**Original Article**

# Current trends in antimicrobial susceptibility pattern of *Salmonella typhi* and *paratyphi*

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**Objective:** To evaluate the current trend of antimicrobial susceptibility pattern of *Salmonella typhi* and *paratyphi*.

**Methodology:** This observational laboratory based study was conducted at Department of Microbiology, Khawaja Muhammad Safdar Medical College, Sialkot from January 1, to June 30, 2019. Blood culture samples were collected aseptically, sub cultured and identified as *Samonella typhi* or *paratyphi A,* as recommended by clinical laboratory standard institute.

**Results:** A total of 2773 samples were collected, among these 1945(70%) were from neonates and were excluded from the study. Among rest 828(30%) blood culture samples, 55(6.64%) yielded growth of *Salmonella typhi* and *paratyphi*. Out of total *Salmonella* species, 44(80%) were *Salmonella typhi* and 11(20%) were *Salmonella Paratyphi A*. Multidrug resistant salmonella were 47% and extensively drug resistant salmonella were 16%. Meropenem and azithromycin showed 100% sensitivity while ceftriaxone in 84% cases.

**Conclusion:** Trends of antibiotic susceptibility are changing as flouroquinolones are less effective than first line drugs. Extensively drug resistant cases of typhoid are also detected, which needs regular monitoring of sensitivity pattern. (Rawal Med J 202;45:291-294).

**Keywords:** Antibiotics, MDR salmonella, resistance, XDR salmonella.

## INTRODUCTION

Infecting organisms are becoming extremely drug resistant day by day.[1] One of the most common infection faced by developing world is typhoid fever.[2] In year 2017, around 116,800 deaths have been reported globally by Global Health Data exchange. Out of these global deaths, 6,700 deaths were from Pakistan.[3] The microorganism responsible for typhoid fever is transmitted via contaminated food and water. And people who have more risk for acquiring this infection are those who have no access to safe drinking water and all those who live in poor sanitation conditions.[3,4]

The sensitivity pattern of causative organism is changing day by day.[5] First line treatment for typhoid fever i.e. ampicillin, trimethoprin-sulfamethaxazole and chloramphenicol was very effective till early 1980s. Then resistance among salmonella developed and organisms which were resistant to all three antibiotics were called multidrug resistant (MDR) salmonella.[6] Flouroquinolones were the next option to treat MDR infections. Till 2005 resistance to flouroquinolones also developed so that empirical therapy shifted mostly to third generation cephalosporin or azithromycin. Now cases of ceftriaxone and azithromycin resistant salmonella are being reported. Due to rapidly developing drug resistance we are facing the danger of handling a super bug, which will eventually be resistant to all available antimicrobials.[5] The incidence of MDR Salmonella reported from South Asia has been 17-23%.[7]

*Salmonella typhi* and *paratyphi* when become resistant to all first line antityphoid agents plus ceftriaxone and flouroquinolone is termed as extremely drug resistant (XDR).[7] And the first case of XDR *Salmonella typhi* was reported in 2016 from Hyderabad, Pakistan and since then WHO has reported around five thousand cases of XDR *Salmonella typhi* from Pakistan.[3,7,8] Physicians in periphery are not convinced to advise blood culture and mostly use empirical therapy. Keeping in view the current prevalence and emergence of XDR strains and decline in resistance to first line antityphoid drugs, this study was conducted to

evaluate the current trend of antimicrobial susceptibility pattern of *Salmonella typhi* and *paratyphi* isolated in our setup.

## METHODOLOGY

This observational laboratory based study was conducted at Department of Microbiology, Khawaja Muhammad Safdar Medical College, Sialkot from 1st January to 30th June 2019. Non probability convenient sampling technique was used. Samples were collected from patients of Allama Iqbal Memorial Teaching Hospital and Govt. Sardar Begum Hospital, Sialkot. Ethical approval for conducting the study was obtained from the ethical review committee of the institute.

All *Salmonella typhi* and *paratyphi*, isolated from the blood cultures were included in the study. Organisms other than *Salmonella typhi* and *paratyphi* were excluded from the study.

For each sample, 5-10 ml of venous blood was drawn after full aseptic measures and was inoculated in special blood culture bottles containing 50 ml of Brain heart infusion (BHI) broth (Oxoid, UK). All samples were incubated for 5 days at 37°C and then subcultured on 2nd, 3rd and 4th days on MacConkeys agar (Oxoid, UK).[7-9] API 20E (Biomerieux, France) was used to identify the isolates. Serotyping was done by group and type specific antisera (Bio Rad). Modified Kirby Bauer disk diffusion method was used to determine the antimicrobial sensitivity of isolates. Following antibiotic discs were used to check susceptibility pattern as recommended by clinical laboratory standard institute (CLSI) ampicillin (10µg), trimethoprin sulfamethoxazole (25µg), chloramphenicol (10µg), ciprofloxacin (5µg), azithromycin (15µg), meropenem (10µg) and ceftriaxone (30µg).[7-9]

**Statistical Analysis:** The data were analyzed by SPSS version 21.

## RESULTS

Out of 2773 samples, 1945(70%) were from neonates and were excluded from the study. Among rest 828(30%) blood culture samples, 55(6.64%) yielded *Salmonella typhi* and *paratyphi* A. Out of total Salmonella species, 44(80%) were *Salmonella typhi* and 11(20%) were *Salmonella Paratyphi A*, 34(61.8%) were from males and 21(38.2%) from female patients. The commonest age group was 10 years to 20 years.(Table 1).

**Table 1. Age distribution of Samonella typhi and Salmonella paratyphi isolates.**

| Age range | *Salmonella typhi* (n=44) | *Salmonella paratyphi* A (n=11) | Total 55 (100%) |
|---|---|---|---|
| 1-10 years | 9 | 2 | 11(20%) |
| 11-20 years | 18 | 5 | 23 (42%) |
| 21-30 years | 5 | 3 | 8(14.5%) |
| 31-40 years | 6 | 1 | 7 (13%) |
| 41-50 years | 4 | 0 | 4 (7%) |
| 51-60 years | 2 | 0 | 2(3.5%) |
| 61-70 years | 0 | 0 | 0 |

**Table 2. Sensitivity percentages of *Salmonella typhi* and *Salmonella paratyphi A* strains.**

| Antimicrobial | *Salmonella typhi* (n=44) | *Salmonella paratyphi* A (n=11) | Total *Salmonella* species (n= 55) |
|---|---|---|---|
| Ampicillin | 28 (63.6%) | 05(45.4) | 33 (60%) |
| Chloramphenicol | 30 (68%) | 07 (63.6%) | 37 (67%) |
| Trimethorpim sulamethoxazole | 24 (54.5%) | 05(45.4) | 29 (53%) |
| Ciprofloxacin | 6 (13.6%) | 03(27.7%) | 09(16%) |
| Azithromycin | 44 (100%) | 11(100%) | 55 (100%) |
| Ceftriaxone | 35(79.5%) | 11(100%) | 46 (84%) |
| Meropenem | 42(95.4%) | 11(100%) | 53 (96%) |

*Salmonella typhi* strains showed highest (100%) sensitivity to azithromycin and meropenem. Whereas *Salmonella paratyphi A* strains showed 100% sensitivity to third generation cephalosporins as well (Table 2). MDR salmonella were 24/55 (47%). A higher percentage 29/55 (53%) of strains turned out to be sensitive to ampicillin, trimethoprim-sulfamethoxazole and chloramphenicol, indicate that the resistance trend might have start reversing. Only 16% isolates of *Salmonella typhi* and *paratyphi* were sensitive to ciprofloxacin which is an alarming situation. So, current trends in salmonella antibiotic susceptibility is that first line anti typhoidal i.e. ampicillin, trimethoprim-sulfmethaxazole and chloram-phenicol are more effective as compared to flouroquinolones. Our

results shows XDR salmonella are 16%, which is also an alarming situation.

## DISCUSSION

The data from our study indicates that ceftriaxone, which has been used for a salvage of MDR strains of *Salmonella typhi* and *paratyphi* will be rendered useless very soon. In our study, only around 84% of the isolates turned out to be sensitive to ceftriaxone. This situation is very alarming. Studies showed incidence of typhoid fever in adults is 0.2% while it was 1.05% in children younger than five years and reported 16 MDR salmonella isolates.[10,11]

Higher flouroquinolone resistance was noted by Shrestha et al from (94%) which is slightly higher than our study.[12] That study reported 21% of strains resistant to ceftriaxone, which is very similar to our study.[13] Recently, Catham-Stephens also reported 5 XDR cases in United States who had travel history to Pakistan and they were only sensitive to meropenem and azithromycin, like our results.[14]

Mutai et al from Kenya reported 70% isolates were resistant to ciprofloxacin, although it is lower but closer to our results.[15] Patil et al reported recently sensitivity of salmonella to chloramphenicol of 94%, which is very encouraging and higher than our results of 67%.[16] A high percentage of isolates appeared to be sensitive to first line antityphoid agents in our study, which is consistent with studies carried out in Bangladesh and India. This reversing of sensitivity to first line antityphoid drugs was also noted by Laghari et al in children.[17]

This might give us some hope that in future we can again start using these antimicrobials for treatment to *Salmonella typhi* and *paratyphi.* To sum up the findings from these studies it was noticed that first line anti-typhoidal drugs were becoming more sensitive and sensitivity to flouroquinolones has decreased.

Pakistan is having an outbreak of XDR typhoid, but the dilemma is that many microbiologists and clinicians are not reporting local statistics from their setups effectively. The incidence of these superbugs in our region is an emergency. There is need to understand the importance of proper reporting, evaluation and monitoring of antimicrobial therapy. Physicians and patients must practice judicious use of antimicrobials in treating typhoid fever. This is an alarming public health concern; antimicrobial stewardship programs must be conducted along with improvement of water, sanitation and hygiene to eradicate this menace.

The study limitations include a short duration and single center study. Longer and multicenter studies should be done to formulate better treatment options for typhoid fever in our setup.

## CONCLUSION

Antibiotic susceptibility pattern is changing as sensitivity to flouroquinolones has decreased as compared to first line antityphoidal agents. As XDR cases are detected, blood culture should be done in every suspected case and third generation cephalosporins could not be used blindly.

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**Conflict of Interest:** None declared
Rec. Date: Dec 23, 2019 Revision Rec. Date: Feb 17, 2020 Accept Date: Feb 25, 2020

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