



COMPARATIVE ANALYSIS OF METHODS FOR THE DIAGNOSIS OF TYPHOID FEVER SUBBULAKSHMI R

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Abstract : Background and Objectives-Typhoid fever continues to be one of the leading causes of morbidity and mortality in our country. Conventional methods of diagnosis are gold standard blood culture and supportive Widal test. This study analyzes Typhoid rapid antibody test, a rapid serological test for the diagnosis of typhoid fever and its usefulness for an early diagnosis, its sensitivity and specificity as compared to Widal test. Materials and Methods-The Typhoid rapid IgM IgG test is a lateral flow immuno-chromatographic test specific for *Salmonella typhi* and separately identifies IgM and IgG antibodies. This study included 81 patients who presented with fever. Clot culture, Widal test and Typhoid rapid antibody test were performed in all patients. Typhoid rapid antibody test and Widal tests were compared for sensitivity and specificity. Results-57 patients out of 81 were clinically suspected to be cases of typhoid fever (Gp-I), while 24 patients were non-typhoid febrile illness (Gp-II). 10 patients (18 percentage) of the Gp-I were positive for clot culture, 32 (56 percentage) were Widal positive, and 44(77 percentage) were positive for Typhoid rapid antibody test. Gp-II had all patients sterile on clot culture, 5 (21 percentage) were Widal positive, while 4 (17 percentage) tested positive for Typhoid rapid antibody test. Amongst 10 culture positive cases in Gp-I, Typhoid rapid test was positive in 9 patients, while Widal was positive in 6 patients, giving sensitivity of 90 percentage and specificity of 83 percentage as compared to Widal which had sensitivity of 60 percentage and specificity of 79 percentage. Conclusion-Typhoid rapid antibody test is an equally reliable, simple test that gives rapid diagnosis and can be helpful in diagnosis and early institution of therapy.

Keyword : Typhoid rapid antibody test, Widal test, Clot culture, Typhoid fever

Introduction:

Typhoid fever is a life threatening systemic infection occurring in under-developed areas of the world and continues to be a major public health problem. There are at least 16 million new cases of typhoid globally ¹. The annual incidence of typhoid fever has been reported as more than 13 million cases in Asia and causing more than six lakhs deaths worldwide annually ². India is the second most populous country of the world with majority inhabiting the rural areas with little access to modern diagnostic tools. Blood culture and Widal test are routinely employed investigations for diagnosis of typhoid fever in all clinical

settings. *Salmonella typhi*, the causative agent, is most frequently isolated from blood during the first week of illness but can also be isolated during the second or third week of illness, during the first week of antimicrobial therapy and during clinical relapse.³ Blood culture, which is the gold standard for the diagnosis of typhoid fever, though highly specific, sensitivity varies from 48-78 percent and the yield is affected by prior antibiotic intake and stage of illness.⁴ Clot culture on the other hand showed the same rate of isolation as that of blood culture.⁵ Advantage of clot culture is that it can be done with the sample taken for Widal test ⁶ and the yield of the test is higher with the modification of method used by Escamilla et al.⁷

The Widal test which is readily available and inexpensive has been used for many years but serious doubts have been raised regarding its validity. It carries disadvantage of being positive in unrelated conditions (anamnesic reactions), test has to be interpreted against a baseline titer in the same geographical area since titers of diagnostic significance differ in endemic and non-endemic areas and a paired sera with a fourfold rise in titer is needed for a meaningful result. Therefore, a fast, reliable, and easy to perform serodiagnostic test with a higher sensitivity and specificity than Widal test is required for rapid diagnosis of typhoid cases, thereby enabling clinicians to initiate an early therapy, reducing morbidity and its complications. Typhoid rapid antibody test is a rapid serological test for the diagnosis of typhoid fever. However, its usefulness in terms of specificity and sensitivity as compared to Widal test has not been studied so far in our region. The present study was conducted to know its utility and effectiveness in terms of diagnostic yields as compared to Widal test. The World Health Organization (WHO) has issued no recommendations on the use of typhoid rapid antibody tests.⁸ Accurate diagnostics for typhoid fever could provide valuable diagnostic information for patient management and make it possible to estimate the incidence of typhoid fever in low-resource settings.

Aim and objectives:

The aim is to provide a fast, reliable, economical and easy to perform serodiagnostic test with a higher sensitivity and specificity for a rapid diagnosis and treatment of typhoid cases

1. To evaluate the usefulness of typhoid rapid antibody test in the diagnosis of typhoid fever

2. To compare results of typhoid rapid test with Widal test and clot cultures and to correlate clinically
3. To determine specificity and sensitivity of typhoid rapid test and Widal test with that of clot cultures

Materials and Methods:

Study period was from October 2014 to December 2014. The Typhoid rapid IgM/IgG test (Oscar Medicare Diagnostics, New Delhi) is based upon lateral flow immunochromatographic principle. The device contains two test strips, one for IgM detection and one for IgG detection. The IgM strip consisting of a dried conjugate pad containing anti-human IgM conjugated with colloidal gold, a nitrocellulose membrane immobilized with *S. typhi* antigen (LPS) at test line region T' and a control line protein at control line region C'. The IgG strip consisting of a dried conjugate pad containing Protein-A conjugated with colloidal gold, a nitrocellulose membrane immobilized with *S. typhi* antigen (LPS) at test line region T' and a control line protein at control line region C'. 5 µl of specimen using micropipette is added followed by 2 drops of buffer into the respective wells and after 15 minutes appearance of pink or purple lines are observed in the result window. Positive controls will give a pink line and negative controls should give no coloured line.

Interpretation:

IgM alone positive – Acute typhoid fever

IgM and IgG positive – Acute typhoid fever (middle stage of infection)

IgG positive – Previous infection, relapse or reinfection with *Salmonella typhi*

IgM and IgG negative – Probably not typhoid

The study included 81 patients of acute febrile illness who presented to our hospital. The patients were divided into two groups. Group I included 57 patients with clinical diagnosis of typhoid fever and Group II comprised of 24 patients of suspected typhoid fever with alternative diagnosis. Clot culture, Widal test and Typhoid rapid antibody test were done in all patients. Results of clot culture, Widal and Typhoid rapid test were compared in all patients for their sensitivity and specificity.

Fig 1: Typhoid rapid antibody test

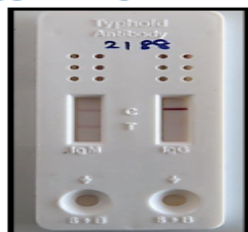


Fig 2: *Salmonella typhi* in DCA plate

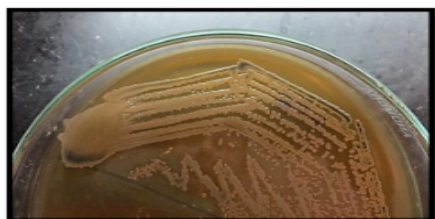
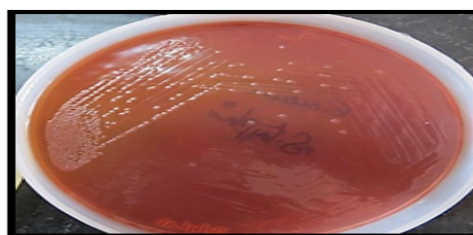


Fig 3: *Salmonella typhi* in MacConkey agar plate



Observations:

Clot cultures was positive in 10 out of 57 patients (Group I), whereas all the 24 patients in group II were sterile on clot culture. 32 patients of Group I were positive for Widal test, whereas 44 out of 57 were positive for Typhoid rapid test. (Table 1). A total of 5 patients in Group II were Widal positive while only 4 tested positive for Typhoid rapid test. On comparative evaluation of Clot culture, Widal test and Typhoid rapid test, clot culture showed a sensitivity of 18% and specificity of 100% whereas Widal test had sensitivity of 56% and specificity of 79%, and Rapid test showed a sensitivity of 77% and specificity of 83%. Among all the 10 patients in Group I who were having positive clot culture, Rapid test was positive in 9 patients, giving a sensitivity of 90%, specificity of 83% and a positive predictive value of 69%, as compared to Widal test which was positive in 6 patients giving a sensitivity, specificity and a positive predictive value of 60%, 79% and 55% respectively. (Table II)

Table I - Comparison of Clot culture, Widal test and Rapid typhoid test

Test	No positive in clinical and culture proven typhoid cases n=57 (Group I)	Non-typhoid cases n=24 (Group II)
Clot culture	10(18%)	0
Widal	32(56%)	5(21%)
Typhoid rapid test	44(77%)	4(17%)

Table II – Comparison of Widal test and Typhoid rapid test in culture proven cases and non-typhoidal cases

Test	No positive in culture proven Typhoid cases n=10	Non-typhoidal cases n=24
Widal test	6(60%)	5(21%)
Typhoid rapid test	9(90%)	4(17%)

Discussion:

Typhoid fever is a systemic illness with a significant morbidity and mortality in developing countries. Poor sanitation, overcrowding, low standard of living, lack of medical facilities, and indiscriminate use of antibiotics lead to endemicity of typhoid fever and multi-resistant strains of *Salmonella typhi* in developing countries. Blood culture has remained the gold standard test in diagnosis of typhoid fever, but its utility in early diagnosis is limited in early phase of illness thereby making the isolation of the organism difficult. Widal test has been used for over a century in developing countries for diagnosing typhoid fever but it has a low sensitivity, specificity and positive predictive value, which changes with the geographical areas. Sharing of O and H antigens by other *Salmonella* serotypes and other members of *Enterobacteriaceae* makes the role of Widal test even more controversial in diagnosing typhoid fever. However, modified Widal test particularly when used along

with conventional widal test has a greater sensitivity. 12 Typhoid rapid antibody test is a new, inexpensive, and reliable serodiagnostic test recently available commercially and studied in many endemic areas with reports of higher sensitivity and specificity. Typhoid rapid test was analyzed for its usefulness in patients of typhoid fever presenting to our hospital and observed that it has a sensitivity of 90% and specificity of 83%, which was higher than that of Widal test.

Conclusion:

Rapid typhoid test is a highly sensitive and specific test in diagnosing typhoid fever. It is a rapid, easy to perform, more reliable test for typhoid fever as compared to Widal test and can be useful in early institution of therapy. However, a larger prospective study would be required to fully evaluate the usefulness of this test in countries endemic to typhoid fever.

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