Prevalence of plasmodium and salmonella infections among pregnant women with fever, presented to three hospitals in Ogun and Lagos states, South-West Nigeria.

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ABSTRACT

Aims: To establish the incidence of Plasmodium falciparum and Salmonella typhi co-infection in pregnant women in Ota general hospital, Igando General Hospital and Covenant University Medical Center, so as to instigate effective control and management measures. To determine the rate of co-infection with respect to the use of widal test and stool culture as diagnostic tools for typhoid fever and To characterize and identify the S. typhi isolates associated with co-infection.

Study design: This research is Cross sectional. To test pregnant women manifesting fever by more than two diagnostic methods in Three hospitals in Ogun and Lagos State.

Place and Duration of study: Covenant university Canaan Land, Microbiology Laboratory October 2012 – June 2013.

Methodology: By Random sampling, Medical examination was done for malaria by Rapid Diagnostic Test using lateral flow test cassettes for the different Plasmodium species and microscopy. Typhoid test for salmonella was by widal test and by culturing the stools.

Results: Of 350 samples, 21 (6%) were positive for either of the disease conditions. 10 (3%) were positive for malaria, 6 (2%) for typhoid and 5 (1%) for both malaria and typhoid. 50 control samples from healthy non-pregnant women were negative for the disease conditions.

Conclusion: Co-infection of Plasmodium falciparum and Salmonella typhi has been confirmed as one of the causes of fever among pregnant women in Nigeria.

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KEYWORDS:
Coinfection, Malaria, Typhoid, Pregnancy.

1: INTRODUCTION

Malaria is a major public health problem especially in tropical and sub-tropical areas; It is estimated to be responsible for about 1 to 3 million deaths and 300-500 million infections annually. Typhoid on the other hand remains an important worldwide cause of morbidity and mortality and continues to be a health problem in developing countries where there is poor sanitation, poor standard of personal hygiene and prevalence of contaminated food. Concurrent malaria and typhoid is often disregarded and untreated. *Plasmodium* and *Salmonella* infections can result in serious complications and conditions such as maternal anemia, fetal anemia, abortion, still-birth, and even death of the child or mother before birth or right after delivery.

Malaria is a tropical disease caused by a parasite that is transmitted from human to human by the Anopheles mosquito (48). The mosquito infects the host with a unicellular parasite called plasmodium, not long after they found out that malaria is transmitted from person to person through the bite of this mosquito which needs blood for her egg, Approximately 40% of the global population is at risk of malaria infection (48).

Malaria is a preventable and treatable disease. If malaria is diagnosed and treated early, the duration of the infection can be considerably shortened, which in turn reduces the risk of complications and death (24).

The vast majority of cases are children under the age of five years and pregnant women (43). There are five parasites causing malaria. Malaria due to *Plasmodium vivax* is mild form of the disease and is generally not fatal, and this type has the widest geographic distribution globally. The *P. vivax* malaria has the widest, About 60% of infections in Indian are caused by *P. vivax*. This parasite has a liver stage and can remain in the body for years without causing sickness. *Plasmodium malariae* also mild and not fatal, it has been known to stay in the blood of some people for several decades. *Plasmodium ovale* is mild and not fatal; It has a liver stage and can remain in the body for years without causing sickness. *Plasmodium falciparum* is the most serious parasite. It is most common in Africa, especially sub-Saharan Africa. *Plasmodium knowlesi* causes malaria in macaques but also infect human (25).

*Salmonella*, a genus of Gram- negative rod shaped bacteria of the family Enterobacteriaceae, causes a wide range of human diseases, such as enteric fever, gastroenteritis, endocarditic and bacteraemia. *Salmonella* associated infections do not present with distinct clinical features, Other bacterial, viral, and even protozoan's may mimic its presentations (9). More than 2,300 *Salmonella* enteric serotypes have been described, only *S. enteric serovar typhi, S. paratyphi, S. typhimurium, S. choleraesuis, S. hadar, S. virehow* and *S. dublin* among others, play important epidemiological roles. Although infections with non-typhoidal *Salmonellae* usually cause self-limited diarrhea illness.
2: MATERIALS AND METHODS

Pregnant women who had fever presented to three hospitals in Ogun and Lagos states, Nigeria were sampled.

2:1 DESCRIPTION OF THE STUDY AREA
This study is a cross-sectional study. This is the first research in Nigeria on coinfection of these organisms in pregnancy. Participants were sampled from Ota General Hospital, Ogun state, Covenant University Medical Center, Canaan land Ogun State and Igando General Hospital, Igando, Lagos State. 350 participants were pregnant women with fever complain, 50 control samples from women that were not pregnant.

2:2 SAMPLE COLLECTION
An intravenous blood sample of 5 ml for all was collected in an EDTA tube in accordance with routine clinical practice for all patients referred for laboratory investigation of malaria infection. Samples site were from 3 hospitals in Ogun state and Lagos state respectively. Three hundred and fifty pregnant women who showed fever and other symptoms suggestive of malaria or typhoid fever that were referred by clinicians after clinical and physical examinations to medical laboratory in Southwest Nigeria for malaria parasite and typhoid tests was used for the analysis. Also, blood samples were collected from 50 seemingly non-pregnant healthy female individuals as controls. Those who participated in the study were given informed consent. A 5mL of blood was taken from each patient for laboratory investigations.

2:3 SAMPLE ANALYSIS

2:3:1 EXAMINATION OF BLOOD SLIDES FOR MALARIA PARASITE:
An intravenous blood sample of 5ml was collected into an EDTA tube. Blood films were made by placing a drop of blood on one end of a slide, and using a cover slide to disperse the blood over the slide’s length. Thick and thin blood films were stained with 10% Giemsa for 10 minutes, thick film was heat fixed and thin film fixed with methanol. It was examined microscopically for malaria parasites. At least 5 blood films were examined for malaria parasite before reporting any film as negative.

2:3:2 RAPID DIAGNOSTIC TESTS (RDTs):
Lateral flow test or immunochromatographic assay cassette was performed using a commercially prepared buffer solution from Orchid Company. It contains two wells, blood sample well and buffer solution well. Following the manufacturers manual the test was done. The appearance of red line of test band and control band indicates positive while just the control band indicates negative.

2:3:3 SEROLOGICAL TEST FOR TYPHOID FEVER:
Widal tests was done using human plasma and a drop of antigen of the chromtest widal test kit was added, It was stirred and rocked for some minutes, following the companies manual. Widal tests were read as positive when O antibody titers were ≥1/80 - 1/160 for S. Typhi.
2:3:4 **BACTERIOLOGICAL TEST FOR TYPHOID FEVER:**

A diagnosis of *Salmonella typhi* was confirmed by testing for the presence of the bacteria in Salmonella Shigella Agar (SSA) \(^{(42)}\). Diarrhea stool samples from widal positive test patients was cultured in Nutrient Agar. The isolates were further sub cultured into SSA, to obtain pure cultures \(^{(28)}\).

2:3:5 **STATISTICAL ANALYSIS:**

Descriptive statistics was used for data analysis. Spearman’s correlation was used to determine their relationship, and chi square distribution was used to analyze the distributions relations to each other. The SPSSPC 17.0 software package (SPSS Inc., Chicago, and Ill., USA) was used for data analysis.

2:3:6 **ANALYTICAL PROFILE INDEX:**

The bacteria pure culture was prepared. A large colony (2-3mm diameter of bacteria pure culture was inoculated into 0.85% NaCL making sure that the suspension is homogenous. The API strip was held up from the table top and inoculated with the bacteria suspension into each well. LDC, ODC, ADH, H2S and URE are filled with sterile mineral oil. The strip is then incubated at 37°C for 18 – 24 hrs. After incubation 1 drop of Kovacs reagent was added to IND and its result is read within a couple of minutes, 1 drop of Barrits A and B to VP and 1 drop of 10% FeCL\(_3\) was added to TDA. Results was read following 1,2 or 4 points for positive reaction for first, second and third tube in each triad, 0 points for negative reaction for first second and third tube in each triad. Oxidase test is done separately and added and is oxidase negative (0). The test includes 21 biochemical reactions and substrates.

**Table 1:** Biochemical test reactions of some bacteria species using API 20E Test kit.

<table>
<thead>
<tr>
<th>TEST</th>
<th>SUBSTRATE</th>
<th>REACTION TESTED</th>
<th>- RESULTS</th>
<th>+ RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ONPG</td>
<td>ONPG</td>
<td>beta – galactosidase</td>
<td>colorless</td>
<td>yellow</td>
</tr>
<tr>
<td>ADH</td>
<td>arginine</td>
<td>argininedihydrolase</td>
<td>yellow</td>
<td>red/orange</td>
</tr>
<tr>
<td>LDC</td>
<td>lysine</td>
<td>lysine decarboxylase</td>
<td>yellow</td>
<td>red/orange</td>
</tr>
<tr>
<td>ODC</td>
<td>ornithine</td>
<td>ornithine decarboxylase</td>
<td>yellow</td>
<td>red/orange</td>
</tr>
<tr>
<td>CIT</td>
<td>citrate</td>
<td>citrate decarboxylase</td>
<td>pale green/yellow</td>
<td>blue-green/blue</td>
</tr>
<tr>
<td>H2S</td>
<td>Nathiosulphate</td>
<td>H2S utilization</td>
<td>colorless/grey</td>
<td>black deposit</td>
</tr>
<tr>
<td>URE</td>
<td>urea</td>
<td>urea hydrolysis</td>
<td>yellow</td>
<td>red/orange</td>
</tr>
<tr>
<td>TDA</td>
<td>tryptophan</td>
<td>deaminase</td>
<td>yellow</td>
<td>brown-red</td>
</tr>
<tr>
<td>IND</td>
<td>tryptophan</td>
<td>indole production</td>
<td>yellow</td>
<td>red (2mins)</td>
</tr>
<tr>
<td>VP</td>
<td>Na pyruvate</td>
<td>acetoin production</td>
<td>colorless</td>
<td>pink/red(10min)</td>
</tr>
<tr>
<td>GEL</td>
<td>charcoal gelatin</td>
<td>gelatinase</td>
<td>no diffusion of black</td>
<td>black diffuse</td>
</tr>
<tr>
<td>GLU</td>
<td>glucose</td>
<td>fermentation/oxidation</td>
<td>blue/blue-green</td>
<td>yellow</td>
</tr>
<tr>
<td>MAN</td>
<td>mannitol</td>
<td>fermentation/oxidation</td>
<td>blue/blue-green</td>
<td>yellow</td>
</tr>
</tbody>
</table>
INOSITOL fermentation/oxidation blue/blue-green yellow
SOR sorbitol fermentation/oxidation blue/blue-green yellow
RHAMNOSA rhamnose fermentation/oxidation blue/blue-green yellow
SUCROSE sucrose fermentation/oxidation blue/blue-green yellow
MELE melibiose fermentation/oxidation blue/blue-green yellow
AMY amygdalin fermentation/oxidation blue/blue-green yellow
ARA arabinose fermentation/oxidation blue/blue-green yellow
OX OXIDASE oxidase colorless/yellow violet

Three test reactions are added at a time to give a 7 digit number, which can then be checked in the code book.

3: RESULTS:

The result of this study is based on establishing the co-infection of *Plasmodium falciparum* and *Salmonella typhi* in pregnant women with fever in some selected locations in Lagos State and Ogun State. It is cross sectional. Out of the 350 blood and stool samples collected, 10 (3%) were positive for malaria by Rapid Diagnostic Test(RDT) and microscopy, 6 (2%) were positive for *S. typhi* by widal test and stool culture. And 5 (1%) were positive for both *Plasmodium* infection and for *Salmonella* infection (Table 2), the both i.e. Co-infection.

Table 2: Is also used to determine the descriptive statistics. The descriptive statistics shows that the minimum number of co-infected women in the three areas surveyed was 1 while the maximum number is 2. The mean distribution for the three locations are 1.97, 1.94 and 1.94 while their deviations are 0.184, 0.239 and 0.240 for Ota, Igando and Covenant respectively. Hence Igando and Covenant have equal mean distributions.

From table 2, Spearman correlation was done to establish the measure of the linear relationship (correlation) between a dependent-variable and an independent variable. The correlation table for the three hospitals surveyed shows that there is a significant positive relationship, between the co-infection prevalence of Malaria and typhoid in Ota, Igando and Covenant. The result further revealed that there is a stronger positive relationship in the co-infection prevalence of malaria and typhoid between Ota and Igando at 0.921 and Igando and Covenant at 0.684 compared to Ota and Covenant at 0.626 all significant at both p<0.01 level of significant. This further indicates that both infections could simultaneously increase and multiply in these three locations at the same time.

Table 3: shows a critical observation of the calculated chi-square ($X^2$) value, given 1 degree of freedom using two tail test ($X^2_{cal}=172.98$, 77.44 and 38.72 for co infection prevalence of Malaria and typhoid in Ota, Igando and covenant respectively) shows that chi-square empirical result was statistically significant at both P less than 0.05 level of significance (Chi square Sig P<0.05). Hence, we can infer that there is existence of the co infections of the two diseases in pregnant women surveyed in Ota, Igando and Covenant university medical center. Therefore the null hypothesis that there is no significant incidence of malaria and *Salmonella* co-infection for pregnant women in Ota, Igando and covenant medical centers cannot be accepted and thus it is discarded and the alternate hypothesis accepted, leading to the
conclusion that there is significant incidence of malaria and *Salmonella* co-infection for pregnant women in Ota General Hospital, Igando General Hospital and covenant University medical center.

Sample 1, 2, 3, 4, 5 and 6 had the same result codes as shown in table 4: after incubation and observation of the colour changes. The organism was confirmed from Biomeriuex co. Inc. USA with code: 4404500 to be *Salmonella typhi*.

Table 5: shows that 5 patients from Ota General Hospital were positive for malaria by RDT and at the same time, the same patients were positive malaria by microscopy. Four patients from Igando General Hospital were positive for malaria by RDT and the same 4 patients were positive for malaria by microscopy. In Covenant University Medical Center 1 patient was positive for malaria by RDT and microscopy. The variations in Sample size examined are due to the population size of each hospital. More patients in Ota than Igando and few in Covenant University.

Table 6: shows that 2 patients from Ota General Hospital were positive for typhoid by widal and at the same time, the same patients were positive for typhoid by stool culture. Two patients from Igando General Hospital were positive for typhoid by Widal test and the same 2 patients were positive for typhoid by stool culture. In Covenant University Medical Center 2 patient was positive for typhoid by Widal test and stool culture.

**Table 2:** Prevalence of *P. falciparum* and *S. typhi* in pregnancy

<table>
<thead>
<tr>
<th>Hospitals</th>
<th>Positive Results</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malaria (%)</td>
<td>Typhoid (%)</td>
</tr>
<tr>
<td>Ota</td>
<td>5 (2.5)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Igando</td>
<td>4 (4)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Covenant</td>
<td>1 (2)</td>
<td>2 (4)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10 (3)</strong></td>
<td><strong>6 (2)</strong></td>
</tr>
</tbody>
</table>
Figure 1: Bar chart showing the total number of samples examined.

Figure 2: Showing the Coinfection Rates in percentage.
Table 3: Hospitals - wise prevalence of malaria and typhoid fever.

<table>
<thead>
<tr>
<th>Zones</th>
<th>Positive</th>
<th>Negative</th>
<th>Total no. Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ota</td>
<td>7</td>
<td>193</td>
<td>200</td>
</tr>
<tr>
<td>Igando</td>
<td>6</td>
<td>94</td>
<td>100</td>
</tr>
<tr>
<td>Covenant</td>
<td>3</td>
<td>47</td>
<td>50</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>16</strong></td>
<td><strong>334</strong></td>
<td><strong>350</strong></td>
</tr>
</tbody>
</table>

Table 4: Showing Biochemical characterization code of isolates using API kit.

<table>
<thead>
<tr>
<th>Triad</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubes</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>16</td>
<td>17</td>
<td>18</td>
<td>19</td>
<td>20</td>
<td>21</td>
</tr>
<tr>
<td>Reaction</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Points</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Add</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7 digital code</td>
<td>4404500</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5: Prevalence of malaria in the three hospitals.

<table>
<thead>
<tr>
<th>Hospitals</th>
<th>RDT (%)</th>
<th>Microscopy (%)</th>
<th>Total no. Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ota</td>
<td>5(2.5)</td>
<td>5(2.5)</td>
<td>200</td>
</tr>
<tr>
<td>Igando</td>
<td>4 (4)</td>
<td>4(4)</td>
<td>100</td>
</tr>
<tr>
<td>Covenant</td>
<td>1 (2)</td>
<td>1(2)</td>
<td>50</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10</strong></td>
<td><strong>10</strong></td>
<td><strong>350</strong></td>
</tr>
</tbody>
</table>
Table 6: Prevalence of Typhoid in the three hospitals.

<table>
<thead>
<tr>
<th>Hospitals</th>
<th>Widal (%)</th>
<th>Stool culture (%)</th>
<th>Total no. Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ota</td>
<td>2(1)</td>
<td>2(1)</td>
<td>200</td>
</tr>
<tr>
<td>Igando</td>
<td>2 (2)</td>
<td>2(2)</td>
<td>100</td>
</tr>
<tr>
<td>Covenant</td>
<td>2 (4)</td>
<td>2(4)</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>6</td>
<td>350</td>
</tr>
</tbody>
</table>

DISCUSSION:

The Co-infection of *P. falciparum* and *S. typhi* among pregnant women studied in this research work shows that there is co-infection of malaria and typhoid in pregnancy. Although, malaria and typhoid fever are said to be endemic in Nigeria, this study shows that malaria is far more likely to cause fever than typhoid fever because all the 350 patients had fever and 10 were positive for malaria but 6 were positive to typhoid. This confirms the results of Eze *et al.*, (17), who observed that though malaria and typhoid share similar symptoms malaria causes fever more than typhoid. Cultural diagnosis of typhoid fever shows a reliable diagnosis of typhoid fever, and so should be done alongside Widal test; Culture should be based on culture of blood, stool and bone marrow. Stool was cultured in this study to isolate *S. typhi*. This agrees with Uneke, (53) who reported culture of stool as the best reliable test method for typhoid fever. However, bone marrow aspirates are difficult to obtain and culture of blood sample delays diagnosis leaving widal as the fast method to be used for urgent situation. So if malaria test and Widal test is done, the patient should be treated for typhoid and malaria. On the other hand, a true co-infection is possible because both typhoid and malaria share social circumstances which are imperative to their transmission. This confirms what Prasanna, observed that excess iron taken to correct anemia in malaria during pregnancy may lead to fatal co-infection (48).

In This study out of the 350 samples tested, only 5 (1%) pregnant women had co-infection of typhoid and malaria by both microscopy, RDT, Widal and stool culture. 10(3%) pregnant women are positive for only malaria by RDT and Slide Microscopy, and 6 (2%) were positive for Typhoid by widal agglutination and by stool culture. The 50 samples as control from healthy women, who are not pregnant, were negative for both malaria and typhoid. The co-infection rate is low but significant; this could be as a result of constant consumption of Intermittent Presumptive Treatment for Plasmodium species (IPTP) and proper training given to pregnant women during their weekly visit to hospitals as antenatal check up. There they are also tutored on how to avoid contaminated food and water, which reduces the risk of contaminating *S. typhi*. 


Erroneous interpretation of the test result may lead to misdiagnosis and mismanagement of the patient, resulting in major 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.

Effective control measures can be determined now that this research has data of true co-infection existence in Pregnancy. A treatment protocol is also necessary to treat the co-infection. But according to present concept we can say for malaria, it is important to tailor control and preventive strategy to the prevailing ecological and epidemiological conditions. The strategy of mortality control involves detecting presumptive cases, determining which cases is parasite positive, and administering effective treatment. Focal interventions to minimize human-vector contact can be effected by the use of insecticide-treated mosquito nets as well as indoor spraying of insecticide. On the other hand, improved personal hygiene, targeted vaccination campaigns and intensive community health education helps.

The correlation test for the three hospitals surveyed, shows that there is a significant positive relationship between the co-infection prevalence of Malaria and typhoid in Ota, Igando and Covenant. That there is a stronger positive relationship in the co-infection prevalence of Malaria and typhoid between Ota and Igando at 0.921 and Igando and Covenant at 0.684 compared to Ota and covenant at 0.626 all significant. (p<0.01).Chi-square empirical result was statistically significant p< .05.

Table 2: shows the prevalence of both malaria and typhoid in the three hospitals.

Table 3: shows that Ota general hospital had the highest prevalence rate of both plasmodium falciparum and salmonella typhi with 7, Igando general hospital next to Ota with 6 and Covenant university medical center had the least with 3. This is true if we write about numbers. But Prevalence, in epidemiology, is the proportion of a population found to have a disease. It is arrived at by comparing the number of people found to have a disease with the total number of people studied.Thus, the prevalence of both plasmodium falciparum and salmonella typhi in Igando and Covenant was higher (6%) than in Ota (3.5%) .

Table 4: shows the characterization of the typhoid specie isolated, the code obtained above was confirmed to be S.typhi. by Biomeriux co. USA.

From table 5: showing the prevalence of malaria, it shows that 10 patients in all were positive to malaria by RDT and these patients were also positive to malaria by microscopy, this study shows that Rapid diagnostic test is required to be reconfirmed by observing the morphology of the parasite to ascertain that the patient was positive for the said malaria. Table 6: shows A total of 6 patients were positive for typhoid by the use of widal test and stool culture, after widal test it is advisable to culture the blood sample or stool sample to reconfirm that the positive patient for widal had the bacteria responsible for typhoid grow in the required medium. This confirms what Prasanna, (48) said that each of the infections gold standards for testing should be performed and reconfirmed by another.

4: CONCLUSION

In Nigeria, malaria is still the leading cause of fever characteristic of typhomalaria signs and symptoms. About one-third of the pregnant patients presenting with fever neither have malaria, typhoid nor typhoid malaria fever. Therefore, presumptive treatment of fever as malaria or typhoid fever should be discouraged. Typhoid fever is currently over diagnosed in Nigeria since Widal test is essentially used in its diagnosis. The use of Widal test alone in the diagnosis of typhoid fever is unreliable, misleading and should be therefore, discouraged. If it must be used, it should be done alongside culture of stool or blood samples. Where, culture facilities are lacking and patients are positive for both malaria and Widal tests, malaria and typhoid should be treated. Only when malaria has been ruled out and there is a strong
Clinical suspicion of typhoid fever that is when such pregnant patients should be treated for typhoid fever. Co-infection of *Plasmodium falciparum* and *Salmonella typhi* has been confirmed as one of the causes of fever among pregnant women in Nigeria.

**ACKNOWLEDGMENT**

We acknowledge Covenant university Laboratory scientists for their help and support. We also appreciate The Medical Directors.

**COMPETING INTERESTS**

We therefore declare that there are no competing interests to this research paper.

**AUTHORS’ CONTRIBUTIONS**

Authors may use the following wordings for this section: “‘Author A’ designed the study, ‘Author B’ performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript, managed the analyses of the study, managed the literature search. Author C and D assisted Author B in the laboratory analysis. All authors read and approved the final manuscript.”

**CONSENTS**

All authors declare that ‘written informed consent was obtained from the Pupils (or other approved parties) for publication of this case report. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.”

**ETHICAL PERMIT**

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.”

**ETHICAL CLEARANCE**

Scientific and Ethical clearance were obtained from the Nigerian Institute of Medical Research Institutional Review Board (NIMR – IRB), and Covenant University Ethics committee for this work. The Ogun State and Lagos state Ministry of Health (Hospitals Management Board) was also informed and clearance obtained for this study. Written informed consent was obtained from patients prior to recruitment into this study.

**REFERENCES**


