the Graphpad Prism version 4® (Graphpad software, San Diego, CA). Differences between groups were determined by the one-way analysis of variance (ANOVA) or paired t- test with the level of significance set at $p < 0.05$.

RESULTS

Out of the 190 children studied, 112 were male and 78 were female, a male:female ratio of 1.43:1. The age range was 6months to 11years, mean age 2.81 years. 146 of the patients (76.84%) were below 5 years of age and 42.1% of the patients were in the 1 to 2 years age group (Table 1).

Malaria Parasite

Malaria parasite was detected in 104 patient blood sam-

ples (Table 2). 12 of these patients also had samples that yielded significant bacterial growth. Thus 92 patients had samples positive for malaria parasite only, meaning that the proportion of fevers attributable to malaria only was 48.42% (95% CI: 41.32 - 55.52). Over half of the patients with malaria parasitaemia were from the 1 to 2years age group. The proportion of malaria parasite positive slides fell with increasing age.

Bacterial growth

42 samples obtained from 36 patients yielded significant bacterial growth indicative of bacterial infection (Table 3). 12 of these patients were also positive for malaria parasite. Thus the proportion of fevers attributable to only bacterial growth was computed for the 24 patients (12.63%; 95% CI: 7.93 - 17.33).

16 urine samples (8.42%), 15 ear swab samples (7.89%) and 11 throat swab samples (5.78%) yielded significant bacterial growth. Majority of these samples were also from patients within the 1 to 2 years age group. There were no differences in distribution between the sexes for the urine and ear swab samples, but all the positive throat swab samples were from male children.

Table 3. Frequency of positive bacterial culture according to sample type.

Age (years)	Ear swab +ve	Urine m/c/s +ve	Throat swab +ve
<1	-	3 (18.7%)	2 (18.2%)
1 to 2	10 (66.7%)	10 (62.5%)	4 (36.4%)
3 to 4	4 (26.7%)	-	2 (18.2%)
5 to 6	1 (6.67%)	3 (18.7%)	3 (27.3%)
7 to 8	-	-	-
9 to 10	-	-	-
11	-	-	-
Total	15	16	11

Table 4. Frequency of co-morbidities.

Positive samples	No.
MP, Urine m/c/s	1
MP, ear m/c/s	3
MP, throat m/c/s	5
MP, throat m/c/s, ear m/c/s	3
Ear m/c/s, throat m/c/s, urine m/c/s	2

Co-morbidities

Two patients had three samples (urine, ear swab and throat swab) which yielded significant bacterial growth, but no malaria parasites detected in the blood. As stated earlier, 12 patients had malaria parasites detected in the blood and bacterial growth in at least one of the other samples (Table 4).

Undetectable causes of fever

In 62 of the patients (32.63%: 95% CI: 25.97 - 39.29), the cause of the fever could not be determined as all the samples from these patients were negative for malaria parasite and significant bacterial growth (Figure 1).

White blood cell count and febrile illnesses

There were no significant differences in white blood cell count and differentials between patients with no detectable cause of fever, those with only malaria parasite infestation, and those with significant bacterial growth (Figure 2).

DISCUSSION

There is a difficulty in differentiating between causes of febrile illness in children in malaria-endemic regions as there is overlapping of manifestations between malaria and bacterial infections. This is compounded by the lack of requisite diagnostic facilities in many healthcare

settings, so presumptive treatment of all fevers as malaria holds sway.

In our study, there was male a preponderance of patients. Most of the patients with either bacterial infection or malaria parasite infestation were within the 1 to 2 years age group. Our results suggest that children within this age group are more vulnerable to infectious illnesses. This might be due to the fact that they might be transiting from maternal antibody protection to developing their own immunity.

In almost half of the patients (48.42%), fevers were attributable to malaria only. This is similar to the 46.1% and 52.4% of positive slides for malaria obtained respectively in two other studies (Reyburn et al., 2004; Mabunda et al., 2009). Our results are also in conformity with the observation in a previous study that half of the children presenting with fever in public clinics in Africa do not have malaria (Gething et al., 2010).

This is different from results obtained in another study where 60.3% of fevers were due to malaria (Nadjm et al., 2010), or the 80.5% observed in a Nigerian study (Olasehinde et al., 2010). However, it means that a sizeable number of patients would have been treated only for malaria even though there was no parasitological diagnosis. Treatment of malaria in children without parasites is believed to have a high probability of poor clinical outcomes because other causes of illness are missed (Reyburn et al., 2004; Okiro and Snow 2010).

Investigations to detect bacterial infections should be included in tests to determine the causes of fever in children. We observed that bacterial infections were responsible for fever in about one-eighth of the children (12.63%). This means that a sizeable proportion of fever

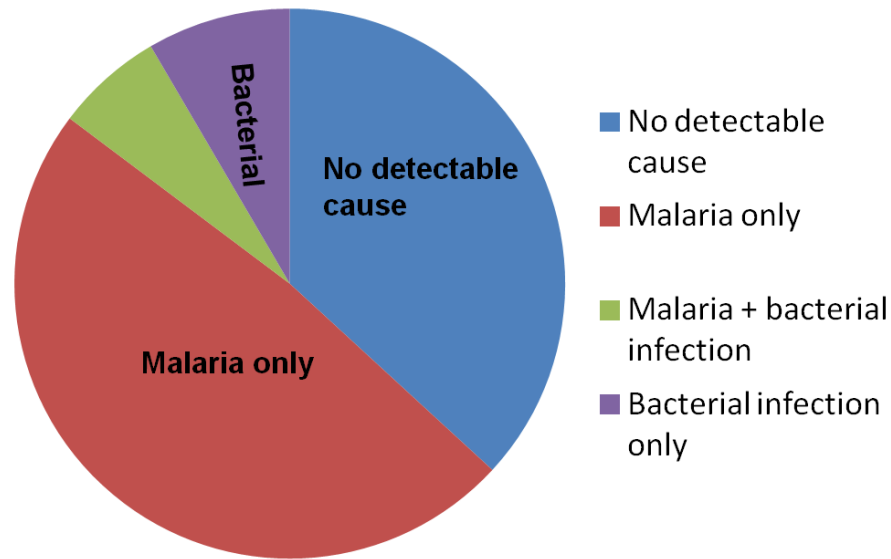


Figure 1. Proportion of detectable causes of febrile illness in children.

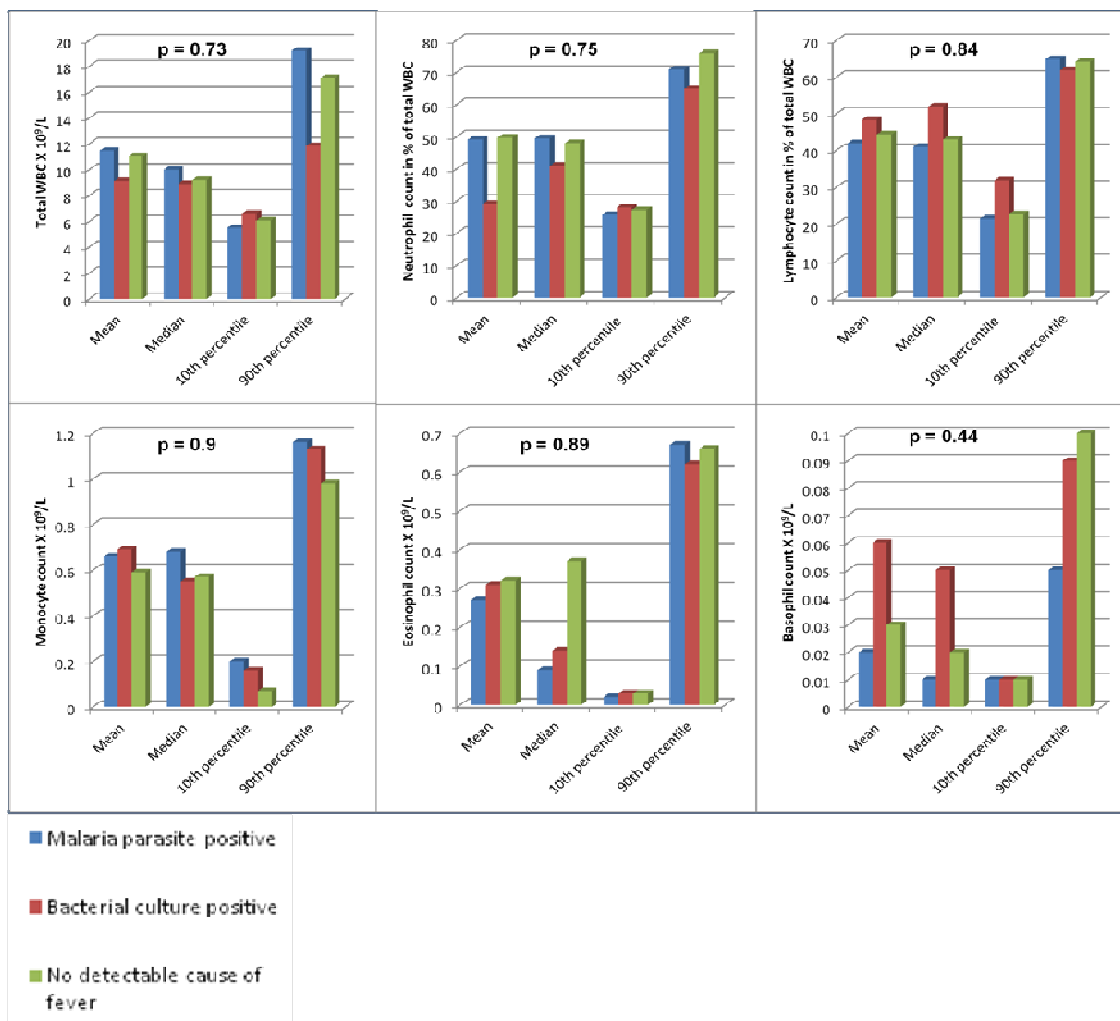


Figure 2. Comparison of white blood counts among the three categories of patients. The mean, median, 10th percentile and 90th percentile values were compared. P- values are shown for each parameter compared.

in children in our environment is caused by bacterial infection. Our figures are higher than the 7.2% observed in a previous study in Australia (Craig et al., 2010), but lower than the figures obtained in another study where one in five children presenting to hospital have significant bacterial illness (Bruel et al., 2011). It also implies that in resource-poor settings like ours where bacterial cultures are not routinely done for febrile children, these children would not be treated with antibiotics. It has been observed that a third of children with invasive bacterial disease are not identified by the current WHO guidelines, and half of isolated micro-organisms are resistant to recommended antimicrobials (Nadjm et al., 2010). Facilities which can do malaria parasite testing should therefore be empowered to do bacterial cultures for diagnosis.

No cause of fever could be detected in almost a third of the study subjects. The fevers in these children could be attributed to viral causes. They could also be due to anaerobic bacterial infections, as no anaerobic cultures were done.

The use of white blood cell counts in the management of childhood fevers has been controversial (Luszczak, 2001). White blood cell counts did not provide any diagnostic value in the determination of the causes of febrile illnesses in this study. This is in agreement with the findings in a review of laboratory tests used in the diagnosis of febrile illnesses in children (Bruel et al., 2011). This calls for prioritization of investigations ordered for children with febrile illnesses in resource-poor settings like ours. It is unhelpful for indigent parents to be made to pay for full blood count tests when more useful tests like malaria parasite or urine cultures have not been done.

Rapid Diagnostic Tests (RDTs) have been shown to be useful in the diagnosis of malaria and are increasingly being used in sub-Saharan Africa (Hopkins et al., 2008; Hopkins, Asiimwe et al., 2009). However, despite being in the National plan (Federal Ministry of Health 2008), they are yet to be widely used in Nigeria especially in the Niger Delta region. Provision of RDTs and the training of health workers to use them would help reduce morbidity and mortality.

Our findings point to the contribution of bacterial infections in causing fevers in children in a malaria-endemic setting. It therefore follows that physicians should have other causes of fever in mind when attending to children with febrile illnesses. Investigations for such febrile illnesses should go beyond detection of malaria parasite. Whilst early appropriate treatment for malaria is necessary, that for other causes of fever in children could reduce morbidity and mortality. The WHO integrated approach to management of sick children, was meant to address the issue of focusing on a single disease entity, but not much seems to have changed. There is therefore the need to revisit the Integrated Management of Childhood Illnesses (IMCI) in order to

accommodate the recent WHO policy on treatment of malaria only after parasitological confirmation (World Health Organization 2010).

CONCLUSION

A sizeable proportion of fevers are caused by bacterial infections even in malaria-endemic settings like the NDUTH. Urinary tract infection, otitis media and pharyngitis are important causes of fever in children in this setting and should be sought for in acutely febrile children. Diagnostic facilities have to be strengthened together with training of requisite staff.

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