Overdiagnosis and overtreatment of malaria in children in a secondary healthcare centre in Sekondi-Takoradi, Ghana

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Abstract

Overdiagnosis and overtreatment of malaria is a major problem in children in malaria-endemic countries. This retrospective study identified children who were admitted with fever and were treated with or without anti-malarial medications and discharged at the Paediatric Unit of the Effia-Nkwanta Regional Hospital. The medical records of all children were searched, retrieved and assessed. A total of 1160 records from children (age range, 0–12 years) were reviewed and evaluated. Of the total number, 21.3% had laboratory confirmed malaria, 38.4% were malaria negative, while 40.3% had no malaria tests performed. In addition, the results showed that 4.5% of the laboratory confirmed malaria positive cases were not given anti-malarial medication while 84.1% of the malaria negative cases were given these incorrectly. Furthermore, 78.2% of the children with no malaria tests were prescribed anti-malarial medication. The presumptive diagnosis of malaria should be abandoned and the installation of a functional laboratory services promoted.

Keywords

Overdiagnosis, malaria, children, overtreatment, healthcare

Introduction

Malaria remains a serious public health concern in sub-Saharan Africa. However, with concerted efforts over the years, malaria mortality rates have decreased by 47% worldwide and by 54% in Africa. Apart from the burden of the disease, overdiagnosis and overtreatment of malaria remains a worrisome problem. There is documented evidence in many countries where cases of febrile illness were incorrectly diagnosed as malaria and malarial treatment given, allowing other possible fatal causes of febrile illness to go untreated. In a typical clinical setting in sub-Saharan Africa, where malaria is endemic, it is a very common practice to prescribe anti-malarial treatment to patients presenting with febrile illness, without recourse to laboratory diagnosis. The practice of presumptive diagnosis based on the assumption that every febrile illness is malaria until proven otherwise has contributed to the continued prescription of anti-malarial medication even when the malaria laboratory test result is negative. The justification given is the fact that a delay in prompt treatment of the disease can cause rapid progress to severe disease and subsequent mortality.

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Malaria diagnosis and treatment is crucial, and the World Health Organization (WHO) has recommended the Integrated Management of Childhood Illnesses strategy to ensure early and prompt treatment.\(^9\) However, the contribution of malaria to febrile illnesses, based on parasitological confirmation of suspected malaria, continues to decrease\(^10,11\) necessitating the WHO to review the treatment guidelines in endemic areas. The current WHO standard treatment guideline for malaria recommends that all suspected cases should be promptly confirmed by microscopy or alternatively by Rapid Diagnostic Test (RDT).\(^2\) Though the WHO still acknowledges that clinical judgment in malaria diagnosis is reasonable practice especially in places where parasitological confirmation is not accessible, clinical diagnosis remains inaccurate and there is an obvious advantage of parasitological confirmation.\(^12\) Therefore, blind treatment of malaria without parasitological confirmation falls short of the required best practice in malaria case management. Consequently, adherence to the correct policy on malaria care will result in a rational use of medication, thereby preventing wastage of extremely limited resources, delaying drug resistance and ensuring that other non-malarial fevers are appropriately managed and not glossed over.\(^6,13\)

Despite this progress in malaria diagnosis, antimalarial medicines are still prescribed even when the malaria blood test is negative,\(^3\) or treatment given without recourse to available microscopy test in the facility.\(^7\) In Ghana, malaria burden has been on a decline since 2009 as evidenced by epidemiological and hospital data.\(^14,15\) Thus, it was apt that Ghana adopted the current WHO test-based treatment guideline as best practice. Adopting this guideline nonetheless requires the availability of the necessary tools in hospitals, clinics and health centres in the country. Scaling up the diagnostic capacity of hospitals and health centres to meet this demand of test-based treatment have been a challenge not only for Ghana but for many other countries in sub-Saharan Africa.\(^8,16\) Current poor infrastructure has created doubts that the implementation of the WHO policy is feasible, it being portrayed as a 'case of learning to run before being able to walk'.\(^17\)

Furthermore, availability of diagnostic capacity is not the only issue that mitigates against adherence to recommended guidelines. The attitude of physicians and other health workers towards the whole idea of

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**Table 1.** Characteristics of the children treated with anti-malarial medications.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Laboratory confirmed malaria diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaria positive</td>
<td>(n = 78)</td>
<td>(n = 104)</td>
<td>(n = 65)</td>
<td>(n = 1160)</td>
</tr>
<tr>
<td>Malaria negative</td>
<td>(n = 91)</td>
<td>(n = 163)</td>
<td>(n = 192)</td>
<td></td>
</tr>
<tr>
<td>Malaria diagnosis not done</td>
<td>(n = 162)</td>
<td>(n = 118)</td>
<td>(n = 187)</td>
<td></td>
</tr>
<tr>
<td><strong>Age groups</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1 year</td>
<td>16 (20.5)</td>
<td>32 (30.8)</td>
<td>22 (33.8)</td>
<td>99 (51.3)</td>
</tr>
<tr>
<td>2–4 years</td>
<td>26 (33.3)</td>
<td>47 (45.2)</td>
<td>26 (40)</td>
<td>345 (29.7)</td>
</tr>
<tr>
<td>≥5 years</td>
<td>36 (46.2)</td>
<td>25 (24)</td>
<td>17 (26.2)</td>
<td>321 (27.7)</td>
</tr>
<tr>
<td><strong>Sex</strong>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43 (55.1)</td>
<td>62 (59)</td>
<td>34 (54.8)</td>
<td>661 (57.7)</td>
</tr>
<tr>
<td>Female</td>
<td>35 (44.9)</td>
<td>43 (41)</td>
<td>28 (45.2)</td>
<td>485 (42.3)</td>
</tr>
</tbody>
</table>

\(P < 0.001\) for all comparisons.

*Missing data (14).
test-based treatment is another problem entirely. There is documented evidence that some healthcare workers disregard negative malaria microscopy and RDT test results and treat patients nonetheless with anti-malarial medication.

Previous studies of this issue were done in district hospitals and primary care centres as most cases present initially to these centres. However, our study in a regional centre, supposedly with more qualified and experienced healthcare workers and fully equipped diagnostic capacities, examines whether best practices are actually adhered to.

Materials and Methods

This retrospective study was conducted at the Effia-Nkwanta Regional Hospital (ENRH) in the Sekondi-Takoradi metropolis. Children admitted between 2010 and 2012, recorded with fever as one of the presenting complaints, successfully treated with or without anti-malarial medications and discharged, were included. Medical records of malaria laboratory diagnosis of these children were searched, retrieved, reviewed and assessed. Information on the demographics, clinical and laboratory findings were collected. Anti-malarial drugs prescribed to the children were documented. Treatment histories were also documented as well as the duration of admission.

Malaria was defined as the presence of any asexual blood stages of *Plasmodium falciparum* species of any density in the thick and thin smear blood film. At ENRH, malaria parasite diagnoses were performed using: (1) *P. falciparum* specific rapid diagnostic test kits (Premier Medical Corporation Ltd.); and (2) confirmation using microscopy with Giemsa staining. This study was approved by the Ghana Health Service Research Ethical Review Committee, Accra, Ghana.

Univariable analyses were performed and results were presented as proportions. Statistical significance

![Figure 2. The proportion of children by year and age groups treated with anti-malarial drugs without laboratory confirmed malaria positives.](image-url)
for cross-tabulations were performed using Pearson $\chi^2$ test for categorical variables and ANOVA for the comparison of mean of the continuous variable. The tests were two-tailed and $P$ value of $\leq 0.05$ was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics version 21.0 (IBM Corporation, Armonk, NY, USA).

Results

Out of 1240 children listed as having been admitted with fever, only 1160 records of children aged <12 years were retrieved for this study. Their mean age was 3.2 ± 3.1 years. There were 247 (21.3%) confirmed cases of malaria, 446 (38.4%) had tests with no malaria found and 467 (40.3%) had no malaria tests performed at all. The absolute number of confirmed cases of malaria decreased from 78 (23.3%) in 2010 to 65 (14.6%) in 2012 (Figure 1), while the number with no evidence of malaria increased from 91 (27.5%) to 192 (43.2%). In this period, though, the number who had no malaria tests performed remained constant (Figure 1).

There were no significant differences between boys and girls in the prevalence of laboratory confirmed malaria diagnosis each year (Table 1). By contrast, the proportion of children testing positive differed between the three age groups each year, the highest prevalence being in infants (Table 1).

When children with laboratory confirmed parasitaemia were excluded from the data analysis, 46% of children aged less than 1 year were treated with anti-malarial medications, a higher proportion than in those aged 2–4 years (27%) or >5 years (27%) ($P = 0.028$) (Figure 2). Overall, more children who had been confirmed to be aparasitaemic, or had not been tested, were treated with anti-malarial medications than children with proven parasitaemia.

The types and combinations of treatments received by the children are summarized in Figure 3.

A documented fever with axillary temperature $\geq 38^\circ$C was significant among children with confirmed malaria ($P < 0.001$) (Table 2). Of these, anti-malarial medication was appropriately prescribed in 95.5% (236/247), but inappropriately prescribed in 84.1% (375/446) with aparasitaemia and in 78.2% (365/467) with no laboratory tests performed (Figure 4). Moreover, children admitted <3 days were more likely to be treated for uncomplicated malaria ($P < 0.001$) irrespective of their laboratory malaria diagnosis.
Table 2. Symptomatic presentations of the admitted children.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Malaria positive (n = 222) (%)</th>
<th>Malaria negative (n = 437) (%)</th>
<th>Malaria diagnosis not done (n = 422) (%)</th>
<th>Total (n = 1081) (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever and vomiting</td>
<td>47 (21.2)</td>
<td>45 (10.3)</td>
<td>57 (13.5)</td>
<td>149 (13.8)</td>
</tr>
<tr>
<td>Fever</td>
<td>58 (26.1)</td>
<td>73 (16.7)</td>
<td>79 (18.7)</td>
<td>210 (19.4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (0.9)</td>
<td>22 (5)</td>
<td>15 (3.6)</td>
<td>39 (3.6)</td>
</tr>
<tr>
<td>Fever, vomiting and frequent stooling</td>
<td>13 (5.9)</td>
<td>40 (9.2)</td>
<td>35 (8.3)</td>
<td>88 (8.1)</td>
</tr>
<tr>
<td>Fever, vomiting and cough</td>
<td>11 (5)</td>
<td>26 (5.9)</td>
<td>22 (5.2)</td>
<td>59 (5.5)</td>
</tr>
<tr>
<td>Fever, vomiting and convulsion</td>
<td>5 (2.3)</td>
<td>4 (0.9)</td>
<td>5 (1.2)</td>
<td>14 (1.3)</td>
</tr>
<tr>
<td>Fever and cough</td>
<td>14 (6.3)</td>
<td>62 (14.2)</td>
<td>56 (13.3)</td>
<td>132 (12.2)</td>
</tr>
<tr>
<td>Fever, vomiting, frequent stooling and cough</td>
<td>6 (2.7)</td>
<td>23 (5.3)</td>
<td>11 (2.6)</td>
<td>40 (3.7)</td>
</tr>
<tr>
<td>Cough</td>
<td>0 (0)</td>
<td>21 (4.8)</td>
<td>28 (6.6)</td>
<td>49 (4.5)</td>
</tr>
<tr>
<td>Vomiting and frequent stooling</td>
<td>9 (4.1)</td>
<td>43 (9.8)</td>
<td>31 (7.3)</td>
<td>83 (7.7)</td>
</tr>
<tr>
<td>Frequent stooling</td>
<td>1 (0.5)</td>
<td>11 (2.5)</td>
<td>8 (1.9)</td>
<td>20 (1.9)</td>
</tr>
<tr>
<td>Fever and convulsion</td>
<td>32 (14.4)</td>
<td>20 (4.6)</td>
<td>17 (4)</td>
<td>69 (6.4)</td>
</tr>
<tr>
<td>Fever and frequent stooling</td>
<td>6 (2.7)</td>
<td>23 (5.3)</td>
<td>17 (4)</td>
<td>46 (4.3)</td>
</tr>
<tr>
<td>Fever, frequent stooling and cough</td>
<td>1 (0.5)</td>
<td>6 (1.4)</td>
<td>13 (3.1)</td>
<td>20 (1.9)</td>
</tr>
<tr>
<td>Vomiting, frequent stooling and cough</td>
<td>0 (0)</td>
<td>5 (1.1)</td>
<td>2 (0.5)</td>
<td>7 (0.6)</td>
</tr>
<tr>
<td>Vomiting and cough</td>
<td>1 (0.5)</td>
<td>6 (1.4)</td>
<td>8 (1.9)</td>
<td>15 (1.4)</td>
</tr>
<tr>
<td>Fever, convulsion and cough</td>
<td>3 (1.4)</td>
<td>2 (0.5)</td>
<td>1 (0.2)</td>
<td>6 (0.6)</td>
</tr>
<tr>
<td>Fever, vomiting, convulsion, frequent stooling and cough</td>
<td>2 (0.9)</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td>4 (0.4)</td>
</tr>
<tr>
<td>Convulsion</td>
<td>6 (2.7)</td>
<td>3 (0.7)</td>
<td>9 (2.1)</td>
<td>18 (1.7)</td>
</tr>
<tr>
<td>Vomiting and convulsion</td>
<td>3 (1.4)</td>
<td>1 (0.2)</td>
<td>2 (0.5)</td>
<td>6 (0.6)</td>
</tr>
<tr>
<td>Frequent stooling and cough</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (0.9)</td>
<td>4 (0.4)</td>
</tr>
<tr>
<td>Fever, convulsion and frequent stooling</td>
<td>2 (0.9)</td>
<td>0 (0)</td>
<td>1 (90.2)</td>
<td>3 (0.3)</td>
</tr>
</tbody>
</table>

*Data not documented (missing data = 79).

Figure 4. The proportion of children prescribed or denied anti-malarial medications with malaria diagnosis. The bars represent 95% confidence interval (CI).
Discussion

The major reason why anti-malarial treatment is prescribed despite a malaria negative test appears to be lack of trust in the results.16 This distrust may be due to a limited number of trained and competent laboratory personnel19–21 and/or poorly maintained and malfunctioning laboratory equipment.22 However, such distrust is unjustified if rapid antigen diagnostic tests are used as these are simple and objective. In our study, children aged <1 year had more presumptive malaria treatment than children of other age groups. While this practice was advocated for children <5 years within the context of an Integrated Management of Childhood Illness,9,23 the WHO now recommends testing in all cases.24

There are strong arguments indicating that the malaria burden is declining in most endemic areas and that a febrile child may be affected by other dangerous febrile illness.18 Symptomatic diagnosis of malaria has proven grossly unreliable in several studies25–28 and the differential diagnosis is legion.29–31 Furthermore presumptive malaria treatment is likely to increase drug resistance,32–34 and the financial burden of inappropriate treatment is obvious.35

Limitations in our study are that the turnaround time for malaria testing was not examined and the exclusion of children who died, as these clearly have an impact on assessing the extent of overdiagnosis and overtreatment. Further limitations are our inability to check for discrepancies between rapid testing and microscopy.

Nonetheless, with the advent of rapid testing for malaria, treatment should, except in extreme circumstances, no longer be given in the absence of a positive result.

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