

MALARIA TYPHOID CO-INFECTION AMONG FEBRILE PATIENTSSamatha P¹, Chalapathi Rao K², Sai Sowmya B³**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: Malaria and typhoid fevers, caused by different organisms are major public health problems in developing countries. People in endemic areas are at risk of both infections concurrently. These are the important cause of fevers in many endemic areas especially during rainy season. Each of these diseases can substantially contribute to mortality if not diagnosed and treated early. The present study was designed to find the Sero prevalence of Malaria, Typhoid and Typho malarial co-infections in febrile patients. **METHODS:** A cross sectional study was conducted from June 2014 to May 2015. A total of five hundred and eighty two subjects were screened for Malaria and Typhoid is included in study irrespective of their age & sex. Data was analysed on the basis of Demographic factors & Serological results. The results were analysed statistically. **RESULTS:** The seroprevalence of malarial infection was found to be 58.41%, Typhoid as 1.8% whereas, True Typho Malarial co-infection was seen in 0.7%. **CONCLUSION:** The present study reports the Prevalence of Malaria, Typhoid and Typho Malarial Co- infection which are important when planning large scale vaccine trials as well as making health policies and a Protocol is required to treat these infections to limit the mortality and morbidity.

KEYWORDS: Malaria, Typhoid, blood culture, Typho Malarial co-infection.

INTRODUCTION: Malaria and typhoid fevers are common causes of fevers in many parts of Andhra Pradesh during rainy season. Concurrent infection with two agents can result in an illness having overlapping symptoms creating a diagnostic dilemma for the treating physician. The similarity in symptoms and differential diagnoses of these diseases often mimic and thereby makes accurate clinical diagnosis and treatment difficult without laboratory confirmation.⁽¹⁾ Malaria is one of the febrile illnesses and the most common fatal disease in the world caused by one or more species of plasmodium. Approximately half of the world population is at risk of malaria. According to the World malaria report 2011, there were about 216 million cases of malaria and an estimated 655,000 deaths in 2010.⁽²⁾

Typhoid fever is a systemic infectious disease caused by salmonella serotypes. It is characterized by an acute illness, the first typical manifestations of which are fever, headache, abdominal pain, relative bradycardia, splenomegaly, and leucopenia.⁽³⁾ The estimated total number of world typhoid fever episode in 2010 was 13.5 million. Many infections including malaria and typhoid are known to complicate HIV/AIDS in sub-Saharan Africa,^(4,5) Malaria and typhoid fever usually present with similar symptoms particularly at the beginning of typhoid fever. Owing to the fact that it is very difficult sometimes to differentiate clinically the presentation of typhoid fever from that of malaria without laboratory support, many clinicians usually request that both tests were performed on individuals presenting with fever of typho malarial signs and symptoms.

An association between malaria and typhoid fever was first described in the medical literature in the middle of the 19th century, and named as typho malarial fever by an Army Doctor, Woodward in 1862 among young soldiers during the American civil war.⁽⁶⁾ Typhoid and malaria

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share social circumstances which are imperative to their transmission. Individuals in endemic areas for both the diseases are prone to infection. Rampant and unnecessary use of iron supplementation to correct possible anemia in malaria is dangerous, since excess iron may predispose to salmonellosis.⁽⁷⁾ Intracellular bacteria, such as Salmonella has an obligate requirement for iron to support for its intracellular growth and survival. The objective of this study is to determine the prevalence of Malaria, Typhoid fever and their co-infection among febrile patients. Study of prevalence is important to understand and assess magnitude of disease in the community, and also to plan better control and prevention strategies.

MATERIALS AND METHODS: Study Area, Population, and Design: The study was conducted from June 2014 to May 2015 at KMC&H, Guntur. Five hundred and eighty two febrile patients suspected for malaria and/or typhoid fever who had not taken antimalarial drug and/or antibiotics within 2 weeks were included. Patients with underlying diseases were excluded from the study.

Specimen Collection and Processing: Data on the demographic and clinical characteristics of the study participants were collected using pretested structured questionnaire by interview. After taking consent 7-10mL blood sample was collected from patients by experienced laboratory technician and was processed.

TYPHOID FEVER DIAGNOSIS: Bacteriological Test for Typhoid Fever: Blood cultures were performed for samples following standard cultural procedures for Salmonella Serotypes as stated in Monica cheesebrough.⁽⁸⁾ Salmonella was identified on the basis of cultural, microscopic and biochemical characterization.⁽⁸⁾

Serological Test: Widal test is the only specific diagnostic investigation available in most tropical regions. The Widal test which is available was introduced as a serologic technique to aid in diagnosis of typhoid fever and has been used for more than a century.

Widal tests were done using a commercially prepared antigen suspension (TYDAL, Lab Care Diagnostics (India) by following the manufacturer's instructions. First Slide agglutination test was done for typhoid fever screening using somatic (O) and flagellar (H) antigens kits of Salmonella species. If slide agglutination test is positive, then subjected to Tube agglutination. Tube Widal tests were read as positive when O antibody titres were $\geq 1/80$ and H antibody titres were $\geq 1/160$.

Malaria Diagnosis: Stained blood film remains currently the "Gold standard" for detecting and identifying malaria parasites.⁽⁹⁾

Examination of Blood Smears for Malaria Parasite: A drop of fresh blood through pinprick is collected. Thick and thin blood films were prepared, stained with 3% Giemsa for 30min and examined for malarial parasites. At least 200 fields were examined for malaria parasite before reporting as negative.

Statistical Analysis: The result of study was subjected to Chi-square test to determine if the relationships between the malaria parasite infection and Typhoid fever are actually significant.

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RESULTS: Table 1 shows the results of laboratory diagnosis of malaria parasite and Widal tests for febrile patients. Three hundred and two of the febrile patients (51.89%) were positive for malaria parasite test only, 132(22.6%) were positive for Widal test only, 38(6.5%) were positive for both malaria parasite and Widal tests while, 110(18.9%) were negative for both tests.

Table 2 shows the results of examination of malaria parasite and blood culture examination of typhoid fever for the febrile patients. Three hundred and thirty six(57.7%) of the patients had malaria parasite only, 7(1.2%) positive for growth of Salmonella only, 4(0.7%) positive for both malaria parasite and Salmonella and 235(40.3%) negative for both malaria parasite and Salmonella infection.

In this study, only samples, which had growth of Salmonella were regarded as positive for Typhoid fever. Three hundred and forty (58.41%) of the fever patients had malaria while, 11(1.8%) of them had typhoid fever.

Infection	Fever patients
Positive for Malaria only	302(51.89%)
Positive for Widal only	132(22.6%)
Co infection	38(6.5%)
Negative for co infection	110(18.9%)
Total	582(99.99%)

Table 1: Examination of malaria parasite and Widal test in febrile patients

Infection	Fever patients
Positive for malaria only	336(57.7%)
Positive for growth of salmonella	07(1.2%)
Positive for malaria and growth of salmonella	04(0.7%)
Negative for malaria and growth of salmonella	235(40.3%)
Total	582(99.99%)

Table 2: Examination of Malaria parasite and typhoid fever by blood culture in febrile patients

Malaria was significantly associated with fever ($\chi^2=128.6$; $p<0.0001$) but there was no significant association between typhoid fever and fever ($p=>0.5$). There was no significant association for co-infection with malaria and typhoid fever among the febrile patients.

While, 170(29.2%) of the febrile patients were positive for Widal test, only 7(1.2%) had growth of Salmonella 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 6.5%. However, when typhoid was diagnosed by blood culture, the prevalence of co-infection with malaria and typhoid fever was 0.7%.

DISCUSSION: Despite the fact that malaria and typhoid are endemic in Andhra Pradesh, the result of this study has indicated that malaria is far more likely to cause fever than typhoid fever. Malaria and Typhoid share common geographical endemic areas especially in rainy season. It is very common to

see patients in many parts of the tropics, undergoing both typhoid and malarial treatment even if their diagnosis has not been confirmed.⁽¹⁰⁾

Cultural diagnosis of Salmonella species has revealed the unreliability of Widal agglutination test, which is basically the diagnostic procedure used in many suspected cases of Typhoid fever. For an accurate and reliable diagnosis of Typhoid fever, the use of Blood culture method should highly be taken into consideration. This could be followed by stool and bone marrow.⁽¹⁰⁾ It should be noted that bone marrow aspirate is highly difficult to obtain and culture from stool has the tendency of increasing the prevalence rate by 10-15%. This leaves the blood as an alternative and reliable method in the diagnosis of salmonella infection.⁽¹¹⁾

Reason for Co-infection: Although there are so many cases of concurrent typhoid and malaria due to cross reactivity of antigen, true co infection also exists. The precise mechanism underlying the association between malaria and salmonella is still not fully understood. However, it has been shown that hemolysis, which occurs in malaria, may predispose to typhoid fever. It has also been shown that acute malaria reduces antibody response to the somatic (O) antigen of Salmonella typhi.

It is a well-known fact that anemia due to massive hemolysis or dyserythropoiesis occur in malaria which leads to deposition of iron in the liver. Short-lived red blood cells might save patients from malaria; the iron they dump out could lead to death. The extra iron seems to feed the bug that causes typhoid fever.⁽¹²⁾ However intracellular bacteria such as Salmonella also have an obligate requirement for iron to support its intracellular growth and survival.⁽¹³⁾ Patients suffering from severe anemia show increased susceptibility to salmonella.^(14,15) On the other hand, iron overload of the liver in malaria can support the growth of salmonella in liver.

Of the 38 patient's positive for both malaria and Widal tests, only 07 actually had typhoid fever as revealed by the results of the blood cultures. Therefore, one can conclude that the other 31 patients were actually malarial patients who only tested positive for Widal test confirming the findings of Onuigbo and Nsutebu et al.,^(16,17) that malaria may lead to over-diagnosis of typhoid fever.

This could be due to cross reactivity between malaria parasite antibodies and Widal antigens.⁽¹⁸⁾ Petit and Wamola (1994) reported a false positive Widal test reaction in 35% of malarial patients.⁽¹⁹⁾ Mbuh et al.,2003⁽¹⁰⁾ reported a false positive Widal test reaction in 36.7% of malarial patients. Our study reports a false positive widal reaction in 19.25% 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 four patients had mixed infection of malaria and typhoid fever as against 38 patients positive for both malaria and Widal test. But Ammah et al reported that in 200 patients with fever, 17% had concurrent malaria and typhoid fever based on bacteriological proven diagnosis as compared to 47.9% based on the Widal test.⁽²⁰⁾ However, co-infection with malaria and typhoid was reported among typho malarial patients in Cameroon.⁽²⁰⁾

This study shows one drawback of presumptive diagnosis. Two hundred and thirty five (40.3%) 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.⁽²¹⁾

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CONCLUSION: In order to rule out any case of malaria with mimicking symptoms the practical use of blood culture for the diagnosis of typhoid fever is strongly recommended. This will help improve patient's management by cutting down cost of treatment and eliminate other risks associated with misuse of antibiotics. In conclusion the prevalence of malaria and typhoid fever co-infection in endemic areas will be greatly reduced if diagnosis of typhoid fever will be based on culture method. Early recognition along with meticulous monitoring and targeted supportive care is the cornerstone of a successful outcome both in malaria and enteric fever.

RECOMMENDATIONS:

1. The need of hour is to further strengthen the Awareness programmes.
2. Improved personal hygiene, Targeted Vaccination, community health education could help to prevent & control.
3. The use of blood culture techniques in diagnosing typhoid should be encouraged.
4. The community should be encouraged to use proper sanitation to reduce the burden of high prevalence.

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