Dual Infection with Typhoid and Malaria in Febrile Patients in Ikare Akoko, Nigeria

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Abstract: Malaria and typhoid continues to be a major public health problem worldwide and are known to present with clinically similar symptoms with fever being the major presentation. This study was carried out to investigate the prevalence of malaria and distribution of sero-antibodies to etiologic agents of typhoid in patients with febrile illness in General hospital, Ikare Akoko, Ondo state, Nigeria. The 234 patients with febrile illness clinically presenting with symptoms of malaria and typhoid without prior laboratory diagnosis for malaria and typhoid were used for the study. Giemsa stained thick and thin blood films were used to determine malaria parasitaemia. Serological prevalence of *Salmonella* species was done using the Widal agglutination tests. Of 234 patients with febrile illness studied, 173 (73.9%) and 88 (37.6%) were positive for typhoid and malaria, respectively. The 43 (18.3%) had malaria-typhoid co-infection. Malaria infection was higher in males 93 (53.7%) as compared to typhoid which was more prevalent in females, 47 (53.4%). The age group <5-15 years had the highest prevalence of malaria 27 (30.7%) and typhoid prevalence was highest in the age group 26-35, 66 (38.2%). *S. typhi* somatic O antigens was the most prevalent cause of typhoid 54 (23.1%) this was followed by *S. paratyphi* B-O 41 (17.5%), *S. paratyphi* C-O 39 (16.7%), *S. paratyphi* A-O 32 (13.7%), *S. paratyphi* A-H 31 (13.2%), *S. typhi* H 18 (7.7%), *S. paratyphi* B-H 15 (6.4%) and *S. paratyphi* C-H 10 (4.3%). The prevalence of typhoid and malaria was high in the subjects studied; typhoid was more prevalent than malaria, screening for typhoid among febrile patients of Ikare Akoko will be of utmost benefit.

Key words: Malaria, typhoid, sero-antibodies, prevalence, febrile patients, clinical symptoms, *S. typhi*

INTRODUCTION

Fever is the most common cause of consultation in the tropics and sub tropics where most fever are of infectious origin of which typhoid and malaria accounts for a majority. Both malaria and typhoid are among the most endemic diseases in the tropics, they are associated with poverty and under development with significant morbidity and mortality (World Health Organization, 2011).

Malaria is caused by some *Plasmodium* species notably, *Plasmodium falciparum*, *Plasmodium malariae*, *Plasmodium ovale* and *Plasmodium vivax* (Sutherland *et al.*, 2010). Typhoid infection is transmitted faeco-orally through contaminated water or food and is caused by *Salmonella* species. Four species has been known to have an etiological role in symptoms consequently known as typhoid viz; *Salmonella typhi*,

Salmonella paratyphi A, *S. paratyphi* B, *S. paratyphi* C (Parry *et al.*, 2002). Co-infection with different serotypes of *Salmonella* species causing typhoid is a common finding (Kanjilal *et al.*, 2006) hence the need for screening for the various species.

Malaria and typhoid are highly prevalent in Nigeria and other sub-Saharan Africa where the highest population of the world's poor live (Mbuh *et al.*, 2003). Both diseases are an indication of neglect of control of the environment. While both diseases and most especially typhoid are going extinct in the wider world, their case in Africa remains an alarming one as they are been recorded to constitute a major cause of hospital admissions in Africa (World Health Organization, 2011). Although, typhoid and malaria are caused by very different organisms-one a gram negative bacilli, the other a protozoan and transmitted via different mechanisms, both diseases share rather similar symptomatology

(Ohanu *et al.*, 2003). Malaria and typhoid often presents with mimicking symptoms, especially in the early stages of the diseases such as fever, general weakness of the body and malaise (Ohanu *et al.*, 2003). Clinical syndromes produced by both diseases often present with diagnostic difficulties and in some cases could lead to diagnostic confusion.

Diagnosis of both diseases is done using the serological Widal agglutination tests and thick and thin stained films for typhoid and malaria, respectively (Olopoenia *et al.*, 2000). Though the thick and thin films remains the gold standard for diagnosing malaria, the Widal test for the laboratory diagnosis of typhoid has its short comings which is as a result of cross-reactions of antigens to somatic O antibodies and to non-typhoidal *Salmonella* species (Koeleman *et al.*, 1992; Olopoenia *et al.*, 2000).

In many African countries like Nigeria, Widal test is the most widely used method in typhoid fever diagnosis because it is easy to perform, requires minimal training and equipment, faster and relatively cheaper (Mbuh *et al.*, 2003). Patients are commonly treated for typhoid fever based on a single Widal test and are a common practice amongst doctors to prescribe anti malaria treatment and antibiotics simultaneously because typhoid fever is endemic and difficult to exclude on clinical ground. This study thus aimed to determine the prevalence of malaria and typhoid among febrile patient with clinically compatible symptoms in Ikare Akoko, Ondo State, Nigeria.

MATERIALS AND METHODS

Study population: This study was carried out at the General hospital; Ikare Akoko a major government owned hospital in Ikare Akoko, Ondo State, Nigeria. The hospital serves the general medical needs of the people of Ikare Akoko and neighboring communities (up to about 25 communities). Ondo State is located in the western part of Nigeria and it is bordered by Edo State on the right, Bight of Benin to the South, Ogun State to the left and Ekiti and Kogi States in the North.

A total of 234 patients presenting to the hospital with febrile conditions suggestive of malaria or typhoid were recruited for the study. Blood samples were obtained by veni-puncture. About 5 mL of venous blood was drawn aseptically into plain bottles and after 1 h centrifuged to obtain serum.

Widal agglutination test for *Salmonella typhi* antibodies:

Widal agglutination test was performed using the Widal agglutination kit (Biotech lab, United States) containing

somatic (O) and flagella (H) antigens of *Salmonella typhi*, *Salmonella paratyphi* A-C. A negative saline control was introduced in each batch of test.

Analysis for *S. typhi* antibodies was initially carried out on a tile. Drops of Widal *S. typhi* antigens were placed unto sera and observed for agglutination. The sera were then tested at a dilution of 1/10 and when positive, it was further tested at 1/20, 1/40, 1/80, 1/160 in 0.9% normal saline and the result read immediately after. A positive Widal test was considered as one that gave a reaction titer of 1/80 or greater in a single test.

Malaria microscopy: Thick and thin Giemsa stained blood smear was examined under the microscope. Thick smears were examined on 100 high powered microscope fields before recorded as negative. The presence of any peripheral parasitaemia at least one per 100 thick fields was considered to be significant as the entire patient presented with fever.

RESULTS AND DISCUSSION

The 234 patients were studied for presence of setiologic agents of malaria and typhoid. Total 173 (73.9%) were sero-positive for sero-antibodies to *Salmonella typhi* antibodies and 88 (37.6%) were positive for malaria. The 43 (18.4%) febrile patients had co-infection of malaria and typhoid. Typhoid was higher among males 93 (53.7%) as compared to 80 (46.2%) for females and malaria was more prevalent in females 47 (53.4%) as compared to males 41 (46.6%) (Table 1). Age wise distribution shows that infection rate for malaria was higher among lower aged febrile patients, age group <5-15 years had highest prevalence of malaria 27 (30.7%) with the age group >45 years having the lowest prevalence of malaria, 2 (2.3%). Typhoid was more prevalent in the age group 26-35 years 66 (38.2%) with age group >45 having the lowest prevalence 10 (5.8%) (Table 2).

Sero-antibodies prevalence shows that more than one antigen were responsible for infection in majority of the patients. Agglutination sero-positivity of somatic O antigens 166 (70.9%) was higher among the febrile

Table 1: Prevalence of malaria and typhoid among febrile patients in Ikare Akoko

Parameters studied	No. positive (%)	Males n = 113	Females n = 121
Typhoid	173 (73.9)	93 (53.7)	80 (46.2)
Malaria	88 (37.6)	41 (46.6)	47 (53.4)
Typhoid-Malaria	43 (18.4)	16 (14.2)	27 (22.3)
Co-infection			

Total no. of patients = 234

Table 2: Age wise prevalence of malaria and typhoid among febrile patients studied

Age (years)	No. tested	Malaria no. infected (%)	Typhoid no. infected (%)
<5-15	48	27 (30.7)	27 (15.6)
16-25	56	16 (18.2)	47 (27.2)
26-35	79	35 (18.6)	66 (38.2)
36-45	33	3 (3.4)	23 (13.3)
>45	18	2 (2.3)	10 (5.8)
Total	234	88 (37.6)	173 (73.9)

Table 3: Distribution of *S. typhi* antigens in the patients studied

Antigens	Sero-types	No. positive (%)
Somatic O antigens		
	<i>S. typhi</i> O	54 (23.1)
	<i>S. paratyphi</i> A-O	32 (13.7)
	<i>S. paratyphi</i> B-O	41 (17.5)
	<i>S. paratyphi</i> C-O	39 (16.7)
Flagella H antigens		
	<i>S. typhi</i> H	18 (7.7)
	<i>S. paratyphi</i> A-H	31 (13.2)
	<i>S. paratyphi</i> B-H	15 (6.4)
	<i>S. paratyphi</i> C-H	10 (4.3)

Total no. of patients = 234

patients when compared to flagella H antigens 74 (31.6%) Table 3. The distribution of sero-antibodies for typhoid shows that *S. typhi* somatic O antigens 54 (23.1%) was the most prevalent cause of typhoid in the patients studied (Table 1). This was followed by *S. paratyphi* B-O 41 (17.5%), *S. paratyphi* C-O 39 (16.7%), *S. paratyphi* A-O 32 (13.7%), *S. paratyphi* A-H 31 (13.2%), *S. typhi* H 18 (7.7%), *S. paratyphi* B-H 15 (6.4%) and *S. paratyphi* C-H 10 (4.3%) (Table 3).

Typhoid fever and malaria are still of major public health importance in the tropics. A total of 234 patients were used in this study and samples were collected during the acute phase of the fever. Following up patients to study prevalence of typhoid using their convalescent sera presented enormous difficulties which arose from non-compliance from patients.

Out of all 234 patients who presented to the hospital with fever, 173 (73.9%) were positive for typhoid Widal agglutination test and most cases were due to *Salmonella typhi* which is known to be the most common germ responsible for typhoid in West Africa (Lerner and Lerner, 2003). Malaria is also a highly endemic disease in Sub-Saharan Africa and other tropical countries in the study 88 (37.6%) of febrile patients studied were found to have malaria. Some studies have reported a higher prevalence of malaria than typhoid in febrile patients (Agwu *et al.*, 2009) but the study showed that typhoid was a more common cause of fever in Ikare Akoko. Higher prevalence of typhoid as against malaria has been reported among febrile patients (Jhaveri *et al.*, 1995; Mbuh *et al.*, 2003). The probable cause of high prevalence of typhoid can be as a result of poor environmental and hygiene practices in this locale. Inadequacies of housing

facilities is common, most houses do not have a toilet and also no existence of proper sewage disposal facilities. Defecation is done at any place accessible and this leads to the spread of the bacteria a well-known infection transmitted by the faeco-oral route.

This research agreed with research of Ammah *et al.* (1999) who found that 26% of patient with fever and signs compatible with typhoid actually had typhoid. It contradicts findings of Emmanuel *et al.* (2003) where only 2.5% out of 200 patients had typhoid. Clinical diagnosis the most widely used approach is unreliable because the symptoms of malaria are very non-specific. Widal test is the commonly used method for diagnosing typhoid in mutual settings like this as it is cheaper, easy to perform and faster (Olopoenia *et al.*, 2000). In endemic areas, the Widal test is still of significant diagnostic value provided judicious interpretation of the test is made against a background of patient information, especially data which relate to agglutinin levels in normal individuals and in non typhoidal fevers common in the region (Olopoenia *et al.*, 2000).

Age and sex wise prevalence of malaria and typhoid was studied; malaria was more prevalent in females than in males while typhoid was more common in males than females. Previous studies have reported a higher prevalence of malaria parasitaemia in males (Osazuwa and Ayo, 2010), though the difference in prevalence was not significantly it adds to the growing body of knowledge that males in tropical countries tends to have higher prevalence of malaria parasitaemia.

Somatic O antigens serologically were more common cause of typhoid in febrile patients in Ikare Akoko. *S. typhi* O was the most prevalent with 54 (23.1%) of the patients being sero-positive for its antibodies. This was closely followed by *S. paratyphi* B-O antigens with a prevalence of 14 (17.55) with the least being *S. paratyphi* C-H 10 (4.3%). In an earlier study done in University of Nigeria, Enugu and Abeokuta using febrile students as subjects highest prevalence for antibodies to etiologic agents of typhoid found Somatic *S. typhi* O antibodies to be most prevalent. This confirms that the patients have active infection of typhoid. Seropositivity for somatic antigens is known to indicate the presence of active infection in patients affected, especially in areas known to have high endemicity (Ibekwe *et al.*, 2008). Urgent care has to be instituted to avoid possible mortality consequent of typhoid infection.

The Widal agglutination tests are known to have some inadequacies due to possible cross-reaction with other antigens having common somatic or flagella recognition proteins. Widal agglutination tests have been used for decades as a tool in the diagnosis of typhoid and

are still being used in many centers in Africa and in Nigeria. This result of the study cannot be disregarded as the study was done in the part of the world where typhoid is known to be highly endemic with a large population having antibodies to one or more typhoid causing *Salmonella* species (Ibekwe *et al.*, 2008).

A limitation to this study was the inability to determine sero-positivity for Widal using convalescent sera. This was due to non-compliance by the patients who felt they have been cured after their diagnosis and taking anti-typhoidal drugs and felt there was no reason to come for further examination. Only 21 Widal salmonella agglutinin positive patients showed for examination for convalescent sera for typhoid causing antibodies as this represented a smaller portion of the positive. Their results were disregarded as this could not represent the needed result to base the report on.

CONCLUSION

In this study, malaria and typhoid fever is highly prevalent among febrile patients in Ikare Akoko, Ondo state, Nigeria. Sero-antibodies for typhoid were quite high (73.9%). The inclusion of screening for typhoid and malaria should be instituted as a routine test among febrile patients presenting with clinical symptoms similar to malaria or typhoid.

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