Original Research Article

Typhoid in pediatric age group in a rural tertiary care center: present scenario

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ABSTRACT

Typhoid fever is predominantly a disease of school age children and young adults. The present study was undertaken to study the incidence of typhoid fever in children in the age group of 0–15 years by various diagnostic methods and to determine the antibiotic susceptibility profile of the isolates. A total of 96 cases with clinically suspected typhoid fever were included in the study group. Blood culture and Widal test were done by standard methods. All S. typhi isolates were subjected to antibiotic susceptibility test using modified Kirby-Bauer disc diffusion method. Enterocheck WB test was done to detect IgM antibodies to S. typhi using the instruction of the manufacturer. Out of 96 clinically suspected children, blood culture was positive for Salmonella typhi in 11 (11.4%) cases and Enterocheck WB test was positive in 9 (9.37%) cases. Even if blood culture is a gold standard method for diagnosing the typhoid fever, we found encouraging results of Enterocheck WB test for detection of IgM antibodies in early phase of disease. We found all S. typhi isolates were sensitive to Ceftriaxone but increasing antibiotic resistance in surrounding is matter of concern.

Keywords
S. typhi, Blood culture, Typhoid fever, Widal test, Enterocheck WB test, Pediatric

Introduction

Typhoid fever is a still a serious disease, with mortality that ranges between 5% and 20%. It is a systemic infection caused by the bacterium, Salmonella enterica serotype typhi (S. typhi). This highly adapted, human specific pathogen has evolved remarkable mechanisms for its persistence in its host that help the organism to ensure its survival and transmission (Parry et al., 2008). The organism is transmitted by faeco-oral route; thus the disease is often associated with poor sanitation and hygiene. The socio-economic impact of the disease is huge, in developing countries like India. A limited study in an urban slum showed 1% of children up to 17 years of age suffer from typhoid fever every year. However it is reported to be milder in infants and young children. The condition is predominantly a disease of school age children and young adults. Typhoid fever cases are observed through-out the year. The peak incidence is reported during the period July-September, which coincides with the rainy season and an increase in fly population (Park, 2011).
Conventionally the diagnosis of typhoid fever is confirmed by blood culture, clot culture, stool culture and Widal test. Low rates of detection of typhoid in preschool children may be due to milder, atypical presentation and difficulties in collecting recommended quantity of blood for conventional diagnostic techniques (Sinha et al., 1995). Even under the best conditions, the organism may not be isolated from blood, especially due to antimicrobial treatment. Simpler methods for diagnosis of typhoid in developing countries would be very useful where the disease is endemic. Serologic tests based on antibody detection have been suggested as a rapid and easy alternative to culture for the diagnosis of typhoid. The most widely used serologic test is Widal test (Dutta et al., 2006). Encouraging results are given by some authors for use of rapid serological tests in diagnosing typhoid fever (Olsen et al., 2004; Anush et al., 2011; Kinikar et al., 2012).

Appropriate antibiotic therapy is essential to cure typhoid fever with minimal complications. The choice of drug and the duration of therapy depend upon several factors such as the clinical severity of the case, the patient’s condition, and drug resistance and more importantly the physician’s experience and available resources (Maripandi et al., 2010).

Result and Discussion

Out of 96 clinically suspected children there were 70 males and 26 females in age group ranging 0–15 yrs. (Fig. 1 and 2). Blood culture was positive for Salmonella typhi in 11 (11.4%) cases. Widal test was positive in 50 (52%) cases and Enterocheck WB test was positive in 9 (9.37%) cases (Table 1). Antibiotic susceptibility testing showed sensitivity to Ampicillin (54.5%), Chloramphenicol (54.5%), Cotrimoxazole (63.6%), Ciprofloxacin (72.7%), Ofloxacin (72.7%) (Table 2). All the S. typhi isolates were sensitive to Cefixime, Ceftriaxone and Cefaperazone.

Typhoid fever continues to be prevalent in several countries around world, mostly in those countries with inadequate sanitation and hygiene. In the present study, a total of
62 (64.8%) children belonged to the age group of 5–15 years, while 30 (31.2%) children belonged to the age group of 1–5 years, indicating involvement of school age children. Raman et al. (1994) in his study of typhoid fever, reported average age as 5.6 years and male to female ratio as 3:2. In an epidemiological study of typhoid in Karachi, Pakistan in 1998, the median age of afflicted patient was 5.8yrs old, with 71% of total subjects being under age of ten years (Luby et al., 1998). Sinha et al. (1999) challenged the common view that typhoid fever is a disorder of school age children and reported that it is a common and significant cause of morbidity between 1 and 5 years of age. However, shift in predominance of seropositivity in the early age group (>15≤30yr) from the pediatric age group (0≤15yr) was reported by Banerjee et al. (2014).

Male to female ratio was found to be 2.6:1 in our study which is higher, may be due to rural tendency of male dominancy. Gosai et al. (2000) in his study reported male to female ratio as 1.4:1 (88 males and 62 females). Blood culture positivity in our study was found to be 11.4%, as compared to few of Indian studies which have reported 16% and 5.3% respectively as mentioned by Beig et al. (2009) and Gosai et al. (2011). The studies conducted abroad in Ghana by Florian Marks et al. (2012) reported 2.5% culture positivity in children (0–15 years). There are considerable advantages of blood culture in diagnosing typhoid fever as they are 100% specific, but also provide antimicrobial sensitivity of the clinical isolate (Kundu et al., 2006). Widespread antibiotic availability and irrational prescription is another reason for the low sensitivity of blood culture. The blood culture positivity is maximum in first week of disease and there by gradually decreases (Bhutta, 2006).

Widal test has been widely used for the diagnosis of typhoid fever, simply owing to the fact that no other sero-diagnostic test of sufficient sensitivity and specificity along with cost effectiveness has been developed specially in typhoid endemic areas (Olopenia and King, 2000). We found 52.0% seropositivity of Widal test in suspected cases of typhoid undertaken in the present study. The seropositivity of Widal test was higher than blood culture, owing to many samples collected during the second and third week of the disease. Use of paired sera was not opted in the present study, as being the only tertiary care hospital and considering the type of rural population that we are catering to. Patients rarely return for outpatient follow up once treated hence obtaining a second sample in such clinical settings becomes difficult. Sensitivity of Widal test below the accepted optimal levels generally results from negativity in early infection, prior antibiotic therapy and failure to mount an immune response by certain individuals (Keddy et al., 2011; Olopenia and King, 2000).

In rural areas due to lack of health care facilities, the typhoid cases may go unnoticed and even the diagnosis may be delayed. In such cases, use of typhoid rapid antibody tests can play a significant role in a developing country like India. Several commercial rapid diagnostic tests namely Typhidot and Tubex have shown sensitivity and specificity of 70% and 80%, respectively in surveillance studies worldwide, apart from being costlier than the agglutination test (Ley et al., 2010). We used one of the rapid test (Enterocheck WB) to detect IgM antibodies specific to S. typhi which showed seropositivity as 9.37%. Madhu et al. (2014) reported higher seropositivity for the same test as 92% in under 15 yr children. Higher sensitivities for detection of IgM antibodies by ELISA and dipstick have been reported earlier.
**Table 1** Different test results done in study population

<table>
<thead>
<tr>
<th>Test (n=96)</th>
<th>Positive</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood culture</td>
<td>11</td>
<td>11.4</td>
</tr>
<tr>
<td>Widal test</td>
<td>50</td>
<td>52</td>
</tr>
<tr>
<td>Enterocheck WB</td>
<td>09</td>
<td>9.37</td>
</tr>
</tbody>
</table>

**Table 2** Antibiotic sensitivity pattern in *S. typhi* isolates

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Sensitivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>54.6</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>54.5</td>
</tr>
<tr>
<td>Co-trimaxazole</td>
<td>63.6</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>72.7</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>72.7</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>81.8</td>
</tr>
<tr>
<td>Nalidixic Acid</td>
<td>72.7</td>
</tr>
<tr>
<td>Cefixime</td>
<td>100</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>100</td>
</tr>
<tr>
<td>Cefoperazone</td>
<td>100</td>
</tr>
</tbody>
</table>

**Figure 1** Age wise distribution of study population
The emergence of multidrug resistant *Salmonella typhi* (MDRST) infection has posed many problems relating to diagnosis and therapy. Since 1990s *S. typhi* has developed resistance simultaneously to all the drugs used in first line of treatment (chloramphenicol, cotrimoxazole and ampicillin). Fluoroquinolones (Ciprofloxacin/Ofloxacin) showed 72.7% of sensitivity in our study. But in-vitro sensitivity of fluoroquinolones has showed clinical failures in real. Resistance of nalidixic acid could be a surrogate marker which predicts the fluoroquinolones failure (Kundu et al., 2006).

In our study all of *S. typhi* isolates were sensitive to III generation cephalosporins (Cefixime, Ceftriaxone and Cefoperazone). Higher cure rates are associated with the treatment of typhoid fever with third generation cephalosporins (Maripandi et al., 2010). But recently, High degree of susceptibility to Ampicillin and Co-trimozaxole has once again made us to think of their use in practice (Choudhary et al., 2013).

Interpretation and conclusion of this study is there is no challenge that blood culture is still a gold standard method, being 100% specific for diagnosing the typhoid fever with its antibiotic susceptibility advantage. We found that Enterocheck WB test for detection of IgM antibodies is equally capable to diagnose infection at earliest in children.

Due to difficulty in getting culture reports, patients have to wait for definitive therapy. This rapid test will be useful in places where culture facilities are not available. The test can be performed without formal training and in absence of specialized equipment. Hence, it will be useful as complementary test to blood culture and Widal test in diagnosis of typhoid fever. The Widal test with its limitations is still helpful in second and third week of disease. Though all *S. typhi* isolates were sensitive to cephalosporins, in our study, the emerging drug resistance cannot be overlooked.
Acknowledgement

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References


