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Evaluation of Diagnostic Methods for Typhoid Fever Disease in Ondo State, Nigeria

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Author's contribution

The sole author designed, analyzed and interprets and prepared the manuscript.

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ABSTRACT

Aim: Typhoid fever is caused by *Salmonella enteric* serovar Typhi and *S. enteric* serovar Paratyphi A. B. C. Accurate diagnosis of this illness will greatly reduce the mortality and morbidity associated with it. This study therefore evaluated the available diagnostic methods for typhoid fever among 44 clinical laboratories in Ondo State of Nigeria.
Methods: A simple but well-structured questionnaire filled by the most senior scientist, was administered on forty-four (44) out of the forty seven clinical laboratories registered by government and the monitoring agency to assess the various methods used by individual laboratory.
Results: All respondent laboratories used serological method (Widal's Agglutination Test) while none used neither bone marrow culture nor molecular technique (PCR). Widal tests were reported by 93.2% of the laboratories without titration. Blood and stool cultures were sparingly and inconsistently used by about 48% of the laboratories, thereby being unable to generate information about species prevalence and

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susceptibility pattern of the pathogens.
Conclusion: The contribution of the clinical laboratories to the seeming treatment failure of typhoid fever became obvious from this study since no proper treatment or control measures can be effective without proper diagnosis. It is therefore suggested that our clinical laboratories be properly equipped for accurate diagnosis of typhoid fever.

Keywords: Typhoid fever; Salmonella enteric serovar typhi; Ondo state; diagnosis; blood culture; Widal's agglutination test; Nigeria.

1. INTRODUCTION

Typhoid fever is a systemic infection caused by human adapted pathogen called *Salmonella enteric* serovar Typhi (*Salmonella* Typhi*)* and *S. Enteric* serovar Paratyphi A, B, C (*Salmonella* Paratyphi A, B, C). These organisms cause both severe typhoid and mild paratyphoid fever illnesses in crowded and impoverished population with inadequate sanitation and that are exposed to contaminated water and food [1]. Faecal-oral route remains the major mode of transmission. The organisms are pathogenic to both man and other mammals causing inflammatory reactions in the intestinal tract. Once in the body, the organisms multiply and spread from the intestines into the bloodstream. Co-infection of malaria and typhoid fever has been reported by various researchers [2-4]. Typhoid fever is an endemic disease in the Tropics and sub-Saharan Africa, where it has become a major public health problem [5]. The annual incidence of typhoid is estimated to be about 17million cases worldwide. In the year 2000, typhoid fever cases were estimated at 21.7million and 217,000 deaths while paratyphoid fever was the cause of 5.4million illnesses worldwide [6]. In Nigeria, typhoid fever prevalence rates were put at 42% in Owerri [7]; 80.1% in Abeokuta among patients with febrile illness [8] and 81.5% in Minna [9].

Like in most infectious diseases, accurate diagnosis of typhoid fever is germane to reduction of mortality and morbidity often associated with typhoid infections. Bone marrow culture remains the gold standard diagnostic test for enteric fever [10]. Widal's agglutination test, which is the commonest serological test for typhoid fever often lacks sensitivity and specificity. Blood culture is often the first choice for both patient diagnosis and epidemiological evaluation of *S. enteric* serovar Typhi (*S. typhi)* and *S. enterica* serovar Paratyphi A, B, C (*S. paratyphi*) burden. However, most enteric fever occurs in low and middle income countries where blood culture are often unavailable, unaffordable or inconsistently done [11]. Stool and urine cultures are often done with little success.

Ondo State is one of the 36 States of the Federal Republic of Nigeria, and it is located in the South western part of the country. It has a population of 4.5millions of inhabitants and 776 health facilities. The highest number of visits to these facilities is due to typhoid fever. This study is therefore designed to evaluate the diagnostic methods available in Ondo State's clinical laboratories.

2. MATERIALS AND METHODS

2.1 Study Area

This study was carried out among clinical diagnostic laboratories located in Ondo State, Nigeria. This State is located in the South western part of Nigeria, covering a land area of

20,959 square kilometers, comprising 18 local government areas. It is ranked 20th among the States of Nigeria. There were forty-seven registered clinical laboratories, three have closed down operation by the time of this study.

2.2 Data Collection

A questionnaire was administered on forty-four (44) clinical laboratories comprising 19 government-owned and 25 private laboratories. Registration with both government and regulating body was the only inclusion criterion. The questionnaire filled out by the most senior scientist in each laboratory was to reveal the methods each laboratory use for the diagnosis of typhoid fever.

3. RESULTS

None of the 44 laboratories used bone marrow culture and molecular technique for the diagnosis of typhoid fever. Alll aboratories performed the Widal's agglutination test as serological method. In government-owned laboratories, 42.1% used blood culture, while only 20% of the private laboratories performed this method (Table 1).The commonly used culture media are glucose broth, blood agar and MacConkey agar for isolation, while Meuller-Hinton agar is used for susceptibility test of the isolates. Only 3 (6.8%) of the laboratories used quantitative serological methods for diagnosis.

Table 1. Diagnostic methods used in clinical laboratories for typhoid fever detection in Ondo, Nigeria

Methods	Government-owned laboratories (%)	Private laboratories (%)
Stool culture	15(78.9)	12(48.0)
Blood culture	08(42.1)	05(20.0)
Bone marrow culture	00(0.0)	00(0.0)
Widal's test	19(100.0)	25(100.0)
Molecular (PCR)	00(0.0)	00(0.0)
Blood film	09(47.4)	19(76.0)
Total	19(100)	25(100)

4. DISCUSSION

Definitive diagnosis remains the major step to adequate and effective treatment of typhoid fever in view of the increasing morbidity and mortality resulting from this illness. Bone marrow culture, which is the gold standard diagnostic test for enteric fever [10,12], was not used by any of the clinical laboratories in the studied area. This was expected because, bone marrow aspiration is not a technique that can be done by a non-medically qualified personnel, coupled with the cost of analysis which many patients will not be able to afford since the larger populations are low income earners. As sensitive as this diagnostic method is, these important limitations worked against its application.

Many studies were done using the serological method popularly known as Widal'test [7,8,13]. Apart from the low sensitivity and specificity of this method, interpretation of the results has been the greatest source of misinformation. In this study, 93.2% reports Widal's test without titration. All respondents use a single test to determine a positive reaction, whereas, a standard interpretation of Widal's test will require a demonstration of four-fold

rise in titre within two weeks of the onset of the illness [14,15]. This brings to the open, a major flaw in the diagnosis of typhoid fever.

Blood culture has limited and inconsistent use among the laboratories. Although, this is the second best method for the diagnosis of typhoid fever, because of duration of investigation, (usually between 5 and8 days) both the patient and the laboratory personnel are usually negatively disposed to this method. Patients will only appear for laboratory test when all self-medications have failed and at this point, they can no longer wait but needed a result to either confirm or not their self-diagnosis. Blood culture will equally provide information about the species being isolated and the susceptibility pattern of the isolates especially in view of multidrug resistance being reported among *Salmonella* sp [16-18]. This method in combination with stool culture is important for epidemiological studies [19]. Molecular characterization is only possible if and when proper cultural techniques are put in place. This further reinforces the need for all clinical diagnostic laboratories in the study area to add cultural methods to serological method, if they must continue to be relevant in the diagnosis of typhoid fever. The higher number of cultures recorded among the government laboratories in stool and blood culture are likely due to government assistance which invariably reduces cost and increases patronage.

Molecular typing and genomic sequency of *S. enteric* serovar Typhi has been reported by some researchers [20,21], this gives insight into the genetic make-up of these organisms and provide useful information about possible use of genetic manipulation in its control. This is an advantage of accurate laboratory diagnosis, however, our laboratories are still not well equipped for this aspect of diagnosis as none of the laboratories use molecular analysis. If the mortality and morbidity resulting from typhoid fever must be reduced, our clinical laboratories will need to be well equipped and do more than their present status. No doubt, inappropriate diagnosis contributes in no small way to emergence and re-emergence of typhoid fever in our society because without proper diagnosis, there cannot be adequate and effective treatment of typhoid fever.

5. CONCLUSION

The commonest method for the diagnosis of typhoid fever in Ondo State of Nigeria is the serological method (Widal's agglutination test). The more reliable and specific cultural methods are hereby advocated, since proper diagnosis contributes in no small way to the effective treatment and control of typhoid fever.

CONSENT

Not applicable.

ETHICAL APPROVAL

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.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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