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Incidence of Malaria and Typhoid Fever Co-Infection Among Patients Attending Rimingado Comprehensive Healthcare Centre, Kano State, Nigeria.

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Abstract
The research was carried out to determine the incidence of malaria-typhoid co-infection among patients attending Rimingado comprehensive healthcare centre, Kano state, Nigeria. Patients' bio- data were obtained through structured questionnaire and diagnosis was done using venous blood sample obtained from the participants. Rapid diagnostic test was used for analysis of malaria parasites while widal test was used for the analysis of enteric fever. Of the 150 patients enrolled for the study (85 females and 65 males), 60 (40.0%) had malaria and typhoid fever co-infection (P<0.05). The incidence of malaria-typhoid co-infection was highest among those in the age group range between 11-20 years (12.0%). However, with regard to the marital status, those that were single had the highest incidence of coinfection (27.3%) than the married. Poor sanitary habits, poverty and ignorance are the predisposing factors for the development of malaria and typhoid infections.

Keywords: Co-infection, Incidence, Malaria, Rimingado, Typhoid.

INTRODUCTION
Malaria-typhoid co-infection is a disease of public health importance which happens to be endemic in the tropical and subtropical countries including Nigeria (Isa *et al*., 2020). Typhoid and malaria fever are two leading febrile illnesses affecting humans, especially in sub-Saharan Africa. They remain the diseases of major public health importance and the cause of morbidity and mortality. An association between malaria and typhoid fever was first described in 1862 in North America as an entity called typho-malaria fever (Smith, 1982). Both diseases are common in many countries of the world where poor sanitary habit, poverty and ignorance exist. The first non-specific manifestations include fever, headache, abdominal pain and vomiting. Despite the importance of concurrent malaria and typhoid fever in the tropics, the challenges associated with the diagnosis and the public health implications have not been comprehensively reviewed (Simon-Oke and Akinbote, 2020). This disease condition during pregnancy and child age can have adverse effects on both mother and fetus as well as the

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children including maternal anemia, fever, fetal anaemia, abortion, still-birth and even death of the child or mother before birth or soon after delivery (Isa *et al*., 2020). Moreover, malaria-infected pregnant women are said to be more prone to typhoid fever because of the increased haemolysis in malaria which is said to increase the availability of iron in the tissues especially the liver and Salmonella species are believed to thrive more in iron rich tissues (Crump *et al*., 2014). It is worthy of note that both typhoid and malaria in pregnant women present with management problems since most drugs used in the treatment of both diseases are contra-indicated in pregnancy (Pam *et al*., 2018).

Malaria is caused by obligate intracellular parasites, which live in host erythrocytes and remodel these cells to provide optimally for their own needs. It is a major public health problem in tropical areas, and it is estimated that malaria is responsible for 1 to 3 million deaths and 300 to 500 million infections annually (Iwuafor *et al*., 2016). Malaria remains the most complex and overwhelming health problem, facing humanity in vast majority of tropical and sub-tropical regions of the world, with 300 to 500 million cases and 2 to 3 million deaths per year (WHO, 2017). About 90% of all malaria deaths in the world today occur in the sub-Saharan Africa and this is because majority of infections are caused by *Plasmodium falciparum* (WHO, 2018). Nigeria accounts for about 50% of malaria deaths (Okpe *et al*., 2016; WHO, 2017). Malaria has social consequences and exerts heavy burden on economic development. The disease is transmitted by the biting of female anopheles' mosquitoes, and the symptoms usually begin ten to fifteen days after being bitten (Isa *et al*., 2020). Malaria causes symptoms that typically include fever, fatigue, vomiting, and headaches. In severe cases it can cause yellow skin, seizures, coma, or death (Caraballo, 2014).

Typhoid fever (enteric fever) is a systemic prolonged febrile illness caused by certain Salmonella serotypes (Birhanie *et al*., 2014). Gram-negative, motile, non-sporing, non-capsulate bacilli which exist in nature primarily as parasites of the intestinal tract of humans and other animals. *Salmonella typhi* and the paratyphoid bacilli are found only in the intestinal tract of man for whom they have a high degree of pathogenicity and in which they frequently cause invasive disease that causes symptoms which may vary from mild to severe and usually begin six to thirty days after exposure with gradual onset of a high fever after several days (Ammah *et al*., 2013). 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 (Crump and Mintz, 2010). *Salmonella typhi* is the etiologic agent of man illness like typhoid fever, gastroenteritis and bacteremia in the blood (Callaway *et al*., 2008; Wain *et al*., 2015). There are about 33 million cases of typhoid annually in the world resulting in 216,000 deaths in endemic areas (Crump *et al*., 2014). The World Health Organization (WHO) identifies typhoid as a serious public health problem with high incidence on children, young adults and pregnant women (WHO, 2014). Outbreaks of typhoid fever are frequently reported from sub-Saharan Africa and countries in Southeast Asia (Baddam *et al*., 2012; Crump *et al*., 2014).

In a research conducted by Odikamnoro *et al*. (2018) involving 350 participants in Ebonyi state Nigeria, prevalence of 127 (36.2%) for malaria-typhoid co-infection was reported. In a similar study by Simon-Oke and Akinbote, (2020) involving 200 university students in Akure Nigeria, 103 (51.5%) prevalence was recorded. This research was carried out to determine the incidence of malaria-typhoid co-infection and risk factors associated with malaria and typhoid fever.

MATERIALS AND METHODS

Study Area

The study was conducted at Primary Healthcare Centre, Rimingado Local Government Area, Kano State; it's located in Rimingado local government area, 20km from Kano state capital. It provides basic healthcare to people of Rimingado and the neighboring community. Geographically, It is located between latitude $11^{0}57'54''$ N and longitude $8^{0}15'00''$ E with an area of 225km^2 (Wikipedia, 2021). The study population comprises of all patients of different age and sex attending Rimingado Comprehensive Healthcare Centre for the diagnosis of malaria and typhoid fever.

Ethical Approval

Ethical approval was obtained from the research Ethics committee of Kano State Ministry of Health and patients consent were sought out prior to the research.

Sample Size Determination

The sample size for this study was determined using the formula by (Naing *et al*., 2006) for sample size calculation at 0.05 level of precision as follows;

$N = Z^2Pq/d^2$

Where: n = required sample size

Z = standard normal deviation at the required confidence interval (1.96) which corresponds to 95% confidence interval.

P = prevalence of malaria-typhoid co-infection from previous study (4.5%) (0.1) (Pam *et al*., 2018).

Q = 1 – p = 0.9

d = degree of precision expected (0.05)

N = (1.96) (0.1) (0.9) / (0.05) = 3.8416×0.09/0.0025 =0.3457/0.0025=138.3 =138

To minimize error, this was however rounded up to 150 samples.

Sample Collection and Processing

About 3ml of venous blood sample was collected from each 150 patients presented with fever aseptically into a plain container. Some portion of the collected whole blood was used for the detection of malaria parasites antigen using RDTs while the remaining other portion was centrifuged at 1,200rpm for 5 minutes to obtain the serum which was used for widal test (Cheesbrough, 2010).

Malaria diagnosis using rapid diagnostic test (RDT)

The test was performed according to the manufacturer's guidelines. The test kit (Paracheck-Pf test kit) was detached from its seal and the blood from the EDTA bottle was blotted into sample window (S) present on the test kit, two drops of Malaria parasite test kit buffer was added to the blood sample in the sample window (S) and allowed to flow through the chamber labeled test (T) and control (C) windows. The test was allowed to run for 5 mins and the result interpreted based on the appearance of red band on the test and control lines.

Widal test for typhoid fever

The test was carried out using Cal-Test Diagnostic Inc. Chino, U.S.A. Widal commercial antigen suspensions, for the somatic (O) and flagella (H) antigens. One drop of the widal antigen suspension was added to the reaction circles containing the patient's serum. The

content of each circle was uniformly mixed over the entire circle with separate mixing sticks. The slides were gently rocked back and forth, and observed for agglutination for one minute. Any serum sample with antibody titre ≥ 1:160 to the O and H antigens of *S. typhi* was considered positive (Simon-Oke and Akinbote, 2020).

Statistical analysis

The data obtained were analyzed using statistical package for social sciences (SPSS) version 19.0 (Chicago, USA). Chi-square (χ^2) was used to determine if the relationships between the Malaria and typhoid co-infection is statistically significant.

RESULTS

A total of one hundred and fifty (150) patients with febrile illness were enrolled, 108 (77.0%) were malaria positive, 80 (53.3%) were typhoid fever positive. Of this number, the incidence of malaria and typhoid fever co-existence using widal and malaria RDT test was 60 (40.0%) (Table 1).

The results of the incidence of malaria-typhoid co-infection in relation to the patient's age group is depicted in table 2; patients in the age group of 11-20years had a highest incidence of malaria and enteric fever co-infection of 18(12.0%) while the age group of 81-90years had the least incidence of 1(0.7%). With respect to the educational class, those with primary education had the highest incidence of 19(12.7%) and those with tertiary education had the least incidence of 10(6 .6%) (Table 3). Furthermore, the malaria-typhoid coinfection with respect to marital status, those that are single have the highest incidence of 41(27.3%) than those that are married 19(12.7%) (Table 4).

Table 5 shows the incidence of malaria-typhoid co-infection in relation to patient's sex. Females were found to have higher incidence of malaria-typhoid co-infection 36 (24.0%) than the males 24 (16.0%).

Table1: Overall incidence of malaria, typhoid fever and co-infection

Illness	No. tested	No. positive (%)
Malaria		108 (77.0)
Typhoid	n=150	80 (53.3)
Coinfection		60 (40.0)

Table 2: Malaria and typhoid fever co-infection among patients with respect to age group

Age group	No. tested	No. malaria (%)	No. typhoid (%)	No. co-infection (%)
(1-10)	27	19 (12.7)	12 (8.0)	10 (6.7)
(11-20)	43	30 (20.0)	26 (17.3)	18 (12.0)
(21-30)	30	22 (14.7)	16 (10.6)	13 (8.7)
(31-40)	17	14 (9.3)	7 (4.7)	6 (4.0)
(41-50)	14	9 (6.0)	6 (4.0)	5 (3.3)
(51-60)	6	5 (3.3)	4 (2.7)	3 (2.0)
(61-70)	6	3 (2.0)	5 (3.3)	2 (1.33)
(71-80)	5	4 (2.7)	3 (2.0)	2 (1.33)
(81-90)	2	2 (1.3)	1 (0.7)	1 (0.7)
Total	150	108 (72.0)	80 (53.3)	60 (40.0)

Table3: Malaria and typhoid fever co-infection among patients with respect to education.

Education level	No. tested	No. Positive (%)
Non formal	45	18(12.0)
Primary	35	19(12.7)
Secondary	50	13(8.7)
Tertiary	20	10(6.6)
Total	150	60(40.0)

Table 4: Malaria typhoid co-infection among patients with respect to marital status.

Marital status	No. tested	No. positive (%)
Married	33	19(12.7)
Single	117	41(27.3)
Total	150	60(40.0)

Table 5: Malaria and typhoid co-infection among patient with respect sex distribution.

Sex distribution	No. tested	No. positive (%)
Female	85	36 (24.0)
Male	65	24 (16.0)
Total	150	60 (40.0)

DISCUSSION

Malaria and typhoid fever still remain diseases of major public health importance in the tropics. They are major aetiological considerations in both acute and prolonged fever of unknown origin in the tropics. Co-infections of malaria and typhoid fever are common in the tropics because of the high incidence of such illnesses (Odikamnoro *et al*. 2018; Simon-Oke and Akinbote, 2020). However, the actual and precise underlying mechanisms to explain the association between malaria and typhoid fever infection is still uncertain, although there are few postulations which may explain why malaria may predispose to Salmonella bacteremia and sepsis (Keong and Sulaiman, 2006). This study investigated the association between malaria and typhoid infections among patients with fever symptoms that reported for testing at healthcare center Rimin Gado Local Government Area of Kano State, Nigeria between August and September, 2021. During the study period, a total of 150 febrile patients reported for testing, of these, 65 (43.3%) were males and 85 (56.7%) were females. Only 42 (28.0%) fever patients did not test positive for any of the two infections. A total of 108 (72.0%) fever patients tested positive for the plasmodium parasite. Among these, positive male cases were 45 (30.0%) and female positive cases were 63 (42.0%). A co-infection of 60 (40.0%) is reported in our studies which is higher than the results obtained by Okpara *et al*. (2011) that a reported a non-significant co-infection prevalence of 22% in Imo State, Nigeria. In another study in Pakistan, it was found that subjects with co-infection were found to have significantly higher rates of nausea, vomiting, abdominal pain, and diarrhoea (Khan *et al*., 2009). Based on the result of this study, malaria and typhoid fever infections are higher in the raining/wet season (August) than drier seasons. This is mainly due to the mode of transmission and reproductive cycles of the Plasmodium parasite and Salmonella bacteria. This study recorded higher malaria and typhoid infections especially in the peak periods of the raining season. Infections for both diseases were high from the months of July to August, coinciding with months of heavy rainfall.

In a research conducted by Odikamnoro *et al*. (2018) involving 350 participants in Ebonyi state Nigeria, prevalence of 127 (36.2%) for malaria-typhoid co-infection was reported. In a similar study by Simon-Oke and Akinbote, (2020) involving 200 university students in Akure Nigeria,

103 (51.5%) prevalence was recorded. These results however agree with our present study which reported a significant co-infection rate.

Malaria and typhoid fever are diseases of the tropics accompanied by poverty and ignorance. Higher incidences were observed in patients lacking formal education and middle aged individuals. Lack of up-to-date diagnosis facilities, poor socio-economic lifestyle, poor disease prevention measures and poor treatment options are all factors related to the high incidence of malaria and typhoid infections.

CONCLUSION

Almost 85% of the febrile patients presenting with fever symptoms in this study had malaria, typhoid, or both. There was a strong association between having fever and that of having malaria or typhoid fever infections. Higher incidence of malaria and typhoid co-infection was observed. Also fever among patients was more likely to be caused by malaria than typhoid according to this study.

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