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Comparative clinical utility of Widal and Typhidot in the diagnosis of typhoid fever

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Abstract

Timely and accurate diagnosis of typhoid fever is considered as the key factor to stop its alarming morbidity and mortality rates in our country. Typhoid fever is usually diagnosed by Widal and Typhidot, while from comparative diagnostic point of view blood culture is considered as gold standard of diagnosis. Current Study correlates Widal and Typhidot results with blood culture to evaluate reliability, sensitivity and specificity of these techniques. Blood samples from 91 patients were collected by aseptic technique and blood culture, Typhidot and Widal tests were performed for detection of *Salmonella typhi*. In group I about 76 patients were suspected for typhoid, while in group II, 15 controls (non-typhoidal) patients were included. Out of 76 samples 44 (58%) were positive for blood culture, 51 (67%) positive for Typhidot and 33 (43%) were Widal positive. From group II all 15 cases showed no growth on blood culture. About 2 (13%) cases were Typhidot reactive while only 4 (27%) cases were Widal positive. Amongst 44 culture positive cases from group I, 41 patients were positive for Typhidot and 31 were reactive against Widal, showing sensitivity of 93 % and specificity of 87% while, Widal sensitivity was 70% and specificity was 73%. The results of this study showed that blood culture is a standard diagnostic test for early diagnosis of *Salmonella typhi*. Typhidot is still sensitive, specific, safe and simple method for the diagnosis of typhoid fever in the underdeveloped areas of the world.

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Introduction

Typhoid fever continues to be endemic public health problem in the resource limited countries, where pure water supply is limited and it has been eradicated from developed countries of the world (Ananthanarayan *et al.,* 2013). Typhoid fever is commonly caused by *Salmonella typhi* a non-spore former, gram-negative rods and facultative anaerobe (Grimont *et al.,* 2000), transmitted by contaminated water or food (Siddiqui *et al.,* 2006). Men are well known Reservoir of Salmonella typhi and remain infectious as long *as Salmonella* is found in urine or stool (Park k *et al.,* 2005*).* After incubation period of 1-2 weeks Salmonella *typhi* enters in small intestine and attaches with epithelium to penetrate in sub-mucosa where it is engulfed by monocytes. It multiplies in monocytes and prevents itself from intracellular killing of monocytes. Finally it reaches in blood stream and causes primary bacteraemia. The bacteria then infect the gallbladder via either bacteraemia or direct extension of infected bile. The result is that the organism re-enters the gastro-intestinal tract in the bile and reinfects peyer patches and causes inflammation (Rao, 2009). The clinical pathogenicity of disease may vary from mild stage to fatal due to inappropriate diagnosis, treatment and preventive measures (Ananthanarayan *et al.,* 2013).

Typhoid fever is still most common health problem in sub-Saharan regions of Africa and Indian subcont-inent where hygienic conditions are not suitable (Bhan *et al*., 2005; Crump *et al*., 2004; Karkey *et al*., 2008; Parry *et al*., 2002)**.** While multidrug resistance (MDR) in India, leading to further complications (Dutta S *et al.,* 2006). Worldwide typhoid reported results showed 200,000 deaths annually (Karkey *et al*., 2008). It is also reported in 2003 that among water borne diseases *S. typhi* is a major death causing infectious disease in Pakistan (Shah *et al*., 2003).

Laboratory tests are necessary tools for early diagnosis and accurate treatment with suitable antibiotics to overcome further complications and speedy recovery due to non-specific sign and symptoms of typhoid fever (Dutta S *et al.,* 2006).

As 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 (Ananthanarayan *et al.,* 2013). Serological techniques including Widal, immunoch-romatographic test (ICT) and semi-quantitative tube agglutination test are considered as quick and simplest methods for the diagnosis of *Salmonella* (Aziah *et al*., 2007)**.**

Widal is still commonly used in endemic areas of developing countries (Pang and Puthucheary 1983). And performed as rapid diagnostic test but it is a test with medial sensitivity and specificity (Postoor R *et al.,* 2008). The immunechromatographic test (ICT) Typhidot is considered as a confirmatory test which detects the presence of specific antibodies IgG and IgM in presence of specific membrane protein coated antigens (Ismail, 1991).

Pakistan is the sixth populous country in the world with minor access to expensive advance diagnostic facilities like blood culture in rural areas. In our country widal and typhidot are routinely performed for typhoid fever diagnosis in primary healthcare units. Widal test has been used frequently in our region but with intermediate sensitivity and specificity. While Typhidot is considered as specific, sensitive and reliable test. But, its reliability with respect of sensitivity and specificity as compared to widal is not been so far evaluated in our region. While some studies conducted in India and other Asian countries have reported encouraging results. This study was undertaken to evaluate comparative utility of Typhidot and Widal test in term of specificity and sensitivity.

Materials and methods

Study area and duration

This comparative epidemiological study was conducted at Department of Medical lab Technology, Central Research Laboratory, University of Haripur. Samples were collected at three pathology laboratories from different private Hospitals of Taxila city, during Jan, 2015 to Jun, 2015.

Samples Collection and transportation

Approximately 91 clinically diagnosed typhoid fevers individual as well as control individual samples were collected at pathology laboratories of Ali Family Clinic, Care Clinical Laboratories and Ahmad Clinical Lab Taxila, Pakistan. Both indoor and outdoor patient were considered in the study.

At the time of specimen collection proper consent was taken from each patient or guardian in case of children. While previously vaccinated individual against typhoid fever were excluded. 8 ml of blood was taken 5ml for blood culture and 3ml for serology. In order to minimize degradation of serum antibodies, the samples was kept at -20°C and transported to lab within 2-3 hour for further analysis.

Culture and Subculture medium

Blood was cultured in blood culture medium (brain heart infusion) and incubated at 37°C for seven days. It was subcultured on both blood and Mac Conkey agar after twenty four hours till the 7th day. The growth of *Salmonella* isolates was confirmed by as per standard protocol (API 20E Biomerieux).

Widal and Typhidot test

Patients with positive blood culture were further tested with Typhidot according to the instructions provided by manufacturer (Sherwal BL *et al*., 2004;

Olsen SJ *et al*., 2004). It is qualitative antibody detection test that contains antigen coated strips for detection of IgM and IgG antibodies to *Salmonella typhi*. Widal test was performed by using tube agglutination by antigen O, H and Vi particulate antigen with serum antibodies (Bio Rad).

Interpretation

Widal was considered positive when a titre of ≥ 1: 160 was observed (Old DC *et al.,* 1996) according to routine laboratory procedures.

Results and discussion

Blood culture was positive in 44 out of 76 susceptible cases for typhoid fever from group I. whereas among 15 group II (non-typhoidal cases) shown no growth even by one case on blood culture. Typhidot was positive in 51 out of 76 patients among group I unlike Widal which was reactive among 33 (43%) patients as shown (table A). Among 15 group II control patients 4 (27%) were Widal positive and only 2 (13%) were reactive against typhidot (table 1).

Table 1. Comparison of blood culture, Typhidot and Widal test.

Test	Culture proven typhoid cases Group I (sensitivity) n = 76	Non-typhoidal cases Group II (sensitivity) n = 15
Blood culture	44 (58%)	0
Typhidot	51 (67 %)	2 (13%)
Widal	33 (43 %)	4 (27%)

On comparative diagnostic point of view typhidot, widal and blood culture, typhidot had sensitivity of 67% and specificity of 87%, while widal showed sensitivity of 43% and specificity of 73%. Unlike typhidot and widal blood culture results showed sensitivity of 58% with 100% specificity.

Amongst 44 culture proven cases from group I, 41 were typhidot reactive with sensitivity of 93%, specificity of 87% with positive predictive value of 93%. Whereas Widal test was positive in 31 cases with sensitivity of 70.45%, specificity of 73% and 70.45% of positive predictive value respectively.

Typhoid fever a multi-systemic infectious disease still (21stcentury) considered as endemic public health problem in developing countries caused by *Salmonella typhi* (Lin FY *et al.,* 2000; Otegbayo JA *et al*., 2003). Anotheremerging problem in developing countries is use of empiric antibiotics among suspected typhoid fever patients (Glory T G; Khan M *et al.,* 1998). Which ultimately leads towards increased antibiotics resistance among common pathogens. It is necessary to use a simple, clinical and inexpensive laboratory tests for decision making therapy.

Current study also highlights disadvantages of delayed diagnosis of typhoid fever leading towards sever complications in developing countries, where patients persist symptoms as long as for two weeks prior to admission in hospital (Wongsawat J *et al.*, 2002; Otegbayo J A *et al.*, 2003; Tohme A *et al.*, 2002).

This study assures reliability of typhidot test with encouraging results in terms of sensitivity and specificity, recorded as 93% and 87% respectively. Current study results are comparable with studies conducted in 2002, 2004 and 2010 among different parts of India with sensitivity of 100%, 92.6% and 92% respectively (Jesudasson M *et al.*, 2002; Sherwal BL *et al.*, 2004; Narayanappa D *et al.*, 2010). Similarly two different studies conducted in 1999 and 2002in Malaysia reported that typhidot had sensitivity of 90.3% and 98% with specificity of 91.9% and 76.6% respectively (Choo KE *et al.*, 1999; Gopalakrishan V *et al.*, 2002). Another study conducted in Pakistan reported sensitivity of typhidot 94 % and specificity of 77%; while Widal test was reported asmore specific (83%) and least (63%) sensitive (Butta ZA *et al.*, 1999). Our results also showed that Widal test is still considered sensitive 70.45% and specific 73% (Table 2) where typhoid fever is endemic. Above mentioned studies confirmed that typhidot test in contrast to Widal is considered as simplest, sensitive and easy to use for diagnosis of typhoid fever.

Table 2. Comparison of Typhidot and Widal test in culture proven cases and non-typhoidal cases.

Test	Culture proven typhoid cases	Non-typhoidal cases
	N = 44 (sensitivity)	N = 15 (sensitivity)
Typhidot test	41 (93 %)	2 (13%)
Widal test	31 (70.45 %)	4 (27%)

Conclusion

Typhi dot testis still sensitive and specific for the diagnosis of typhoid fever, 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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