

Original article:

Current pattern of Salmonella Typhi antimicrobial susceptibility in the era of antibiotic abuse

Riyaz chungathu, Jayavardhana A

Dept of Pediatrics, PSGIMSR, Coimbatore

Name of the Institute/college: PSG Institute of Medical Sciences and Research , Coimbatore , India.

Corresponding author: Jayavardhana A

Abstract

Multidrug resistance in Salmonella Typhi has emerged as a significant problem. Given the difference in the sensitivity patterns reported for Salmonella Typhi, this study aimed to evaluate antimicrobial susceptibility patterns of Salmonella Typhi in a tertiary care hospital, coimbatore in south India. Salmonella Typhi positive blood cultures from children up to 14 years of age, over a period of 18 months from June 2011 to November 2012 were analyzed . Kirby-Bauer disc diffusion method was used to evaluate antimicrobial susceptibility. Results: Of the total of 50 isolates studied, all the isolates were susceptible to ceftriaxone, most were responsive to Ampicillin, Chloramphenicol, Cotrimoxazole, and Ciprofloxacin. Out of 50, only 4 cases were sensitive to Nalidixic acid. Isolates that showed high nalidixic acid resistant (34/50) had elevated minimum inhibitory concentration (MIC) for ciprofloxacin, ranging from 0.135 to 0.91 µg/mL (average 0.25 ± 0.11 µg/mL) RSC. Only 2 isolates were multi drug resistant. Though multi drug resistance is less common, high level of nalidixic acid resistance and elevated MIC for fluoroquinolones is a concern in this population.

Key words: Antimicrobial susceptibility, Salmonella typhi, multidrug resistant typhoid fever

Introduction

Typhoid fever is a bacterial disease, caused by Salmonella typhi. It is transmitted through the ingestion of food or drink contaminated by the faeces or urine of infected people. It is a worldwide problem and widely prevalent in the tropical developing countries with an estimated 12-33 million cases (1) and 6 lakhs death occurring annually (2). Major contribution is from Asia (3) and it is endemic in the most parts of Indian subcontinent (4). Appropriate antibiotic therapy reduces mortality from 30% to less than 1% (5). Multidrug resistant (MDR) enteric fever (resistant to chloramphenicol, ampicillin and cotrimoxazole) has emerged across the world in the recent times (6). Salmonella Isolates with reduced susceptibility to fluoroquinolones have now reported

in the Indian subcontinent and other regions (7, 8).The current worldwide increase in antimicrobial resistance and lack in the development of new antibiotics have serious public health and economic implications. The reason for increasing resistance is multifactorial, but the main cause is the high level of inappropriate antibiotic usage. About 80% of antibiotics are used in the community and the rest are used in hospitals (9, 10). It is estimated that 20-50% of all antibiotics use is inappropriate, resulting in an increased risk of side effects, higher costs and higher rates of resistance in other community pathogens (11). In this context, it was essential to find out the current sensitivity pattern of the Salmonella strains isolated from blood in our region.

Materials and Methods

It is a cross-sectional, hospital based study spanning over a period of 18 months from June 2011 to November 2012. Inpatients and outpatients of department of Paediatrics of PSG IMSR with confirmed diagnosis of Salmonella typhi including locales in and around Coimbatore including referred cases up to 14 years of age were included. Institution human ethics committee approved the study. All the suspected cases of typhoid fever on the basis of clinical features of high grade fever, headache, hepatosplenomegaly, and with other Constitutional symptoms were investigated. Blood culture was performed by collecting 5cc venous blood and diluting it 4 times under normal circumstances and 10 times if treated with antibiotics, and then injecting into a bulb containing 20-30cc of 5% bile broth. The bulb is incubated for 24-48 hrs at 37°C and subcultures were made on McConkey's medium. Cultures were declared negative after incubation for 10 days. Antibiotic sensitivity pattern was assessed by the Kirby-bauer disc diffusion method where discs containing antibiotics were placed onto an agar plate upon which bacteria were growing. If the bacteria is sensitive to the antibiotic a zone of inhibition is seen around the disc. Minimum inhibitory concentrations (MIC) of isolates resistant to chloramphenicol, ampicillin and nalidixic acid were determined by agar dilution test using purified antibiotic powders. Data were evaluated using descriptive statistics.

Results

A total of 50 cases of salmonella typhi isolates from blood culture were included for analysis. Out of these, 36 (72%) were males and 14(28%) were females. Of the 50 cases 39(78%) were between 5-14 years and 11(22%) cases were less than 5 years. Fever was noted in all the cases (100%). Average duration of symptoms before admission was 4.5 days. Other predominant symptoms were pain abdomen (26%), diarrhea (28%), vomiting (22%) and cough (14%). Hepatomegaly(60%) and Splenomegaly(68%) were the major clinical findings. Toxic look was present in 18 % of cases. Leucopenia (<4000/cumm) was present in only 5 cases. In the present study (table-1), all the isolates were susceptible to ceftriaxone(100%) , most were responsive to Ampicillin (48/50,96%), Chloramphenicol (47/50,94%), Cotrimoxazole (45/50,90%) and Ciprofloxacin (48/50,96%). Out of 50, only 4 cases were sensitive to Nalidixic acid. Isolates that showed high nalidixic acid resistant (34/50) had elevated MIC for ciprofloxacin, ranging from 0.135 to 0.91 µg/mL (average 0.25 ± 0.11 µg/mL) RSC. Only 2 isolates were multi drug resistant (simultaneous resistance of bacteria to chloramphenicol, ampicillin and trimethoprim-sulfamethoxazole) in this study. No mortality in the study group. Mean duration of hospital stay was 6.5±3 days. Mean defervescence time after initiation of antibiotic therapy in ceftriaxone treated group (36/50) was mean 4.5±2 days and ciprofloxacin (14/50) treated group was 5±3 days.

Table -1, showing antibiotic sensitivity pattern

Antibiotics	Sensitive N=50	Intermediate	Resistant
chloramphenicol;	46(92%)	1(2%)	3(6%)
ampicillin;	45(90%)	3(6%)	2(4%)
ceftriaxone;	50(100%)	0	0
ciprofloxacin;	34(68%)	14(28%)	2(4%)
trimethoprim- sulfamethoxazole	40(80%)	5(10%)	5(10%)
nalidixic acid;	4(8%)	12(24%)	34(68%)
multidrug resistance	-	-	2(4%)

Discussion

Typhoid fever is endemic in most parts of the India and it remains a major public health problem in many similar developing countries. This organism is highly adaptable and has remarkable mechanisms of survival and transmission in the host (12). Growing drug resistance is an important factor in the morbidity and mortality of the typhoid fever. Reports from different parts of India documented an increasing resistance of *S. Typhi* strains to commonly used first line drugs especially ciprofloxacin (13, 14, 15). The resistance pattern varies with geographical locations. This study was done in tertiary care teaching hospital Coimbatore, India.

All the isolates in our study were sensitive to ceftriaxone in contrast to the recent studies (16, 17) that recorded resistance to ceftriaxone. Nalidixic acid sensitivity has been validated as a screening test for susceptibility to ciprofloxacin. High level of nalidixic acid resistance is associated with a high MIC of ciprofloxacin, which is associated with treatment failure(18,19). In this present study, 34of

50 isolates were nalidixic acid resistant and were associated increased resistance to ciprofloxacin. The fluoroquinolones resistance is said to be due to altered DNA gyrase sub-unit but, recently plasmid-mediated resistance pattern has also been reported (20). In developing countries such as India, ciprofloxacin continues to be the mainstay in the treatment of typhoid fever as it is orally effective and economical.

The emergence of ciprofloxacin resistance is a concern in many developing countries. There is no significant difference in response to fever in children treated with ceftriaxone and ciprofloxacin in this study. Only 4% multidrug resistant isolates in this region is notable. This study has few limitations. As it was small hospitals based study, these findings may not truly reflect the sensitivity pattern in the community. Despite the fact that multi drug resistance is less common, high level of nalidixic acid resistance and elevated MIC for fluoroquinolones in the pediatric age group warrants rational prescription of antibiotics.

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