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Research Article

# Incidence of malaria and salmonellosis co-infection in Ahmadu Bello University Teaching Hospital, Zaria, North-West Nigeria

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## Abstract

Malaria and enteric fever infection co-exists in tropical region of the biosphere due to prevailing climatic conditions and poor hygiene practice. This work is aimed at determining the incidence of malaria-typhoid co-infection among patients in Ahmadu Bello University Teaching Hospital Zaria, Kaduna State, Nigeria. Patients' bio-data were obtained through structured questionnaire and diagnosis was done using venous blood sample obtained from the participants. Blood smear was used for analysis of malaria parasites while widal test and blood culture was used for the analysis of enteric fever. The temperature of the respondents was ≥ 38°c. Of the 216 patients enrolled for the study (141 females and 75 males), 49 (22.7%) had malaria and typhoid fever co-infection using Widal test, and none (0.0%) was positive for typhoid fever using blood culture. The prevalence of Malaria-typhoid co-infection was highest among those in the age group > 60 years (66.7%), those into tertiary education (30%), the Yoruba ethnic group (25%), those in the weight group 41-50 (40%), the employed (24%) and those who are married (30%). A substantial association exist in the malaria-typhoid fever co-infection between the age groups at ($x^2 = 3.06$, $p > 0.05$). There was a statistical relationship between malaria and typhoid fever at ($r = 0.967$, $p > 0.05$). Therefore, blood culture should be adopted as a decisive diagnosis for typhoid fever in order to remarkably reduce the assumingly high prevalence of typhoid and its co-infection with malaria and to avoid the indiscriminate use of antibiotics without laboratory confirmation.

## Introduction

Malaria is a life threatening protozoan illness of human and monkeys. In the ecosphere today, about 80% of these cases and 90% of deaths cause by malaria arises in the sub-Sahara Africa [1-4]. Globally, Nigeria accounts for about 50% of malaria deaths [5,6]. Malaria has social consequences and exerts heavy burden on economic development [7,8]. About 3.3 billion individuals worldwide remain at danger of malaria in addition to emerging ailment [9]. Clinical diagnosis of malaria is based on the patient's signs and symptoms at physical examination [9,10].

Pregnant women are more susceptible to attacks of malaria and develop antibodies and become semi-immune which is being suppressed particularly by *Plasmodium falciparum* [11,12]. In spite of all effort by government, WHO and non-governmental organization, malaria parasites are endemic in the tropical district [13]. Malaria account for 60% of outpatient visits, 30% of hospitalizations, 30% of children below 5 years mortalities, 25% infants deaths and 11% maternal deaths [14-16].

Typhoid fever is a major public health concern in tropical developing countries, especially in areas where access to clean water and other sanitation measures are limited [17-19]. *Salmonella typhi* is the etiologic agent of man illness like typhoid fever, gastroenteritis and bacteria in the blood [20,21]. Growth period of *Salmonella typhi* is from 3 to 60 days, and signs are usually obtainable from 1 to 14 days of infection [22].

Malaria and typhoid fever are ailments of community health concern in the sub-Sahara area of the biosphere with similar clinical symptoms and fever being the foremost medical presentation [23]. According to Ohanuet al. [24], these infectious diseases are common in Nigeria like other tropical and sub-Sahara Africa areas of the ecosphere. In view of this, people in Nigeria are at high risk of infections of both malaria and typhoid fever either at the same time or as an acute infection [25]. Malaria and typhoid fever share clinically related symptoms, but malaria causes difficult fever than typhoid fever [26]. This study was carried out to determine the prevalence co-infection of malaria and typhoid fever infections among patients with febrile illness. The study also aimed at determining the reliability of Widal test and blood culture in the diagnosis of typhoid fever.

## Materials and methods

### Study area

The study was carried out in Ahmadu Bello University Teaching Hospital, Zaria of Kaduna state, North West Nigeria. The coordinates are along latitude 10°,20 'N and longitude 7°,45'E. The state shares boundaries with Niger State to the west, Zamfara, Kastina and Kano states to the north, Bauchi and Plateau States to the east and FCT Abuja

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and Nassarawa State to the south.

### Study design

It was a cross-sectional hospital-based study that was used to determine the co-infection of malaria and typhoid fever in Ahmadu Bello University Teaching Hospital, Zaria, Kaduna State.

### Target population

All patients attending General Out Patients Department of ABUTH with febrile illness were enrolled for the study.

### Inclusion criteria

Patients of both sexes and all age groups with febrile illness attending Ahmadu Bello University Teaching Hospital, Zaria, North-west, Nigeria were enrolled in the study.

### Exclusion criteria

Patients with catheterization done within 6 days before the study were excluded.

### Ethical clearance

Ethical approval for this work was gotten from the Health Research Ethics Committee of Ahmadu Bello University Teaching Hospital (ABUTH) Zaria, North-west, Nigeria (Protocol number: ABUTHZ/HREC/U10/2016).

### Informed consent

Written informed consent was sought from participants/guardian preceding enrolment into the work. Information about the work was described to the participants in English and Hausa languages especially those that could not comprehend English Language. Participation in the study was voluntary and those who declined to take part in the study were still given due attention without any bias.

### Sample size

Precisely 216 participants were used, and the sample size was calculated with a 95% CI and precision level of 4% using the formula by Daniel [27].

$n = z^2 \times pq/d2$

Where: n = Sample size

z = 1.96 at 95%

P= Prevalence rate (10%) = 0.1 [28].

d = Sampling error that can be tolerated (0.04)

### Data collection

Structured questionnaire was given to patients/guardians that gave their permission in order to get information concerning their socio-demographic details, symptoms of the disease and protective measures to prevent infection.

### Sampling technique

A purposive sampling technique was used.

### Sample collection

Blood samples were collected at General Out Patients Department (GOPD) of Ahmadu Bello University Teaching Hospital, Zaria, North-west Nigeria. Two hundred and sixteen blood samples of enrolled patients with fever, headache, vomiting, and fatigue were used for this study. Respondents upper hand were fastened using tourniquet, and cotton wool was soaked in methylated spirit to clean and sterilized the site for blood collection. 5 ml syringe with 21 g needle was used to withdraw 4mls of blood from each patient. Dry cotton wood was placed at the site of venipuncture and needle was gently removed while sharps were safely disposed in the sharp box.

Two millilitre (2 mL) of the blood was aseptically introduced into a culture bottle containing Brain Heart Infusion broth, the remaining 2 mLs of the blood into an Ethylene Diamine Tetra-acetic Acid (EDTA) bottle for malaria parasite determination and allow to settle to obtained serum for serological test.

### Diagnosis of malaria parasite

Thick and thin film stained with Giemsa was prepared for the microscopic examination of the malaria parasite. The thin films were fixed with methanol and all films were stained with 3 % Giemsa stain of pH 7.2 for 45 min [29].

### Microscopic examination of blood films

Blood films were examined microscopically using 100X (oil immersion) objectives as described by [30]. The thick films were used to determine the parasite densities while thin films were used to identify the parasite species and infective stages. For thick films, the ring form, trophozoites and gametocytes was looked for. The presence of *Plasmodium species* at one per 100 high-power thick fields was considered to be substantial under oil immersion by a train microscopist.

## Diagnosis of typhoid fever

### Blood culture

Two millilitres (2ml) of the blood samples that was directly inoculated into a culture bottle containing Brain Heart Infusion Broth was incubated at 37°C for a period of 7 days. This was sub-cultured on day 3 and 7 on MacConkey agar and Blood agar base (Oxoid) [30,31]. Blood culture media was thrown away as negative after 10 days if no growths occur.

### Widal test

Serological tests were done on all blood specimens by rapid slide titration technique with commercially prepared antigen suspension (Omega diagnostic kit) manufactured by Hill foots business village Alva FK12 5DQ, Scotland, United Kingdom for somatic (O) and flagella (H) antigens [29]. A single drop of each reactant in the direction, paratyphi A, B, C and typhi D of O antigen and paratyphi A, B, C and typhi D of H antigen were placed in the first and second row on white rectangular tile. The serum was obtained from each blood sample using Pasteur's pipette and was added to each reactant and mixed with a stirrer, and the stirrer was dried with cotton wool after each stir. The tile was gently rocked for one minute and was observed for agglutination. A significant titer was considered positive for any serum specimen with antibody titre more than or equal to 1 in 160 for somatic (O) and flagella (H) antibodies.

### Statistical analysis

Data from all the questionnaires was coded, entered and analyzed using statistical package for social science (SPSS), version 23. Result

of the research findings was subjected to Chi-square test and Pearson correlation coefficient

## Results

A total of two hundred and sixteen (216) patients with febrile illness were enrolled, 75 (34.7 %) males and 141 (65.3 %) females were examined for malaria and enteric fever co-infection. Of this number, the incidence of malaria and typhoid fever co-existence using Widal test was 22.7 % while none 0.0 % had malaria and typhoid fever co-infection using blood culture techniques (Table 1).

On the malaria-typhoid fever co-infection among participants with respect to age, education and marital status (Table 2), those in the age bracket > 60 years had a higher incidence of malaria and enteric fever co-infection of 66.7% while the age group 1-10 years had the least prevalence of 7.9 %. There is a significant association between Salmonella co-infection with malaria among the age group ($p > 0.05$). Those in the tertiary had the highest incidence of malaria and typhoid fever co-existence of 30.0 %, of which females 24.5 % and males 40.1 % while the primary had the least 13.6 %. The married had 30.0 % incidence of malaria-typhoid fever co-infection compared to single 15.0 % in this study.

However, on the co-infection of malaria and typhoid fever among participants with respect to weights, ethnicity and occupation (Table 3), the highest incidence of malaria and enteric fever co-infection 40.0 % was recorded among 11-20 and 41-50 weight groups while no case of co-infection was recorded among the weight group 21-30 and 91-100. The unemployed had the incidence of 22.0 % compared to the employed 24 %. Also, the Yoruba ethnic group had higher incidence of malaria and typhoid fever co-infection 25.0 % than other tribes (Table 3).

The participants' attitude towards medication before laboratory diagnosis (Figure 1) showed that 29.6 % took antimalarial drugs before the laboratory test, 7.4 % took antibiotics while 10.6 % took both antimalarial and antibiotics. It was also found that 52.3 % did not take either antimalarial or antibiotic drugs. 19.0 % of the respondents reported that the drugs were prescribe and administered to them by doctor, 7.8 % by nurse, 3.2 % by laboratory scientist, 4.2 % by pharmacist and 13.4 % was self-medication (Figure 1).

**Table 1.** Overall prevalence of malaria and typhoid fever co-infection using Giemsa stain, widal test and blood culture respectively.

| Illness | No. examined | No. co-infected using widal (%) | No. co-infected using blood culture (%) |
|---|---|---|---|
| Malaria and Typhoid Co-infection | 216 | 49(22.7) | 0.0(0.0) |

**Table 2.** Malaria-typhoid fever co-infection among participants with respect to age, education and marital status.

| Age group (years) | No. Examined | No. Positive (%) | Male Examined | Male Positive (%) | Female Examined | Female Positive (%) |
|---|---|---|---|---|---|---|
| 1-10 | 38 | 3(7.9) | 11 | 2(18.2) | 27 | 1(3.7) |
| 11-20 | 52 | 9(17.3) | 26 | 2(7.7) | 26 | 7(26.9) |
| 21-30 | 55 | 18(33) | 15 | 5(33.3) | 40 | 13(32.5) |
| 31-40 | 38 | 12(32) | 10 | 5(50) | 28 | 7(25) |
| 41-50 | 18 | 3(16.7) | 6 | 1(16.7) | 12 | 2(16.7) |
| 51-60 | 9 | 0(0.0) | 3 | 0(0.0) | 6 | 0(0.0) |
| >60 | 6 | 4(66.7) | 4 | 2(50) | 2 | 2(100) |
| Total | 216 | 49(22.7) | 75 | 17(22.7) | 141 | 32(22.7) |
| $X^2 = 3.06$, | df = 6, | $p > 0.05$ | | | | |
| Education | $X^2 = 3.95$ | df = 3 | $p > 0.05$ | | | |
| Nonformal | 36 | 9(25) | 10 | 1(10) | 26 | 8(30.7) |
| Primary | 44 | 6(13.6) | 16 | 3(18.8) | 28 | 3(10.7) |
| Secondary | 65 | 13(20) | 27 | 4(14.8) | 38 | 9(23.7) |
| Tertiary | 71 | 21(30) | 22 | 9(40.1) | 49 | 12(24.5) |
| Total | 216 | 49(23) | 75 | 17(22.7) | 141 | 32(22.7) |
| Marital Status | $X^2 = 0.07$ | df = 1 | $p > 0.05$ | | | |
| Married | 110 | 33(30) | 29 | 11(37.9) | 81 | 22(27.1 |
| Single | 106 | 16(15) | 46 | 6(13.0) | 60 | 10(16.7) |
| Total | 216 | 49(22.7) | 75 | 17(22.7) | 141 | 32(22.7) |

**Table 3.** Co-infection of malaria and typhoid fever among participants with respect to weights, ethnicity and occupation.

| Weights | No. Examined | No. Positive (%) | Male Examined | Male Positive (%) | Female Examined | Female Positive (%) |
|---|---|---|---|---|---|---|
| 11-20 | 10 | 4(40) | 3 | 3(100) | 7 | 1(14.3) |
| 21-30 | 36 | 0(0.0) | 14 | 0(0.0) | 22 | 0(0.0) |
| 31-40 | 25 | 6(24) | 12 | 1(8.3) | 13 | 5(38.5) |
| 41-50 | 35 | 14(40) | 9 | 3(33.3) | 26 | 11(42) |
| 51-60 | 42 | 11(26) | 19 | 4(21.1) | 23 | 7(30.4) |
| 60-70 | 28 | 8(28.6) | 10 | 4(40) | 18 | 4(22.2) |
| 70-80 | 22 | 3(13.6) | 3 | 1(33.3) | 19 | 2(10.5) |
| 81-90 | 14 | 3(21.4) | 4 | 1(25) | 10 | 2(20) |
| 91-100 | 4 | 0(0.0) | 1 | 0(0.0) | 3 | 0(0.0) |
| Ethnicity | $X^2 = 1.47$ | df = 3 | $p > 0.05$ | | | |
| Hausa Fulani | 136 | 32(24) | 53 | 11(20.8) | 83 | 21(25.3) |
| Yoruba | 24 | 6(25) | 6 | 1(16.7) | 18 | 5(27.8) |
| Igbo | 7 | 0(0.0) | 1 | 0(0.0) | 6 | 0(0.0) |
| Others | 49 | 11(22) | 15 | 5(33.3) | 34 | 6(17.6) |
| Total | 216 | 49(23) | 75 | 17(22.7) | 141 | 32(22.7) |
| Occupation | $X^2 = 8.94$ | df= 1 | $p > 0.05$ | | | |
| Employed | 75 | 18(24) | 31 | 11(35.5) | 44 | 7(15.9) |
| Unemployed | 141 | 31(22) | 44 | 6(13.6) | 97 | 25(25.8) |
| Total | 216 | 49(23) | 75 | 17(22.7) | 141 | 32(22.7) |

$X^2 = 5.62$, df = 8, $p > 0.05$

## Discussion

The co-existence of malaria and typhoid fever is of significant public health challenge in Zaria, Kaduna State, Nigeria. These infectious diseases are ranked among the most frequent causes of morbidity and mortality especially among children [32,33]. In developed countries of the world, the incidence of cases and death of malaria and typhoid fever has drastically diminish due to a combination of better-quality sanitation and hygiene, vaccine, anti-malarial and antibiotic chemotherapy and effective vector control.

In this study, fortynine (22.7 %) had co-infection of malaria and typhoid fever using Widal test (Table 1). The observed prevalence rate of malaria-typhoid fever co-infection was similar to the results obtained by previous investigators in other parts of the country and neighboring countries [34,35]. Opara et al. [34] and Ukagaet al. [35] reported 22 % and 20 % respectively in Owerri. This high incidence could be attributed to haemolytic anaemia and malaria parasites specific factors which raise the patients' vulnerability to non-typhoidal *Salmonella* serotypes (NTS) as reported by Mbuh et al. [36]. This could also be due to the fact that study was carried out during raining season alone (July to October) when infection rate was high. However, Nwuzoet al. [37], Samathaet al. [38], and Mbuh et al. [36] recorded low prevalence rate of 5.6 %, 6.5 %, and 10.1% in Enugu, Guntur and Zaria respectively. Also, the result of Salmonella co-infection with malaria was 0.0% using blood

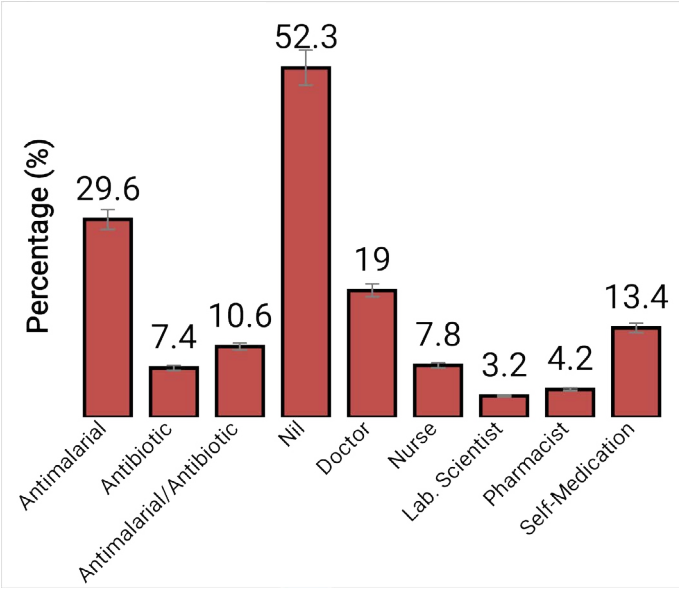


**Figure 1.** Participants attitude towards medication before laboratory diagnosis in the study area.

culture (Table 1) is in agreement with earlier reports by Mbuhet al. [36], Samathaet al.[38], Oroket al. [39], Sundufuet al. [40], and Nwuzoet al. [37], that reported 0.5 %, 0.7 %, 0.8 %, 0.6 % and 0.8 % in Zaria, Guntur, Calabar, Sirra Leone and Abakaliki respectively. However, this result is in contrast with the finding of Akinyemi et al. [41] and Ohanuet al. [24] that recorded 19.95 % and 26.6 % in Lagos and Enugu respectively. The disparity could be as a result of environmental friendly and climatic variance in many parts of the country, poor hygiene and lack of potable water. This low prevalence rate (0.0 %) obtained using blood culture could be due to the volume of blood collected or the use of antibiotics by patients prior to the time of the test.

In this study, 66.7 %, 30 %, and30 % of age group greater than 60 years, tertiary and married participants respectively had the highest prevalence of Salmonella co-infection with malaria (Table 2). Also, the weight group 11-20 and 41-50 had 40 % prevalence with no infection among the weight group 21-30 and 91-100 (Table 3). The high prevalence rate could probably be attributed to more exposure to contaminated water and malaria parasite due to bad environmental conditions. Cross-reactions with other antigens as well as those from non-typhoidal Salmonella and malaria antigens can occur as a consequence of latent and post-infectious diseases widespread in the tropics like amoebiasis, tuberculosis, pneumonia, rickettsia diseases, rheumatoid arthritis and chronic active hepatitis [42]. Complement components like Clq and C4 deficiency are associated with Salmonella co-infection with malaria. Complement activation during malaria consumed complement components and impaired the host defense [43]. It is a common habit among patients in Zaria to receive malaria and typhoid fever treatment instantaneously before laboratory analysis or rely on the cheaper and quick Widal test for the diagnosis of typhoid fever.

## Conclusion

This study observed an antigenic cross reaction between malaria parasites and other Salmonella species in the blood which could be the reason for the much talk of malaria and typhoid fever co-infection in Zaria, Kaduna State. The use of blood culture techniques should be advocated in the diagnosis of typhoid fever. This will greatly diminish the high prevalence of malaria-typhoid co-infection in Nigeria and other malaria endemic areas of the world. The prevalence of malaria among the participants was high in spite of various control measures. Hence, there is need to strengthen and scale up various malaria control programs.

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## Author Contributions

Author B.E.I. got the concept and design of the study. Authors G.C.E., P.C.I, and O.J. participated in the revision of the work. Authors S.I.R.O., I.B.O. and O.M.O. carried out the statistical analysis and the data interpretation. Author S.I.R.O. managed the literature searches and critical review of the manuscript for important intellectual content. The final version for publication was written by B.E.I. All the authors read and approved the final version for publication.

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