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Comparison of the Prevalence of Symptomatic Malaria and Symptomatic Typhoid Fever in Bayelsa State

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Abstract **Review Article**

Enteric fever also known as typhoid fever is caused by *Salmonella typhi*, is a disease that is endemic in the tropic and sub-tropic regions of the world and has become a major public health concern in the developing world with an estimated annual incidence of 540 cases per 100,000 patients. Malaria parasitaemia which is caused by *Plasmodium falciparum* and transmitted by female anopheles mosquito is a leading cause of febrile illness among low-income and poor sanitary environments. The study was aimed at comparing the prevalence of symptomatic malaria and symptomatic typhoid fever in Bayelsa State. This research was carried out in Federal Medical Center in Bayelsa State, Molecular research Laboratory in Niger Delta University and Niger Delta University Teaching Hospital, Bayelsa State in Nigeria. Samples were collected from both febrile and non-febrile patients in Bayelsa State. A total of one thousand (1000) subjects recruited for this study, blood samples were collected in the selected areas of Bayelsa State and samples of febrile and nonfebrile patients attending Federal Medical Center and Niger Delta University Teaching Hospital, Okolobiri were examined. Sample processing for this study included blood film for malarial parasites, Widal test using blood sample for both Tube and Tile Method, the results revealed the prevalence of both malarial parasitaemia and typhoidal antibodies (co infection) was 51(51.7%) Females had a higher percentage of co-infection than males 32(5.7%) and 19(4.3%) respectively. This study also revealed that of the 205 febrile patients screened, 175 (85%) were positive for malaria parasitaemia, whereas 15(7.4%) were positive for typhoidal antibodies. This shows that malaria is more likely to cause fever than typhoid, although both share rage in their symptomatology. In conclusion, this study revealed a strong relationship between malaria and typhoidal antibodies as both share some social circumstances and diagnostic symptomatology. Efforts must be made to confirm the diagnosis by paired sera investigation more than is presently the case.

Keywords: Typhoidal Antibody, Malaria Parasitaemia, *Salmonella typhi*, Typhoid fever, Co-infection, Bayelsa State

INTRODUCTION

1.1 Background of the Study

Enteric fever also known as typhoid fever is caused by *Salmonella typhi,* is a disease that is endemic in the tropic and sub-tropic regions of the world and has become a major public health concern in the developing world with an estimated annual incidence of 540 cases per 100,000 patients (11). Although, typhoid fever is widespread in various regions of the world, the genuine burden of the infection is weakly defined within most endemic countries. The well-known occurrence of multidrug-resistant typhoid fever also complicates the issue (2).

Salmonella species are intracellular pathogens (6) with some serotypes causing serious illness. Nontyphoidal serotypes can be transferred from animal to human viz a viz. They usually invade only the gastrointestinal tract and cause *Salmonella* food poisoning and their symptoms resolve without antibiotics. *Salmonella species* are Gram-negative facultative intracellular pathogens that infect their hosts via contaminated food and water. The genus *Salmonella* is part of the family of Enterobacteriaceae.

The definitive diagnosis of enteric fever in patients with compatible clinical pictures is the isolation of the *Salmonella* from blood, bone marrow, stool or urine (Ibwekwe *et al.,* 2008) and the demonstration of the 4 fold rise in the antibody titre to both the O and the H antigens of the organism between the acute and the convalescent phase sera, (14) and this part of the world do have paucy data on the localised antibodies titre for *Salmonella* infection in humans at various age gaps unlike the developed countries like the USA and Britain (5).

1.2 Malaria

Malaria parasitaemia which is caused by *Plasmodium falciparum* and transmitted by female anopheles mosquito is a leading cause of febrile illness among low-income and poor sanitary environments (18) and remains a major public health problem worldwide. Malaria and its complications are controlled by preventing infection and prompt diagnosis and effective treatment (17). Africa accounts for 91% of all malaria deaths and, with an estimated 57.5 million cases and 225,000 deaths per year. Nigeria accounts for 27% of the total African malaria burden (15). Within Nigeria, malaria is a major cause of illness, death, and poverty, and a significant drain on the economy and wellbeing of the nation. It is estimated that 50% of Nigeria‘s adult population will have at least one episode of malaria each year and children under five will have 2–4 attacks annually (10).

MATERIALS AND METHODS

2.1 Study Area

This research was carried out in Federal Medical Center in Bayelsa State, Molecular research Laboratory in Niger Delta University and Niger Delta University Teaching Hospital, Bayelsa State in Nigeria. Samples were collected from both febrile and non-febrile patients in Bayelsa State.

2.2 Study Design

This study was a comparative study and a random sampling method was used to carry out among 1000 subjects recruited for this study, blood and stool samples were collected from 200 subjects whereas only blood samples was collected from 800 subjects based in Bayelsa State.

2.3 Sample Size

To estimate sample size of 0.801 proportion (80.1%) at a confidence level of 95% with an acceptable difference/Error Margin of 0.05 (5%).

The sample size was determined using the equation as described by Niaing *et al*. (2006). The prevalence of 33.5% in a similar study obtained by Okafor and Ogugua (2017) was used to determine the sample size using the formulae below: -

$$N = \frac{PQ}{\left(\frac{E}{Z}\right)^2}$$

P = prevalence of previous study 33.5 % (Okafor *et al*., 2020)

2.4 Demography

The age, sex, geographical location, medical history of the patients, occupation, types of samples was all recorded.

2.5 Sample Collection

Of the One thousand (1000) subjects recruited for this study, blood and stool samples were collected from two hundred (200) subjects whereas only blood sample was collected from eight hundred (800) subjects in the selected areas of Bayelsa State and samples of febrile and nonfebrile patients attending Federal Medical Center and Niger Delta University Teaching Hospital, Okolobiri were examined. Information relating to biological and demography of the patients and environment was also recorded. A well designed questionnaire was administered to the patients.

2.6 Exclusion Criteria

Subjects who were on antibiotics before the date of sample collection for less than two weeks was excluded from the study

2.7 Inclusion Criteria

Subjects who had not been on antibiotics for more than two weeks before the date of sample collection were included in the study.

2.8 Ethical Considerations

2.8.1 Consent Form

Informed consent from parents/guardians of the wards and outpatients was sought before collection of samples.

2.9.2 Ethical Approval

Ethical approval was sought and obtained from the Federal Medical Center Yenagoa and Niger Delta University Teaching Hospital, Okolobiri before commencement of the study.

2.10 Sample Processing

Sample processing for this study included blood film for malarial parasites, Widal test using blood sample for both Tube and Tile Method, Culture method in which Deoxycholate Citrate agar (DCA), Nutrient agar, Selenite F, MacConkey and Salmonella-Shigella Agar were the culture media used for the stool samples. Biochemical test using API20E, antibiotic susceptibility testing and polymerase chain reaction (PCR) were also carried out to check for the resistant genes of antibiotics and characterization of *salmonella* species.

2.10.1. Thick Blood Film for Malaria Parasite:

Fields stain and Giemsa stain were used to stain the blood films for proper identification of malarial parasite

2.10.1.1 Widal Examination using Blood Samples

2.10.1.2 Tile Method

All reagents were allowed to return room temperature and mixed very well, a drop of serum sample (25µl) was added into each reaction circle (tile) labelled as O, H, AH, BH and CH according to given antigen solutions, 1 drop of positive control (25µl) and negative control was added and marked PC and NC respectively followed by the addition of antigen solutions of *Salmonella typhi* _O‘, *Salmonella typhi* _H‘, *Salmonella paratyphi* _AH‘ _BH and CH‘ to circles labelled as O, H, AH, BH and CH respectively in which test samples has been added. It was then mixed thoroughly with the aid of applicator stick and the tile was rocked gently and observed for agglutination based on rate of agglutination.

2.10.1.3 Tube Method

The reagents were allowed to return to room temperature and mixed very well and 4 sets of test tubes were assembled for individual antigen, each set

containing 1- 8 tubes. 1.9 ml of 0.85% sterile saline was added to tube no. 1 of each antigen set and to tube no. 2-8 of all sets 1 ml of physiological saline was added. 0.1 ml of test sample to be tested was added to tube number 1 of all sets and 1ml was transferred from tube number of all sets to tube number 2, from 2 to tube number 3 respectively and mixed very well and 1ml was discarded in each set of tube number 7 while tube 8 in all sets served as control.So the dilutions of the serum sample from tube No. 1 to 7 respectively in each antigen set were 1:20, 1:40, 1:80, 1:160, 1:320, 1:640, 1:1280 and to all the tubes (1 to 8) of each set, one drop of H and O Widal antigen respectively was added, mixed well and the tubes were covered and incubated at 37^0c overnight. The sediment button was dislodged gently and observed for agglutination.

2.11 Data Analysis

The data's and date of the samples were collected, during collection of the specimen. A structured questionnaire (Appendix I) was used to collect clinical and socio demographic information including age, gender and suspected diagnosis of the clinical specimen was also collected from the subjects presenting at the laboratory for diagnostic investigations.

2.12 Statistical Analysis

SPSS Version 21 and Winlept Version 11.4 (Describe program Version 2.72 was the statistical software or packaged that was employed in this study. Frequency distribution was done, Kruskal-wallis, Chi square, and Kappa was also used to check for association.

The demographic distribution of participants by age, gender, and febrile revealed that out of 1000 subjects studied, 205 were febrile of which 89(43.4%) and116 (56.6%) were febrile males and females respectively.

The study also showed that 328 subjects were between 31-40 (32.8%) years of age of which 26(29.2%) and 38(32.8%) were febrile males and female respectively.

Furthermore, 323(32.3%) patients were between the age group 21-30 years of which febrile male were 21 (23.6%) and febrile female were 44(37.9%). (Table 4.1).

Table 3.1: Demographic Distribution of Participants by Age, Gender, and Febrile

Age Group	Male		Female		Total
(Years)	Febrile	Non Febrile	Febrile	Non Febrile	
11 - 20	15 (16.9%)	35 (10.0%)	12 (10.3%)	37 (8.3%)	99 (9.9%)
21 - 30	21 (23.6%)	116 (33.2%)	44 (37.9%)	142 (31.8%)	323 (32.3%)
31 - 40	26 (29.2%)	111 (31.8%)	38 (32.8%)	153 (34.3%)	328 (32.8%)
41 - 50	19 (21.3%)	62 (17.8%)	18 (15.5%)	80 (17.9%)	179 (17.9%)
51 - 60	8 (9.0%)	25 (7.2%)	4 (3.4%)	32 (7.2%)	69 (6.9%)

61 - 70	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (1%)
Total	89 (8.9%)	349 (34.9%)	116 (11.6%)	446 (44.6%)	1000 (10.0%)

Table 3.2: Gender and Health Status of both Tube and Tile Typhoidal Antibodies Titre

Variables	No. Tested	Prevalence (%) Tube method	Prevalence (%) Tile method	Co titre of Tile and Tube
Male	438	21(4.7)	31(7.1)	12(2.7)
Female	562	29(5.1)	67(11.9)	17(3.0%)
Febrile	205	15(7.4)	27(13.1)	8 (3.9)
No febrile	795	35(4.4)	71(8.9)	21(2.6)

The distribution of typhoidal antibodies using Tube method and Malaria parasitaemia by febrile status revealed that out the of 205 febrile patients 15(7.4%), 175(85%) and 35(17.1%) had significant typhoidal antibodies, malaria parasitaemia and and both parasitaemia and typhoidal antibodies whereas 795 of non-febrile subjects 35(4.4%), 142(17.8%) and 12(1.5%) had typhoidal antibodies, malaria parasitaemia and both typhidal antibodies and malaria parasitaemia respectively in which the malaria parasitaemia based on health status was statistically significant at $P < 0.05$ and the typhoidal antibodies based on health status was not statistically significant at $P > 0.05$

Table 3.3: Distribution of participants with typhoidal antibodies using Tube Method and Malaria by Febrile Status

Health Status	Number Tested	Typhoidal antibodies Positive	Malaria parasitaemia Positive	TA/MP Positive
Febrile /Hospitalized	205	15 (7.4%)	175(85%)	35(17.1%)

Non Febrile /Not Hospitalized	795	35 (4.4%)	142 (17.8%	12(1.5%)
Total	1000	50 (5.0%)	317(31.7%	47(4.7%)

For Widal Tube method, X^2 =0.88, p =2.915, and Malaria X^2 =149.668 and p =0.000

The distribution of typhoidal antibodies using Tile method and Malaria parasitaemia showed that out of 205 febrile patients 27(13.1%), 175(85%) and 14(2.8%) had significant typhoidal antibodies, malarial parasitaemia and both parasitaemia and typhoidal antibodies respectively.

The findings also revealed that out of 795 of non-febrile subjects examined, 17(8.9%), 142(17.8%) and 37(4.6%) had typhoidal antibodies, malaria parasitaemia and both typhidal antibodies and malaria parasitaemia respectively in which the malaria parasitaemia based on health status was statistically significant as $P < 0.05$ and the typhoidal antibodies based on health status was not statistically significant at $P > 0.05$

Table 3.4: Distribution of Participants with Typhoidal Antibodies using Tile Method and Malaria Parasitaemia by Febrile Status

Health Status	Number Tested	Typhoidal Antibodies (Tile) Positive	Malaria Parasitaemia Positive	TA/MP
Febrile / Hospitalized	205	27 (13.1%)	175(85%)	14(4.8%)
Non Febrile / Not Hospitalized	795	71 (8.9%)	142 (17.8%)	37(4.6%)
Total	1000	98 (9.8%)	317(31.7%)	51 (5.1%)

For widal Tile Method, X^2 =3.314, p=0.069 and for Malarial X^2 =149.668, p =0.000

4.1 DISCUSSION

Enteric fever is a disease that is endemic in this region and has become a major public health challenge in our society owing to misinterpreted diagnosis, inaccurate interpretation of Widal test results or lack of baseline titre leading to to the indiscriminate use of antibiotics even when not needed.

The prevalence of both malarial parasitaemia and typhoidal antibodies (co infection) was 51(51.7%) which is higher than (10.33%) reported by (Mohammed, 2012) in Sokoto, (15.2%), (Mbah & Agu, (2014) in Zaria and (28%) by Orok *et al.* (2016) in Calabar. However, there was a significant difference between the numbers of individuals that had both malarial parasitaemia and typoidal antibodies and those that don't have ($P < 0.05$). Females had a higher percentage of co-infection than males 32(5.7%) and 19(4.3%) respectively, and the age group 31-40 years old had the highest percentage of co-infection 18(5.5%). This does not agree with the report of (Orok *et al*., 2016), in which the highest co-infection rate was (37.5%) amongst in the age group of 1-15 years.

This study also revealed that of the 205 febrile patients screened, 175 (85%) were positive for malaria parasitaemia, whereas 15(7.4%) were positive for typhoidal antibodies. This shows that malaria is more likely to cause fever than typhoid, although both share rage in their symptomatology. This result agrees with Igbeneghu *et al.,* (2009) findings in Ibadan, who observed 50.4% of malaria against 4.7% of typhoid fever. However, the result varies with the observations made by Nwuzo *et al*., (2008) in Abakaliki, Opara *et al.,* (2011) in Owerri and Igharo *et al*., (2012) in Ondo, who observed higher prevailing rates of typhoid than malaria in febrile patients; with overall rates of (21.20% typhoid vs. 13.20% malaria), (42% typhoid vs. 39% malaria, Opara *et al*., 2011) and (73.9% typhoid vs. 37.6% malaria) in Ighara *et al*., (2012) respectively

4.2 Conclusions

This study revealed a strong relationship between malaria and typhoidal antibodies as both share some social circumstances and diagnostic symptomatology. The prevalence of both malarial parasitaemia and typhoidal antibodies (co infection) was 51(51.7%) which indicates a close association and therefore, other tools of prevention and treatment are essential to avoid this problem.

4.3 Recommendations

Based on the findings and conclusions made in this study, it is pertinent to suggest that

1. Efforts must be made to confirm the diagnosis by paired sera investigation more than is presently the case.
2. Every treatment of fever should be preceded by an adequate laboratory diagnosis that can establish the actual aetiological agent.
3. There should be provision of other preventive measures such as personal and environmental hygiene, long lasting insecticidal nets and insecticides.

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