

Original Research Article


A comparative study of Widal test and Typhidot (IgM and IgG specific assay) test in the diagnosis of enteric fever

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Abstract

Background: Enteric fever (Typhoid fever) is a common systemic infectious disease worldwide, especially in developing countries like India and continues to be one of the leading causes of morbidity and mortality. It is caused by the bacterium *Salmonella typhi* or *Salmonella paratyphi* serotypes A, B and C. The clinical diagnosis of Enteric fever traditionally depends on Blood culture and Widal tests. However limitations such as longer time for Blood culture results and difficulties in the interpretation of Widal tests make them unpractical for screening patients in endemic regions and lead to misdiagnosis and missed diagnosis.

Aim and objectives: Purpose of the study was to compare the sensitivity and specificity of Widal test and Typhidot based IgM and IgG assay with the Blood culture (taken as gold standard) in the diagnosis of Enteric fever.

Materials and methods: This comparative study was done on 120 patients in the General Medicine Department of Indira Gandhi Institute of Medical Sciences, Patna. All patients above 11 years of age of either sex with acute febrile illness suspected to have Enteric fever were included in this study. Febrile patients with other diagnosis were excluded. Blood culture, Widal test, Typhidot (IgM and IgG) test and other routine investigations were performed in all patients. Typhidot tests and Widal tests were compared for sensitivity and specificity.

Results: Out of 120 clinically diagnosed cases of Enteric fever, 18(15%) patients were Blood culture positive for *Salmonella typhi*, 27(22.5%) patients were positive on Widal tests and 36(30%) were Typhidot positive. Out of 18 Blood culture positive patients for *Salmonella typhi*, 10 patients were

positive and 8 were negative on Widal testing. Out of 36 Typhidot positive patients 16 patients were positive and 20 were negative on Blood culture.

Conclusions: Traditionally Blood culture and Widal test are used in the diagnosis of Enteric fever. However Typhidot (IgM & IgG assay) tests are simple and rapid screening tests that simultaneously detect and differentiate between IgM and IgG antibody to Salmonella typhi and paratyphi produced in response to infection, thus aiding in determination of current or previous exposure. It offers the advantage of early and rapid diagnosis and helps in early institution of therapy. Preliminary data have shown sensitivity and specificity of 95% and 86% respectively of Typhidot tests.

Key words

Enteric fever, Widal test, Typhidot test, Blood culture, Salmonella typhi.

Introduction

Enteric fever (Typhoid fever) is a systemic disease mostly occurs in developing countries and continues to be a major public health problem [1, 2]. It is caused by dissemination of Salmonella typhi or Salmonella paratyphi serotypes A, B and C. Enteric fever is a major cause of morbidity and mortality worldwide, causing an estimated 27 million cases with 200000-600000 deaths annually [3]. The subcontinent India bears the brunt of the disease both in terms of absolute number of cases and drug resistant strains [3, 11]. The annual incidence is highest (>100 cases/100000 population) in south-central and southeast Asia; medium (10-100 cases/100000 population) in the rest of Asia, Africa, Latin America and Oceania (excluding Australia and New Zealand); and low in other parts of the world. In disease endemic area like India, the annual incidence of Enteric fever is about 1% [3]. The development of severe disease (occurs in \approx 10-15% of patients) depends on host factors (immunosuppression, antacid therapy, vaccination, previous exposure), strain virulence, inoculum size and choice of antibiotic therapy. Because the clinical presentation of Enteric fever is relatively non-specific, laboratory tests are important for accurate diagnosis and early treatment with suitable antibiotics for speedy recovery, prevention of emergence of complications, morbidity and deaths and also for the control of transmission [4]. The definitive diagnosis of Enteric fever requires the isolation of Salmonella typhi or paratyphi from blood, bone marrow, other sterile

sites, rose spots, stool or intestinal secretions which consumes a lot of time and energy [5]. Widal test has been used as a rapid serological test but it has moderate sensitivity and specificity and positive predictive value. However, it becomes positive only in the second week of illness [6], and paired sera are required for confirmation of the diagnosis [7]. Complexity and higher costs of other molecular test hinders its routine use [12-15]. Therefore to overcome the limitations of conventional methods a serological test (Typhidot test) which is a rapid inexpensive, early to perform, reliable with high sensitivity and specificity for diagnosis of Enteric fever and appropriate for outpatient settings has been introduced. Hence present study was done to compare the sensitivity and specificity of Widal test and Typhidot test in our region.

Materials and methods

This was a comparative cross sectional study done on 120 patients in the General Medicine Department of Indira Gandhi Institute of Medical Sciences, Patna. All patients above 11 years of age of either gender attending the Medicine Department with acute febrile illness and suspected to have Enteric fever were included in this study. Febrile patients with other diagnosis were excluded. Blood culture, Widal test, Typhidot (IgM and IgG) test and other routine investigation (CBC, urine analysis and culture, liver function tests, chest X-ray PA view) were performed in all patients. 15 ml of venous blood samples were collected from every patient.

Around 10 ml of blood sample was inoculated into Brain Heart Infusion biphasic medium and transported to the laboratory for culture (taken as gold standard). The remaining blood specimen was kept for serum separation in a sterile test tube that was used for Widal and Typhidot (IgM and IgG) test. Typhidot (CTK biotech) is a test consisting of a dot ELISA kit that detects IgM and IgG antibodies against the 50 KD outer membrane protein (OMP) of Salmonella typhi. The test becomes positive within 2-3 days of infection and gives result within 15 minutes.

Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of Typhidot and Widal test were estimated.

Sensitivity = $\frac{TP}{TP+FN} \times 100$, TP= True positive

Specificity = $\frac{TN}{FP+TN} \times 100$, TN= True negative

Positive predictive value (PPV) = $\frac{TP}{TP+FP} \times 100$, FP= False positive

Negative predictive value (NPV) = $\frac{TN}{TN+FN} \times 100$, FN= False negative

Accuracy = $\frac{TP+TN}{TP+TN+FP+FN} \times 100$

Results

Out of 120 clinically diagnosed cases of Enteric fever, 18(15%) patients were Blood culture positive for Salmonella typhi, 27(22.5%) patients were positive on Widal test and 36(30%) were Typhidot positive (**Table - 1, Figure – 1**). Out of 18 Blood culture positive patients, 10 patients were positive and 8 were negative on Widal testing. Out of 27 patients who were positive for Widal test, 10 patients were positive and 17 patients were negative to Blood culture (**Table – 2**). However, out of 36 Typhidot positive patients, 16 tests positive and 20 tests negative to Blood culture. Meanwhile out of 18 Blood culture positive patients, 16 were positive and 2 patients were negative on Typhidot tests (**Table – 3**). The sensitivity, specificity, positive and negative predictive value of Typhidot test were found to be 88.9%, 80.4%, 44.4% and 97.6% respectively. However sensitivity, specificity, positive and negative predictive value of Widal test were 55.6%, 83.3%, 37%, and 91.4% respectively. The diagnostic accuracy of Typhidot and Widal test were 81.7% and 79.2% respectively (**Table – 4**).

Table – 1: Comparison between Blood culture, Widal test and Typhidot test.

RESULT	BLOOD CULTURE	WIDAL TEST	TYPHIDOT TEST	BLOOD CULTURE
	NO. OF PATIENTS (%)	NO. OF PATIENTS (%)	NO. OF PATIENTS (%)	NO. OF PATIENTS (%)
POSITIVE	18 (15%)	27 (22.5%)	36 (30%)	18 (15%)
NEGATIVE	102 (85%)	93 (77.5%)	84 (70%)	102 (85%)
TOTAL	120 (100%)	120 (100%)	120 (100%)	120 (100%)

Table – 2: Comparison between Blood culture and widal test.

		BLOOD CULTURE		
		POSITIVE	NEGATIVE	TOTAL
WIDAL TEST	POSITIVE	10	17	27
	NEGATIVE	8	85	93
	TOTAL	18	102	120

Figure - 1: Positive cases on Blood culture, Widal test and Typhidot test.

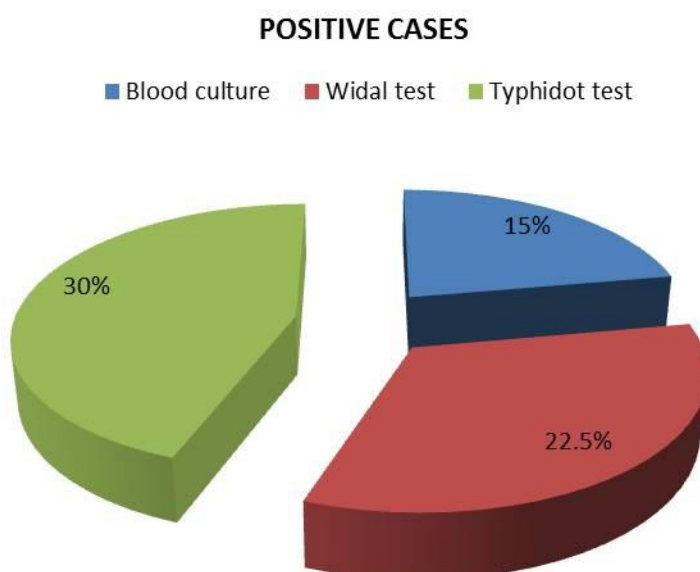


Table – 3: Comparison between Blood culture and Typhidot test.

		BLOOD CULTURE		
		POSITIVE	NEGATIVE	TOTAL
TYPHIDOT TEST	POSITIVE	16	20	36
	NEGATIVE	2	82	84
	TOTAL	18	102	120

Table – 4: Observation of outcome of Typhidot test and Widal test.

TEST	SENSITIVITY %	SPECIFICITY %	PPV%	NPV%	DIAGNOSTIC ACCURACY
TYPHIDOT	88.9	80.4	44.4	97.6	81.7%
WIDAL	55.6	83.3	37	91.4	79.2%

PPV: Positive predictive value, NPV: Negative predictive value

Enteric fever results in significant amount of morbidity, mortality and loss or absence from work hours in developing countries. Low standard of living, poor sanitation and hygiene, overcrowding and injudicious use of antibiotics lead to endemicity of Enteric fever and emergence of multi-resistant strains of *Salmonella typhi* in developing countries [1, 2]. For diagnosis of Enteric fever Blood culture remains the gold standard but its utility in early and rapid diagnosis is limited in early phase of the disease thereby making the isolation of

Salmonella typhi and paratyphi troublesome. Widal test has been used for diagnosis of Enteric fever since many decades but its low sensitivity, specificity, positive predictive value and sharing of O and H antigens by other *Salmonella* serotypes and other Enterobacteriaceae makes the role of this test more controversial [8, 9]. Typhidot test is a new, reliable, cost effective, rapid serological test for the qualitative detection and differentiation of IgM and IgG anti *Salmonella typhi* and paratyphi in human serum or plasma. Preliminary data have shown

sensitivity and specificity of 95% and 86% respectively [10].

Conclusion

Typhidot test is simple, easy to perform, more reliable, rapid screening test having high sensitivity and specificity as compared to Widal test in diagnosing Enteric fever. Typhidot test becomes positive within 2-3 days of infection and gives result within 15 minutes which allows medical professional to take immediate action and early institution of therapy. So Typhidot test seems to be a practical alternative to Widal test in early diagnosis and early starting of antibiotics and helps to lessen the brunt of the disease in developing countries like India.

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