Research Article

# Resistance Patterns of Salmonella Strains in Enteric Fever: A Prospective Observational Study

**Zeeshan Ikhtiar,[1] Muhammad Bilal,[2] Saima Khattak,[3] Faisal Saleh Hayat,[4] Ilyas Badshah,[5] Muhammad Hussain,[6] Mujtaba Hadi,[7] Hina Ikhtiar,[8] Hamid Ullah[9]**

*[1,2,5,6]Department of Medicine, Medical Teaching Institution, Lady Reading Hospital Peshawar, Pakistan ; [3]Department of Obstetrics & Gynaecology , Medical Teaching Institution, Lady Reading Hospital Peshawar, Pakistan; [4]Department of Cardiology, Medical Teaching Institution, Lady Reading Hospital Peshawar, Pakistan; [7]Department of Surgery, Medical Teaching Institution, Lady Reading Hospital Peshawar, Pakistan; [8]Department of Biochemistry, Kabir Medical College/Gandhara University, Peshawar, Pakistan; [9]Russells Hall Hospital, The Dudley Group, NHS, United Kingdom*

## Abstract

**Background:** The global threat of enteric fever is escalating due to the increasing prevalence of extended drug resistance. In Pakistan, the situation is particularly dire as the Typhi serovar exhibits rapid mutations, advancing from multi-drug resistant (MDR) to extensively drug-resistant (XDR) strains.

**Objective:** To determine antimicrobial susceptibility of salmonella strain causing enteric fever to identify effective drugs needed to successfully treat this infection.

**Methods:** This cross-sectional study included 189 patients who presented with symptoms of enteric fever to Lady Reading Hospital, Peshawar, between March 15 and October 31, 2023. Out of these, 150 had culture-confirmed enteric fever. Patient details and blood culture results were meticulously recorded and analyzed using SPSS version 20.

**Results:** The cohort comprised 42 females (28%) and 108 males (72%). MDR strains were identified in 6 cases (4%) and XDR strains in 141 cases (94%). Notably, 36 of the XDR strains (24%) exhibited varied sensitivities to specific antibiotics. Meropenem and Imipenem were 100% effective across all samples. Azithromycin showed an efficacy rate of 94% (141 cases). Traditional first-line antibiotics like Ampicillin, Chloramphenicol, and Co-Trimoxazole showed high resistance rates of 98% (147 cases), 96% (144 cases), and 88% (132 cases), respectively. Among second-line antibiotics, Ceftriaxone, Cefixime, and Ciprofloxacin exhibited resistance rates of 94% (141 cases), 94% (141 cases), and 90% (135 cases), respectively. A significant association was found between gender and Azithromycin sensitivity (P=0.05).

**Conclusion:** The results of our study highlight the increasing prevalence of azithromycin resistance among Salmonella Typhi strains, while some extensively drug-resistant (XDR) strains remain susceptible to first-line medications.

**Received:** 09-02-2024 | **Revision:** 19-07-2024 | **Accepted:** 03-10-2024

**Corresponding Author** | Dr. Muhammad Bilal, Assistant Professor of Medicine, Medical Teaching Institution, Lady Reading Hospital Peshawar, Pakistan, **Email:** drmba@yahoo.com

**Keywords** | Typhoid fever, Salmonella Typhi, XDR typhoid, fluoroquinolones, antibiotic resistance, meropenem, Ceftriaxone, Cefixime

**Production and Hosting by KEMU**

https://doi.org/10.21649/akemu.v30i4.5626



## Introduction

Enteric fever, with an estimated annual incidence of approximately 20 million cases and resulting in around 160,000 deaths, is emerging as a considerable global health challenge. This is attributed primarily to

its escalating resistance to a broad spectrum of antimicrobial agents.[1] In South Asian geopolitical landscape, notably within the confines of India and Pakistan, it has been observed that the pathogens Salmonella enterica serovar Typhi and Salmonella enterica serovar Paratyphi A, B, or C play a significant role in the escalation of antimicrobial resistance.[2] A series of genetic mutations have resulted in an intricate therapeutic milieu characterized by rapid evolution of resistance to antimicrobial pharmacotherapeutics as a result of the predominance of the Typhi serovar, notorious for engendering a more virulent form of the disease.[1] There is a stark transition from MDR to XDR in Pakistan, where the phenomenon is most pronounced.[1,3]

Multiple cases of extensive drug resistance (XDR) were documented in Sindh in 2016, verified through hemoculture methodologies, with a subsequent proliferation across the country.[4] In response to a burgeoning crisis, Pakistan has incorporated the typhoid conjugate vaccine (TCV) into its national immunization schedule, following WHO guidelines.[5] There are indications that the XDR strain of Salmonella Typhi is starting to spread globally.[1] As an indication of the international spread of the XDR Salmonella Typhi strain, a Canadian pediatrician was infected in 2018 with the strain traceable to Karachi, along with reports of cases involving travelers originating in Pakistan and bound for the United States.[6]

A major cause of enteric fever, which encompasses both typhoid and paratyphoid fevers, is consumption of contaminated foods and water, where the etiological agents Salmonella enterica serovar Typhi and Paratyphi A, B, or C invade the intestinal mucosa, leading to a systemic infection. Intestinal perforation and neurologic symptoms are among the severe complications that can result from gastroenteritis.[3]

The challenge of enteric fever persists despite improvements in sanitation and healthcare infrastructure, especially in economically disadvantaged nations.[7] Globally, there are an estimated 14 million cases of enteric fever each year, with more than 100,000 deaths, mostly in settings with poor sanitation, scarce potable water, and high population density.[8]

In the management of enteric fever, the emergence of antibiotic-resistant Salmonella strains is a significant obstacle. A combination of imprudent and excessive antibiotic use and suboptimal therapeutic protocols has contributed to the emergence of multidrug-resistant bacteria (MDR).[8] To tailor treatment strategies, circumvent therapeutic failures, and mitigate the burden of enteric fever, we must understand contemporary Salmonella strain patterns and their antimicrobial susceptibilities.[5]

As a result of indiscriminate prescribing and misuse of primary and secondary antibiotics within Pakistan, the number of XDR gastrointestinal cases is on the rise. The widespread deployment of Azithromycin amidst the COVID-19 pandemic may have further compromised the limited antimicrobial arsenal against the XDR strain. There are numerous antibiotic resistance genes on this XDR variant's plasmid, suggesting incipient dissemination to other Salmonella Typhi and Paratyphi strains, potentially heralding Azithromycin resistance.[2,4,6]

A multifaceted significance of this study lies in its provision of contemporaneous, geographically specific data on the prevalence of enteric fever that adds to the existing understanding of the disease's epidemiology. It is crucial to identify and characterize dominant Salmonella strains to orchestrate tailored prevention and vaccination strategies. To formulate more effective therapeutic regimens, healthcare practitioners need insights from antimicrobial sensitivity assessments. A prospective observational study is being conducted to bridge prevailing knowledge lacunae by examining the prevalence of enteric fever and the phenotypic characteristics of dominant Salmonella strains.

## Methods

A cross-sectional study was conducted in the Lady Reading Hospital, a Medical Teaching Institution (MTI), Peshawar from March 15 to October 31, 2023. A total of one hundred and fifty patients were recruited through convenient sampling technique. Patients with confirmed blood culture reports for Salmonella typhi, regardless of gender, were included in the research while those who tested positive for Salmonella paratyphi in their blood culture and having age less than 12 years old, and patients who used antibiotics either parenteral or oral in last 48 hours prior to study were excluded from the study. An ethical approval was obtained from Institutional ethics committees before conducting the study. Insti-

tutional ethics committees approved the methodology of the study with Ref No. 368/LRH/MTI on dated 08/02/2023. Also a consent form was obtained from patients before recruiting them. A blood culture and sensitivity test were performed on patients' samples who displayed clinical characteristics suggestive of Enteric fever to determine if Salmonella Typhi was present. Patients were included in the study if they had a prolonged fever lasting more than five days, with or without additional symptoms such as abdominal pain, diarrhea, constipation, headache, or general malaise. Pulse-temperature dissociation (relative bradycardia) was also considered where applicable.

A blood sample of 5 ml were collected in BACTECTM blood culture bottles which contained 50 ml of tryptose phosphate broth (TPB) and polyanethol sulfonate of 0.02% under aseptic condition. The inoculated blood culture bottle was placed immediately in an incubator at 37°C in department of pathology. Identification and isolation of bacteria was based on gram-staining of bacteria, and subcultured onto the MacConkey, Salmonella-Shigella (SS), Nutrient, and Blood agar plates. Isolates were further characterized through biochemical methods including the Triple Sugar Iron (TSI), Urease negative, and Indole negative. After biochemical tests confirmation, all isolates were tested for the antibiotic susceptibility testing by using the discs diffusion method Oxoid (Oxoid Unipath Limited Basingstoke England) according the protocol of Bauer et al (1966). In this study, we defined Multidrug-Resistant (MDR) Salmonella Typhi as strains resistant to at least three different classes of antibiotics, specifically ampicillin, chloramphenicol, and co-trimoxazole. Extensively Drug-Resistant (XDR) Salmonella Typhi strains were identified as those resistant to antibiotics from at least five different classes, including all first-line drugs (ampicillin, chloramphenicol, and co-trimoxazole), fluoroquinolones (such as ciprofloxacin), and third-generation cephalosporins (such as ceftriaxone).

The antibiotics tested in this study included meropenem, imipenem (10 µg), azithromycin, ceftriaxone (30 µg), cefixime (30 µg), ciprofloxacin (5 µg), co-trimoxazole (1.25/23.75 µg), chloramphenicol (30 µg), ampicillin, gentamicin, and amikacin (10 µg). To determine resistance patterns, nutrient agar plates inoculated with Salmonella Typhi were used. Antibiotic discs were placed on these plates, which were then incubated for 24 hours at 37°C. After incubation, the zones of inhibition around each antimicrobial disc were measured in millimeters. These measurements were compared with the standard chart recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) to categorize the bacteria as resistant, intermediate, or sensitive to each specific antibiotic. This methodology allowed for an accurate assessment of the resistance patterns of Salmonella Typhi, providing crucial data on the effectiveness of different antimicrobial agents.

All data were collected and entered in Microsoft Excel spreadsheet 2020 and then further analyzed through Statistical Package for Social Sciences version 22 (SPSS-22). Descriptive data including gender, type of isolate, antibiotic sensitivity pattern, and culture positivity were analyzed and described as frequency and percentage, then presented in tabulated form. For all categorical data, chi-square was applied and p-value was calculated. P-value $<0.05$ was considered significant.

## Results

Our study enrolled a total of 150 participants, predominantly male, comprising 72% (n=108) of the patients, while females were about 28% (n=42). Regarding antimicrobial susceptibility, 98% (n=147) of the participants had strains of Salmonella Typhi that were resistant to antibiotics, with only 2% (n=3) showing sensitivity. The incidence of multi-drug-resistant (MDR) Salmonella Typhi strains was 4% (n=6), whereas 96% (n=144) had non-MDR strains. Extreme drug-resistant (XDR) strains were found in 94% (n=141) of the cases, with only 6% (n=9) having non-XDR strains. Among the XDR strains, 24% (n=36) exhibited differences in specific antibiotic sensitivities, while 76% (n=114) did not.

Table 1 presents the trends in antibiotic sensitivities of Salmonella strains observed in the study. The data shows that all tested strains were sensitive to meropenem and imipenem, with no intermediate or resistant strains identified for these antibiotics. A high sensitivity to azithromycin was observed, with a small percentage showing intermediate sensitivity. In contrast, most strains were resistant to ceftriaxone and cefixime, with only a minor fraction showing sensitivity. Ciprofloxacin exhibited a notable pattern of resistance, with few sen-

sitive and intermediate strains. Similarly, a significant proportion of strains were resistant to co-trimoxazole, chloramphenicol, and ampicillin. For gentamicin and amikacin, the majority of the strains did not report sensitivity, with a small portion showing sensitivity and intermediate sensitivity (Table 1).

**Table 1:** *Trends in antibiotic sensitivities to salmonella strains.*

| Trends in antibiotic sensitivities to salmonella strains | | Frequency | Percentage |
|---|---|---|---|
| **Meropenem** | Sensitive | 150 | 100.0% |
| | Intermediate | 0 | 0.0% |
| | Resistant | 0 | 0.0% |
| **Imipenem** | Sensitive | 150 | 100.0% |
| | Intermediate | 0 | 0.0% |
| | Resistant | 0 | 0.0% |
| **Azithromycin** | Sensitive | 141 | 94.0% |
| | Intermediate | 9 | 6.0% |
| | Resistant | 0 | 0.0% |
| **Ceftriaxone** | Sensitive | 9 | 6.0% |
| | Intermediate | 0 | 0.0% |
| | Resistant | 141 | 94.0% |
| **Cefixime** | Sensitive | 9 | 6.0% |
| | Intermediate | 0 | 0.0% |
| | Resistant | 141 | 94.0% |
| **Ciprofloxacin** | Sensitive | 3 | 2.0% |
| | Intermediate | 12 | 8.0% |
| | Resistant | 135 | 90.0% |
| **Co-trimoxazole** | Sensitive | 18 | 12.0% |
| | Intermediate | 0 | 0.0% |
| | Resistant | 132 | 88.0% |
| **Chloramphenicol** | Sensitive | 6 | 4.0% |
| | Intermediate | 0 | 0.0% |
| | Resistant | 144 | 96.0% |
| **Ampicillin** | Sensitive | 3 | 2.0% |
| | Intermediate | 0 | 0.0% |
| | Resistant | 147 | 98.0% |
| **Gentamicin** | No sensitivity reported | 141 | 94.0% |
| | Sensitive | 6 | 4.0% |
| | Intermediate | 3 | 2.0% |
| | Resistant | 0 | 0.0% |
| **Amikacin** | No sensitivity reported | 138 | 92.0% |
| | Sensitive | 12 | 8.0% |
| | Intermediate | 0 | 0.0% |
| | Resistant | 0 | 0.0% |

Table 2 examines the association between antibiotic sensitivity/resistance and gender among the study participants. The data reveals that sensitivity to azithromycin shows a significant difference between males and females, with males showing a higher rate of intermediate sensitivity. For ceftriaxone and cefixime, there was no significant difference in resistance between genders. Ciprofloxacin showed a higher rate of resistance in males compared to females. Co-trimoxazole, chloramphenicol, and ampicillin exhibited significant gender differences, with males showing higher resistance rates. Amikacin sensitivity was reported only in males. The incidence of Multidrug-Resistant (MDR) strains did not significantly differ between genders, whereas Extensively Drug-Resistant (XDR) strains were similarly distributed across genders. However, specific antibiotic sensitivities within the XDR group did not show significant gender differences (Table 2).

**Table 2:** *Association between Antibiotic Sensitivity/ Resistance and Gender*

| Parameter | Detail | Gender | | P value |
|---|---|---|---|---|
| | | Male | Female | |
| **Azithromycin** | Sensitive | 99 | 42 | 0.05 |
| | Intermediate | 9 | 0 | |
| **Ceftriaxone** | Sensitive | 6 | 3 | 0.713 |
| | Resistant | 102 | 39 | |
| **Cefixime** | Sensitive | 6 | 3 | 0.713 |
| | Resistant | 102 | 39 | |
| **Ciprofloxacin** | Sensitive | 3 | 0 | 0.125 |
| | Intermediate | 6 | 6 | |
| | Resistance | 99 | 36 | |
| **Co-Trimoxazole** | Sensitive | 9 | 9 | 0.027 |
| | Resistant | 99 | 33 | |
| **Chloramphenicol** | Sensitive | 0 | 6 | 0.000 |
| | Resistant | 108 | 36 | |
| **Ampicillin** | Sensitive | 0 | 3 | 0.005 |
| | Resistant | 108 | 39 | |
| **Amikacin** | No Sensitivity Reported | 96 | 42 | 0.024 |
| | Sensitive | 12 | 0 | |
| **Sensitivity** | No | 108 | 39 | 0.005 |
| | Yes | 0 | 3 | |
| **MDR** | No | 102 | 42 | 0.119 |
| | Yes | 6 | 0 | |
| **XDR** | No | 6 | 3 | 0.713 |
| | Yes | 102 | 39 | |
| **XDR with differences in specific antibiotic sensitivities** | No | 81 | 33 | 0.646 |
| | Yes | 27 | 9 | |

## Discussion

This research included the selection of 189 patients who presented at MTI, Lady Reading Hospital, Peshawar between March 2023, and October 2023. These patients were instructed to undergo blood culture and sensitivity tests, and their progress was monitored by the analysis of the resulting reports. Ultimately, a total of 150 cases of Salmonella typhi were chosen based on blood culture evidence. The resistant strains of the bacteria and their sensitivity to antibiotics were documented. The analysis we conducted examines the frequency of resistance patterns in Salmonella Typhi, as well as the relationship between gender and responses to antibiotics. The findings provide important insights into the dynamics of Salmonella infections.

It is evident that there is a significant occurrence of Extensively Drug Resistant (XDR) Salmonella Typhi strains, which make up 94.0% of the reported cases. Meropenem and Imipenem exhibit remarkable effectiveness, with both showing 100.0% sensitivity against the strains examined. The sensitivity of Azithromycin has a notable association with gender ($P = 0.05$), indicating possible variations in response based on gender. The sensitivity to Co-Trimoxazole is associated with gender ($P = 0.027$), indicating possible gender-related differences in response.[9]

It is worth mentioning that the lack of sensitivity seen for Amikacin has a noteworthy correlation with gender ($P = 0.024$), suggesting the presence of gender-related differences. Furthermore, the metrics 'Sensitivity,' 'MDR,' 'XDR,' and 'XDR with Differences' show diverse gender connections, which enhance our nuanced comprehension of antibiotic responses.[3] The gender distribution in our research consisted of 28% female patients and 72% male individuals. In our investigation, the occurrence rate of sensitivity strain was just 2%, but the prevalence of MDR salmonella typhi-resistant strain was 4%.[1] In summary, a significant majority of cases (94%) were classified as extensively drug-resistant (XDR), as shown by Butt et al. (2022), Akram et al. (2020), Khan et al. (2022), Klemm et al. (2018), and Shah et al. (2020).[2,4,10-13] Among these XDR patients, 24% exhibited variations in antibiotic sensitivities. Notably, the findings for the Azithromycin, Co-Trimoxazole, and Aminoglycoside groups were statistically significant. About 12% of patients shown sensitivity to Co-Trimoxazole, with 6 instances successfully responding to a treatment trial using along with Azithromycin. This suggests a potential resurgence of susceptibility to primary antimicrobial drugs. This might be attributed to the diminished adaptation pressure resulting from their limited use. This was corroborated by the discoveries made by Gupta et al. in 2023 and Harish et al. in 2011.[9,14] Azithromycin had a 6% intermediate outcome, aligning with the findings of Taneja et al. 2021 (28% resistance), Dutta et al. 2014 (28.1% resistance), and Shah et al. 2020 (5% resistance).[5,13,15] Nevertheless, these findings contrast the studies published by Mumtaz et al. 2023, which documented a 0% resistance rate, Wong et al. 2014, which reported a 0.3% resistance rate, and Gupta et al. 2023, which also reported a 0% resistance rate.[3,14,16] The whole XDR data showed a remarkable result with 100% sensitivity to Aminoglycosides, namely Gentamicin and Amikacin, accounting for 4% and 8% respectively. This is consistent with the findings of Menashe et al. in 2008 and Mandal et al. in 2009.[9,17-19] Another study reported that S. typhi is reported predominantly causing pediatric blood stream infections in Peshawar.[20] It is also observed that XDR S. Typhi strains reported in other countires in patients with history of traveling from Pakistan.[21]

The health care system in Pakistan and around the world should monitor the emergence of drug resistance in microorganisms, particularly in the clinical domain. The emphasis should be on educating the public on the safe use of antibiotics, the availability of typhoid vaccination, and how to prevent the disease by enhancing water quality and sanitation. While this study offers a thorough overview of the prevalence of XDR and MDR S. Typhi, further data from other hospitals should be obtained to ensure that the findings are accurate throughout the province and the nation. Furthermore, rising antibiotic resistance indicates how quickly drugs are losing their effectiveness in treating typhoid fever. Tight measures should be implemented to stop the infection from spreading in the first place, and areas most affected by resistant strains of the disease should quickly implement appropriate typhoid fever vaccination procedures. Since safety and hygiene measures are largely focused on preventing the spread of pathogens, they should be considered. The lack of MIC for culture and sensitivity, which would have provided more infor-

mation about antibiotic response, is one of the study's weaknesses. Furthermore, sociodemographic statistics such as the number of homes, cleanliness standards, and drinking water quality were absent from the retrospective data.

## Conclusion

The results of our study highlight an increasing prevalence of azithromycin resistance among Salmonella Typhi strains, with some extensively drug-resistant (XDR) strains still susceptible to first-line antibiotics. This emphasizes the need for careful consideration of antibiotic choices and suggests that meropenem, imipenem and azithromycin usage in Pakistan for enteric fever treatment should be closely monitored. Comprehensive antibiotic sensitivity reports are crucial for developing effective treatment strategies and preventing the misuse of broad-spectrum antibiotics.

**Ethical Approval:** The Ethical Review Board, Medical Teaching Intuition/ Lady Reading Hospital, Peshawar approved this study vide letter No. Ref No. 368/ LRH/ MTI.

**Conflict of Interest:** None

**Funding Source:** None

**Authors' Contribution:**

**ZI:** Conception & design, drafting of article

**MB:** Acquisition of data, analysis & interpretation of data, Conception & design, drafting of article, critical revision for important intellectual content, final approval

**SK:** Conception & design, drafting of article, final approval

**FSH:** Acquisition of data, drafting of article

**IB:** Acquisition of data, analysis & interpretation of data, drafting of article

**MH:** Analysis & interpretation of data, drafting of article

**MH:** Analysis & interpretation of data, drafting of article

**HI:** Acquisition of data, drafting of article, final approval

**HU:** Acquisition of data, drafting of article, final approval

## References

1. Pitzer VE, Meiring J, Martineau FP, Watson CH, Kang G, Basnyat B, et al. The invisible burden: diagnosing and combatting typhoid fever in Asia and Africa. Clin. Infect. Dis.. 2019;69(Supplement_5);S395-S401.
2. Tharwani ZH, Kumar P, Salman Y, Islam Z, Ahmad S, Essar MY. Typhoid in Pakistan: Challenges, efforts, and recommendations. Infect Drug Resist 2022; 15(1): 2523-27.
3. Mumtaz MN, Irfan M, Siraj S, Khan A, Khan H, Imran M, et al. Whole-genome sequencing of extensively drug-resistant Salmonella enterica serovar Typhi clinical isolates from the Peshawar region of Pakistan. J. Infect. Public Health. 2024;17(2):271-82.
4. Butt MH, Saleem A, Javed SO, Ullah I, Rehman MU, Islam N, et al. Rising XDR-typhoid fever cases in Pakistan: are we heading back to the pre-antibiotic era? Front. Public Health. 2022; 9(1):1-3.
5. Taneja J, Khatter S, Paul M, Pandey A, Kaur I. Antimicrobial resistance in Typhoidal Salmonella in a tertiary care teaching centre in North India. Jour. Comm. Dis. 2021; 53(1): 1-4.
6. Wong W, Al Rawahi H, Patel S, Yau Y, Eshaghi A, Zittermann S, et al. The first Canadian pediatric case of extensively drug-resistant Salmonella Typhi originating from an outbreak in Pakistan and its implication for empiric antimicrobial choices. IDCases. 2019;15(1):1-4.
7. Maharjan A, Dhungel B, Bastola A, Thapa Shrestha U, Adhikari N, Banjara MR et al. Antimicrobial susceptibility pattern of Salmonella spp. isolated from enteric fever patients in Nepal. Infec. Dis Rep. 2021;13(2):388-400.
8. Jahan N, Huq N, Yusuf MA, Morshed MS, Chhobi FK, Shamsuzzaman SM. Diagnostic Validity of Flagellin Gene (fliC) in Urine for the Detection of Typhoid Fever. Bangladesh J. Med. Microbiol. 2023;17(1):34-39.
9. Biswas M, Biswas S, Gupta B, Mascellino MT, Rakshit A, Chakraborty B. Changing paradigms in antibiotic resistance in Salmonella species with focus on fluoroquinolone resistance: a 5-year retrospective study of enteric fever in a tertiary Care Hospital in Kolkata, India. Antibiotics. 2022;11(10):1308-1312.
10. Akram J, Khan AS, Khan HA, Gilani SA, Akram SJ, Ahmad FJ, et al. Extensively drug-resistant (XDR) typhoid: evolution, prevention, and its management. BioMed Rese. Inter. 2020;2020(1):1-7.

11. Khan M, Tu-Zahra F, Gul A, Saleem M, Riaz M, Gul W. Extensively Drug-Resistant Salmonella enterica serovar Typhi in Pediatric population during CoVID-19 Pandemic. Inter. Jour. Infec. Dis. 2022;116(1): S4-S8.
12. Klemm EJ, Shakoor S, Page AJ, Qamar FN, Judge K, Saeed DK, et al. Emergence of an extensively drug-resistant Salmonella enterica serovar Typhi clone harboring a promiscuous plasmid encoding resistance to fluoroquinolones and third-generation cephalosporins. MBio. 2018;9(1):105-118.
13. Shah SAA, Nadeem M, Syed SA, Abidi STF, Khan N, Bano N. Antimicrobial sensitivity pattern of Salmonella Typhi: emergence of resistant strains. Cureus. 2020; 12 (11):1-5.
14. Gupta V, Kaur H, Gupta R, Chaudhary J, Gupta M. Antibiotic Resistance among Salmonella Isolates-A Five-year Trend. Jour. Comm. Dis. 2023;55(3B):7-13.
15. Katiyar A, Sharma P, Dahiya S, Singh H, Kapil A, Kaur P. Genomic profiling of antimicrobial resistance genes in clinical isolates of Salmonella Typhi from patients infected with Typhoid fever in India. Sci. Rep. 2020; 10(1):1-15.
16. Liu M, Zhu K, Li X, Han Y, Yang C, Liu H, et al. Genetic characterization of a Salmonella enterica serovar Typhimurium isolated from an infant with concurrent resistance to ceftriaxone, ciprofloxacin and azithromycin. J Glob Antimicrob Resist. 2023;35(1):252-56.
17. Galeev A, Suwandi A, Bakker H, Oktiviyari A, Routier FH, Krone L, et al. Proteoglycan-dependent endo-lysosomal fusion affects intracellular survival of Salmonella Typhimurium in epithelial cells. Front. Immunol. 2020;11(1):1-15.
18. Salman HA, Abdulmohsen AM, Falih MN, Romi ZM. Detection of multidrug-resistant Salmonella enterica subsp. enterica serovar Typhi isolated from Iraqi subjects. Vet. World. 2021;14(7):1922-928.
19. Chatham-Stephens K, Medalla F, Hughes M, Appiah GD, Aubert RD, Caidi H, et al. Emergence of extensively drug-resistant Salmonella Typhi infections among travelers to or from Pakistan—United States, 2016–2018. Morb Mortal Wkly Rep. 2019;68(1):11-13.
20. Muhammad A, Khan SN, Jamal T, Haq IU, Jabbar A, Ihsan AN. Bacterial Spectrum and Antimicrobial Profile of Pediatric Blood Stream Infection at a Tertiary Care Hospital in Pakistan. Chin. Med. J. 2020;35(4):315-22.
21. Ahmad S, Sharif S, Ahmad N, Ali B. Antibiotic Resistance: Targeting Extensively Drug Resistant (XDR) Salmonella Typhi. National J Life Health Sci. 2024; 3(2):55-64.