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A Study on the Clinical Profile, Blood Profile and Culture Sensitivity Pattern of Salmonella Typhi in Paediatric Patients

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ABSTRACT

Objective: To study clinical profile, blood profile and culture sensitivity patterns of Salmonella typhi in paediatric patients and factors associated with multi-drug resistant pattern.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Paediatrics and Microbiology Department, Combined Military Hospital Peshawar from Jan 2021 to Jan 2022.

Methodology: A total of 97 paediatric patients with a confirmed diagnosis of Salmonella typhi were included in the study. A detailed clinical proforma was designed to document all the symptoms this patient had since admission. In addition, all baseline blood investigations and culture sensitivity analysis were requested during clinical evaluation. Basic demographic factors were associated with the presence of multi-drug resistant disease patterns in study participants.

***Results*:** Out of 97 children in the study, 65 (67.1%) were males, while 32 (22.9%) were females The mean age of the children in our study was 9.82±3.26 years. 61 (62.8%) patients had Salmonella typhi, which was not multi-drug resistant, while 36 (37.2%) had multi-drug resistant disease. Fever was the commonest symptom reported by our study participants. No organism was found resistant to Meropenem. Statistical analysis revealed that raised C-reactive protein levels at the time of assessment had a statistically significant relationship with the presence of multi-drug resistant disease (*p*-value=0.001).

Conclusion: A considerable number of pediatric patients with typhoid had multi-drug resistant illnesses in our study participants. Therefore, special attention should be paid to children who had raised C-reactive protein levels at the time of initial assessment.

Keywords: Culture sensitivity, Multi-drug resistance, Salmonella typhi.

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INTRODUCTION

Typhoid fever is an invasive infection caused by a gram-negative bacterium, Salmonella Typhi. It consists of a polysaccharide capsule which provides the added benefit of virulence of the bacterium by protecting phagocytosis. It is a major health issue in developing countries like Pakistan, which is endemic and presents with fever. About 21 million patients have been affected with typhoid fever annually, leading to 161,000 cases ending in fatality.[1] It is the commonest bacterial cause of fever in returning travellers and migrants from these areas.[2] The frequency of enteric fever is high in children aged 1–15 years. The typical presentation of typhoid fever consists of gradual onset of fever, chills, hepatosplenomegaly and abdominal pain.[3] Early detection is the key to managing these patients. It is mostly a clinical diagnosis; therefore, history and examination are of utmost importance. Blood culture is the gold standard for diagnosis and helps guide the clinician in management by providing data about sensitivity pattern.[4] However, and it is not a highly sensitive test. It is a resource and time-limited, resulting in 7-10 days.[5]

The clinical picture has worsened and resulted in absenteeism, morbidity, mortality and a constraint on resources. Typhoid fever spreads from drinking water contaminated with urine or faeces of infected people. Poor sanitation, low socioeconomic status, and inadequate hygiene are the most common culprits.[6] Complications may arise due to inadequate treatment or due delay in diagnosis, including typhoid intestinal perforation leading to gastrointestinal haemorrhage, hepatitis, cholecystitis, myocarditis, shock, encephalopathy, pneumonia, and anaemia.[7]

Antimicrobial resistance has developed to the traditional first-line medications, which include Chloramphenicol, Ampicillin, and Trimethoprim-Sulfamethoxazole. There is increasing resistance to the broad-spectrum Cephalosporins, but it is more common in non-typhoidal strains. Azithromycin is currently used and mostly found to be sensitive for managing

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uncomplicated typhoid.[8] The term MDR describes resistance to Ampicillin, Trimethoprim-Sulfamethoxazole, and Chloramphenicol during XDR exhibit resistance to Chloramphenicol, Ampicillin, Co-Trimoxazole, and Fluoroquinolones, as well as thirdgeneration Cephalosporins.[9] Pakistan has one of the most lethal and resistant types of bacterium. Residents of the Pakistani provinces of Punjab and Sindh have been declared to be most at risk of developing typhoid out of all 16 Asian countries where typhoid is prevalent.[10] Limited local has been available regarding the detailed clinical, haematological profile and culture sensitivity patterns. We, therefore, planned this study with the rationale of studying the clinical profile, blood profile and culture sensitivity patterns of Salmonella typhi in paediatric patients and factors associated with multidrug resistant patterns.

METHODOLOGY

This cross-sectional study was conducted at the Departments of Pediatrics and Microbiology, Combined Military Hospital (CMH), Peshawar Pakistan from January 2021 to January 2022. Research Evaluation and Ethical Committee approved (Ref No. CPSP/REU/PED-2018-017-4978) the study, and informed consent in written form was taken from the patients' parents. The sample size was calculated using the WHO calculator by keeping the population prevalence of multi-drug resistant typhoid fever at 52% and the margin of error as 10%.[11] The data was collected via the non-probability consecutive sampling technique.

Inclusion Criteria: All the paediatric patients (1 to 12 years) having a fever of (temperature >38'C) for the last five days, abdominal pain, nausea and vomiting with a positive culture sensitivity test for Salmonella typhi were included in the study.

Exclusion criteria: Patients who required intensive care on admission, those with chronic diseases, those who developed complications of disease or those who were severely dehydrated were excluded from the study. Those who refused to undergo culture and sensitivity tests or other investigations were also not included in the study.

Typhoid fever was diagnosed using relevant clinical and laboratory parameters per hospital protocol by a consultant pediatrician.[12] All of these patients underwent tests such as complete blood count, C-reactive protein, blood culture and sensitivity. Blood culture and sensitivity were performed according to set protocols. Blood was collected in three designated bottles and sent to the hospital's laboratory, where it was processed and examined by a consultant microbiologist, and then culture and sensitivity pattern was determined.[13] Multi-drug-resistant typhoid was defined as if a culture-sensitivity pattern showed resistance to all first-line antibiotics as described in guidelines.[14] All relevant socio-demographic, clinical and laboratory information was entered in a proforma designed for this study.

The statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS version 23.0). Mean and standard deviation were calculated for the age of patients. In addition, frequency and percentage were calculated for gender, clinical and laboratory profile parameters. Pearson chi-square test was used to assess the association between age, gender, use of boiled water and raised C- reactive protein with multidrug resistant pattern by keeping the *p*-value less than or equal to 0.05 as significant.

RESULTS

Of the 97 typhoid fever patients, 65 (67.1%) were male, and 32 (32.9%) were female. The overall mean age of the patients was 9.82±3.26 years. Table-I showed study participants' basic demographic, clinical and haematological profiles.

Table-I: Demographic, Clinical and Hematological Findings of Enrolled Patients (n=97)

Study Parameters	Frequency (%)
Mean Age	9.82±3.26 years
Gender	
Male	65 (67.1)
Female	32 (32.9)
Hemoglobin	
Within range	70 (72.1)
Deranged	27 (27.9)
White Cell Count	
Within range	21 (21.6)
Deranged	76 (78.4)
Platelet Count	
Within range	37 (38.1)
Deranged	60 (61.9)
C-reactive Protein	
Within range	68 (70.1)
Deranged	29 (29.9)
Clinical Profile	
Fever for >5 days	97 (100)
Constipation	19 (19.5)
Diarrhea	29 (29.8)
Vomiting	34 (25.1)
Headache	9 (9.3)
Splenomegaly	18 (18.5)
Hepatomegaly	25 (25.7)
Oral ulcers	06 (6.1)
Others	02 (2.1)

Fever of more than 5 days was present in 97 (100%) patients , vomiting in 35.1%, constipation in 19.5%, diarrhoea in 29.8% and headache in 9 (9.3%) patients. Hepatomegaly was seen in 25 (25.7%), splenomegaly in 18 (18.5%) and in oral ulcers 6 (6.1%) patients.

Table-II summarized the sensitivity pattern of Salmonella typhi in patients included in our study. 18 (18.5%) patients were resistant to Ciprofloxacin, 16 (16.4%) were resistant to Azithromycin, while none of the samples was found resistant to Meropenem.

Table-II: Sensitivity pattern of culture positive salmonella typhi(n=97)

Drug name	Sensitivity pattern		
	Sensitive n(%)	Intermediate n(%)	Resistant n(%)
Amoxicillin	45 (46.4)	1 (1.1)	31 (31.9)
Ampicillin	44 (45.4)	0 (0)	53 (54.6)
Chloramphenicol	36 (37.1)	0 (0)	71 (73.2)
Ciprofloxacin	77 (79.3)	2 (2.2)	18 (18.5)
Ceftriaxone	79 (81.4)	0 (0)	18 (18.5)
Cefixime	77 (79.3)	0 (0)	20 (20.6)
Azithromycin	81 (83.5)	0 (0)	16 (16.4)
Meropenem	96 (98.9)	1 (1.1)	0 (0)

Table-III showed the results of the statistical analysis. Raised C-reactive protein at the time of assessment was statistically significantly associated with the presence of multi-drug resistant disease (*p*-value-0.001) while age (*p*-value-0.868), gender (*p*-value-0.345) and use of boiled water (*p*-value-0.739) had no such association.

Table-III: Factors Associated with Multi-Drug Resistant Typhoid(n=97)

Factors Studied	Non-resistant Typhoid n(%)	Multi-drug Resistant Typhoid n(%)	*p*-value
Age			
<8 years	45 (73.7)	26 (72.2)	0.868
8-12 years	16 (26.3)	10 (27.8)	
Gender			
Male	43 (70.5)	22 (61.1)	0.345
Female	18 (29.5)	14 (38.9)	
Use of Boiled Water			
No	36 (59.1)	20 (55.6)	0.739
Yes	25 (40.9)	16 (44.4)	
Raised C-reactive Protein			
No	50 (81.9)	18 (50.0)	0.001
Yes	11 (18.1)	18 (50.0)	

DISCUSSION

Our study revealed that routine first-line treatment resistant typhoid is common in our part of the world, and raised inflammatory markers like CRP at the time of presentation may be associated with multi-drug resistant illness. Typhoid is still one of the commonly encountered infectious diseases with predominant abdominal symptoms. Lower and middle-income countries not only bear this disease in general but also face the treatment-resistant form of illness, which may result in potentially life-threatening complications. Due to limited data for this disease in children in Pakistan, we conducted this study to assess the clinical profile, blood profile and culture sensitivity patterns of Salmonella typhi in paediatric patients and factors associated with multi-drug resistant patterns in children managed at CMH Peshawar.

Bhutta *et al.* conducted a study on paediatric patients presenting at Agha Khan University Hospital Karachi regarding the presentation and clinical features of multi-drug resistant typhoid.[15] They concluded that 20% of the patients suffering from typhoid had treatment-resistant strain and clinical symptoms were more severe in these patients. Furthermore, duration of admission, mortality and coagulation profile was significantly more deranged in patients with multi-drug resistant disease than in other children.

Vigiho *et al.* in 2021 determined the risk factors associated with extensively drug-resistant typhoid fever in Pakistani children.[16] They revealed that patients using community water supply and eating from street vendors had more chances of having the drug-resistant disease. Our study design and parameters differed from that of Vigiho *et al.* but the use of boiled water was not significantly associated with the presence or absence of multi-drug resistant typhoid in our study participants. The reason may be the inclusion of patients from a military setting where patients may not be the true representative of the general population.

Socio-demographic, clinical manifestations, complications, antibiotic sensitivity pattern, treatment, and outcome in hospitalized enteric fever patients were studied by Behera *et al.* in 2021.[17] It was concluded that fever was the most commonly reported symptom followed by vomiting and diarrhoea. Around 73% had raised CRP in their study participants. Our study showed similar results, and paediatric patients with multi-drug resistant illnesses were frequently seen during the study period. Raised C-reactive protein levels at the initial assessment were also common and related to multi-drug resistance in our patients.

Six-year retrospective data regarding enteric fever in children was conducted from a tertiary care hospital in Singapore in 2016.[18] It was found that around 16% of patients had multi-drug resistance disease. Anaemia was also a common finding in children managed at their hospital. Around 28% of our study participants had anaemia, and approximately 36% of cases diagnosed with typhoid had multidrug resistance.

This study adds to the statistics of multi-drug resistant typhoid in our world. C-reactive protein emerged as an important biochemical marker to predict the resistant form of illness at initial assessment.

LIMITATIONS OF STUDY

A longitudinal study may have generated better results. Excluding complicated cases may prone the data towards bias as they may have been treatment-resistant cases. Prior use of antibiotics was ascertained by the recall ability of family members, which increases the chance of recall bias. The microbiology laboratory of its own hospital was used for culture and sensitivity. Reconfirmation from another source regarding sensitivity patterns may have increased the generalizability of our results.

CONCLUSION

All the patients in our study presented with fever. Many paediatric patients with typhoid had multi-drug resistant illnesses in our study participants. Special attention should be paid to children who had raised C-reactive protein levels at the time of initial assessment. Meropenem should be reserved for cases resistant to all other options.

Conflict of Interest: None.

Author's Contribution:

HU: Literature review and research, AR: Review approved final draft, AMA: Study design, critical review and edit of final draft, RR: Conceived and designed the study, initial drafts, SA: Statistical analysis and review, AA: Data collection and compilation, research.

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