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# CULTURE AND SENSITIVITY PATTERN OF *SALMONELLA TYPHI* AND *SALMONELLA PARATYPHI* IN CHILDREN WITH TYPHOID FEVER

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**Abstract**

*The present study aimed to investigate the culture and sensitivity pattern of Salmonella typhi and Salmonella paratyphi in children with typhoid fever at the Department of Paediatrics in Balochistan Institute of Child Health Services Quetta from July 2022 to January 2023. The total blood samples of 150 patients were used in which 72 samples were positive for Salmonella typhi and 41 were positive for Salmonella paratyphi. Out of which 93 were females and 57 were males. The samples were incubated overnight at 37°C. The blood culture bottles were processed on BD Bactec automated blood culture system. Gram stain and subsequent subcultures were performed on MacConkey's Agar, Sheep Blood Agar, and Chocolate Agar from the positive samples for S. typhi and S. paratyphi by Bactec. The Positive cultures were confirmed serologically with BD Difco™ Salmonella species O Antiserum Factor 9, Antiserum Vi, and Antiserum Factor 2 antisera. The results of the study show that Azirthromycin and Meropenum are least resistant and highly sensitive to both S. typhi and S. paratyphi. Ampicillin, Cotrimoxazole and Ceftriaxone shows minimum sensitivity and maximum resistance for S. typhi and S. paratyphi. Whereas, Cotrimoxazole and Ceftriaxone shows zero sensitivity and hundred percent resistance toward S. typhi and S. paratyphi. Hence, the antibiotics which show maximum resistance for Salmonella isolates should be excluded from the category of first line drugs. However, those which showed least resistance for Salmonella isolates should be given as first line drugs. In contrast, need for more research is required for the development of new drugs.*

**Keywords:** *Antibiotics, Resistance, Sensitivity, S. typhi, S. paratyphi*

## INTRODUCTION

The bacterial infection caused by *Salmonella typhi* and *Salmonella paratyphi* affecting all countries around the world is known as Enteric fever. It the most important and common disease since present (1). It is one of a major cause of morbidity and mortality particularly in developing countries. Whereas, if this disease is not treated properly, it can result in multiple problems likewise, gut perforation, hepatitis, hypo-tension, encephalitis and stupor or ultimately death (2).

There are about 11-21 million typhoid fever cases reported throughout the world annually with the total death rate around 128000 to 161000 (3). In contrast, in the subcontinent, the cases of enteric fever reported in Pakistan are huge in number such as 451.7 per 100,000 cases in comparison to India where it was reported 214.2 per 100,000 cases per year (4). The estimated cases of Enteric fever with fatality rate worldwide were around 0.95% in 2017, making the highest fatality rate being in the old population, pediatric population and in those living in underdeveloped and poor countries (5).

At present, antimicrobial resistance is one of the major problems and challenges that modern world is facing in the field of medicine. A study reports that more than 35000 people have died in USA due to antibiotic resistance (6). However, the treatment of enteric fever based on culture and sensitivity pattern varies from country to country and region to region with the emergence of Managed Detection Response (MDR) and Extended Detection Response (XDR) of enteric fever in under developing countries which is due to the

misuse of antibiotics. In Pakistan, a study was conducted mainly in Karachi, which reported higher incidences of enteric fever due to the unneeded use of antibiotics and ingestion of contaminated food (7). Accordingly, to combat with this disease trimethoprim-sulfamethoxazole, and chloramphenicol were used to cure enteric fever. In 1980s, resistance to these first line antibiotics was first seen. In South Asia multi-drug resistance enteric fever has now become a common problem with figures reaching up to 44% in Pakistan and 13% in India (17). This has led the researchers to explore more antibiotics hence., Fluoroquinolones were used as a treatment for typhoid fever. In contrast, the resistance to Fluoroquinolones for *S typhi* then appeared to be seen likewise, in Pakistan it was reported to be 90% as per SEAP (Surveillance Of enteric Fever in Asia Project) report (8). After the resistance to Quinolones clinicians has started using third-generation that is Cephalosporins and resistance against them was seen rarely (9). However, in Karachi and Interior Sindh, Pakistan, in 2016, the resistance to third generation Cephalosporins has also emerged. Therefore, the researches shift towards the use of new antibiotics such as Azithromycin and carbapenem which are the most commonly used agents now a days to treat enteric fever. So far, the resistance towards these two antibiotics is rare. In contrast, there is a lack of current local data in Punjab province regarding the antibiotic sensitivity pattern of enteric fever and in Baluchistan the focus of researchers towards this issue is not such highlighted.

*Salmonella typhi* and *Salmonella paratyphi* are an evolving and dynamic organism, affecting millions of children and adults. However, the antibiotics which are used to control this disease leads to the development of resistance over time. Hence, researchers must be aware of the current trends of antibiotic sensitivity pattern and resistance pattern to effectively control the spread of this disease. The people should be aware of their prescribing habits to avoid the development of antimicrobial resistance and to avoid overuse of antibiotics which could leads to the development of antibiotic resistance (6). Consequently, the data obtained from this study will be helpful in this regard and it will also help in the formulation of standard guidelines for the treatment of enteric fever. The study will also help to prevent the use of antibiotics which have developed resistance with time and must be replaced by the addition of antibiotics. The objectives of this study were to find out the frequency of positive blood culture in clinically diagnosed cases of enteric fever; and the resistance to antibiotics and sensitivity pattern in culture positive cases of *Salmonella typhi* and *Salmonella paratyphi*.

## MATERIALS AND METHODS

This study was carried out in the Department of Pediatrics in Balochistan Institute of Child Health Services Quetta from July 2022 to January 2023 which is a specialized tertiary care hospital in Baluchistan. The totals of 150 patients were tested for typhoid fever. Furthermore, the blood culture and sensitivity to antibiotics was done in all clinical enteric fever cases who were aged between four to twelve years old. The reports were collected before the patients have started given antibiotics. Mostly, the blood cultures of the patients in the study grew *S. typhi and S. paratyphi* in both fresh and recurred cases in the present study. The samples were incubated overnight at 37°C. The blood culture bottles were processed on BD Bactec automated blood culture system. Gram stain and subsequent subcultures were performed on MacConkey's Agar, Sheep Blood Agar, and Chocolate Agar from the positive samples for *S. typhi* and *S. paratyphi* by Bactec. The Positive cultures were confirmed serologically with BD Difco™ *Salmonella species* O Antiserum Factor 9, Antiserum Vi, and Antiserum Factor 2 antisera (10). Whereas, all the isolates were tested for their susceptibility according to the given guidelines (Clinical and Laboratory Standard Institute Guidelines).

### ANTIBIOTIC SUSCEPTIBILITY

Antibiotic susceptibility data was collected whereas, the pattern of antibiotic resistance was analysed in the cultures with positive cases. The commonly used antibiotics tested in the laboratory and included in the study were Ampicillin, Azirthromycin, Ceftriaxone, Cotrimoxazole, Cefotaxime, Ciprofloxacin, and Meropenem.

## RESULTS AND DISCUSSION

The total number of patients included in the study was 150 out of which 57 were male and 93 were female. The duration of time of appearance of symptoms for enteric fever in children was 4-6 days between which the blood samples were collected and examined in the laboratory. The children were aged between 4-12 years old. The common species which were identified in the study were *Salmonella typhi* and *Salmonella paratyphi.*

**Table I.** Age and gender wise distribution

| Species | Age | Gender | |
|---|---|---|---|
| | | Female | Male |
| *Salmonella typhi* | 4-12 years | 57 | 33 |
| *Salmonella para typhi* | 4-12 years | 36 | 24 |

However, the blood culture presented with enteric fever particularly for *Salmonella typhi* female patients were 57 females and 33 males. Whereas, in case of *Salmonella paratyphi* there were 36 females and 24 males' patients as shown in Table I.

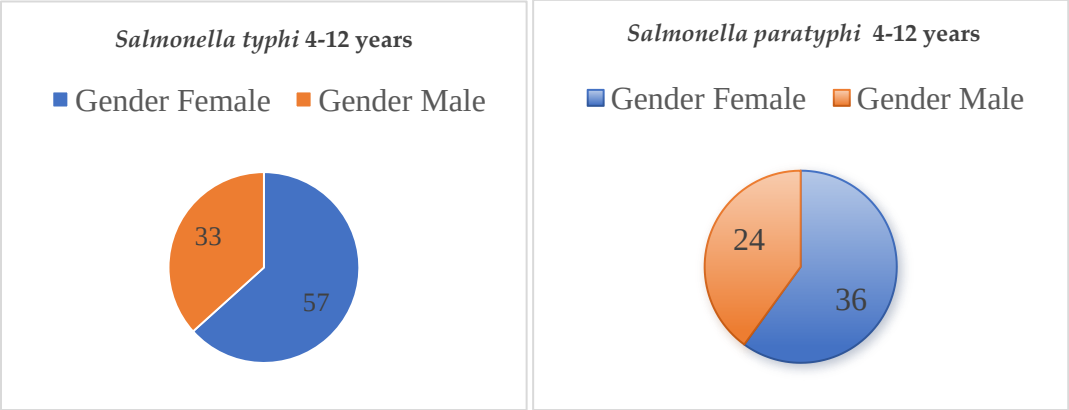


**Fig. 1.** The age wise and gender wise distribution of blood samples for *S. typhi* and *S. paratyphi*

The patients included in the study were both male and females whose blood culture were investigated for *S. typhi* and *S. paratyphi* were aged between four to twelve years as shown in Fig. 1.

**Table II.** Positive and negative blood samples for *S. typhi* and *S. paratyphi*

| Species | Positive samples | Negative samples |
|---|---|---|
| *Salmonella typhi* | 72 | 18 |
| *Salmonella paratyphi* | 41 | 16 |

Out of 90 patients the blood cultures positive for *S. typhi* were 72 samples and 18 samples were tested negative. In contrast, out of 60 patients the blood cultures positive for *S. paratyphi* were 41 samples and 16 samples were tested negative as shown in Table II.

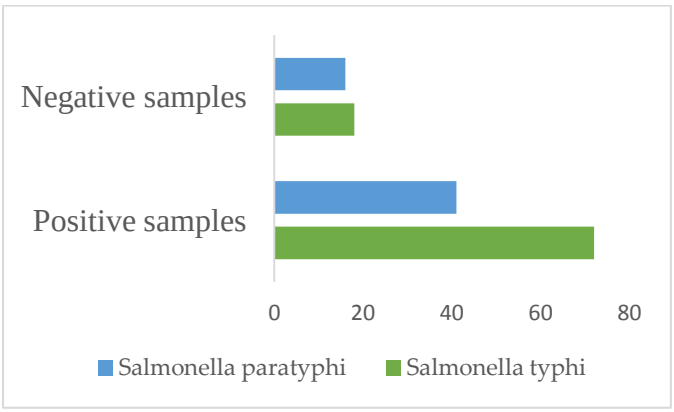


**Fig. 2**. The margin for positive and negative cases for *S. typhi* and *S. paratyphi*

The Fig. 2 indicated that the blood culture for positive patients with *S. typhi* are greater in number in comparison with *S. paratyphi* and same in case of negative blood samples both for *S. typhi* and *S. paratyphi*.

**Table III**. Sensitivity and resistance pattern of *S. typhi* and *S. paratyphi* against multiple antibiotics

| Antibiotics | Sensitivity pattern *S. typhi* | %age | Resistance pattern *S. typhi* | %age | Sensitivity pattern *S. paratyphi* | %age | Resistance pattern *S. paratyphi* | %age |
|---|---|---|---|---|---|---|---|---|
| Ampicillin | 7 | 9.72% | 65 | 90.2% | 8 | 19.5% | 33 | 80.4% |
| Ciprofloxacin | 0 | 0% | 72 | 100% | 1 | 2.44% | 40 | 97.5% |
| Ceftriaxone | 4 | 5.55% | 68 | 94.4% | 3 | 7.31% | 38 | 92.6% |
| Cotrimoxazole | 3 | 4.16% | 69 | 95.8% | 4 | 9.75% | 37 | 90.2% |
| Cefotaxime | 0 | 0% | 72 | 100% | 1 | 2.43% | 40 | 97.5% |
| Azirthromycin | 72 | 100% | 0 | 0% | 41 | 100% | 0 | 0% |
| Meropenum | 72 | 100% | 0 | 0% | 41 | 100% | 0 | 0% |

Resistance and sensitivity to typhoid is gaining attention day by day. Whereas, the results of the current study shows that Azirthromycin and Meropenum are 100% sensitive, and 0% resistant to *S. typhi*. In the same way, the results for *S. paratyphi* suggests that Azirthromycin and Meropenum are 100% sensitive, and 0% resistant to *S. paratyphi* as shown in table 3. This explains that these two antibiotics should be given as the first line drugs to the patients in order to combat with the effects of this disease. The suggested results were in accordance with the study performed in Peshawar, Pakistan (11–13). Ampicillin, shows 9.72% sensitivity and 90.2% resistance for *S. typhi*. Cotrimoxazole showsed 4.16% sensitivity and 95.8% resistance to *S. typhi*. Ceftriaxone shows 5.55% sensitivity and 94.4% resistance. Whereas, in case of *S. paratyphi*, Ampicillin shows19.5% sensitivity and 80.4% resistance for the given antibiotic. Cotrimoxazole showed 9.75% sensitivity and 90.2% resistance to *S. paratyphi*. Ceftriaxone shows 7.31% sensitivity and 92.6% resistance as given in Table III. The following results shows that these drugs are highly resistant to *S. typhi* and *S. paratyphi*. Therefore, they should be excluded as first line drugs against this disease. The results were in accordance with the study reported in 2022 and 2009 which shows that these drugs are very resistant to *S. typhi* and *S. paratyphi* (14, 15). Both Ciprofloxacin and Cefotaxime shows 0% sensitivity and 100% resistance towards *S. typhi*. Similarly, Ciprofloaxacin and Cefotaxime are 0% sensitive and 100% resistant to *S. paratyphi* as shown in table 3 which shows that these drugs must be excluded from antienteric fever drugs. Hence, the given results suggest that these two antibiotics are highly resistant for *S. typhi* and *S. paratyphi*. Therefore, these two drugs shall also be exuded from the criteria of first line drugs. The given results were in accordance with the results reported in Peshawar Pakistan which shows similar results as reported in the present study (11, 16).

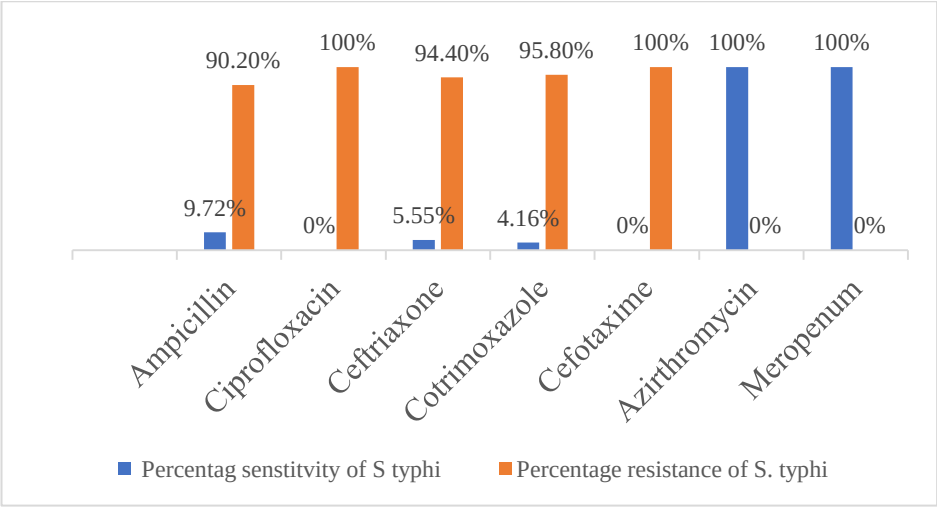


**Fig. 3.** The percentage sensitivity and resistance of *S. typhi*

The Fig. 3 shows the values of antibiotics used in the study which explains that Azirthromycin and Meropenum are 100% sensitive and 0% resistant to *S. typhi*. Ampicillin, Ceftriaxone and Cotrimoxazole are least sensitive and highly resistant to *S. typhi*. While, Cefotaxime and Ciprofloxacin are zero percent sensitive and hundred percent resistant toward *S. typhi*.

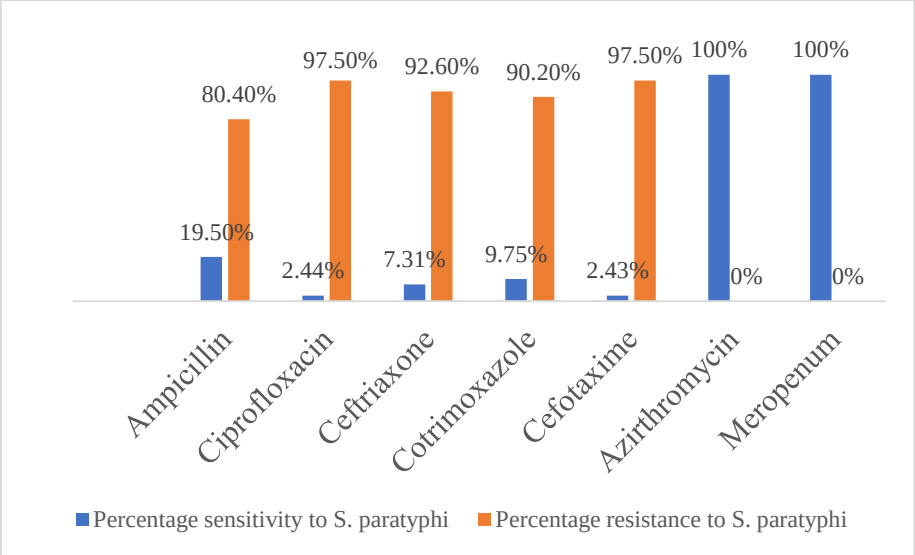


**Fig. 4.** The percentage sensitivity and resistance of *S. paratyphi*

The Fig. 4 illustratesd that the values of antibiotics used in the study shows that Azirthromycin and Meropenum are hundred percent sensitive and zero percent resistant to *S. paratyphi*. Whereas, Ampicillin, Ceftriaxone and Cotrimoxazole shows some value for sensitivity and around eighty to ninety percent resistance for *S. paratyphi*. While, Cefotaxime and Ciprofloxacin are highly resistant and least sensitive towards *S. paratyphi*.

# CONCLUSION

The current study highlights that as antibiotic resistance continues to increase over time, it is crucial to discontinue the use of antibiotics that have developed significant resistance against Salmonella isolates as first-line treatments. Instead, antibiotics that demonstrate higher sensitivity and lower resistance should be prioritized as first-line therapies to protect children from the effects of typhoid fever.

## Future Recommendations:

Further studies are needed to assess the effectiveness of antibiotics not included in this research against *S. typhi* and *S. paratyphi*. Additionally, more research is required to identify new drugs for treating enteric fever caused by *Salmonella* isolates.

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