

Value of Widal Test in the Diagnosis of Typhoid Fever

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Abstract

Typhoid Fever occurs worldwide primarily in developing nations where sanitary conditions are poor. The absence of specific symptoms and signs makes the clinical diagnosis difficult. Definitive diagnosis requires the isolation of *S. typhi* from blood or other body fluid. But in developing countries culture facilities often not available & diagnosis rely upon clinical features and the detection of antibodies by the Widal test. Numerous studies however have cast serious doubts on the value of the test. The aim of the study was to reassess the utility of a single Widal test in the diagnosis of typhoid fever. The descriptive study was carried out on 100 adult patients with suspected cases of typhoid fever, in the Department of Medicine, Chittagong Medical College Hospital for a period of one year from January to December 2009. Blood samples were collected to perform culture and Widal test. TO titre $\geq 1:160$ were considered as significant. AO or BO $\geq 1:160$ was also considered as significant. The results showed 24 among 100 clinically suspected typhoid fever cases yielded growth of *S. typhi*. Widal test was found significant in 20(83.33%) out of 24 cultured confirmed cases. Results revealed significant difference in Widal test results between culture positive and negative cases, X^2 value 5.601, P value 0.018(<0.05). The study concluded that use of Widal test may be justified in second week of illness as a suggestive test for clinical diagnosis or in patients who have clinical typhoid fever but are culture negative.

Keywords: Value, Widal test, Typhoid fever

Introduction

Typhoid Fever also known as Enteric Fever is a fatal multisystem illness caused primarily by *salmonella typhi*. The variable manifestations of typhoid fever make this disease a true diagnostic challenge. The classical presentation includes, fever, malaise, diffuse abdominal pain & constipation. Untreated typhoid fever is an exhausting illness that may progress to delirium, intestinal hemorrhage, bowel perforation & even death. Survivors may be left with long or permanent neuropsychiatric complications¹. Typhoid Fever occurs worldwide primarily in developing nations where sanitary conditions are poor, poor standard of personal hygiene and frequent contamination of food¹. It is sporadic disease in developed countries that occurs mainly in returning travelers, with occasional point-source epidemics². Delay in diagnosis, emergence of resistance strain, the lack of availability of safe, effective and cheap vaccine is contributing factors. Typhoid fever is endemic in Asia, Africa, Latin America, and the Caribbean & Oceania¹. *S. typhi* has been a major human pathogen for thousands of years, thriving in conditions of poor sanitation, crowding & social chaos. It may have responsible for the Great Plague of Athens at the end of the Peloponnesian War. The name *S. typhi* is derived from the ancient Greek "typhos" an ethereal smoke or cloud that was believed to cause disease & madness. In the advanced stage of typhoid fever, the patient's level of consciousness is truly clouded. Although antibiotics have markedly reduced the frequency of typhoid fever in the developed world, it remains endemic in developing countries¹. In view of the doubt expressed on the value of the Widal test in different studies^{2,3,7} due to above mentioned causes; we thought it worthwhile to reassess the utility of a single Widal test in the diagnosis of typhoid fever.

Materials and Methods

This descriptive study was carried out for a period of one year from January 2009 to December 2009, in the Department of Medicine, Chittagong Medical College and Hospital, Chittagong Bangladesh. The study place is a 1000 bed teaching and referral hospital with more than 10 million populations in its catchment area. Total one hundred patient of clinically suspected Typhoid fever were selected considering the inclusion criteria like

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1. Clinically diagnosed case of Typhoid fever based on insidious onset of fever above 38° C (100.4° F) for > 7 days and < 14 days plus two or more of the following in history or physical examinations -Frontal headache, Toxic look, Constipation, Diarrhea, Coated tongue, Diffuse abdominal tenderness, Relative bradycardia, Splenomegaly or hepatomegaly, Rose spot.

2. Age: 18 years to 60 years, both male & female. And Exclusion Criteria like Other causes of fever like Malaria and other organ specific infections with localizing sign and symptoms like UTI and RTI etc.

Those who did not agree with written informed consent to participate in the study.

Semi-purposive sampling technique was followed in this study.

Results

We could enroll 100 patients of clinically diagnosed Typhoid fever over the study period. Results obtained as baseline characteristics of the subjects, different clinical and laboratory parameters are shown in tabulated form and in diagram. Statistical analysis was done to see the significant difference of Widal test results between blood culture positive and blood culture negative cases. The results obtained were compared and analyzed to observe statistical significance.

Blood culture results

Blood culture was performed among study subjects to see the culture positivity and establish the diagnosis of typhoid fever in clinically suspected individuals. The results shown in the following (figure-I)

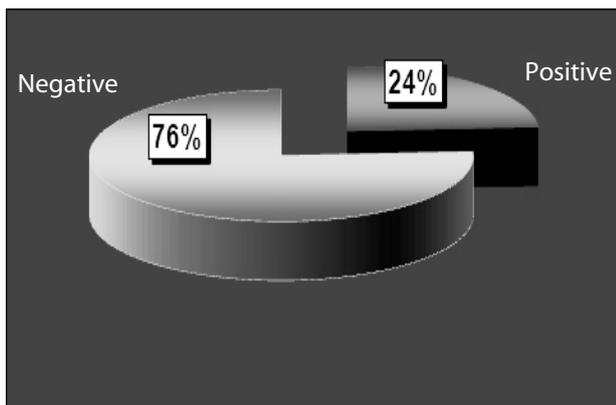


Figure- I: Distribution of blood culture results among the study subjects (n=100)

Figure I shows the distribution of blood culture results among the study subjects. Among clinically suspected Typhoid fever cases, blood culture for *S Typhi* was found positive in one quarter of subjects but rest of the subject did not show growth of *Salmonella* in blood culture.

Widal test results among study subjects

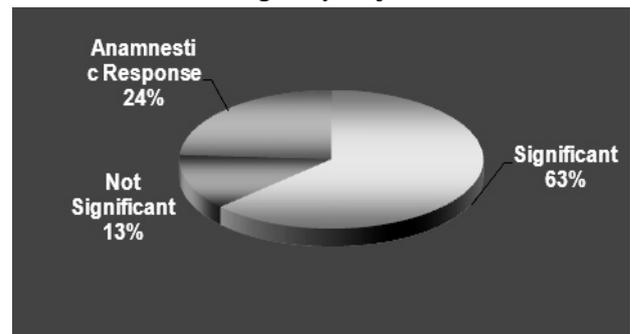


Figure- II (a): Distribution of Widal test result among study subjects (n=100)

Figure II (a) shows the distribution of Widal test results among study subjects. The results showed that Widal test was found significant in majority (2/3rd) of the subjects but rest of the cases did not show any significant rise of titre. Widal test was also performed in blood cultured confirmed typhoid cases. The results showed in the following figure.

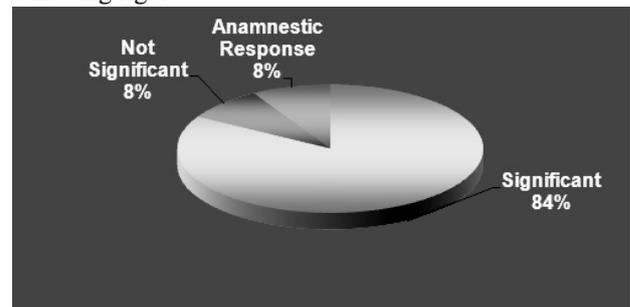


Figure-II (b): Distribution of Widal test results among blood culture positive cases (n=24)

Figure II (b) shows the distribution of Widal test results among blood culture positive cases. Results revealed that Widal test was found significant in most of the blood culture positive cases but few patients with blood culture positive did not show any significant titre.

Distribution of Widal agglutination titre among study subjects

Table I shows the distribution of TO and TH titre ($\geq 1:160$) status in blood culture confirmed typhoid fever cases. The results revealed that TO ($\geq 1:160$) was found significant in majority of blood culture positive Typhoid fever cases. Results showed that both the titre was raised though TO titre raises slightly higher than the TH titre.

Table - I: Distribution of TO and TH ($\geq 1:160$) status among the blood culture positive subjects (n = 24)

TITRE	<1:160	$\geq 1:160$	TOTAL
TO	08(33.3)	16 (66.6)	24
TH	10 (41.6)	14(58.3)	24

Figures in parentheses indicate percentages

Table II shows the significant AO titre (≥ 160) in study subjects, both cultures positive and culture negative cases. Result revealed that AO titre was found significant more in blood culture positive cases. No significant BO titre was found in study subjects.

Table- II: Distribution of AO status among the study subjects (n = 100)

BLOOD CULTURE	≥ 160	< 160	TOTAL
Positive	4(16.6)	20(83.3)	24
Negative	8(10.5)	68(89.4)	76
N	12	88	100

Figures in parentheses indicate percentages

Widal test result in blood culture positive and culture negative Typhoid fever cases.

Table III Shows the Widal test result in blood culture positive and culture negative Typhoid fever cases. Results revealed that there is difference in Widal test results between blood culture positive and blood culture negative cases. The difference is statistically significant (X^2 value = 5.601, df = 1, P value = < 0.05). So the result confirmed that Widal test is found significant in most of the blood culture positive Typhoid fever cases.

Table -III: Widal test results in culture positive and culture negative Typhoid cases (n = 100)

		BLOOD CULTURE		TOTAL
		Positive	Negative	
WIDAL TEST	Significant	20 (83.3)	43 (56.6)	63 (63.0)
	Not Significant	02 (08.0)	11 (14.4)	13 (13.0)
	Anamnestic Response	02 (08.0)	22 (28.9)	24 (24.0)
Total		24(100.00)	76(100.00)	100(100.00)

Figures in parentheses indicate percentages.

Chi-square test statistics: $X^2 = 5.601$; df = 1; P = 0.018; Significant (< 0.05).

Discussion

A simple Widal test in agglutination titre of TO $\geq 1:160$ were observed in 2/3rd of cases of culture positive and culture negative patients with strong clinical suspicion of Typhoid fever. The test was found significant in more than 3/4th of culture-positive typhoid fever cases which is comparable to other studies. Some studies found Widal test significant in more than 90% of blood cultured confirmed Typhoid fever cases⁸. In our study it was found that at a titre more than or equal to 1:160, the positivity of the 'TO' titre (66.6%) was greater than that of the 'TH' titre (56.6%). Hence, the 'TO' titre may be considered to be of greater diagnostic significance. Similar observations are made by Kulkarni *et al.* & Willke^{9,10}. AO (*S. paratyphi A*) was found

significant (titre $\geq 1:160$) in 16% of blood culture positive typhoid fever cases which is similar to other studies which was around 20% in different studies, but it was 40% in other study⁴. No significant elevation of BO titre was found in our study. Some studies also reported significant elevation of BO titre ($\geq 1:160$) in 2 to 3% cases⁵.

In the present study blood culture was found positive in one quarter of cases with the clinical diagnosis of typhoid fever which was similar to other study⁶. In other studies however with varying clinical manifestation, *S. typhi* has been isolated from 40 to 60 % cases. This difference could be due to unknown reasons as found in other studies, also have been contributed by prior antibiotic use and also amount of blood taken for culture. Present study revealed that some patients of suspected typhoid fever with positive blood culture had no significant elevation of titres of O or H antibodies. Although these patients may have had antibodies at a lower titre, they may have a negative Widal test throughout the course of their illness. This lack of antibody response among patients with blood culture-positive typhoid fever may be attributed to undefined host or bacterial factors or prior antibiotic treatment or late appearance of antibody titres⁸. In our study we had some limitations like we had no sufficient data about how many patients received prior antibiotic and also blood culture was performed in the 2nd week of the illness which decreased the rate of growth of salmonella in culture due to prior antibiotic use. We had no control group, so risk factors for negative blood culture or insignificant Widal test could not be evaluated and sensitivity and specificity of the test could not be done. We could not confirm bacteriologically or serologically (four fold rise of titre) of Typhoid fever in 76 percent cases. The study concluded that Widal test result is positive in significant titre in most cases of blood culture positive Typhoid fever cases and use of Widal test may be justified in the second week of illness as a suggestive test for clinical diagnosis of typhoid fever or in patients who have clinical typhoid fever but are culture negative or in regions where culture facilities are not available. Observing the findings of the present study following recommendations is put forward for consideration of future researchers as well as relevant authority.

Further study with larger sample size, antibiotic free samples and case control study is needed to see the significance of Widal test in clinically suspected enteric fever.

To establish the role of Widal test in enteric fever needs information on sensitivity and specificity in laboratory confirmed typhoid fever cases.

References

1. Brusck JL, Garvey T, Corales R, Schmitt SK. Typhoid Fever: Overview-eMedicine Infectious Diseases. 2008.
2. Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. Typhoid Fever: Review Article. The New Engl J Med. 2002; 34:1770-1782.
3. Olopoenia, LA and King AL. (Widal Agglutination test-100 years later: still plagued by controversy. Postgrad Med J. 2000;76:80-84.

4. Jog S, Soman R, Singhal T, Rodrigues C, Mehta A, Dastur FD. Enteric fever in Mumbai- Clinical profile, sensitivity patterns and response to antimicrobials. *J Assoc Physicians India*. 2008;56:237-240.
5. Kabir S, Azahar MA, Ekram S, Islam QT, Ahmed I. Current clinical profile of Enteric fever in a teaching Hospital. *TAJ, RMC, Rajshahi*. 2002;15(2):81-83.
6. Abuzejo PE, Capending MR, Lupisan SP, Arcay J, Sombrero LT, Ruutu P, et al. Blood culture confirmed typhoid fever in a provincial hospital in Philippines. *Southeast Asian J Trop Med Public health*. 2001;32(3):531-6.
7. Itah AY, Akpan CJ. Correlation studies on Widal agglutination reaction and diagnosis of typhoid fever. Department of Microbiology university of Uyo, Akwa Ibom state, Nigeria. 2004;35(1):88-91.
8. Parry CM, Hoa NT, Diep TS et al. Value of a single Widal test in diagnosis of typhoid fever in Vietnam. *J Clin Microbiol*. 1999;37:2882-86.
9. Willke A, Ergonul O, Bayar B. Widal test in the diagnosis of Typhoid fever in Turkey. 2002;19:938-941.
10. Kulkarni ML, Rego SJ. Value of single Widal test in the Diagnosis of Typhoid Fever. *J.J.M medical College, Davangree-Karnataka*. 1994.
11. Mahmud AK, Chowdhury AJ, Sarkar ZM, Miah RA, Saleh AA, Mandal RM, et al. Typhoid Fever. *Mymensing Med J*. 2008;17(2):236-44.
12. Aftab R, Khurshid R. Widal agglutination titre: A rapid serological diagnosis of typhoid fever in developing countries. *Pak J physiol*. 2009;5(1):65-67.
13. Anwar PM, Rasool S, Sharif MK. Typhidot test and blood culture for the diagnosis of typhoid fever. *Professional Med J*. 2002;99(2):139-44.
14. Bhutta ZA. Current concepts in the diagnosis and treatment of typhoid fever. *B Med J*. 2006;333:78-82.
15. Chart H, Cheasty T, Pinna ED, Siorvens L, Wain J, Alam D, et al. Serodiagnosis of Salmonella enterica serovar Typhi and salmonella enterica serovars paratyphi A, B and C human infections. *J Med microbial*. 2007;56:1161-1166.
16. Crump JA, Youssef FG, Luby SP, Wasty MO, Rangel JM, Taalat M, et al. Estimating the incidence of typhoid fever and other febrile illnesses in developing countries. *Emerging infectious diseases*. 2003;9(5):539-544.
17. Hernaningsih Y, Betty AT, Aryati. Diagnostic value of slide assay using one phage type local antigen compared with four phage types in typhoid fever patients in Surabaya. *Folia Medica Indonesiana*. 2010;46(2):95-101.
18. Devrim I, Erguany K, Kara A, Tezer H, Cengiz AB, Ceyhan M, et al. The comparison of culture, Widal agglutination test and polymerase chain reaction as a diagnostic tool in typhoid fever. *Cent Euro J Med*. 2008; 3(4):470-474.
19. Dimitriov T, Udo EE, Albaksami O, Shehab SA, Kilani A, Shehab M, et al. Clinical and microbiological investigations of typhoid fever in an infectious disease hospital in Kuwait. *J Med Microbiol*. 2007;56:538-544.
20. Dong B, Galido CM, Shin E, Acosta CJ et al. Optimizing typhoid fever case definitions by combining serological tests in a large population study in Hechi City, China. *Epid & infection*. 2007;135:1014-1020.
21. Gopalkrishnan V, Sekhar WY, Soo EH, Vinsent RA, Devi S. Typhoid fever in Kuala Lumpur and a comparative evaluation of two commercial diagnostic kits for the detection of antibodies to salmonella typhi. *Singapore Med J*. 2002;43(7):354-358.
22. Hosolgu S, Bosnak V, Akalin S, Geyik MF, Ayaz C. Evaluating of false negativity of the Widal test among culture proven typhoid fever cases. *The J of Infect in Developing Countries*. 2008;2(6):475-478.
23. House D, Wain J, Ho VA, Diep TS, Chinh NT, Bay PV, et al. Serology of Typhoid fever in an area of endemicity and its relevance to diagnosis. *J Clin Microbiol*. 2001;39:1002-7.
24. Khoharo HK, Ansari S, Qureshi F. Evaluating single acute-phase Widal test for the diagnosis of typhoid fever. *Medical Channel*. 2010;16(1):2-43.
25. Ibekwe AC, Okonoko IO, Onunkwo AU, Donbraye E, Babalola ET and Onoja BA. Baseline salmonella agglutinin titers in apparently healthy freshmen in Awka, south eastern Nigeria. *Sci Res and Essay*. 2008;3(9):425-435.
26. Jamil B, Lashari I, Bhatti S, Hasan RS. Enteric fever in adult patients: Clinical features, outcome & antibiotic susceptibility patterns. *Infectious dis J of Pakistan*. 2003; 68-71.
27. John LB, Thomas G, Roberto C, Steven S. Typhoid Fever Overview. Department of Medicine and Infectious Disease Service, Cambridge Health Alliance. 2008.
28. Mathura KC, Gurubacharya DL, Shrestha A, Pant S, Basnet P, Karki DB. Clinical profile of typhoid fever. *Kathmandu University Med J*. 2003;1(2):135-137.
29. Mohanty SK, Ramana KV. Single and unpaired sera tube Widal agglutination test in enteric fever. *Saudi J Gastroenterol*. 2007;13:213.
30. Neopane A, Poudel M, Pradhan B, Dhakal R, Karki DB. Enteric Fever: Diagnostic Value of Clinical Features. *Kathmandu Univ Med J (KUMJ)*. 2006;4(3):307-15.
31. Ochai RL, Acosta CJ, Danovaro-Holliday MC, Baiging D, Bhattacharia SK, Agtini MD, et al. A study of typhoid fever in five Asian countries: Disease burden and implications for controls. *Bulletin of WHO*. 2008; 86(4):241-320.

32. Omuse G, Kohli R, Revothi G. Diagnostic utility of single Widal test in diagnosis of typhoid fever at Aga Khan Univ Hospital, Nairobi, Kenya. *Trop Doct.* 2010; 40(1):43-44.
33. Onyekwere CA. Typhoid fever: Misdiagnosis or Over diagnosis. *Nigerian Medical Practitioner.* 2007;51(4):76-79.
34. Ruhi A and Rukhsana K. Widal agglutination titre: A rapid serological diagnosis of typhoid fever in developing countries. *Pak J Physiol.* 2009;5(1):5-67.
35. Youssef FG, Parker TM and Daba as (US Naval Res Unit Egypt). A comparative study of blood culture and antibody response with the duration of illness in diagnosis of typhoid fever. *Int J of Mol Med and Adv Sci.* 2007; 3(1):1-5.
36. Vollaard AM, Ali S, Van Asten HAGH, Widjaja SC, Van Dissel JT. Risk factors for typhoid and paratyphoid fever in Jakarta, Indonesia. *JAMA.* 2004;291(21):2607-2615.