

# Changing Patterns of Antimicrobial Susceptibility of *Salmonella Typhi* at the Children's Hospital Lahore

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## ABSTRACT

**Objective:** To evaluate the changing pattern of antimicrobial susceptibility of *Salmonella typhi*.

**Study Design:** Observational study

**Place and duration of study:** The Children's Hospital Lahore, from January to December 2010.

**Materials and methods:** Blood cultures of 780 clinically suspected patients were performed using brain heart infusion broth. The antimicrobial susceptibility of *S. typhi* was performed using Kirby Bauer disc diffusion method.

**Results:** A total of 69 isolates of *Salmonella species* were recovered during above stated period. Frequency of *Salmonella typhi* was found to be 60(87%), *Salmonella paratyphi A* 8(12%) and *Salmonella typhimurium* was 1(1%). *Salmonella typhi* was found to be highly sensitive to amikacin (100%), amoxicillin+calvulanic acid (100%), cefotaxime (100%), ceftriaxone (100%), cefuroxime (100%), aztreonam (100%), meropenem (100%), piperacillin-tazobactam (100%), cefixime (90.48%), gentamycin (90.48%), ceftazidime (85.71%), ciprofloxacin (85.71%) and nalidixic acid (85.71%). *S. typhi* was found to be less sensitive to trimethoprim-sulphamethoxazole (23.81%) and ampicillin (23.81%).

**Conclusion:** *S. typhi* is still the major cause of enteric fever in our region but the emergence of more antibiotic susceptible strains may help clinicians in the treatment of this disease to reduce the morbidity.

**Key words:** *Salmonella typhi*. Multidrug resistant *Salmonella typhi*. Antimicrobial susceptibility pattern.

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## INTRODUCTION

Typhoid fever mainly caused by *Salmonella typhi* remains an important public health problem in developing countries<sup>1,2,3</sup>. Despite major advances in understanding of the pathogenesis and risk factors for typhoid fever, the disease is still widely prevalent throughout the developing world. Although difficult to estimate with any degree of accuracy, the population based incidence of typhoid in developing countries ranges from 150-1000 cases per 100,000 populations. In 2000, it was estimated that over 2.16 million episodes of typhoid fever occurred worldwide, resulting in 216,000 deaths and that more than 90% of this morbidity and mortality occurred in Asia.<sup>4</sup> Recent data from South Asia also indicate that contrary to earlier opinion, typhoid fever is widely prevalent among young children less than five years of age with comparatively higher morbidity and hospitalization rates. Although better sanitation, provision of clean drinking water along with antibiotics have markedly reduced the frequency of typhoid fever in the developed world, but it still remains endemic in developing countries<sup>5</sup>.

*Salmonella typhi* is a flagellated aerobic, rod shaped, Gram negative bacteria and a member of family Enterobacteriaceae.<sup>6</sup> Blood culture is the most frequent, accurate means of diagnosing bacteremia in enteric fever.<sup>7</sup> There has been an emerging trend of increased antimicrobial resistance since 1960. Since then, increasing number of multidrug resistant *S. typhi* has become a source of concern for the physicians.

This study was aimed at determining the frequency of *S. typhi* and to evaluate its antimicrobial susceptibility pattern in clinically suspected cases of typhoid fever admitted at Children's Hospital, Lahore.

## MATERIALS AND METHODS

This observational study was conducted at The Children's Hospital and Institute of Child Health, Lahore from January to December 2010. The study population was 780 patients with clinical suspicion of enteric fever regardless of their age and gender. The blood samples were collected by the medical staff in the brain heart infusion broth and sent to the laboratory for culture and sensitivity testing. The blood culture bottles were incubated at 37°C up to 7 days in Microbiology laboratory with the observation of growth indicators every day.

After 18-24 hours of incubation at 37°C, samples were subcultured on blood and MacConkey agar

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(Oxoid) plates and these plates were incubated at 37°C for 24 hours. The plates were observed for bacterial growth on second day. The separate individual colony was selected and studied for cultural characteristics. The characters considered were shape, size, margins and pigmentation around the colonies. In case of growth, Gram's staining and biochemical test/API 20E (bioMerieux) were performed<sup>8</sup>. Antibiotic sensitivity tests were performed on Mueller Hinton agar (Oxoid) using Kirby Bauer disc diffusion method. Interpretation of zone sizes of each disc was made as sensitive or resistant using interpretation chart recommended by Clinical and Laboratory Standards Institute (CLSI)<sup>9</sup>. Data was processed using SPSS version 16.0.

**RESULTS**

A total of 69 *Salmonella* isolates were recovered from 780 blood cultures over a time period of one year in the Microbiology department of the Children's Hospital and Institute of Child Health, Lahore. Frequency of *Salmonella typhi* was found to be 60 (87%) followed by *Salmonella paratyphi A* 8 (12%) and *Salmonella typhimurium* 1 (1%) (Figure I). *Salmonella typhi* was found to be highly sensitive to amikacin (100%), aztreonam (100%), amoxicillin+calvulanic acid (100%), cefotaxime

(100%), ceftriaxone (100%), cefuroxime (100%), meropenem (100%), piperacillin-tazobactam (100%) along with gentamycin (90.48%), cefixime (90.48%), ceftazidime (85.71%), nalidixic acid (85.71%) and ciprofloxacin (85.71%). *S. typhi* was less sensitive to trimethoprim-sulphamethoxazole and ampicillin (23.81% each) (Figure II).

Figure I: Frequency of different *Salmonella spp.* isolated from blood cultures

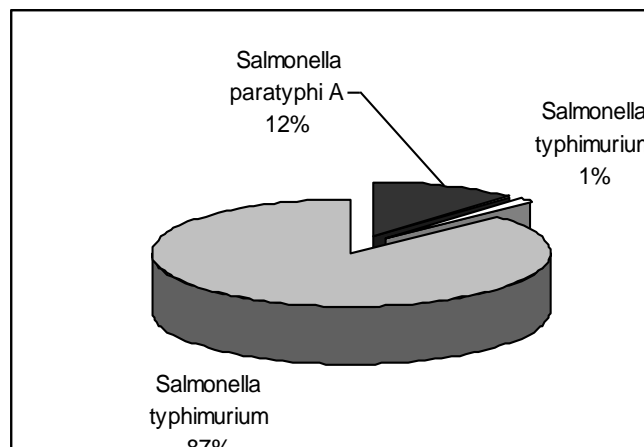
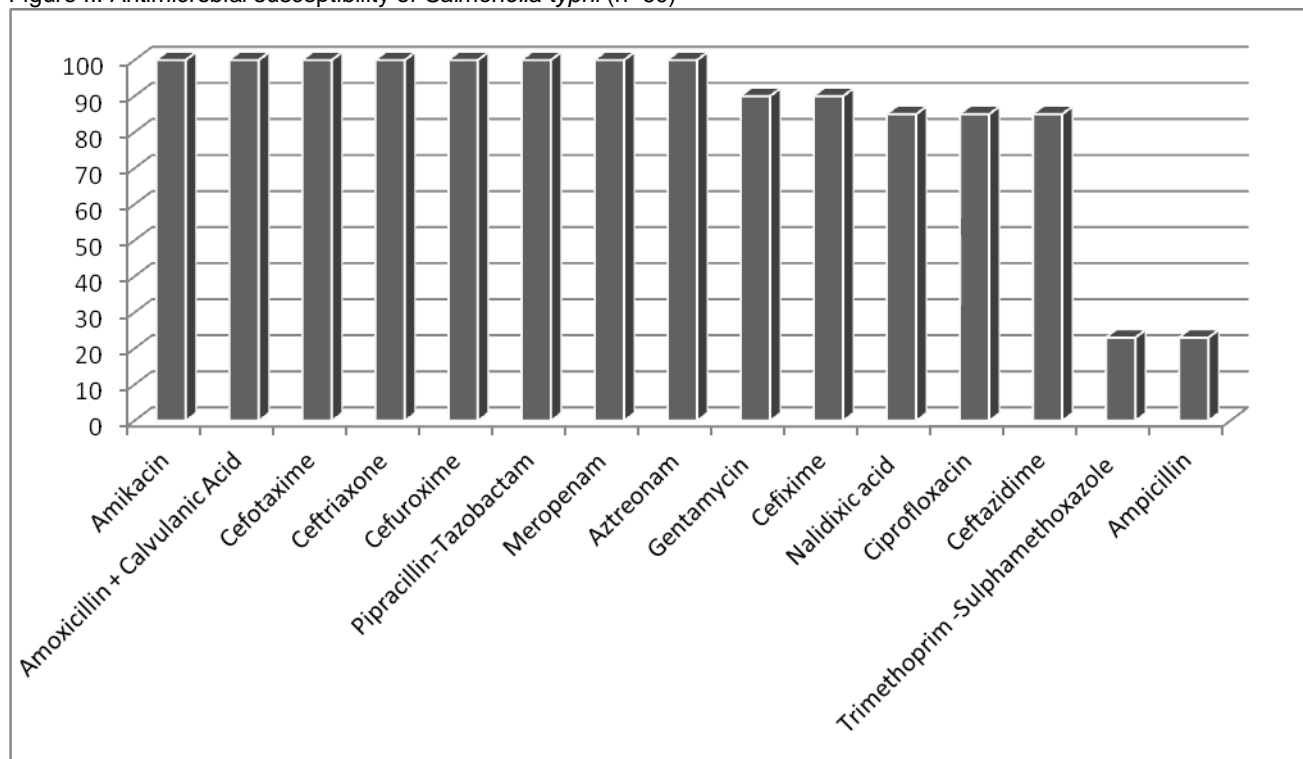


Figure II. Antimicrobial susceptibility of *Salmonella typhi* (n=60)



## DISCUSSION

The morbidity of typhoid fever is very high in South Asian region including Pakistan. The incidence of *Salmonella typhi* in Southeast Asia has been estimated to be 110 cases/100,000 populations which is the third highest incidence rate for any region<sup>10</sup>. However; it is the Indian subcontinent which has the highest incidence (IR) of the disease worldwide. A previous study from Pakistan in 2006 revealed an IR of 170/100,000 (using blood culture) whereas a serology based IR was 710/100,000 (using Typhidot)<sup>10</sup>. Although effective treatment with chloramphenicol was introduced in 1948<sup>11</sup>, the emergence of resistance to chloramphenicol, ampicillin and cotrimoxazole has been of concern<sup>12</sup>. Later on, fluoroquinolones and third generation cephalosporins were considered the drugs of choice for treatment of typhoid fever. However, decreased susceptibility to these agents along with nalidixic acid have been reported which led to the prospect of re-emergence of untreatable typhoid fever and an increasing global burden<sup>13</sup>.

According to the results of the present study, *Salmonella typhi* with a yield of 86.96% was the most frequently isolated organisms among all *Salmonella* species. This is in accordance to a study from Karachi which reported a yield of 83% of *Salmonella typhi* in suspected cases of typhoid fever.<sup>14</sup> Two more studies from Nepal and from Nigeria also reported similar results<sup>15,16</sup>. In contrast, a study from Rawalpindi (Pakistan) reported only 41% of *Salmonella typhi* in suspected cases<sup>17</sup>. Similar results were also reported by researchers from Nepal and India<sup>18,19</sup>.

In the present study, antimicrobial sensitivity pattern for *Salmonella typhi* revealed highest sensitivity to amikacin (100%), amoxicillin+calvulanic acid (100%), cefotaxime (100%), ceftriaxone (100%), cefuroxime (100%), aztreonam (100%), piperacillin-tazobactam (100%), and meropenem (100%). Similar antibiotic sensitivity pattern was demonstrated in a hospital of India where they reported 100% antimicrobial sensitivity to amoxicillin+calvulanic acid and cefotaxime<sup>20</sup>. This may be due to decreased use of these antibiotics in the recent years.

A study conducted at Knti children hospital Nepal reported *Salmonella typhi* to be highly sensitive to ceftriaxone, ofloxacin, chloramphenicol and least sensitive to amoxicillin and ciprofloxacin.<sup>15</sup> This study partially supports the sensitivity pattern reported in our study. Yet, another study at Nepal Medical College Teaching Hospital reported *S. typhi* to be highly sensitive to amikacin and ciprofloxacin that is partially in accordance to the current study<sup>19</sup>.

Another Indian researcher studied antimicrobial resistance of *Salmonella typhi* in Chennai, India<sup>21</sup>. Out of total *Salmonella* isolated, 70% were *Salmonella typhi* which were highly sensitive to cotrimoxazole, quinolones and cephalosporins. This study is in accordance to the present study except for being much resistant to cotrimoxazole.

In a study conducted in Kenya, 83.3% *S. typhi* were resistant to most commonly available drugs like ampicillin. This study supports the results of our study<sup>1</sup>. A study conducted in the Microbiology laboratory of Ziauddin Medical University, Karachi reported high resistance of *Salmonella typhi* to ampicillin<sup>14</sup>. These results are similar to present study where *Salmonella typhi* showed high resistance to ampicillin (77%). Due to frequent use of ampicillin, most of organisms have developed resistance against this drug.

A study of the antibiotic sensitivity pattern of enteropathogenic bacteria from Al-Qasimi Hospital, Sharjah reported the highest sensitivity of *Salmonella typhi* to gentamycin (100%) and lowest sensitivity to trimethoprim-sulphamethoxazole (50%)<sup>22</sup>. These results are close to the results of our study. In the present study, *Salmonella typhi* showed good sensitivity to gentamycin (90%) and lowest sensitivity to trimethoprim-sulphamethoxazole (23 %).

In the year 2008, our study center reported decreased susceptibility of *S. typhi* against amikacin (77%), cefuroxime (79%), ceftazidime (64%), cefixime (77%), ciprofloxacin (49%), and gentamycin (79%)<sup>23</sup>. The results of the present study shows a changing pattern of *S. typhi* against these antibiotics as amikacin and cefuroxime have now improved to be 100% sensitive, cefixime and gentamycin being 90% while ciprofloxacin and ceftazidime being 85% sensitive to *S. typhi*.

Changing pattern of antibiotic sensitivity of *S. typhi* was also observed in a study from India. Multidrug resistance was found in only 11.96% isolates of *S. typhi*. Less than 2% isolates of *S. typhi* showed resistance to ciprofloxacin. A sensitivity of 97% against third generation cephalosporins was observed among *Salmonella typhi* isolates<sup>24</sup>. Another study from central west India has also recently reported changing pattern of antimicrobial susceptibility for *S. typhi*<sup>25</sup>.

Consumption of unboiled water, poor sanitary and domestic conditions are responsible for the high rate of typhoid fever. In order to prevent such outbreaks at global level, recently WHO introduced several household interventions including solar disinfection and use of low cost ceramic filters. Despite large scale global efforts, situation cannot be easily controlled in rural areas yet<sup>26</sup>.

## CONCLUSION

We can conclude that *Salmonella typhi* is still the major causative agent of enteric fever in our region. A positive change that has been observed in this study is the improved pattern of antibiotic sensitivity compared to the pattern previously studied at our center. This indicates that with rational use of antibiotics, we can overcome the problem of increasing antibiotic resistance. A national antibiotic policy should be devised to improve the management of such diseases so that our national resources may be better utilized.

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