

Malaria and Typhoid Fever among Adult Patients Presenting with Fever in Ibadan, Southwest Nigeria

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Abstract: Two hundred and fifty eight adult patients presenting with fever of typhomalarial symptoms were referred to Biomedics Diagnostic Laboratory, an active medical laboratory in Ibadan, Southwest Nigeria, for malaria parasite and Widal agglutination tests. About 161 (62.4%) of the patients had malaria, 43 (16.7%) were positive for Widal test, 130 (50.4%) had malaria only, 12 (4.7%) were positive for Widal test only, 31 (12%) were positive for both malarial parasite and Widal tests and 85 (32.9%) were negative for both tests. Blood cultures carried out on the samples showed that only 2 (0.8%) of the 258 patients were positive for *Salmonella typhi*, the causative organism of typhoid fever. Similar tests were performed on blood samples collected from 100 apparently healthy individuals as controls. The 18 (18%) of the control subjects had malarial infection, 11 (11%) were positive for Widal test, 13 (13%) had malarial infection only, 6 (6%) were positive for Widal test only, 5 (5%) were positive for both malarial parasite and Widal test, 76 (76%) were negative for both malarial and Widal tests and none was positive for growth of *S. typhi*. This study shown that malaria was significantly associated with fever ($\chi^2 = 56.84$; $p < 0.0001$) but typhoid fever was not significantly associated with fever ($p = 0.52$). Co-infection with malaria and typhoid fever was not significant ($p = 0.14$). Although, malaria was significantly associated with fever, $>1/3$ (37.6%) of the febrile patients had no malaria. Typhoid fever was over-diagnosed by Widal test (16.7%) compared to the result of blood culture (0.8%).

Key words: Fever, malaria, typhoid fever, malarial test, Widal test, co-infection

INTRODUCTION

Like malaria, there is a popular belief that typhoid fever is endemic and quite prevalent in Nigeria (Onuigbo, 1990; Ohanu *et al.*, 2003). Patients, who fail to respond to the first line of malaria treatment usually suspect typhoid fever (Onuigbo, 1990). Malaria and typhoid fever usually present with similar symptoms particularly at the beginning of typhoid fever (Petit and Wamola, 1994; Nsutebu *et al.*, 2001). Owing to the fact that it is sometimes very difficult to differentiate clinically the presentation of typhoid fever from that of malaria without laboratory support (Rooth and Bjorkman, 1992), many clinicians usually request that both tests be performed on individuals presenting with fever of typhomalarial signs and symptoms.

In Sub-Saharan Africa, while the gold standard technique for diagnosing malaria is by examination of blood smear for malarial parasite, one reliable diagnostic technique for typhoid fever is culturing of blood, stool and urine samples and isolating *Salmonella typhi*. In

Nigeria, where facilities for culturing are not usually available, diagnosis of typhoid fever is essentially based on Widal agglutination test and it has been argued that diagnosis of typhoid fever by the Widal test alone is prone to error (Edelman and Levine, 1986; Onuigbo, 1990; Jhaveri *et al.*, 1995; Mbuh *et al.*, 2003). Owing to the nonspecific nature of Widal agglutination test, co-infection with malaria and typhoid is believed to be common and therefore the simultaneous treatment of both infections is quite rampant (Nsutebu *et al.*, 2001; Mbuh *et al.*, 2003).

This study was carried out to determine the relationship between fever, malaria and typhoid fever and the prevalence of co-infection with malaria and typhoid among the study population in Ibadan, Southwest Nigeria.

MATERIALS AND METHODS

Two hundred and fifty eight adult patients presenting with typhomalarial fever were referred by clinicians after clinical and physical examinations to Biomedics

Diagnostic laboratory, an active medical laboratory in Ibadan, Southwest Nigeria for malarial parasite and Widal tests. Also, blood samples were collected from 100 seemingly healthy individuals as controls. Those who participated in the study gave informed consent. A 5 mL of blood was taken from each patient for laboratory investigations.

Examination of blood slides for malaria parasite: Thick blood films stained with 3% Giemsa for 30 min were made and examined for malarial parasites. At least 200 blood fields were examined for malaria parasite before reporting any film as negative.

Serological test for typhoid fever: Widal tests were done using a commercially prepared antigen suspension (Cal-Test Diagnostic Inc. Chino, USA) and following the manufacturer's instructions. Widal tests were read as positive when O antibody titres were $\geq 1/160$ for *S. typhi* (Mohammed *et al.*, 1992).

Bacteriological test for typhoid fever: Blood cultures were performed for samples following standard cultural procedures for *S. typhi* as stated in Cheesbrough (2000). *S. typhi* was identified on the basis of cultural, microscopic and biochemical characterization (Cheesbrough, 2000).

RESULTS

Table 1 shows the results of laboratory diagnosis of malarial parasite and Widal tests for febrile and control subjects. One hundred and thirty of the febrile patients (50.4%) were positive for malarial parasite test only, 12 (4.7%) were positive for Widal test only, 31 (12%) were positive for both malaria parasite and Widal tests while, 85 (32.9%) were negative for both tests. Thirteen (13%) of the control subjects had malarial infection only, 6 (6%) were positive for Widal test only, 5 were positive for both malaria parasite and Widal test, 76 (76%) were negative for both tests.

Table 2 shows the results of microscopic examination of malarial parasite and cultural examination of typhoid fever for the febrile and control subjects. One hundred and sixty (62.0%) of the patients had malarial parasite only, 1 (0.4%) positive for growth of *S. typhi* only, 1 (0.4%) positive for both malaria parasite and *S. typhi* and 96 (37.2%) negative for both malarial parasite and *S. typhi*.

In this study, only samples, which had growth of *S. typhi* were regarded as positive for typhoid fever. One hundred and sixty one (62.4%) of the fever patients had malaria while, 2 (0.8%) of them had typhoid fever. On the other hand, 18 (18%) of the control subjects had malarial

Table 1: Microscopic examination of malarial parasite and Widal agglutination test for the febrile and control subjects

Infection	Subjects (%)	
	Febrile	Control
Positive for malarial parasite only	130 (50.4)	13 (13.0)
Positive for Widal only	12 (4.7)	6 (6.0)
Positive for malarial parasite + Widal	31 (12.0)	5 (5.0)
Negative for malarial parasite + Widal	85 (32.9)	76 (76.0)
Total	258 (100.0)	100 (100.0)

Table 2: Microscopic examination of malarial parasite and bacteriological diagnosis of typhoid fever for febrile and control subjects

Infection	Subjects (%)	
	Febrile	Control
Positive for malarial parasite only	160 (62.0)	18 (18.0)
Positive for growth of <i>S. typhi</i> only	1 (0.4)	0 (0.0)
Positive for malarial parasite + growth of <i>S. typhi</i>	1 (0.4)	0 (0.0)
Negative for malarial parasite + growth of <i>S. typhi</i>	96 (37.2)	82 (82.0)
Total	258 (100.0)	100 (100.0)

infection, while none had typhoid fever. Malaria was significantly associated with fever ($\chi^2 = 56.84$; $p < 0.0001$) but there was no significant association between typhoid fever and fever ($p = 0.52$). There was no significant association for co-infection with malaria and typhoid fever among the febrile patients ($p = 0.14$).

While, 43 (16.7%) of the febrile patients were positive for Widal test, only 2 (0.8%) had growth of *S. typhi* as shown by blood culture results. When, typhoid fever was diagnosed by single Widal agglutination test, the prevalence of co-infection with malaria and typhoid fever was 12%. However, when typhoid was diagnosed by blood culture, the prevalence of co-infection with malaria and typhoid fever was 0.4%.

DISCUSSION

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. Cultural diagnosis of typhoid fever shows the unreliability nature of Widal test, which is basically used in the diagnosis of typhoid fever in Nigeria. A reliable diagnosis of typhoid fever is based on culture of blood, stool and bone marrow (Edelman and Levine, 1986). However, bone marrow aspirates are difficult to obtain and culture from stool sample delays diagnosis leaving blood culture as the reliable method in the absence of other alternatives (Mbuh *et al.*, 2003).

Owing to lack of facilities, cultures are not usually performed in the diagnosis of typhoid fever in Nigeria. Therefore, all 43 patients who tested positive for Widal test would normally be considered as having typhoid fever. However, blood cultures results shown that only

2 of the patients actually had typhoid fever. This emphasized the importance of a reliable diagnostic procedure for typhoid fever. The unreliability characteristic of Widal test has been reported by Onuigbo (1990) and Ohanu *et al.* (2003). Widal test positively has been associated with: non-typhoid fevers resulting from anamnestic reactions (Pang and Puthuchear, 1983), sub-clinical typhoid infection in a typhoid fever endemic area (Pang and Puthuchear, 1983; Kustner *et al.*, 1987), cross-reacting antibodies produced by non-typhoid *Salmonellae* (Reynolds *et al.*, 1970), malaria (Onuigbo, 1990; Ohanu *et al.*, 2003) and cirrhosis and hepatitis (Protell *et al.*, 1971).

Of the 31 patients positive for both malaria and Widal tests, only 1 actually had typhoid fever as revealed by the results of the blood cultures. Therefore, one can conclude that the other 30 patients were actually malarial patients who only tested positive for Widal test confirming the findings of Onuigbo (1990) and Nsutebu *et al.* (2001) that malaria may lead to over-diagnosis of typhoid fever. This could be due to cross reactivity between malaria parasite antibodies and Widal antigens (Jhaveri *et al.*, 1995). Petit and Wamola (1994) reported a false positive Widal test reaction in 35% of malarial patients. Mbuh *et al.* (2003) reported a false positive Widal test reaction in 36.7% of malarial patients. This study reports a false positive Widal test reaction in 18.6% of malarial patients. Therefore, when patients are positive for both malaria and Widal tests and there are no facilities for culture, it is advisable to first of all treat malaria.

In this study, only one patient had mixed infection of malaria and typhoid fever as against 31 patients positive for both malaria and Widal test. This study is line with that of Mbuh *et al.* (2003), who did not observe any significant relationship between malaria and typhoid fever. However, co-infection with malaria and typhoid was reported among typhomalarial patients in Cameroon (Ammah *et al.*, 1999). Also, typhomalaria concomitant relationship of 16% was observed in children with cerebral malaria in Northern Nigeria (Prada *et al.*, 1993). This study shows the one draw back of presumptive diagnosis. Ninety-six (37.2%) of the fever patients neither had malaria nor typhoid fever. Patients presenting with fever clinically suspected to be either malaria or typhoid should be subjected to laboratory diagnosis for confirmation. Diagnosing on the basis of clinical evidence alone is unreliable, misleading and could lead to development of drug resistance, increase in adverse reactions, accumulation of toxic malarial drug and increase in drug budgets (Wernsdorfer and Payne, 1991; Jonkman *et al.*, 1995).

CONCLUSION

In Nigeria, malaria is still the leading cause of fever characteristic of typhomalaria signs and symptoms. About one-third of the patients presenting with fever neither have malaria nor typhoid 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. The use of culture techniques in diagnosing typhoid should be embraced and encouraged. Where, culture facilities are lacking and patients are positive for both malaria and Widal tests, malaria should be treated. Only when malaria has been ruled out and there is a strong clinical suspicion of typhoid fever should such patients be treated for typhoid fever.

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