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Dispelling the Malaria-Typhoid Co-infection Myth in Nigeria: A Literature Review

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Abstract

Malaria and typhoid fever are public health concerns in Nigeria, with high prevalence rates. The perception of a widespread co-infection between these diseases may be misleading, due to limitations in diagnostic methods, particularly the Widal test for typhoid fever. This literature review examines the prevalence of malaria-typhoid co-infection in Nigeria and identifies factors contributing to misdiagnosis, including non-specific symptoms, limited diagnostic resources, and the diagnostic accuracy of tests employed. Additionally, the review discusses the implications of misdiagnosis, such as the overuse of broad-spectrum antibiotics leading to a rising incidence of antimicrobial resistance. Strategies to address this issue are explored, emphasizing the need for improved diagnostic methods, enhanced healthcare provider education, and comprehensive health education campaigns to empower patients and curb antibiotic misuse. While acknowledging limitations in available research done in Nigeria, this review underscores the urgency of addressing the malaria-typhoid co-infection myth to improve healthcare outcomes and combat antimicrobial resistance in Nigeria.

Keywords: Malaria; Typhoid; Malaria-Typhoid co-infection; Widal test; Multi-microbial resistance.

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1. Background

Malaria and typhoid are infectious diseases endemic to Nigeria [1]. In 2021, malaria had an estimated prevalence of 68 million cases and resulted in 194,000 deaths, making Nigeria the global leader in malaria burden, contributing to nearly 27% of cases worldwide [2].

Typhoid, with approximately 290,000 annual cases, is also endemic in Nigeria [3]. Studies have shown that co-infection between typhoid and malaria is highly prevalent, particularly in low-income countries with poor sanitary measures and limited access to adequate medical resources [4, 5]. However, several studies have also shown that the overestimation of co-infection rates between these diseases in recent years can be attributed to the diagnostic and screening methods for typhoid fever, particularly the Widal test [6, 7]. This test, while highly sensitive, has low specificity, leading to a higher rate of false positives and potentially skewing the reported prevalence of malaria and typhoid co-infection [6, 8,7]. The Widal test is unable to distinguish between a patient's past infection, current infection, or vaccination for S. Typhi, and test results may yield false positives in cases of typhus, acute falciparum malaria, chronic liver disease, rheumatoid arthritis, nephrotic syndrome, and myelomatosis [9].

Debunking the misconception of high coinfection prevalence is crucial to reducing unnecessary antibiotic prescriptions and mitigating the growing threat of antibiotic resistance in Nigeria.

Malaria is an infectious disease transmitted by the bite of a female Anopheles mosquito carrying the Plasmodium species parasite [10]. The parasites initially proliferate in liver cells before infesting red blood cells [11]. Within the bloodstream, successive generations of parasites develop inside red blood cells, leading to their destruction and the release of daughter parasites, perpetuating the cycle by infecting additional red blood cells [11]. This illness poses a life-threatening risk, manifesting symptoms ranging from flu-like manifestations to multiorgan failure, coma, and eventual fatality [12].

Conversely, typhoid fever spreads through a fecal-oral route, by the Salmonella bacterium. Individuals with typhoid fever harbor the bacteria in their bloodstream and intestinal tract [13]. Symptoms include prolonged high fever, fatigue, headache, nausea, abdominal pain, and either constipation or diarrhea, sometimes accompanied by a rash [13]. Despite the distinct etiologies, pathogenesis, and modes of transmission of malaria and typhoid fever occasionally present with non-specific symptoms, leading to confusion and misdiagnosis by health providers.

Patients falsely diagnosed with typhoid alongside malaria in Nigeria are typically initiated on broad-spectrum antibiotics in addition to anti-malarial medications without undergoing confirmatory tests such as blood or bone marrow culture. This widespread administration of broad-spectrum antibiotics has contributed to the escalating incidence of antimicrobial resistance, consequently amplifying mortality rates [14, 15, 16].

2. Objectives

The objective of this review is to analyze literature pertinent to identifying gaps in the diagnosis of typhoid fever and malaria. Additionally, it aims to explore strategies aimed at reducing the overestimation of co-infection rates. The overall goal is to propose novel approaches to mitigate the excessive use of broad-spectrum antibiotics among

patients who do not have typhoid fever.

3. Factors Contributing to Misdiagnosis

3.1. Non-specific Symptoms

Malaria and typhoid are prevalent diseases in low-income countries, affecting a significant portion of the population due to poor hygiene and low living standards [14]. Both illnesses exhibit nonspecific symptoms, including fever, body aches, vomiting, diarrhea, and constipation, complicating their independent diagnosis based solely on clinical presentation [17]. Physicians who rely solely on clinical assessments without confirming through laboratory testing are prone to prematurely diagnosing malaria-typhoid coinfections and initiating empirical antibiotic treatment. More than half of Nigeria's population is estimated to experience at least one episode of malaria each year, contributing to approximately 30% of outpatient visits, 20% of all hospital admissions, and 10% of hospital deaths [18]. The use of antibiotics stemming from false positives in typhoid diagnoses following multiple hospital presentations heightens the risk of antibiotic resistance [7].

3.2. Limited Diagnostic Resources and Presumptive Treatment by Healthcare Providers

Malaria and typhoid fever are particularly prevalent in the northern regions of Nigeria, characterized by high levels of poverty and limited economic resources [19, 20]. The inadequate access to healthcare facilities exacerbates the situation, resulting in a scarcity of diagnostic equipment essential for accurate malaria and typhoid diagnoses [19]. Consequently, healthcare providers often resort to presumptive diagnoses of coinfections based solely on nonspecific clinical symptoms.

In these resource-constrained settings, healthcare practitioners frequently prescribe anti-malarial drugs and broad-spectrum antibiotics empirically to cover both diseases [21, 22]. Even for patients presenting repeatedly, the standard practice remains consistent, with the same medications administered on each occasion. Unfortunately, this indiscriminate use of medications contributes significantly to the emergence of antimicrobial resistance [23].

3.3. Diagnostic Accuracy of the Utilized Tests

In Nigeria, the primary diagnostic methods for malaria and typhoid fever are the thick and thin blood smear and the Widal test, respectively [24]. These tests are widely available and affordable across most regions of the country, although their accuracies in predicting each disease vary significantly [6, 24].

The thick and thin blood smear test involves microscopic examination of the patient's blood to detect Plasmodium species and quantify their numbers, which can also indicate the severity of the infection [24]. This method is considered the gold standard for diagnosing malaria, particularly when both thin and thick smears are meticulously conducted [25]. Additionally, rapid diagnostic tests (RDTs) for malaria are commonly used in various healthcare settings in Nigeria [24].

The diagnosis of typhoid fever in many cases relies on the Widal test, although the gold standard remains

microscopy and blood and/or bone marrow culture [3]. However, these gold standard tests are often unavailable in many parts of Nigeria due to economic constraints and the need for skilled personnel, leading to the widespread use of the Widal test for confirmation [3].A study conducted in the USA compared the efficacy of RDTs to traditional blood smear examinations for malaria diagnosis [26]. The findings revealed that RDTs exhibited superior sensitivity (97%) compared to traditional Giemsa blood smear (85%), with a better negative predictive value (99.6% vs. 98.2%) [26]. Notably, the most significant difference in performance was observed in diagnosing Plasmodium falciparum, where RDTs demonstrated 100% sensitivity compared to 88% sensitivity for blood smears [26]. The lower sensitivity of microscopy may be attributed to the expertise required for accurate interpretation.A cross-sectional survey conducted in Tanzania compared the performance of the Widal test with stool cultures in 158 patients [8]. The Widal test showed 81.5% sensitivity, 18.3% specificity, 10.1% positive predictive value, and 89.7% negative predictive value [8]. In contrast, stool culture exhibited 31.3% sensitivity, 91.5% specificity, 29% positive predictive value, and 91.5% negative predictive value [8].Another study in Nepal compared the diagnostic accuracies of the Widal test with the ELISA test.[27] Among 1371 febrile cases, blood culture-confirmed Salmonella typhi in 237 patients [27]. The sensitivity and specificity of IgG and IgM ELISA were significantly higher compared to the Widal test at a titer level ≥1:200 [27]. The positive predictive value of ELISA was also substantially higher than that of the Widal test [27].Furthermore, a comparative analysis of commercially available typhoid point-of-care tests conducted in Kenya and Pakistan evaluated 2942 blood culture samples [28]. The Widal test demonstrated very low sensitivity and specificity (47.7% and 79.4%, respectively), indicating its inadequacy as a diagnostic tool for typhoid fever [28].

A study conducted in Zaria, Nigeria, to assess the rate of co-infections of malaria and typhoid fever revealed notable findings [29]. The rate of co-infection was notably higher when typhoid fever was diagnosed using the Widal test (10.1%) compared to the blood culture method (0.5%) [29]. Additionally, a correlation analysis indicated that there was no significant relationship between the malaria parasite load and the level of Salmonella antibody titers in malaria patients [29]. The correlation coefficients were found to be 0.05 and 0.08 for somatic and flagella antigens of Salmonella typhi, respectively [29].

3.4 Clinical Symptoms Overlap with Other Endemic Diseases

Regions endemic to malaria and typhoid fever also exhibit a high prevalence of other infectious diseases, such as dengue fever, Lassa fever, HIV, lower respiratory infections, and diarrheal diseases caused by various pathogens [30, 31]. These illnesses often present with similar clinical symptoms to malaria and typhoid fever, potentially leading to misdiagnosis and inappropriate treatments [30].

4. Discussion

Over the years, a widespread belief has taken root among Nigerians, asserting that malaria and typhoid fever commonly occur together and necessitate concurrent treatment. This misconception stems from extensive false diagnoses made by physicians in Nigeria, either through presumptive means or because of inefficient testing methods. This misinformation has become deeply ingrained in the population, to the extent that some patients, even when experiencing minor symptoms, resort to self-medication with antimalarial and antibiotic medications.

A study conducted via a national survey in Nigeria has revealed that more than a third of the public consumes antibiotics without a prescription from a doctor [23].In many hospitals in low-income communities, the only diagnostic tests available in their laboratories are the Widal test and microscopes used for blood films to detect malaria parasites. Consequently, physicians practicing in such facilities often rely solely on these available tests when diagnosing patients.However, studies cited above have demonstrated that the Widal test is an ineffective method for diagnosing typhoid fever, given its high likelihood of yielding false positives among uninfected individuals. Conversely, when blood cultures are employed instead of the Widal test, the prevalence of malaria and typhoid coinfections significantly decreases. This disparity suggests that the number of presumed coinfections is greatly exaggerated due to the poor accuracy of the Widal test, which is commonly utilized throughout the country.Nigeria is grappling with rising antimicrobial resistance, as highlighted by a national survey [23]. Shockingly, the number of deaths attributed to antimicrobial resistance surpasses those caused by various other significant health conditions, including enteric infections, respiratory infections, tuberculosis, maternal and neonatal disorders, neglected tropical diseases, malaria, and cardiovascular diseases [32]. Many of these conditions lead to mortality due to repeated exposure to antibiotics, resulting in infections with drug-resistant strains of microorganisms. To address this pressing issue, concerted efforts are needed to limit over-the-counter access to antibiotics, reduce the indiscriminate prescription of antibiotics, implement proper and effective diagnostic testing, and provide comprehensive health education to deter the rate of self-prescribing medications.Health education campaigns on the perils of antibiotic overuse are crucial for raising awareness among Nigerians and empowering them to make informed decisions about their healthcare. Furthermore, healthcare professionals, including physicians, should receive education on the limitations of the widely used Widal test and the risks associated with prescribing antibiotics solely based on a positive Widal result. Instead, physicians should be encouraged to utilize blood cultures for diagnosing typhoid fever, particularly when there is a strong suspicion of the disease.It is crucial to recognize the limitations of this literature review, especially concerning the data collection methods and study designs of the studies reviewed. The regions where most of these studies were conducted may have encountered challenges in securing the necessary funding to screen and test a large sample size effectively. Additionally, while this review aims to gather information on malaria and typhoid co-infections in Nigeria, many of the papers reviewed were from populations like Nigeria but not specifically from Nigeria. This is due to the limited available research conducted on this topic in Nigeria. These factors emphasize the necessity for further research and resources to effectively address antimicrobial resistance in Nigeria.

5. Conclusion

The prevalent practice of conducting concurrent testing with the Widal test for typhoid fever and microscopic analysis of blood smears for malaria among patients exhibiting nonspecific symptoms has resulted in the perceived exaggeration of malaria and typhoid coinfections. This phenomenon is primarily attributed to the lower diagnostic accuracy of the Widal test, notably its low specificity and positive predictive value. Consequently, false-positive results from the Widal test have spurred the widespread overuse of antibiotics, thereby exacerbating the escalating incidence of antimicrobial resistance in Nigeria. To address this critical issue, it is imperative to allocate additional research and resources toward developing more accurate methods for diagnosing patients with typhoid fever in Nigeria.

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