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ENTERIC FEVER IN ERA OF ANTIBIOTIC RESISTANCE A RETROSPECTIVE STUDY

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ABSTRACT

Background: Salmonella typhi and Salmonella paratyphi are the common causes of enteric fever, a gastrointestinal infection that is characterized by systemic clinical signs. The oral-fecal pathway is the main means of transmission, and humans are the only known reservoir for this bacteria. Within 14 days of infection, clinical signs usually show up as fever, vomiting, diarrhea, and abdominal pain. Due to its high rates of morbidity and mortality, enteric fever is a major global health concern. Children are more prone to this ailment, especially in the summer and during the rainy season.

Objective: To examine antibiotic resistance in enteric fever in children.

Study design: An analytical cross-sectional study

Place and Duration: This study was conducted in Pir Abdul Qadir Shah Jilani Institute of Medical Sciences Gambat from September 2022 to September 2023.

Methodology: children with enteric fever symptoms were selected at random from a hospital with a well-functioning laboratory. Two blood samples were drawn from different locations and submitted for sensitivity and culture testing. Our study comprised children whose Salmonella typhi or paratyphi isolates were positive. Considering the patients' ages, we separated them into three groups. Patients in the first group were under 2 to 5 years of age; those in the second group were between 6 to 10 years old; and those in the third group were 11 to 15 years of age.

Results: A total of 200 children were included in this research. Overall 136 participants were male, while 64were female. Considering the patients' ages, we separated them into three groups. Patients in the first group were under 2 to 5 years of age (n = 42), those in the second group were between 6 to 10 years old (n = 108), and those in the third group were above 11 to 15 years of age (n = 50).

The age range with the highest levels of antibiotic resistance was 6 to 10 years old. Furthermore, resistance rates were noticeably greater in those who had taken antibiotics before seeking medical assistance.Antibiotic resistance was more common in male patients than in female patients.
Conclusion: Patients between the ages of 6 to 10 years showed a considerably higher level of resistance than patients under the age of 2 to 5 years or patients over the age of 11 to 15 years.

Keywords: Salmonella typhi, enteric fever, antibiotic resistance, sensitivity, children

INTRODUCTION

Salmonella typhi and Salmonella paratyphi are the common causes of enteric fever, a gastrointestinal infection that is characterized by systemic clinical signs [1]. The oral-fecal pathway is the main means of transmission, and humans are the only known reservoir for this bacteria [2, 3]. Within 14 days of infection, clinical signs usually show up as fever, vomiting, diarrhea, and abdominal pain [4]. It's also conceivable for atypical symptoms to appear, which would add them to the list of potential reasons for fevers of unknown origins.

Due to its high rates of morbidity and mortality, enteric fever is a major global health concern [5]. Children are more prone to this ailment, especially in the summer and during the rainy season. According to recent estimates, there may be as many as 21 million cases of typhoid fever worldwide each year, with between 128,000 and 161,000 deaths reported [6]. When cases are mishandled or go untreated, mortality rates can skyrocket to 30%; however, with prompt treatment, mortality can drop to less than 1% [7, 8]. Resistant salmonella species are thought to be the cause of 35,000 deaths each year in the USA alone [9]. Increased rates of sickness and mortality have been linked to the rise of extensively drug-resistant (XDR) and multi-drug-resistant (MDR) strains of enteric fever across Asia.

The first effective antibiotic to treat enteric fever was discovered in 1940 [10]. Newer and more effective drugs were created over time. But the enteric fever-causing bacteria have quickly changed, becoming resistant to these medications. The number and proportion of enteric fever patients that have developed treatment resistance have increased globally. Even medications that were formerly quite successful in treating enteric fever are becoming less effective and developing resistance.

First reported in 1970, multi-drug-resistant (MDR) enteric fever is defined by resistance to three main antibiotics: co-trimoxazole, ampicillin, and chloramphenicol [11]. Beginning in the 1990s, fluoroquinolones were the drug of choice for treating MDR enteric fever. Fluoroquinolone-resistant strains, however, have become more common due to the extensive usage of these drugs, especially in regions of Asia like our own country [12]. Notably, the World Health Organization (WHO) was notified in 2016 when a novel extensively drug-resistant (XDR) strain of typhoid fever appeared in some parts of Karachi, Pakistan [13]. The purpose of this study was to assess how well antibiotics work in treating typhoid fever in order to reduce the risk of resistance developing and the related financial burden.

METHODOLOGY

This study was approved by the ethical review committee of the hospital. All information was entered into a patient-focused, well-laid-out questionnaire. We appended a form in both Urdu and English to the treatment records with their signed approval. children with enteric fever symptoms were selected at random from a hospital with a well-functioning laboratory. Two blood samples were drawn from different locations and submitted for sensitivity and culture testing. Our study comprised children whose Salmonella typhi or paratyphi isolates were positive.

Exclusion criteria: children less than 2 years of age were excluded. Moreover, patients having fever due to other symptoms, individuals with blood cultures negative for Salmonella typhi, and children with respiratory infections were also not included in this study.

In our study, patients had to be between 2 to 15 years of age. Considering the patients' ages, we separated them into three groups. Patients in the first group were 2 to 5 years of age; those in the second group were between 6 to 10 years old; and those in the third group were above 11 to 15

years of age. Using the antibiotic sensitivity found in culture reports, antibiotic resistance was evaluated in each of the three patient groups. With reference to their prior usage of antibiotics and their status as naïve patients, we divided these patients into two groups. With SPSS version 25, all of the data wereexamined.

RESULTS

A total of 200 children were included in this research. Overall, 136 participants were male, while 64 were female. Considering the patients' ages, we separated them into three groups. Patients in the first group were 2 to 5 years of age (n = 42), those in the second group were between 6 to 10 years old (n = 108), and those in the third group were above 11 to 15 years of age (n = 50). The age range with the highest levels of antibiotic resistance was 6 to 10 old. Furthermore, resistance rates were noticeably greater in those who had taken antibiotics before seeking medical assistance. Antibiotic resistance was more common in male patients than in female patients. These individuals either purchased antibiotics over-the-counter or used them for shorter periods of time and at lower doses than recommended. Table 1 shows the demographics and treatment options for different resistance classes of S. typhi.

Table No. 1: demographics and treatment options for different resistance classes of S. typhi.

Variables	N	%
Gender		
● Male	136	68
● Female	64	32
Age (years)		
● 2.5	42	21
● 6.10	108	54
● 11.15	50	25
History of antibiotic		
● Yes	152	76
● No	48	24
Cephalosporin resistance		
● Yes	98	49
● No	102	51
Cephalosporin sensitivity		
● Yes	104	52
● No	96	48
Quinolones resistance		
● Yes	120	60
● No	80	40
Quinolones sensitivity		
● Yes	81	40.5
● No	119	59.5
Macrolides resistance		
● Yes	14	7
● No	186	93
Macrolides sensitivity		
● Yes	188	94
● No	12	6

Table number 2 shows the comparison of antibiotic resistance and sensitivity among the patients with and without the history of antibiotics.

Table No. 2: comparison of antibiotic resistance and sensitivity among the patients with and without the history of antibiotics.

Variables	Antibiotic history	
	Yes	**No**
Cephalosporin resistance		
● Yes	80	18
● No	72	30
Cephalosporin sensitivity		
● Yes	74	30
● No	78	18
Quinolones resistance		
● Yes	108	12
● No	44	36
Quinolones sensitivity		
● Yes	58	36
● No	94	12
Macrolides resistance		
● Yes	12	2
● No	140	46
Macrolides sensitivity		
● Yes	142	46
● No	10	2

Table number 3 shows the comparison of antibiotic resistance and sensitivity with respect to gender.

Table no. 3: comparison of antibiotic resistance and sensitivity with respect to gender.

Variables	Gender	
	Male	**Female**
Cephalosporin resistance		
● Yes	69	29
● No	67	35
Cephalosporin sensitivity		
● Yes	68	36
● No	68	28
Quinolones resistance		
● Yes	84	36
● No	52	28
Quinolones sensitivity		
● Yes	52	29
● No	84	35
Macrolides resistance		
● Yes	11	2
● No	125	62
Macrolides sensitivity		
● Yes	126	62
● No	10	2

DISCUSSION

Although the emergence of antibiotic resistance in enteric fever is a global concern, poor countries, especially those in the Indo-Pak area, are especially concerned about it as this is the region where

salmonella antibiotic resistance is most common [14]. This puts people afflicted by the bacteria in grave danger, in addition to placing a heavy financial burden on our nation.

When antibiotic resistance first appeared in 1948, it reduced the efficacy of first-line treatments and caused salmonella typhi strains to become resistant to these medications by 1950 in the United Kingdom [15]. In South Asia, cases of multidrug-resistant (MDR) typhoid were documented in the 1980s [16]. Fluoroquinolones were recognized as the main therapeutic option for typhoid fever after the 1980s; nevertheless, resistance to these medications was observed in the UK as early as 1992 [17]. For a long period of time, injectable ceftriaxone and ciprofloxacin were used with encouraging results. Significantly, over 5,000 cases of extensively drug-resistant (XDR) typhoid fever were recorded in the Sindh Province in less than two years after instances were first detected in Hyderabad, Pakistan, in November 2016 [18]. There have also been a few reports of XDR cases from the USA and the UK [19]. The widespread and inappropriate use of antibiotics in our nation—resulting from their unregulated sale—has been a major factor in the emergence of salmonella strains that are resistant to antibiotics [20].

Fluoroquinolones were the most resistant salmonella species in our study, which is consistent with our patients' frequent use of them. Both types of patients who had previously received these medicines and those who had not exhibited quinolone resistance rose to 60%. Between the ages of 6 to 10 years, this resistance was most noticeable, and more male patients than female patients were impacted. The increase in quinolone resistance that we have shown in our research is probably a direct result of its careless prescribing, not only for typhoid fever but for other illnesses as well. This pattern is consistent with findings from other research projects that have raised comparable issues about the use of antibiotics.

Azithromycin is unique in that it is the only oral antibiotic available for the treatment of typhoid fever in this worrisome situation of increasing resistance. But because it is widely used to treat upper and lower respiratory infections, its efficacy is also compromised. Additionally, resistance to macrolides was found in our investigation. Treatment options for extensively drug-resistant (XDR) typhoid, such as carbapenem, are expensive for patients and place a significant financial burden on impoverished countries. The results of our investigation are consistent with other studies, emphasizing the difficulties in managing typhoid infections in this setting of rising resistance.

CONCLUSION

Given the increasing trend of antibiotic resistance, especially with regard to salmonella infections, it is essential to choose antibiotics carefully, placing special emphasis on prescriptions based on culture.

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Conflict of Interest: None

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