International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article

A Comparative Study of Widal Test and Typhidot in Rapid Diagnosis of Typhoid Fever

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ABSTRACT

Background: Typhoid fever is a major public health problem and a leading cause of morbidity and mortality globally. It is usually diagnosed by conventional methods like Blood culture and Widal test. Typhidot is a rapid and reliable serological test for diagnosis of typhoid fever. The aim of the present study was to evaluate the utility of Typhidot test in rapid diagnosis of typhoid fever in terms of sensitivity and specificity.

Materials and Methods: The study group included 85 clinically suspected typhoid fever cases of all age groups and both sexes. Blood culture, Widal test and Typhidot test were performed on all the patients. Widal and Typhidot tests were compared for sensitivity and specificity.

Results: Out of total 85 clinically diagnosed typhoid fever cases enrolled in the study, 11 cases (13%) were positive by blood culture, 20 (23.5%) by Widal test and 22 (26%) by Typhidot test. Widal test has a sensitivity of 54%, specificity of 81%, positive predictive value of 30% and negative predictive value of 92% in comparison with blood culture results. Typhidot test has a sensitivity of 91%, specificity of 84%, positive predictive value of 45% and negative predictive value of 98% in comparison with blood culture results.

Conclusion: Typhidot test is a rapid, easy to perform and a reliable diagnostic test and can be useful in early institution of therapy.

Key words: Typhoid fever, *Salmonella typhi*, Blood culture, Widal test, Typhidot test.

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Article History:

Received: 17-01-2017, **Revised:** 01-02-2017, **Accepted:** 14-02-2017

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2017.3.2.017	

INTRODUCTION

Typhoid fever, caused by Salmonella enterica serotype Typhi, is one of the commonest infectious diseases and is endemic in Indian sub-continent[1]. It is a life threatening systemic infection and is a major public health problem, occurring more frequently in developing countries where overcrowding, poor hygiene and sanitation are prevalent[2,3].

Typhoid fever is a major cause of morbidity and mortality globally, causing an estimated 16.6 million new infections and 600,000 deaths each year[4]. The annual incidence of typhoid fever has been reported as more than 13 million cases in Asia[5].

Enteric fever is usually diagnosed by blood culture, stool culture, bone marrow culture, bile culture and serological techniques, among these blood culture is considered as gold standard and becomes positive in first week of fever, but it may not be always available or may not be done properly in many resource poor laboratories[6]. Indiscriminate use of antibiotics also make the isolation of the causative organism difficult from blood[7,8].

On the other hand, serological test like Widal, which is inexpensive, readily available and has moderate sensitivity and specificity, has been in use in all clinical settings for many years. But doubts have been raised regarding its validity as the titers of diagnostic significance in this test differ in different geographical areas, in different populations and in the presence of other febrile diseases.

Therefore, a fast, reliable, and easy to perform serological test with a higher sensitivity and specificity than Widal test is required for rapid diagnosis and management of typhoid cases, thereby enabling clinicians to initiate an early therapy, reducing morbidity and its complications[2].

Typhidot is a rapid serological test for the diagnosis of typhoid fever. This is a dot-enzyme immune assay (EIA), which detects IgG and IgM antibodies to a specific 50 kD outer membrane protein (OMP) antigen of Salmonella enterica serotype Typhi[9]. However, compared to Widal test, its significance in terms of sensitivity and specificity has not been studied much in our region. The present study was done to systematically evaluate the utility and significance of Typhidot in rapid diagnosis of typhoid fever in terms of sensitivity and specificity.

MATERIALS AND METHODS

The study was conducted in the Department of Microbiology, Heritage institute of Medical Sciences, Varanasi. A comparative six month study of Typhidot & Widal test for the diagnosis of typhoid fever was conducted from July 2016 to December 2016. The study group included 85 clinically suspected typhoid fever cases of all age groups as well as both sexes who presented to our hospital whereas febrile patients with alternative diagnosis were excluded from the study. Detailed clinical evaluation as well as routine investigations like complete blood count, smear for malarial parasite, urine and stool routine microscopy and urine culture were also done in all cases.

Blood samples were collected from all the patients included in the study, 15 ml from the adult patients and 7 ml from children. Around 10ml of blood from adult patients and 5 ml from children <12 years was inoculated into the blood culture media (BHI broth) and incubated at 37° C. Subcultures were done on every alternate day till the 7th day.

The growth of *Salmonella* was identified as per standard protocol and confirmed by agglutination with Salmonella polyvalent O, O9 and H:'d' antisera[10]. The Widal test was performed by slide agglutination method and it was considered positive when a titre of equal to or more than 1:160 was observed[11].

Typhidot is a rapid, qualitative dot ELISA test kit which detects IgM and IgG antibodies against a specific 50 kD outer membrane protein of *Salmonella typhi* enterica serotype Typhi strains, which is impregnated on nitrocellulose strips. The test was done as per manufacturer's kit instructions (Typhidot; Malaysian Biodiagnostic Research SDN BHD, Kuala Lumpur, Malaysia). The reaction tray was divided into 2 columns marked as M and G. 250 µl of sample diluent was dispensed in each well and 2.5 µl of test /control was added and then incubated for 20 minutes. The strips were washed with washing buffer three times, then, 250 µl of anti-human IgM and IgG was dispensed in each well and incubated for another 15 minutes. These were washed again, dispensed with 250 µl of colour development solution, and were incubated for another 15 minutes and results were then interpreted.

A positive IgM was interpreted clinically as acute typhoidal illness, while IgM and IgG positive were taken as acute typhoidal illness in middle stage of infection and IgG positive was interpreted as a chronic carrier or previous infection or reinfection.

Results of blood culture, widal, and typhidot test were compared in all the patients for their sensitivity and specificity.

Table 1: Results of Blood culture, Widal and Typhi dot tests among enrolled cases

Results	Blood culture		Widal test		Typhidot test	
	No.	%	No.	%	No.	%
Positive	11	13	20	23.5	22	26
Negative	74	87	65	76.4	63	74
Total	85	100	85	100	85	100

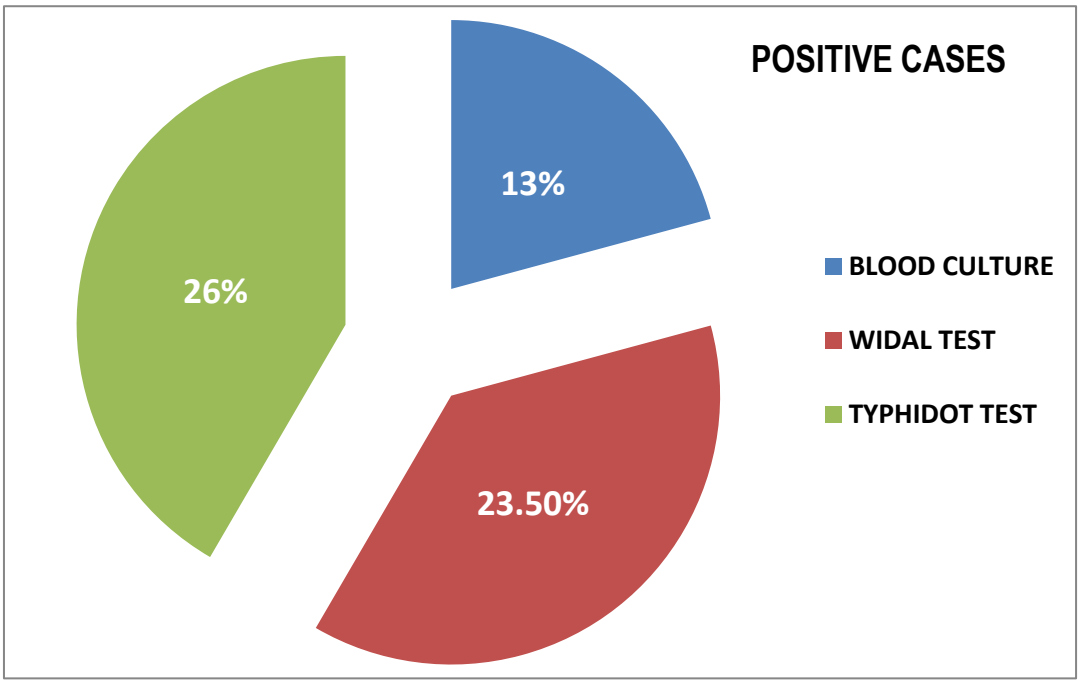

Fig 1: Positive cases of Blood culture, Widal and Typhidot tests

RESULTS

Out of total 85 clinically diagnosed typhoid fever cases enrolled in the study, 11 cases (13%) were positive by blood culture, 20 cases (23.5%) by Widal test and 22 cases (26%) by Typhidot test. [Table-1, Fig-1]

Amongst 11 blood culture positive cases, only 06 cases were positive by Widal test & 05 cases were negative. Out of 20 cases positive by Widal test, only 06 cases were positive and 14 cases were negative by blood culture. Widal test has a sensitivity of

54%, specificity of 81%, positive predictive value of 30%, negative predictive value of 92% in comparison with blood culture results [Table-2, Fig-2]. Out of 85 cases, 22 were positive by Typhidot test. Out of 22 Typhidot positive cases, 10 cases were positive and 12 cases were negative by blood culture. Typhidot test has a sensitivity of 91%, specificity of 84%, positive predictive value of 45% and negative predictive value of 98% in comparison with blood culture results. Out of 11 blood culture positive cases, 10 cases were positive and only 01 case was negative by Typhidot test. [Table-3, Fig-3]

Table 2: Comparison of Widal test with blood culture

		Blood culture		
		Positive	**Negative**	**Total**
Widal test	**Positive**	06	14	20
	Negative	05	60	65
Total		11	74	85

Sensitivity- 54%, Specificity- 81%, PPV- 30%, NPV-92%

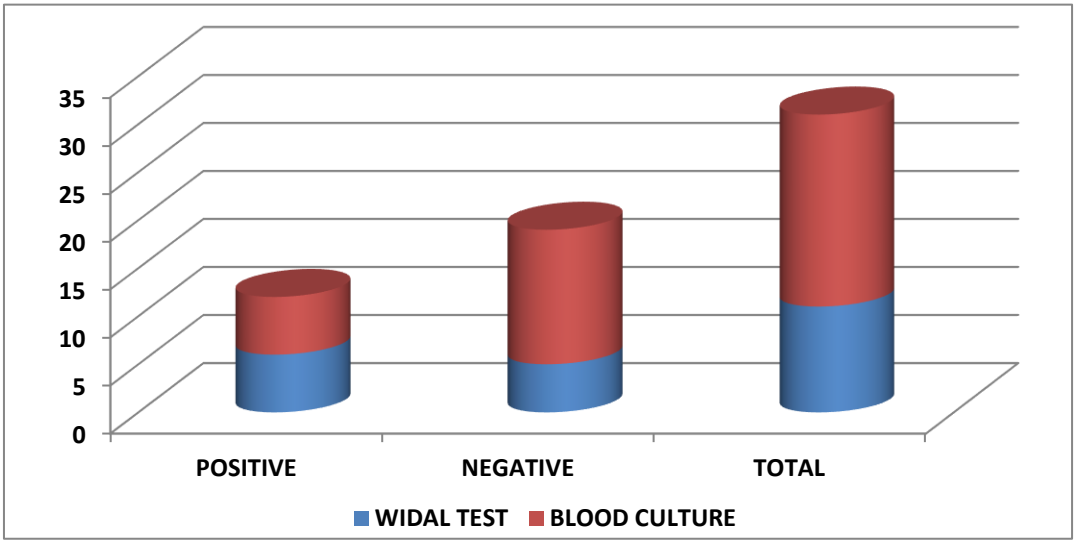

Fig 2: Comparison of Widal test with blood culture

Table 3: Comparison of Typhidot test with blood culture

		Blood culture		
		Positive	**Negative**	**Total**
Typhidot Test	**Positive**	10	12	22
	Negative	01	62	63
Total		11	74	85

Sensitivity- 91%, Specificity- 84%, PPV- 45%, NPV-98%

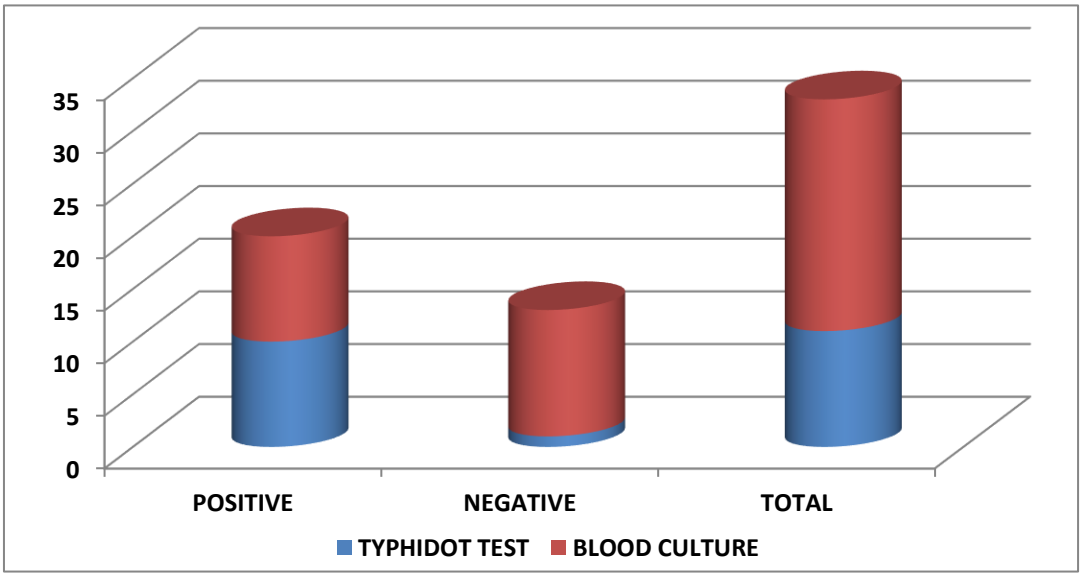

Fig 3: Comparison of Typhidot test with blood culture

DISCUSSION

Typhoid fever is a multi-systemic illness with a significant morbidity and mortality rate in developing countries[2]. Poor sanitation, low standard of living, overcrowding, lack of medical facilities, and indiscriminate use of antibiotics lead to endemicity and prevalence of typhoid fever[12,13]. Emergence of multidrug resistant strains of *Salmonella enterica* serotype *Typhi* has only added to the burden of the disease. Any delay in diagnosis and initiating of appropriate therapy only increases the risk of outcome[14].

Blood culture has been the gold standard for 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. Out of total 85 clinically diagnosed typhoid fever cases enrolled in the study, 11 cases were positive by blood culture, which reports sensitivity of 13%, while culture positivity in other studies have quoted sensitivity ranging from 8.9-43%[15-20]. The relative low rate of isolation from blood culture had been attributed to widespread and irrational use of antibiotics and due to difficulties in obtaining adequate amount of blood obtained for cultures especially among children.

Widal test has been in use for over a century in developing countries but its diagnostic significance and utility has been limited due to low sensitivity, specificity and positive predictive value, which changes with the geographical areas[2]. Decreased sensitivity is due to the long latent period after which the test may become positive, negative result in early infection or due to prior antibiotic therapy, while decreased specificity is attributed to cross reactivity with other Gram negative bacteria and non typhoidal salmonella, pre-existing base line antibodies in endemic areas, anamnestic reactions in unrelated infections and prior TAB or oral typhoid vaccination[21]. 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[22]. In the present study, Widal test came out to be positive in 20 (23.5%) cases amongst 85 clinically diagnosed typhoid fever patients. Widal test was positive in 06 of the 11 blood culture positive patients and 05 of blood culture negative patients. Thus, the test had a sensitivity of 54% and specificity of 81%, which is in agreement with other studies from endemic areas, where there may be high levels of specific and cross reacting antibodies[2,15,23]. Though higher sensitivity and specificity for Widal has been reported, its use in endemic areas should not be encouraged[24].

Typhidot is an inexpensive, easy to perform and reliable serodiagnostic test recently made available commercially and studied in many endemic areas with reports of having good sensitivity and specificity and is based on detection of antibodies which appear in detectable titers as early as second day of illness. The present study was done to evaluate Typhidot test for determining its significance and utility in patients of typhoid fever reporting to our hospital and it was observed that it had a sensitivity of 91% and specificity of 84%. This is higher than widal test and is comparable to other studies done in different parts of India and also with the studies conducted outside[2,14,20,26,28]. A similar study carried out in the southern part of India reported that Typhidot had a sensitivity of 100% and specificity of 80% and recommended its utility together with widal test in early diagnosis of typhoid fever[19]. In another study conducted on typhoid patients in Pakistan, Typhidot test had a comparable sensitivity of 94% and specificity of 77%, while widal test had a sensitivity and specificity of 63% and 83%[27]. Other studies conducted in Malaysia also showed that Typhidot is better and could replace the widal test when used together with blood culture[25,26].

CONCLUSION

Typhidot test is a rapid and highly sensitive and specific test in diagnosing typhoid fever as compared to Widal test and can be useful in early institution of therapy. It should be adopted in routine clinical settings for early detection of typhoid fever where limited advance diagnostic facilities are available.

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Source of Support: Nil.

Conflict of Interest: None Declared.

Cite this article as: Neha Garg. A Comparative Study of Widal Test and Typhidot in Rapid Diagnosis of Typhoid Fever. Int J Med Res Prof. 2017; 3(2):88-92. DOI:10.21276/ijmrp.2017.3.2.017