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A study of Anti Microbial Resistance in *Salmonella Enterica Serovars Typhi* and *Paratyphi A* at CMH Quetta

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ABSTRACT

Objectives: To ascertain the antimicrobial resistance of *Paratyphi A* and *Typhi Serovars* of *Salmonella Enterica*
Study Design: Prospective observational study
Place and Duration of Study: Clinical Microbiology Laboratory at the CMH Quetta, Pakistan November 2022-Septmeber 2023 Patients and
Methodology: The data from the lab were reviewed in this investigation Blood cultures from 1441 admitted patients from the Medicine department supplied to the laboratory of the CMH Quetta between November 2022 and September 2023 were tested for antibiotic susceptibility and Typhoidal Salmonellae were isolated.
Results: Out of total 1441 isolates, 839(58.2%) were isolates of *Salmonela Typhi* and 602(41.8%) were S Paratyphi .These microbes had maximum resistance against Ceftriaxone (71.6%, 67.2%), Ciprofloxacin (70.6%, 66.6%). *S typhi and paratyphi* have minimal resistance to Meropenum 7.7% and 9.13% respectively. These patients had maximum sensitivity for Meropenum.

Conclusion: *S. Typhi and S. Paratyphi* have high rates of multidrug resistance against Ceftriaxone and Ciprofloxacin. Meropenum had found to have minimal resistance.

Keywords: Antibiotic Reistances, Enteric fever, *Salmonella enterica typhi,* and salmonella enterica paratyphi.

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INTRODUCTION:

Typhoid fever affects 21.6 million people worldwide each year and results in about 250,000 fatalities.[1] Typhoid and paratyphoid fever are caused by serovars of Salmonella enterica Typhi, also referred to as Salmonella ser. Typhi and Paratyphi, respectively. Estimates suggest that countries in South and Southeast Asia accounted for more than 90% of all typhoid fever cases.[1] A significant health issue in developing nations remains to be enteric fever, which is brought on by Salmonella enterica serovars Typhi and Paratyphi A, notably in South Asia and Pakistan.[2,3] The H58 S. Typhi haplotype continues to dominate in many parts of South and South-East Asia, where enteric fever is still a major problem. Due in part to the widespread use of this antibiotic family, fluoroquinolone resistance is very common in Asia.[4] Several low- and middle-income countries lack adequate laboratory resources, making standard procedures for a clear diagnosis and a successful antibiotic treatment tough. Typhoid fever is difficult to identify from other types of febrile illnesses.[5] Historically, ampicillin, trimethoprim-sulfamethoxazole, and chloramphenicol were the first-line antibiotic treatments for typhoid fever.[6] The development of antibiotic resistance and the shifting modalities of presentation have made it more challenging to identify and treat enteric fever in many regions of the world. *S. Typhi bacteria* that are resistant to all three of the first-line prescribed medications for treatment are referred to be multidrug resistant (MDR) strains of S. Typhi.[7] *MDR S. Paratyphi* cases have been recorded at up to 25% worldwide incidence.[8] In Hyderabad, Pakistan, in 2016, it was discovered that Salmonella Typhi was highly drug resistant (XDR), which is characterised as having resistance to first-line antibiotics, a fluoroquinolone, and a third-generation cephalosporin.[12] Since then, reports of more than 10,365 infections in Pakistan caused by XDR Salmonella Typhi have been sent to the WHO.[9,10] Fluoroquinolones were the first line of defence against MDR strains after their introduction. But since 2000, there has been a sharp rise in the proportion of *S. Typhi* isolates that are fluoroquinolone resistant. There have been reports of MDR isolates from various parts of South Asia that are less susceptible to

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fluoroquinolones. MDR infections can be treated with azithromycin, ceftriaxone, and cefixime, both of which are cephalosporin antibiotics. Cephalosporins are the medicine of choice in South Asia for empiric therapy because to high levels of fluoroquinolone and multidrug resistance.[11] According to earlier findings from Pakistan, *S. Typhi* and Paratyphi are becoming more resistant to fluoroquinolone antibiotics. Increased availability to antimicrobial drugs, diagnostic gaps brought on by a lack of laboratory capabilities, and inexpensive, subpar fluoroquinolone formulations are some of the main factors contributing to the rise of antimicrobial resistance in developing nations. It is particularly concerning how rarely third-generation cephalosporins are able to combat Salmonella with typhoidal toxins.[12,13] Although enteric fever is a common illness in Pakistan, little is known about the pattern of antibiotic resistance. The objective of this work was to gather information on the pattern of antibiotic resistance among *S. Typhi and S. Paratyphi* isolates from patients admitted to a general hospital in Quetta between 2022 and 2023.

METHODOLOGY

Between November 2022 and September 2023,1441 patients were the subjects of this observational study. Patients reports were referred by the Medicine departments at CMH Quetta to the Pathology Department for a diagnosis of anti microbial resistance of Salmonella *Enterica Serovars Typhi and Paratyphi* A. The patients were chosen through convenience sampling. The CMH Quetta, Pakistan, conducted a review of the work and gave it their approval (IREB-Reference number: CMH QUETTA CASE FILE 09 TRG). Patients aged above 12 years were included in the study. Patients and their parents also provided formal informed consent.

Inclusion Criteria: Patients who have Typhoid fever, admitted in hospital, aged 12 years or above, were included.

Exclusion Criteria: Patients having previous personal or family history of drug resistance. Multiple comorbidities, psychological history, previous history of drug intake were excluded.

Review of *Typhi and Paratyphi* serovars of Salmonella enterica's antimicrobial susceptibility data A isolated from blood cultures sent to the Clinical Microbiology Laboratory at the CMH Quetta by hospitalised patients. following international laboratory standards for conducting business. Patients who had been admitted to hospitals had their venous blood samples obtained. Blood was injected into bottles of the BACTEC aerobic plus/F improved resins. BACTEC Peds Plus/F bottles were used for patients who weighed less than 12.8 kg. The blood culture bottles were sub-cultured onto the MacConkey agar plate once the BACTEC equipment detected bacterial growth. Colonies with biochemical signs of Salmonellae were validated serologically using specific O and H antisera (BD Laboratories).The antibacterial susceptibilities of ceftriaxone, ciprofloxacin, azithromycin, and meropenem were evaluated. Salmonella isolates grown on Muller-Hinton agar were tested for antibiotic susceptibility using the Kirby-Bauerdisk diffusion method. Fluoroquinolone resistance was determined by ofloxacin resistance, while multidrug resistance was determined by ceftriaxone, ciprofloxacin, and azithromycin resistance. Sequencing was avoided in the regions that affect quinolone resistance. SPSS version 26.0 was used to collect, input, and analyse the data.

RESULTS

This prospective study was carried out on 1441 patients isolates of Salmonella *enterica serovars Typhi and Paratyphi*. Distribution according to age is, 12-17 years were 339(23.5%), age 18-22 years were 229(15.9%), age 23-28 years 333(23.2%), age 29-50 years were 380(26.3%) and age >50 years 160(11.1%). Age distribution can be scene in Table-I.

Table-I: Age distribution of respondents

Variables (Age)	Frequency	Percentages
12-17 years	339	23.5%
18-22 years	229	15.9%
23-28 years	333	23.2%
29-50 years	380	26.3%
>50 years	160	11.1%
Total	1441	100%

Out of total 1441 isolates, 839 (58.2%) were Salmonella Typhi positive and 602(41.8%) were Samonella Paratyphi positive, as shown in Table-II.

Table-II: Frequency of S. Typhi and S. Paratyphi

Variables	Frequency	Percentages
S. Typhi	839	58.2%
S. Paratyphi	602	41.8%
Total	1441	100%

Out of total 839, Salmonella Typhi, 71.6% had resistance to Ceftriaxone, 70.31% to Ciprofloxacin, 19.6% to Azithromycin and 7.7% to Meropenum. Out of total 602, Salmonella Paratyphi A, 67.2% had

resistance to Ceftriaxone, 66.6% to Ciprofloxacin, 18.6% to Azithromycin and 9.13% to Meropenum, as shown in Table-III.

Table-III: Anti Microbial Resistance of Salmonella Typhi and Paratyphi A

Variables	Ceftriaxone	Ciprofloxacin	Azithromycin	Meropenum
Salmonella Typhi	71.6%	70.31%	19.6%	7.7%
Salmonella Paratyphi A	67.2%	66.6%	18.6%	9.13%

DISCUSSION

Out of the total isolates used in this prospective observational investigation, 1441 individuals were examined. of those, 839 were Salmonella Typhi and 602 were Salmonella Paratyphi A. The current study supports the research by Farah Naz Qamar et al., in which the bulk of the isolates belonged to the S. typhi species.[14] Present study found that maximum isolates of *S typhi and Paratyphi* were present in age between 18-50 years, the results were not in accordance to a study carried out Nata Pratama Hardjo Lugitoand Cucunawangsih where maximum isolates were present in age between 6-18 years.[15] Our research shown that *S typhi and S paratyphi* were resistant to *ceftriaxone, and ciprofloxacin* supports research by Ugboko H et al., who also discovered the highest levels of resistance against all of these groups.[16] the present study found that *S. Typhi and Paratyphi* had least resistant to Meropenum and Meropenum had maximum sensitivity is in favor of study carried out in Nepal where Meropenum was found to be effective in treating enteric fever.[17] Present study found that *S typhi and paratyphi* is highly resistant to cetriaxone and ciprofloxacin is in favor of study carried out by H. J. Chand et al. where they found resisitance of microorganism against this group.[18] Present study found that S Paratyphi had increasing resistance over time is n favor study carried out by Butt T et al. where MDR rises from 14% to 44% over a period of 5 years.[19] The declining multidrug resistance trend over time in other locations may be attributable to a change in therapy and a reduction in the use of these three drugs.[20,22]

LIMITATIONS

Lack of a control group, observational design, small sample size, exclusion of individuals with normal results, and lack of an association with risk variables were all limitations in the study. Future research can be done with the aforementioned restrictions in mind.

CONCLUSION

Present study concluded that resistance rates against antimicrobials as *S typhi and paratyphi* is high. These microbes had maximum resistance against Ceftriaxone (71.6%, 67.2%), *Cephalosporins* (70.6%, 66.6%). *S typhi and paratyphi* have minimal resistance to *Meropenum* 7.7% and 9.13% respectively. Typhoid vaccination and policies to restrict the overuse and abuse of antibiotics should be devised and put into place to stop the disease and the spread of resistance.

Conflict of Interest: None.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

HN & HS: Data acquisition, data analysis, critical review, approval of the final version to be published.

NT & STA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MZ: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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