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ORIGINAL ARTICLE

Strains of Typhoid Salmonella in Pakistan Causing an Impending Threat for Drug-Resistant

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ABSTRACT

Aim: To estimate the resistant strains of enteric fever in Pakistan.
Study Design: Cross sectional observation based study
Place and Duration of Study: Department of Paediatric Medicine, Arif Memorial Teaching Hospital, Lahore from 1st April 2021 to 30th September 2021.
Methodology: Fifty patients were selected as study participants. All those patients with positive culture for Salmonella typhi and paratyphi were included. The age of the enrolled patients was taken as >12 years. The microbiological testing for typhoid slides was performed after withdrawing 6cc blood from the patients for blood culturing.
Results: The mean age of the patients was 28±5.3 years. Five patients who showed no resistance while 24% had multiple drug resistance and 66% had extensive drug resistance from various antibiotics against typhoid.
Conclusion: Salmonella typhi is the main strain in Pakistan with extensive resistance found posing serious challenges in the treatment of the disease.
Keywords: Enteric fever, Resistant strain, Pakistan, High burden

INTRODUCTION

Enteric fever, commonly known as typhoid is a bacterial infection caused by gram negative bacteria, typically by Salmonella typhi and less commonly by Salmonella paratyphi which lead to high fever, vomiting and diarrhea. Typically, enteric fever is associated with gastrointestinal symptoms (nausea, diarrhea, vomiting and constipation), prolonged fever, fatigue, headache, cough and loss of appetite. Sometimes it also leads to fatal complications such as intestinal perforations, encephalitis and gastrointestinal hemorrhages if not treated timely and properly.[1]

It's a major health challenge for developing countries with ~250000 deaths annually.[2] In lower income or developing countries, high burden of disease is associated with poor sanitation, improper vaccination system and poor food hygiene.[3] Situation is also worst in neighboring countries of Pakistan like India.[4] In 2016, a resistant strain in Pakistan has emerged which got spread to Sindh and Punjab and CDC has issued extra warning and cautious to travellers to Pakistan.[5,6] This strain was resistant to first and second line treatment, including fluoroquinolones.[7,8] Recent study of Jinnah Hospital also showed that, large group of patients were multidrug resistant (MDR) S. typhi cases who were resistant to chloramphenicol, amoxicillin, ciprofloxacin, co-trimoxazole, and ceftriaxone.[9]

Multidrug resistant is an emerging health challenge for growing nations of the world.[10,11] World health organization has defined enteric fever on the basis of their resistance pattern: non-resistant typhoid fever, multidrug-resistant typhoid and extensively drug-resistant typhoid. International studies have proved that, Typhoid caused by XDR and MDR strains is associated with more severe illness and higher chances of prolonged symptoms and complications.[12] Goal of the current study is to highlight the resistant strains of typhoid in Pakistan. This study will also help in determining its related complications

MATERIALS AND METHODS

This study was cross sectional observation based conducted at Department of Paediatric Medicine, Arif Memorial Teaching Hospital Lahore from 1st April 2021 to 30th September 2021. Out of the total visits for typhoid infections, 50 patients were confirmed for Salmonella typhi and paratyphi. The sample size was calculated in accordance with prevalence of 493 per 100000 individuals per annum with typhoid fever with a frequency of disease as 30%. The 95% confidence interval and 5% margin of error were considered for calculating this sample size. All those patients with positive culture for Salmonella typhi and paratyphi were included. The age of the enrolled patients was taken as >12 years. The microbiological testing for typhoid slides was performed after withdrawing 6cc blood from the patients for blood culturing who were clinically showing typhoid symptoms. Patients were observed for any complication formation during their admission in the hospital. The culture as well as resistance pattern were also recorded in addition to the age, gender and clinical features of each patient. These observations were recorded on a well-designed questionnaire. The statistical analysis was conducted through SPSS-25.

RESULTS

Five patients who showed no resistance while 24% had multiple drug resistance and 66% had extensive drug resistance from various antibiotics against typhoid (Table 1).

Table 1: Resistance Pattern in enrolled patients

Resistant Pattern	No.	%
Non resistant	5	10.0
Multidrug resistant	12	24.0
Extensively drug resistant	33	66.0

Table 2: Age, weight Clinical history and Symptoms of enrolled patients (n=50)

Variable	No.	%
Age (years)		
14-25	25	50.0
26-35	15	30.0
36-55	10	20.0
Mean weight	67kg ±7.5	
Clinical history		
Fever >104	34	68.0
<104	16	32.0
Co morbidity	4	8.0
Antibiotic/last 2 months	12	24.0
Clinical Symptoms		
Abdominal pain/nausea	10	20.0
Abdominal tenderness	8	16.0
Hepatomegaly	10	20.0
Splenomegaly	21	42.0

On analysis of various antibiotics for resistance through blood culturing it was observed that meropenem had highest

sensitivity against salmonella followed by azithromycin while Ciprofloxacin had highest resistance pattern followed by ampicillin and cotrimoxazole (Fig. 1).

The mean age of the patients was 28±5.3 years with a mean weight as 67kg in all the enrolled patients. The clinical history showed that 68% of the patients had a fever around 104°F and only 8% had co morbidities. The clinical symptoms showed splenomegaly presentation in 42% of the cases while only 16% presented with abdominal tenderness (Table 2).

The salmonella caused respiratory complications like pleural effusion in 4% and pneumonia in 2% cases while renal problems like hypernatremia was presented in 2% and AKI in 10% cases with hematological complications in 4%. The blood culturing showed that Salmonella typhi was presented in highest number of cases such as 90% while paratyphoid was only presented in 10% blood culture reports (Table 3).

Table 3: Respiratory, Renal complications and Blood culture analysis of patients (n=50)

Variable	No.	%
Respiratory complications		
Pleural effusion	2	4.0
Pneumonia	1	2.0
Hypernatremia (Na>145mcg/L)	1	2.0
AKI	5	10.0
Circulatory Failure	2	4.0
Hematological Complication	2	4.0
Blood Culturing		
Salmonella typhoid	45	90.0
Salmonella Paratyphoid	5	10.0

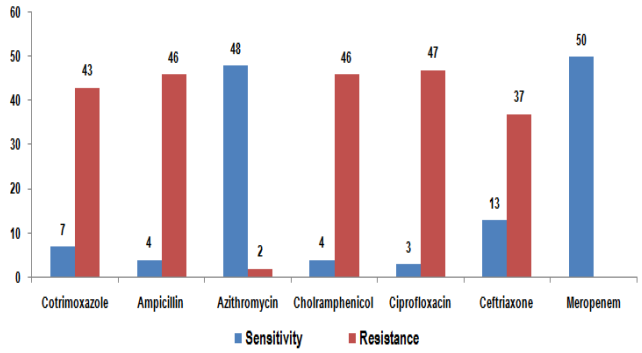

Fig 1: Drug resistance and sensitivity pattern in enrolled patients

DISCUSSION

Increasing number of resistant enteric fever cases is a parallel health problem with COVID-19. Contaminated food, poor hygienic conditions, bad sanitation system are some of the major contributing factors especially in developing region of the world. Extensive and misuse of antibiotics has also worsened the present situation by enhancing resistant cases.[13] In current study, 10%, 24% and 66% of non-resistant, multidrug resistant and extensively drug resistant cases were found, respectively. This high figure increases the duration of toxemia, fever and days of response to antibiotics. Result of this study is somewhat close to other findings.[13,14]

Study from Fiji by Getahun et al[15] showed mean duration of enteric fever symptoms is 11 days, and 11% of the patients showed related complications. High grade fever (104) was also reported by majority of present study participants. Sixty-eight percent of the study participants were showing fever of >104. Splenomegaly was also observed by 42% of the patients and 20% of the patients were showing abdominal pain and hepatomegaly. Similar results have been reported in somewhere else.[16]

Despite the increasing use of vaccination, public health awareness, travelling restrictions and caution by Center for Disease Control and Prevention (CDC) and World Health Organization (WHO), typhoid is still a serious issue for many developing countries such as Bangladesh, India also including Pakistan. Azithromycin is only drug and resistance against this could make the situation more worst. Carbapenems and tigecycline can also be used but due to its high cost, it cannot be used extensively by developing or low income countries.[17,18] A serious and immediate action plan is required by government and heath care policy makers, in a situation where azithromycin resistance in XDR strain is also occurring to save many lives and eradication of this infection.

CONCLUSION

Salmonella typhi is the main strain in Pakistan with extensive resistance found posing serious challenges in the treatment of the disease.

REFERENCES

1. Mogasale V, Desai SN, Mogasale VV, Park JK, Ochiai RL, Wierzba TF. Case fatality rate and length of hospital stay among patients with typhoid intestinal perforation in developing countries: a systematic literature review. PLOS ONE 2014; 9: e93784.
2. GBD 2017 Typhoid and Paratyphoid Collaborators. The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Infect Dis 2019; 19: 369-81.
3. Lee JS, Mogasale VV, Mogasale V, Lee K. Geographical distribution of typhoid risk factors in low and middle income countries. BMC Infect Dis 2016; 16: 732.
4. Mukhopadhyay B, Sur D, Gupta SS, Ganguly NK. Typhoid fever: Control & challenges in India. Indian J Med Res 2019; 150: 437–47.
5. Centers for Disease Control and Prevention (CDC). Extensively drug-resistant typhoid fever in Pakistan. 2019.
6. Zaki SA, Karande S. Multidrug-resistant typhoid fever: a review. J Infect Dev Ctries 2011; 5: 324-37.
7. Center for Infectious disease research and policy (CIDRAP). XDR typhoid outbreak in Pakistan tops 5,200 cases. WHO, 2020.
8. Klemm EJ, Shakoor S, Page AJ, Qamar FN, Judge K, Saeed DK, et al. Emergence of an extensively drug resistant Salmonella entericaSerovarTyphi clone harboring a promiscuous plasmid encoding resistance to fluoroquinolones and third-generation cephalosporins. mBio 2018; 9: e00105-18.
9. Rasheed F, Saeed M, Alikhan NF, Baker D, Khurshid M, Ainsworth EV, et al. Emergence of Resistance to Fluoroquinolones and Third-Generation Cephalosporins in Salmonella Typhi in Lahore, Pakistan. Microorganisms 2020; 8: 1336.
10. Rahman BA, Wasfy MO, Maksoud MA, Hanna N, Dueger E, House B. Multi-drug resistance and reduced susceptibility to ciprofloxacin among Salmonella entericaserovarTyphi isolates from the Middle East and Central Asia. New Microbes New Infect 2014; 2: 88–92.
11. Parry CM. The treatment of multidrug-resistant and nalidixic acid-resistant typhoid fever in Viet Nam. Trans R Soc Trop Med Hyg 2004; 98: 413–422.
12. Kadhiravan T, Wig N, Kapil A, Kabra SK, Renuka K, Misra A. Clinical outcomes in typhoid fever: adverse impact of infection with nalidixic acid-resistant Salmonella typhi. BMC Infect Dis 2005; 5: 37.
13. 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 Res Int 2020.
14. Rasheed MK, Hasan SS, Babar ZU, Ahmed SI. Extensively drug-resistant typhoid fever in Pakistan. Lancet Infect Dis 2019; 19: 242–243.
15. Getahun SA, Parry CM, Crump JA, Rosa V, Jenney A, Naidu R, et al. A retrospective study of patients with blood culture-confirmed typhoid fever in Fiji during 2014-2015: epidemiology, clinical features, treatment and outcome. Trans R Soc Trop Med Hyg 2019; 113: 764–70.
16. Fida S, Mansoor H, Saif S, Iqbal J, Khan AQ. Clinical Perspectives of Multiple and Extensively Drug-Resistant Typhoid; result from a tertiary care hospital from Pakistan. J Infec Developing Countries 2021; 5(04), pp.530-537.
17. Kaurthe J. Increasing antimicrobial resistance and narrowing therapeutics in typhoidal salmonellae. J ClinDiagn Res 2013; 7: 576–9.
18. Parry CM, Thieu NT, Dolecek C, Karkey A, Gupta R, Turner P, et al. Clinically and microbiologically derived azithromycin susceptibility breakpoints for Salmonella entericaserovars typhi and paratyphi A. Antimicrob Agents Chemother 2015; 59: 2756–64.