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# A Study on Antibiotic Sensitivity Pattern of Salmonella Typhi in Pediatric Age Group

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**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 RMMCH, Chidambaram, India. Salmonella Typhi positive blood cultures from children up to 12 years of age, over a period of 22 months from November 2014 to August 2016 were analyzed. Kirby-Bauer disc diffusion method was used to evaluate antimicrobial susceptibility.*
**Results:** *Of the total of 20 isolates studied, all the isolates were susceptible to ceftriaxone, Cefixime and Azithromycin. most were responsive to Ciprofloxacin, Nalidixic acid and Chloramphenicol. Maximum resistant noted against Ampicillin. In this study 10% of isolates were MDR.*
**Key words:** *Antibiotic sensitivity, Salmonella typhi, multidrug resistant typhoid fever, Pediatric age group.*

## Introduction

Typhoid fever is a global health problem[1]. It is a common infectious disease presenting as acute multisystem febrile illness caused by Salmonella typhi and Salmonella paratyphi[2]. It is a major public health problem in India where patients report throughout the year with monsoon clustering patterns. Low standards of living are the main reasons behind the higher endemicity in India. The disease burden is compounded by explosive emergence of multidrug resistant salmonellae which are resistant to conventionally used drugs like chloramphenicol, ampicillin and cotrimoxazole[1]. Growing drug resistance is an important factor in the morbidity and mortality of the typhoid fever.

Blood cultures are the gold standard diagnostic method for diagnosis of enteric fever. 'The sensitivity of blood culture is highest in the first week of the illness and reduces with advancing illness[3]. Overall sensitivity is around 50% but drops considerably with prior antibiotic therapy. Failure to isolate the organism may be caused by several factors which includes inadequate laboratory media, the volume of blood taken for culture, the presence of antibiotics and the time of collection. For blood culture it is essential to inoculate media at the time of drawing blood.

Salmonella can be easily cultured in most microbiologic laboratories with use of routine culture media (Hartley's media, blood agar and MacConkey agar). Automated blood culture systems, such as BACTEC, certainly enhance the recovery rate. Sufficient amount of blood should be collected for culture as the median bacterial count in the peripheral blood is only 0.3 CFU/mL

(inter quartile range 0.1-10; range 0.1-399). At least 10 mL of blood in adults and 5ml in children should be collected. Dilution should be appropriate in order to adequately neutralize the bactericidal effect of serum and a ratio of 1:5-1:10 of blood to broth is recommended[3]. Clot cultures, wherein the inhibitory effect of serum is obviated, have not been found to be of superior sensitivity as compared to blood cultures in several clinical studies. In the laboratory blood culture bottles should be incubated at $37^0$C and checked for turbidity, gas formation and other evidence of growth 1, 2, 3 and 7 days.

For day l, 2 and 3 only bottles showing signs of positive growth are cultured on agar plates. On day 7 all bottles should be subcultured before being discarded as negative. Advantage of blood culture is it is 100% specific and can find antibiotic sensitivity pattern which is important in this drug resistant era. Disadvantage of blood culture is not readily available at all center, time consuming and low sensitivity if antibiotic given earlier.

Fluoroquinolones, third-generation cephalosporins (eg ceftriaxone and cefixime), and azithromycin are currently regarded as the antibiotics of choice for treating MDR strains[2]. However, an issue of great concern is the emergence of strains of S. Typhi with reduced susceptibility to fluoroquino-lones. The matter is further worsened by the fact that etiological diagnosis for cases of pyrexia is available in relatively few centers[1]. This might lead to improper therapy and worsen the drug resistance among Salmonella isolates. Hence study about antibiotic sensitive pattern of Salmonella typhi is crucial in the proper management of typhoid fever, in prevention and control of disease and drug resistance.

**Materials and Methods**

A study to assess the antibiotic sensitivity pattern of enteric fever in children from 1 to 12 years of age in RMMCH was conducted from November 2014 to August 2016.Clinically suspected cases of typhoid fever in 1 to 12 years age among both sexes admitted in Pediatric Department, Rajah Muthiah Medical College and Hospital, Chidambaram using simple random method, constituted the study group.

Children admitted with fever of 5 days or more in duration were screened for enteric fever based on Widal titers blood culture results. Diagnosed enteric fever were studied for laboratory profile and antibiotic sensitivity pattern of the organisms grown. All laboratory values and culture results recorded in proforma. Among culture positive children, antibiotic sensitivity pattern noted. Finally all the laboratory parameters consolidated and tabulated from which antibiotic sensitivity pattern formulated.

**Blood collection- Procedure**

The sterile gloves were worn and the venepuncture site on the patient's skin was disinfected by applying 70% isopropyl alcohol in water with 1% chlorhexidine for at least 1 min and allowed to dry. Around 7 mL of blood from children younger than 12 years who were clinically suspected of typhoid fever was collected. Around 5 mL of blood was inoculated immediately into the culture media and transported to the laboratory. The remaining blood was kept for serum separation in a sterile test tube that was used for Widal. In this study, Brain-heart infusion biphasic medium (BHI agar + BHI broth) with liquid phase 50 mL stored between 2°C and 8°C was used for inoculation.

The blood bottle was then incubated at 37°C for up to 7 days being tilted so that the liquid flowed over the solid medium and checked for turbidity, colony formation and other evidence of growth on day 1, 2, 3 and 7. The bottles showing signs of positive growth were subcultured on blood agar and MacConkey's agar and incubated overnight at 37°C. Non-lactose fermenting smooth colonies detected on the plates were picked up for further identification by biochemical and serological tests.

Antibiotic sensitivity pattern was assessed by the Kirby-baeur disc diffusion method where discs

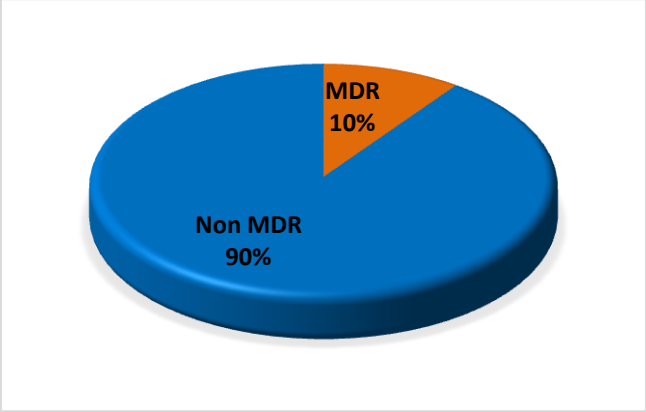
containing antibiotics were placed onto an agar plate upon which bacteria were growing. If the bacteria is sensitive to the antibiotic a zone of inhibition is seen around the disc. Minimum inhibitory concentrations (MIC) of isolates resistant to chloramphenicol, ampicillin and nalidixic acid were determined by agar dilution test using purified antibiotic powders. Ampicillin (10 µg), Chloramphenicol (30 µg), Trimethoprim-Sulphamethoxazole (1.25 & 23.75 µg), Nalidixic acid (30 µg), Ciprofloxacin (5 µg), Ceftriaxone (30 µg) used. Multi drug resistant (MDR) strain were defined as those resistant simultaneously to ampicillin, chloramphenicol and trimethoprim-sulphamethoxazole. Data were evaluated using descriptive statistics.

## Results

**Table 1:** Drug Sensitivity and Resistant pattern of S. Typhi

| Antibiotic | Sensitive | | Resistant | |
|---|---|---|---|---|
| | N | % | N | % |
| Ampicillin | 14 | 70 | 6 | 30 |
| Cotrimoxazole | 16 | 80 | 4 | 20 |
| Chloramphenicol | 18 | 90 | 2 | 10 |
| Nalidixic acid | 18 | 90 | 2 | 10 |
| Ciprofloxacin | 19 | 95 | 1 | 5 |
| Ceftriaxone | 20 | 100 | 0 | 0 |
| Cefixime | 20 | 100 | 0 | 0 |
| Azithromycin | 20 | 100 | 0 | 0 |

**Fig 1:** Multi Drug Resistant Strain Isolated In This Study




Among 140 children in study population, Twenty (14.3%) cases were positive for enteric fever by blood culture. Total of 20 cases of salmonella typhi isolates from blood culture were included for analysis. Out of these, 13 (65%) were males and 7(35%) were females. Of the 20 cases 16(20%) were between 5-12 years and 4(20%) cases were less than 5 years. Fever was noted in all the cases (100%). Average duration of symptoms before admission was 5.7 days. In the present study (table-1), all the isolates were susceptible to ceftriaxone(100%) ,Cefixime (100%) and Azithromycin (100%). Most were responsive to Ciprofloxacin (19/20,95%), Nalidixic acid (18/20,90%), Chloramphenicol (18/20,90%).Cotrimoxazole sensitive in 16 (80%) children. Out of 20, only 14 cases were sensitive to Ampicillin (70%). Chloramphenicol sensitivity is 90% which is higher than ampicillin and cotrimoxazole. Among 20 culture positive children, 2 (10%) were multi drug resistant (figure 1). No mortality in the study group. Mean defervescence time after initiation of antibiotic therapy in ceftriaxone treated group (16/20) was mean 4.6 days and ciprofloxacin (4/20) treated group was 5.4 days.

## Discussion

**Table 2:** Antibiotic Sensitivity Pattern among Salmonella Typhi

| Study series | mpi | o-Tri | hlor | ali | ipro | eftri | efix | zith |
|---|---|---|---|---|---|---|---|---|
| Joshi BG et al [5] | 00 | 00 | 00 | 4 | 8 | 00 | 00 | 2 |
| Riyazchungathu et al [7] | 0 | 0 | 2 | | 8 | 00 | | |
| S Udayakumar et al [8] | 9.5 | 0 | 7.4 | .3 | 0 | 3.5 | 3.5 | 00 |
| Altafahmedtalpur et al [9] | 7.07 | | 3.14 | | 0.48 | 2.68 | 5.60 | |
| Nilesh D. Patel et al [10] | 6 | 0 | 1 | | 3 | 6 | | |
| RanjanaHawaldar et al [11] | 1.25 | 7.5 | | | | 8.73 | 9.37 | |
| Anees Akhtar et al [6] | 3.30 | | 3.30 | 3.30 | 3.30 | 00 | 3.30 | 00 |
| Chandrashekar et al [4] | | 0.3 | | 3.1 | 3.3 | 7.5 | 1.7 | |
| Sudharshan raj et al [12] | 0.7 | .6 | 5.8 | | 00 | 00 | 00 | |
| Hetal N et al [13] | .04 | | 5.11 | 00 | 00 | 00 | 00 | 7.04 |
| Present study | 5 | 0 | 0 | 0 | 5 | 00 | 00 | 00 |

Ampi- Ampicillin. Co-Tri – Cotrimoxazole. Chlor- chloramphenicol. Nali- Nalidixic Acid. Cipro- Ciprofloxacin. Ceftri- Ceftriaxone. Cefix- Cefixime. Azith- Azithromycin.

In this present study 20 isolates are positive for Salmonella typhi all are sensitive (100%) to Ceftriaxone, Cefixime and Ciprofloxacin. Which is comparable with Joshi BG et al, Sudharshan Raj et al and Hetal N et al. Ciprofloxacin have 94.4% sensitivity which is comparable with Nilesh D Patel et al. Ampicillin sensitivity is 95% which is comparable with Riyazchungathu et al and Hetal N et al . Multi drug Resistant is seen in 10%, which less than Anees Akhtar et al and more than Joshi BG et al as shown in table 2.There is re-emergence of strains with high sensitivity to first line antibiotics choramphenicol and cotrimoxazole noted in this study.

## Conclusion

Blood culture is the gold standard for diagnosis of typhoid fever with high specificity. Sensitivity is higher in first week of illness, decline with the increase in the duration of illness and with prior antibiotic usage. Whenever feasible confirmation with blood culture is strongly encouraged especially with the appearance of drug resistance strains in the community. Appropriate diagnosis using blood cultures and using 3rd generation cephalosporins as the first line of drug in treating children with enteric fever can reduce the duration of treatment, promote better compliance, reduce relapse rates, and may decrease multidrug resistant S.typhi/paratyphi strains in the community.

MDR and Quinolone resistant strains are emerging. All the salmonella typhi isolates are fully susceptible to ceftriaxone, cefixime and azithromycin in this study. There is re-emergence of strains with high sensitivity to first line antibiotics choramphenicol and cotrimoxazole noted in this study. The fact that multi drug resistance is 10% in this study, which warrants rational prescription of antibiotics.

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