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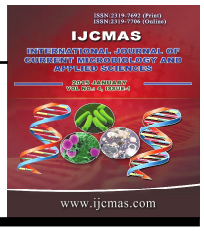

Original Research Article

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

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A B S T R A C T

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.

K e y w o r d s

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).

Materials and Methods

The study was conducted in Department of Microbiology, Rural Medical College, Loni (Maharashtra, India). The study included children from age group 0–15 years with fever for ≥four days with signs and symptoms which were suggestive of typhoid fever. An informed consent was taken from the patients before sample collection. The blood samples were collected for blood culture, Widal test and Enterocheck WB test. The blood culture was done by using brain heart infusion (BHI) broth and was incubated. Subsequent sub-cultures were made on Mac Conkey's agar and blood agar media after 24, 48 and 96 hours and final subculture made on seventh day. The growth of *S. typhi* was identified by the standard biochemical tests and it was confirmed by agglutination with Salmonella polyvalent 'O', 09 and H: d antisera. The Widal test was done by using the standard procedure (Collee *et al.,* 1996). The Widal test was confirmed by the tube agglutination method and it was considered as positive when a titer of equal to or more than 1:160 was observed. The Enterocheck WB test (manufactured by Zephyr Biochemicals) is a rapid, qualitative sandwich immunoassay for the detection of the IgM antibodies to *S. typhi* in human serum/plasma or whole blood specimens. It detects the presence of the IgM class of antibodies to a lipopolysaccharide (LPS) which is specific to *S. typhi* in the specimens.

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 1and 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 (88males 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

Test (n=96)	Positive	Percentage %
Blood culture	11	11.4
Widal test	50	52
Enterocheck WB	09	9.37

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

Antibiotic	Sensitivity (%)
Ampicillin	54.6
Chloramphenicol	54.5
Co-trimaxozole	63.6
Ciprofloxacin	72.7
Ofloxacin	72.7
Gentamicin	81.8
Nalidixic Acid	72.7
Cefixime	100
Ceftriaxone	100
Cefoperazone	100

Figure.1 Age wise distribution of study population

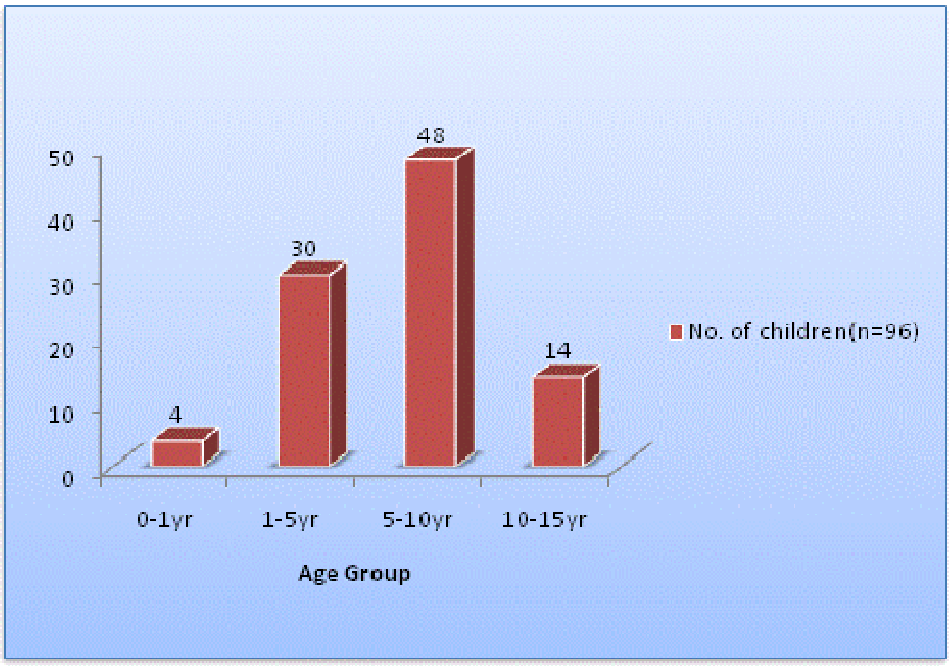
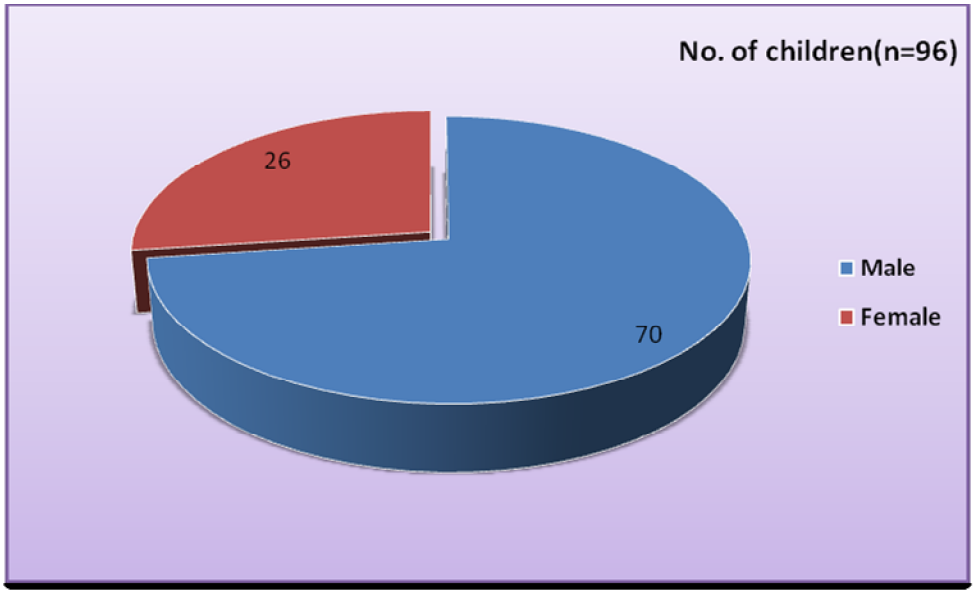


Figure.2 Gender distribution of study population



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). Fluroquinolones (Ciprofloxacin/Ofloxacin) showed 72.7% of sensitivity in our study. But in-vitro sensitivity of fluroquinilones has showed clinical failures in real. Resistance of nalidixic acid could be a surrogate marker which predicts the fluroquinolones 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.

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