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 2:1:160 were considered as significant. AO or BO 2:1:160 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, X² 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 complications.1 Typhoid Fever occurs worldwide primarily in developing nations where sanitary conditions are poor, poor standard of personal hygiene and frequent contamination of food. It is sporadic disease in developed countries that occurs mainly in returning travelers, with occasional point-source epidemics. 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 & Oceania. 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 countries. In view of the doubt expressed on the value of the Widal test in different studies 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
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, Spleenomegaly 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 (≥1:160) status in blood culture confirmed typhoid fever cases. The results revealed that TO (≥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 (≥1:160) status among the blood culture positive subjects (n = 24)

<table>
<thead>
<tr>
<th>Titre</th>
<th>≥1:160</th>
<th>&gt;1:160</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>TO</td>
<td>16 (66.6)</td>
<td>8 (33.3)</td>
<td>24</td>
</tr>
<tr>
<td>TH</td>
<td>14 (58.3)</td>
<td>9 (37.5)</td>
<td>24</td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th>BLOOD CULTURE</th>
<th>≥100</th>
<th>&lt;100</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>4(16.6)</td>
<td>10(33.3)</td>
<td>24</td>
</tr>
<tr>
<td>Negative</td>
<td>8(10.5)</td>
<td>68(89.4)</td>
<td>76</td>
</tr>
<tr>
<td>N</td>
<td>12</td>
<td>88</td>
<td>100</td>
</tr>
</tbody>
</table>

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 (X² 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)

<table>
<thead>
<tr>
<th>BLOOD CULTURE</th>
<th>Positive</th>
<th>Negative</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant</td>
<td>2(8.3)</td>
<td>43(56.6)</td>
<td>65(63)</td>
</tr>
<tr>
<td>Not Significant</td>
<td>02(08.0)</td>
<td>11(14.4)</td>
<td>13(13.0)</td>
</tr>
<tr>
<td>Anamnestic Response</td>
<td>02(08.0)</td>
<td>22(28.9)</td>
<td>24(24.0)</td>
</tr>
<tr>
<td>Total</td>
<td>24(100.00)</td>
<td>76(100.00)</td>
<td>100(100.00)</td>
</tr>
</tbody>
</table>

Figures in parentheses indicate percentages.

Chi-square test statistics: X² = 5.601; df = 1; P = 0.018; Significant (< 0.05).

Discussion

A simple Widal test in agglutination titre of TO ≥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 cases. 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. & Willke9,10. AO (S. paratyphi A) was found significant(titre ≥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 (≥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 titre8. 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


