ABSTRACT

Malaria and typhoid fever are among the most endemic diseases in the tropics. The emergence of multi-drug resistant strains of Salmonella typhi and Plasmodium falciparum poses a big challenge to eradication of both diseases. Both diseases share similar transmission factors, putting individuals in areas endemic for both infections at a substantial risk of contracting both infections concurrently. The main objective of the study was to determine the incidence of malaria and typhoid fever co-infection in the Sunyani and Kumasi metropolises. One hundred and twenty-nine participants were recruited for the study. Twenty-two (17.0%) of the subjects tested positive for typhoid fever, twenty-four (18.6%) tested positive for falciparum malaria, and five (3.9%) were co-infected with falciparum malaria and typhoid fever. No association (P=0.585) was found between malaria and typhoid fever infection.

INTRODUCTION

Malaria is the most important parasitic disease of man, causing over 1 million deaths annually. The disease is caused by the protozoan parasite belonging to the genus Plasmodium. P. falciparum, P. vivax, P. ovale, P. malariae and P. knowlesi are the five species known to cause disease in man. P. falciparum is the most virulent of the four, accounting for almost all malaria deaths [1]. Malaria is transmitted through the bite of an infected female Anopheles mosquito.

Typhoid fever is an acute systemic infection caused by the bacterium Salmonella enterica sub-sp enterica serotype Typhi (or simply Salmonella Typhi). Typhoid is transmitted by the fecal-oral route via contaminated food and water. An estimated 17 million cases of typhoid are reported worldwide each year, resulting in 0.6 million deaths [2]. This is exacerbated by the emergence
and spread of multidrug-resistant strains of *Salmonella* Typhi, and further complication by malaria co-infection [3, 4, 5, 6].

Malaria and typhoid fever are among the most endemic diseases in the tropics. Both diseases have been associated with increasing poverty, deterioration in sanitation, poor public health services, compounded by increasing drug resistance of the two aetiological agents[7, 8]. Although the two infections are caused by very different agents and transmitted via different mechanisms, both diseases share rather similar symptoms [9, 10, 11, 12]. This presents a challenge of diagnostic error. Definitive laboratory-based diagnosis is, thus, required to differentiate the two infections as well as detect co-infections.

High prevalence has been established for both diseases. But it is only within the last two decades that reports of high prevalence of co-infections have been made [9, 10, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23].

Precise incidence of malaria and typhoid fever co-infection is unknown in most areas [24], including Ghana. We, therefore, sought to ascertain the incidence of malaria and typhoid fever co-infection in the Sunyani and Kumasi metropolises in Ghana, and determine the association between malaria and typhoid fever infections in the two metropolises.

**MATERIALS AND METHODS**

**Study area and subjects**

This study was a cross-sectional study. Participants of the study were purposively sampled from the Sunyani regional hospital in the Brong-Ahafo region and Kumasi South hospital Ashanti region of Ghana. Participants were included from patients visiting the Out-Patient Department of the two hospitals. All participants had been clinically diagnosed as having malaria. In all one hundred and twenty-nine (129) participants were sampled for the study.

**Sample Collection**

Three milliliters (3ml) of blood sample was collected from each patient into EDTA tubes by trained and licensed medical laboratory technologists from the two hospitals.

**Typhoid fever diagnosis**

The Widal agglutination test was performed on all blood samples by the rapid slide titration method using commercial antigen suspension (Cal-Test Diagnostic Inc. Chino, U.S.A.) for the somatic (O) and flagella (H) antigen. Initially, 80μl of each participants blood sample was pipetted twice onto a slide, antigens O and H were added to each and then mixed for one (1) minute. The absence of agglutination was recorded as <1:20. But if agglutination occurs, then the test had to be continued with another 40μl of the same blood sample. The test was also continued for samples that showed agglutination to a particular antigen with 40ml, 20ml, 10ml and 5ml consecutively until no agglutination occurred. The corresponding interpretation were 1:40, 1:80, 1:160 and 1:320. A participant was diagnosed positive for typhoid when his/her sample record antibody titre ≥1:80 to the somatic (O) antigen and negative for typhoid if it is <1:80.
Haemoglobin (Hb) count
Haemoglobin level was determined using the Cell Dyn automated blood analyzer.

Malaria diagnosis
First response PfHRP-II malaria rapid-diagnostic (RDT) kit was used for the detection of histidine-rich protein II antigen which is characteristic of *P. falciparum*. A drop of each participant’s blood was dropped onto the sample well of the kit after which two drops (60µl) of assay buffer was added into the buffer well and the results read in 20 minutes at room temperature. A positive reaction was identified by the presence of two rose-pink colour bands at the control (C) and test (T) labels. A visible rose-pink label at the control (C) label only was indicative of a negative reaction.

Data analysis
Data were analysed using Minitab statistical software version 15 and results generated in two-by-two tables. Chi-square analysis was also carried out to ascertain association between malaria and typhoid infections.

RESULTS

The 129 participants recruited into the study comprised 117 females, representing 90.7%, and 12 males representing 9.3%. Participants were aged between 5 and 83 years. Majority of our participants were youthful (mean age = 26.32 years). The mean age of the female participants was 25.69 years, and that of the male participants was 32.41 years.

Participants were generally anaemic, with a mean haemoglobin (Hb) value of 10.6225g/dl, considering that the lowest Hb threshold is 11.0g/dl (for children between 0-5 years) [25]. Anaemia in females was significantly higher than that in males ($\chi^2=8.62$, DF=1, P=0.003).

<table>
<thead>
<tr>
<th>Table 1: Anaemia in male and female participants</th>
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</thead>
<tbody>
<tr>
<td>Normal Hb</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
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<tr>
<td>TOTAL</td>
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<table>
<thead>
<tr>
<th>Table 2: Anaemia in malaria-positive and malaria negative participants</th>
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<tbody>
<tr>
<td>Normal Hb</td>
</tr>
<tr>
<td>Malaria negative</td>
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<tr>
<td>Malaria positive</td>
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<td>TOTAL</td>
</tr>
</tbody>
</table>

Twenty-four (24) out of the one hundred and twenty-nine (129) participants tested positive for malaria constituting 18.6% whilst 105 participants tested negative constituting 81.4%. 2 of the 24 malaria positive participants had normal Hb levels. However, there was no significant difference between anaemia in malaria-positive participants and that in malaria-negative participants ($\chi^2=2.054$, DF=1, P=0.152).
Thirty-two (32) participants tested positive for typhoid fever, representing 24.8%, whilst 97 tested negative, representing 75.2%. About 16.6% of male participants (i.e. 2 of 12) tested positive for typhoid fever, whereas 24.6% of the female participants (i.e. 30 of 117) tested positive. However, there was no significant difference between typhoid fever in the two sexes ($\chi^2=0.470$, DF=1, P=0.493). Twenty-five (25) of the 32 typhoid-positive participants were anaemic, and 80 of the 97 typhoid-negative participants had normal Hb levels. No significant difference ($\chi^2=0.301$, DF=1, P=0.584) was found between anaemia in typhoid-positive participants and that in typhoid-negative participants.

Table 3: Anaemia in typhoid-positive and typhoid-negative participants

<table>
<thead>
<tr>
<th></th>
<th>Normal Hb</th>
<th>Anaemia</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typhoid negative</td>
<td>17</td>
<td>80</td>
<td>97</td>
</tr>
<tr>
<td>Typhoid positive</td>
<td>7</td>
<td>25</td>
<td>32</td>
</tr>
<tr>
<td>TOTAL</td>
<td>24</td>
<td>105</td>
<td>129</td>
</tr>
</tbody>
</table>

Six (6) of the malaria-positive participants were co-infected with typhoid fever, representing a malaria-typhoid fever co-infection prevalence of 4.65%.

Table 4: Malaria-Typhoid fever co-infection

<table>
<thead>
<tr>
<th></th>
<th>Typhoid negative</th>
<th>Typhoid positive</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria negative</td>
<td>79</td>
<td>26</td>
<td>105</td>
</tr>
<tr>
<td>Malaria positive</td>
<td>18</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>TOTAL</td>
<td>97</td>
<td>32</td>
<td>129</td>
</tr>
</tbody>
</table>

We found no association ($\chi^2=0.0001$, DF=1, P=0.981) between malaria and typhoid fever infections. We also found no association ($\chi^2=0.016$, DF=1, P=0.901) between anaemia in malaria and anaemia in typhoid fever.

Table 5: Anaemia in malaria-typhoid fever co-infection

<table>
<thead>
<tr>
<th></th>
<th>Normal Hb</th>
<th>Anaemia</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typhoid negative</td>
<td>23</td>
<td>100</td>
<td>123</td>
</tr>
<tr>
<td>Typhoid positive</td>
<td>1</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>24</td>
<td>105</td>
<td>129</td>
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DISCUSSION

We have, for the first time to the best of our knowledge, described dual infection with malaria and typhoid fever in Ghana.

The precise mechanism underlying the association between malaria and salmonellosis is still not fully understood. However, it has been shown that haemolysis, which occurs in malaria, may predispose to typhoid fever [26]. It has also been shown that acute malaria reduces antibody response to the somatic (O) antigen of S. typhi [27]. We were unable to find any association between malaria and typhoid fever (P=0.981). Six (6) out of the 129 participants had dual malaria and typhoid fever infections, representing 4.65%. Anaemia in 5 of the 6 co-infected participants could not be attributed to the co-infection (P=0.901).
We recorded prevalence of 18.6% and 24.8% respectively for malaria and typhoid fever. These values are very high, corresponding with other works in other endemic regions [9, 10, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23]. This high prevalence in our study sites indicate that much effort should be devoted to controlling the two infections in the sites and the country at large.

Participants were generally anaemic, with a mean Hb value of 10.6225g/dl. The study did not seek to find out the cause of the anaemia. However, regarding the fact that the study was conducted in a low-income country which is endemic for parasitic diseases, one would not neglect poor nutrition and parasites as major causes of anaemia. Nonetheless, we found no association between anaemia and each of the two infections.

CONCLUSION

No association was found between malaria and typhoid fever infections. No direct evidence points to the fact that malaria may predispose to typhoid fever. However, we recommend that the two infections be very well monitored to reduce morbidity.

Acknowledgement

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REFERENCES