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(RESEARCH ARTICLE)

Assessment of co-infection of typhoid and malaria in patients attending F.M.C Umuahia Abia state

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Abstract

Malaria and typhoid fever are major public health problems in tropical and subtropical countries. People in endemic areas are at risk of contracting both infections concurrently. This study was aimed at assessing malaria and co-infection of typhoid fever among patients. A cross-sectional study was conducted on 256 patients suspected for malaria and typhoid fever from March to August 2017 at Federal Medical Centre Umuahia Abia State. Blood samples were collected for blood film preparation and widal test. The prevalence of malaria was 78.90% (n = 202). Among these age groups, (11 – 15), (16 – 20), (21 – 25) and (26 – 30) years were mostly infected. The seroprevalence of typhoid fever was found high and poor hand washing habit were associated with typhoid fever infection. Further studies should be done on malaria and typhoid fever co-infection in different seasons and different study areas.

Keywords: Typhoid; Malaria; Co-Infection; Prevalence; *Plasmodium; Salmonella*

1. Introduction

Malaria is a life threatening serious parasitic disease resulting from infection with *Plasmodium* species transmitted by the bite of female Anopheles mosquitoes. Malaria is a leading cause of illness and death in the developing world and a significant drag on economic development. The parasite was visualized in red blood cells by Lavern in 1880. Sir Ronald Ross subsequently proved that the infection was transmissible by mosquitoes to humans in 1879 [1].

Four species of the parasite transmit human malaria: *Plasmodium falciparum, P. vivax, P. ovale, P. malaria. P. vivax and P. falciparum* together account for almost 90% of malaria infection globally. *P. falciparum*, the most virulent form, is the cause of almost all malaria associated deaths and severe disease. *P. vivax* and *P. ovale* cause relapsing disease and relapses occur weeks to months after initial illness. Most deaths are caused by *P. falciparum* because *P. vivax, P. ovale* and *Plasmodium* malaria generally cause a milder form of malaria [2]. The fifth specie, *P. knowlesi*, rarely cause disease in humans. Malaria is one of the most common infectious diseases and a great public health problem worldwide, particularly in Africa and South Asia.

About three billion people are at risk of infection in 109 countries. Each year, there are an estimated 250 million cases of malaria leading to approximately one million deaths, mostly in children under five years of age [3]. Malaria is one of the most successful parasites ever known to mankind. After thousands of years, it remains the world's most pervasive infection, affecting at least 91 different countries and some 300 million people. The disease causes fever shivering, joint pain, headache and vomiting. In severe cases, patients can have jaundice, kidney failure, and anemia and can lapse into a coma [4]. It is ever present in the tropics and countries in Sub-Saharan Africa, which account for nearly 90% of all malaria cases. The disease is widespread in tropical and subtropical regions that exist in a broad band around the equator [5].

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Malaria is commonly associated with poverty and has a major negative effect on economic development. In Africa, it is estimated to result in losses of US 12 billion a year due to increased healthcare costs, lost ability to work, and negative effects on tourism [6]. Symptoms usually begin ten to fifteen days after being bitten. If not properly treated, people may have recurrences of the disease month later. In those who have recently survived an infection, reinfection usually causes milder symptom. This partial resistance disappears over months to years if the person has no continuing exposure to malaria. Malaria is typically diagnosed by the microscopic examination of blood using blood films or with antigen-based rapid diagnostic tests. Methods that use the polymerase chain reaction to detect the parasite's DNA have been developed, but are not widely used in areas where malaria is common due to their cost and complexity [7].

The risk of malaria disease can be reduced by preventing mosquito bites through the use of mosquito nets and insect repellents, or with mosquito control measures such as spraying insecticides and draining standing water several medications are available to prevent malaria in travelers to areas where the disease is common. Resistance among the parasites has developed to several anti-malarial medications. For example, chloroquine – resistant *P. falciparum* has spread to most malaria areas, and resistance to artemisinin has become a problem in some parts of South East Asia [2].

Typhoid fever is a chronic disease caused by the Bacterium *Salmonella typhi* that is very common in many developing regions of the world. Human is the only reservoir host of this bacterium. A person can be infected by eating contaminated food and water. Typhoid fever is an acute systemic infection caused by the bacterium *Salmonella enterica* serovar *typhi*. *Salmonella enterica* serovars *paratyphi* A, B, and C cause the clinically similar condition, paratyphoid fever. Typhoid and Paratyphoid fevers are collectively referred to as enteric fevers. Typhoid is transmitted by the fecal-oral route via contaminated food and water and is therefore encountered mostly throughout the developing world because sanitary conditions are very poor and use of untreated water from streams and stagnant ponds are common. In the last decade, the emergence of resistance to the antibiotics used for treatment has led to large epidemics, and complicated the management of this disease [8]. The true magnitude of typhoid is difficult to quantify because the clinical picture is often confused with many other febrile illnesses and most typhoid endemic areas in Africa lack facilities to confirm the diagnosis. A good surveillance system that accurately measures the incidence and causes of febrile illness in a region must be able to detect cases as close as possible to the population level and must be supported by modern laboratory diagnostic capacity.

In many afro-tropical countries, parasitic co-existence is common with increased potential for co-infection, which may adversely impact the outcome of the diseases they cause [9]. Of all human diseases caused by protozoan parasites malaria has the greatest burden and is responsible for most deaths amongst young children in Sub-saharan Africa, accounting for 90% of all global cases [10].

The fact that malaria affect more than two-thirds of humans has led to growing interest to understanding their epidemiology and interactions with other infections [11]. Although there is much literature on the epidemiology of malaria separately, little is known about the distribution and impact of their co-infections on the population across the country. Due to the differences in the physiological, anthropological, genetic, immunological or geo ecological factors, infections with malaria may not necessarily be independent within an individual and could result in positive or negative associations in disease manifestation.

The implications of concomitant malaria and co-infections have been mainly explored and indicate that their interactions can decrease the course of malaria infection and disease [12]. Thus, this study sought to determine the incidence and prevalence of malaria and co-infection and evaluate its impact on malaria. The findings from the study will provide useful, information necessary to design strategies to effectively control and manage malaria in the context of co-infection.

2. Material and methods

2.1. Advocacy and mobilization

2.1.1. Study Population

An Ethical clearance was obtained from the F.M.C ethical committee. Written informed consent was obtained from each of the volunteer study subjects or guardian of children. Informed consent of each participant was obtained before blood sample collection. Consent for screening of the children was obtained from their parents. A total of 256 subjects; (126 males and 130 females) blood samples were collected from subjects and questionnaires were administered to the subjects to obtain socio-demographic information, knowledge, attitude and practice about malaria and typhoid fever.

2.1.2. Sample Collection

The method of sample collection employed was Venipuncture technique recommended by Cheesbrough [13].

2.1.3. Laboratory Analysis

The collected blood samples were analyzed within 30-60 minutes of collection. Microscopic examination of stained thick and thin blood films for malaria diagnosis were prepared according to the technique by Cheesbrough, [13]. A drop of each blood sample was placed in the center of a grease-free clean glass slide. Thereafter, the reverse side of the slide was cleaned with cotton wool and kept for air-drying and staining with Giemsa's stain. The slide was held with the dried thick film slide facing downward and dipped in Giemsa's stain for 10 minutes. It was washed off gently in clean water. The back of the slide was cleaned with cotton wool and kept in the draining rack to air-dry for thin film, a small drop of blood was placed on the centre of a grease free microscopic slide. The drop of blood was then spread with a glass spreader held at an angle of 80 to obtain a thin film with a smooth tail end. This was allowed to air-dry in a horizontal position and then fixed with absolute methanol for two minutes. A Giemsa stain was applied on the thin film for 10 minutes. The stain was then washed off using water and also air dried. The stained thick and thin films were viewed using oil immersion at l00x magnification to examine for *Plasmodium* parasites presence of ring forms of *Plasmodium* and Trophozoites of *Plasmodium* indicate positive results. A blood smear was considered negative if no parasite was seen after examination under x100 high power field of microscope.

Typhoid fever infections were diagnosed using patients' blood serum and widal test kits. The widal kit contained reagents with attenuated typhoid antigen which reacted specifically with the body's antibody. Stool sample were aseptically inoculated into selenite – F – enrichment broth and incubated overnight at 37^0C. The selenite -F- culture was sub-cultured using Shigella – Salmonella Agar SSA or DCA and incubated at 37^0C overnight. Suspected colonies were inoculated into Kliger Iron Agar (KIA) Slants and the characteristic fermentation patterns for *S. typhi* and other *Salmonella* species were sought after incubation of the slants at 37^0C overnight.

2.1.4. Identification

Positive specimens were identified on the basis of microscopy for malaria parasite. For typhoid fever, an agglutination reaction in any of the reagents was an indication that Salmonellae was present. The degree of agglutination was recorded in titres as scanty agglutination (1:40), Slight agglutination (1:80), Heavy agglutination (1.160) and Very heavy agglutination (1:320)

The assessment of malaria parasite and typhoid fever was calculated as the proportion of sampled patients with a positive result divided by the number of patients who provided blood samples.

2.2. Statistical Analysis

The data generated from this study were analyzed using descriptive statistics and results were presented in percentages.

3. Results

Out of 256 patients, 202 (78.90%) had malaria, 147 (57.42%) by serology and 38(14.84%) by culture had typhoid fever. Age groups (11-15), (16-20), (21-25) and (26-30) years were mostly infected with malaria and typhoid fever (Table 1).

Analysis of the co-infection of typhoid fever and malaria was statistically analyzed and it was found that typhoid fever was independent of malaria ($P<0.05$).

Although both infections were independent, there was a significant correlation between typhoid fever and malaria ($P<0.05$). This correlation was more pronounced when widal test was used than culture method. *Salmonella typhimurium* with overall prevalence of 4 (1.56%) was isolated in the age groups, 16-20, 21-25 and 26-30, while *Salmonella typhi* 17(6.64%) was isolated in all age groups except 1-5 and 35-40 years. *Salmonella paratyphi* had equal prevalence (Table 2).

Males and females ratio was approximately equal. The difference in prevalence with respect to age group was statistically significant ($P<0.05$).

Furthermore, the study indicated that out of the 202 (78.91%) malaria positive patients, 29(14.36%) had typhoid fever bacteriologically confirmed. Both sexes were approximately equally co-infected. On the other hand, out of the 54 (21.09%) malaria negative patients 9(16.67%) were bacteriologically confirmed positive for typhoid fever (Table 3).

There was no significant difference in infection rate (P>0.05), 88(43.56%) patients had malaria parasite density parasite count of 1000 to 50,000 parasite per micro liter of blood. Among these patients 48(32.65%) and 12(31.44%) had typhoid fever confirmed serologically and bacteriologically respectively. 114(56.44%) of malaria positive patient had parasite density of above 50,000 per micro liter of blood (Table 4).

Among these patients were 99(67.35%) and 26(68. 42%) typhoid fever positive confirmed by widal test and culture respectively. The disparity in the infection rates were statistically not significant by bacteriological method (P>0.05) and significant by serology (P<0.05). Malaria infection was higher in the rainy season than in the dry season (Table 4.5).

3.1. Prevalence of malaria and typhoid fever infection among FMC patients based on Age-group

Age groups 11 – 15, 16 – 20, 21 – 25 and 26 – 30 years were mostly infected with malaria and typhoid fever. Age group 11 – 15 was the highest with prevalence rate of (96.88%) followed by age group 1 – 5 with prevalence rate of 89.47 and the least was age group 35 – 40 with prevalence rate of 46.67%.

Table 1 Prevalence of malaria and typhoid fever infection among FMC patients based on Age-group

Age group (Years)	Number Examined	Malaria	Number Positive	Typhoid fever
			Widal Test	Culture
1-5	19	17(89.47)	5 (26.32)	0 (0.00)
6-10	26	21(80.71)	12(76.15)	2(7.69)
11-15	32	31(96.88)	2(75. 00)	6(18.75)
16-20	46	33 (82.50)	27 (67.15)	8 (20.00)
21-25	52	43(82.69)	37 (71.15)	12(23.08)
26-30	42	33(78.57)	34(57.14)	9(21.14)
31-35	30	17(56.67)	14(46.67)	1 (3.33)
35-40	15	7(46.67)	4(26.67)	0(0.00)
Total	256	202(78.91)	147 (57.42)	38(14.84)

Key: Number in parenthesis = percentage (%), while the number outside is number positive for each test.

3.2. *Plasmodium falciparum* and *Salmonella* species in FMC Patients.

Both malaria and typhoid infection were independent, there was a significant correlation between the two. *Salmonella typhimurium* with overall prevalence of 4 (1.56%) was isolated in the age groups 16 – 20, 21 – 25 and 26 – 30, while *Salmonella typhi* 17(6.64%) was isolated in all age group except age group 1-5 and > 35 years.

Table 2 *Plasmodium falciparum* and *Salmonella* species in FMC Patients

Age in Years	Number Examined	*Plasmodium falciparum*	*Salmonella typhi*	*Salmonella typhimurium*	*Salmonella paratyphi*
1-5	19	17(89.47)	0(0.00)	0(0.00)	0(0.00)

6-10	25	21(80.71)	2(7.69)	0(0.00)	0(0.00)
11-15	32	31(96.88)	2(6.25)	0(0.00)	4(12.50)
16-20	46	33(82.50)	5(12.50)	1(2.50)	2(5.00)
21-25	52	43(82.69)	4(7.14)	2(3.85)	6(11.54)
26-30	42	33(78.57)	3(7.14)	1(2.38)	5(11.90)
31-35	30	17(56.67)	1(3.33)	0(0.00)	0(0.00)
35-40	15	7(46.67)	0(0.00)	0(0.00)	0(0.00)
Total	256	202(78.91)	17(6.64)	4(1.56)	17(6.64)

3.3. Malaria and typhoid Fever Association

Both sexes were approximately equally coinfected. Out of the 54 (21.09%) malaria negative patients, 9(16.67%) were bacteriologically confirmed positive for typhoid fever.

Table 3 Malaria and typhoid Fever association

***Salmonella* isolate**	**Malaria Positive N = 202**			**Malaria Negative N=54**		
	Male	**Female**	**Total**	**Male**	**Female**	**Total**
S. typhi	7(3.47)	6(2.97)	13(6.44)	2(3.70)	2(3.70)	4(7.41)
S. paratyphi A	5(2.48)	7(3.47)	12(5.94)	3(5.56)	2(3.70)	5(9.26)
S. paratyphi B						
S. paratyphi C						
S. typhimurium	3(1.49)	1(0.50)	4(1.98)	0(0.00)	0(0.00)	0(0.60)
Total	15(7.43)	14(6.93)	29(14.36)	5(9.26)	4(7.41)	9(16.47)

Key: Number in parenthesis = percentage (%)

3.4. Relationship between *Plasmodium falciparum* Parasite

Table 4.4, 88 (43.56%) patients had malaria parasite density of 1000 to 50,000 parasite per micro litre of blood. 114 (56.44%) of malaria positive patients had parasite density of above 50,000 per micro litre of blood.

Table 4 Relationship between *Plasmodium falciparum* Parasite

Density and Salmonella Antibody Titres			
P. falciparum	**Malaria Positive**	**Typhoid fever**	**Positive Density Culture**
	Widal test		
1000-50,000	88(43.56)	48(32.65)	12(31.58)
Above 50,000	114(56.44)	99(67.35)	26(68.42)
Total	202(78.91)	147(57.42)	38(14.84)

Key: Number in paranthesis = percentage (%)

Table 5 Malaria and typhoid fever infection in relation to months of the Study

Months	**Malaria positive n=202**	**Typhoid Fever n=38**
August	11(5.45)	2(5.26)
September	14(6.93)	1(2.63)

October	17(8.43)	3(7.89)
November	19(9.41)	4(10.52)
December	23(11.38)	3(7.89)
January	34(16.83)	8(21.05)
February	44(21.78)	12(31.58)
March	40(19.80)	5(13.16)

Key: Number parenthesis = percentage (%)

4. Discussion

The study indicated a positive association between malaria and typhoid fever which is more pronounced when typhoid fever was diagnosed serologically. Erroneous interpretation of the test result may lead to misdiagnosis and mismanagement of the patient, resulting in morbidity and mortality. So, interpretation of widal test results when diagnosing concurrent malaria and typhoid fever must therefore be done with a lot of caution.

Out of the 256 person, those within the age group of 11-15 years had the highest prevalence of malaria 31(96.88%) followed by 1-5 years 19(89.47%) while those in 35-40 years had the least 7(46.67%). This might be due to low immune response against malaria infection, inappropriate use of bed nets and inappropriate use of antimalarial drugs in those children. Also among the age groups, those within the age group of 6-10, 12(76.15%) had the highest prevalence of typhoid fever followed by age group 11-15 2(75.00%). This might be due to their poor handwashing habit, inadequate sanitation and proper use of latrine or toilet. The result of using stool culture was 12(23.08%) for typhoid and this is in agreement with the study in Anambra 26.06%, Ibadan 19.95% and Ebonyi 23.75%. The positivity rates of *Salmonella typhi* and *Salmonella paratyphi* were similar 17(6.64 and 17(6.64%) respectively. But there is a great difference in frequency of *Salmonella typhimurium,* 4(1.56%). The difference in the frequency of the species might be the result of the prevention and control measures employed in the study area.

In this study, the prevalence of malaria and typhoid was almost similar in males and females 15(7.43%) and 14(6.93%) respectively but there was no statistically significant association $P > 0.05$. While other studies showed in Ebonyi, Nigeria females (10.60%) are more affected than males (7.30%). This might be due to the fact that males are sleeping outside their house for agricultural purpose and have greater chance to travel to malaria and typhoid fever endemic area for crop cultivation or daily labor. Also the high co-infection rate among males agrees with the work of Ihongbe who observed that most male farmers and traders spend their time in the farms and markets where they may have no other sources of drinking water and hence have to purchase sachet water.

The result of this study is comparable with the reports from Edo State, Nigeria 180% according to Iroha. But it is less than the reports from Enugu Nigeria where malaria positive is 56 and typhoid fever 15, the discrepancy of the results between the studies might be due to seasonal variation and difference in geographical locations. In this study the malaria and typhoid fever in relation to months of the study was 202 and 38 respectively. This is in agreement with Eneanya, who reported the prevalence rates of 216 and 32 respectively in Azia Community in Anambra State. The ignorance of the people might be responsible for the prevalence of the diseases in the study area, and probably this could be attributed to lack of health education programme as majority of the residents of the study area are mainly traders and farmers.

5. Conclusion

Malaria predisposes to bacterial super-infection possibly through its effect on immune responsiveness. Under special conditions of severe malaria notably heamolysis and impairment of leucocyte and macrophage function due to phagocytosis of parasite and subsequent malaria pigment accumulation, immunosuppression, the invading bacteria would proliferate leading to bacteraemia and septicemia. Malaria and typhoid fever are tropical diseases. Poverty, mal-nutrition, poor sanitary status, poor personal hygiene, poor health facilities, poor social service and low level of education are among the factors that make tropical areas diseases laden. Mal-nutrition gives room to susceptibility infection.

Most people are ignorant of the causative agents, means of transmission, spread and acquisition of some diseases. Typhoid fever is acquired from contaminated water, food, ice creams, but the presence of a symptomatic carriers

worsen the situation as unusual prolonged outbreak of typhoid fever from 1988 to 1994 in Terrassa (Barcelona, Spain) was caused by a casual food handler who was a carrier.

Despite the fact that malaria and typhoid fever are indistinguishable regarding their clinical signs and symptoms and there are some overlaps in their pathology. *Plasmodium* and *Salmonella* are not of the same phylum, cannot share antigens nor have same method of transmission. This association has been co-incidental as both diseases are endemic in Umuahia and environs.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

There is no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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