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Fighting XDR Typhoid: A Hospital Based Study on Clinical Aspects and Treatment Outcome in Tertiary Care Hospital

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Author`s Contribution

[1,3]Substantial contributions to the conception or design of the work; or the acquisition, [2,4,6]Drafting the work or revising it critically for important intellectual content Final approval of the study to be published ,[5]Active participation in active methodology, Statistical analysis.

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ABSTRACT

Objective: The main aim of this study is to find Clinical Aspects and Treatment Outcome in drug resistant Typhoid.

Methodology: Total 120 patients participated in this study. Individuals who received a diagnosis of XDR S.Typhi through a blood culture test were identified from the registry of both healthcare facilities. The medical data of patients suffering from typhoid fever who received treatment as either a hospital inpatient or outpatient between April 1, 2022, and June 30, 2022, were examined for the purpose of screening for inclusion in this investigation. Only typhoid patients who tested positive for S.Typhi in a test to culture blood and the manifestation of insusceptibility to the five classifications of antimicrobials (ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, fluoroquinolone, and 3rd generation cephalosporin (ceftriaxone or cefixime) were examined for potential incorporation in this inquiry.

Results: Among the 120 cases of XDR Typhoid, n= 35 (29.16%) were managed exclusively with azithromycin, while 40 (33.33%) were solely administered meropenem. The remaining 45(37.5%) received a combination of both azithromycin and meropenem. Two patients could not recover after receiving Azithromycin. Full recovery seen in Meropenem. Four patients couldn't recover from combination therapy.

Conclusion: Escalating antibiotic resistance in Salmonella enterica has rendered it a complex ailment to address. Measures ought to be implemented to enhance antibiotic prescription protocols and establish consistent recommendations for the management of highly resistant strains of Salmonella enterica.

Keywords: Typhoid Fever, Extensive drug resistant, Clinical Symptoms, Treatment

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Introduction

Typhoid fever is a systemic disease triggered by the microorganism Salmonella enterica serotype Typhi (Typhi).[1] The illness is mainly distinguished by the existence of continuous high body temperature and may encompass additional indications such as weariness, head pain, loss of appetite, irregular bowel movements, unproductive coughing, and diarrhea. [2] At present, enteric fever poses a worldwide public health challenge, with an estimated yearly occurrence of 11-21 million instances around the globe, leading to 200,000 fatalities.[3] The prevalence of enteric fever is greatest in the Asian area, with 93% of the worldwide occurrences being accounted for in this region.[4] In the time prior to antimicrobial medications, typhoid fever could result in death in as much as 10%–30% of instances; fatality reduces to 1%–2% with suitable therapy.[5] In 2016, a massive epidemic of highly drug-resistant (HDR) typhoid fever associated with polluted water started in Sindh province, Pakistan, and is ongoing to this day.[6] HDR Typhi strains are impervious to medications utilized for managing vulnerable strains, such

as ampicillin, ceftriaxone, chloramphenicol, ciprofloxacin, and trimethoprim-sulfamethoxazole. [7]

The majority of strains obtained from affected individuals in the epidemic have shown sensitivity to azithromycin and carbapenems. [8] Highly resistant Typhi infections have been documented in travelers to and from Pakistan around the world and within the United States. [9] Additionally, an unconnected group of Typhi infections that are resistant to ceftriaxone and linked to Iraq has been reported in both the United States and the United Kingdom. [11]

Given the gravity of the illness, which may be underestimated due to insufficient resources for microbial diagnosis, the fatality rate of enteric fever is anticipated to be elevated and, on the rise, [12] The medical characteristics of individuals diagnosed with the extensively drug-resistant (XDR) variety of enteric fever are slowly becoming evident, with more severe complications, a protracted clinical course, and deaths.[10] As a result of the scarcity of suitable diagnostic equipment and restricted antibiotics, medical practitioners will soon encounter a quandary in treating this illness efficaciously [13]

This study aimed to investigate the medical advancement of extensively drug-resistant (XDR) salmonella by contrasting the intensity of the strain with the multi-antibiotic resistant (MDR) and medication-susceptible strains among both adult and pediatric populations in a tertiary medical facility. Furthermore, the research evaluates the impact of the XDR salmonella strain in all cases of enteric fever, including issues, therapeutic approach, and clinical outcomes

Methodology

A review of past medical records was carried out on patients who were diagnosed with enteric fever at Ayub Teaching Hospital Abbottabad between 1st July, 2021 and 31st December, 2021. The study included all patients, both adult and pediatric, who were confirmed to have enteric fever through culture tests. The information was gathered using the Health Management Informatics System (HMIS). The study was approved by the Institutional Review Board (IRB).

Individuals who received a diagnosis of XDR S.Typhi through a blood culture test were identified from the registry of both healthcare facilities. The medical records of typhoid patients who received treatment as either a hospital inpatient or outpatient between April 1, 2022, and June 30, 2022, were examined for the purpose of screening for inclusion in this investigation. Only typhoid patients who tested positive for S.Typhi in a blood culture test and displayed resistance to the five categories of antibiotics (ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, fluoroquinolone, and 3rd generation cephalosporin (ceftriaxone or cefixime) were considered for inclusion in this inquiry. Individuals with incomplete medical records, specifically those lacking details on antimicrobial treatment, therapy duration, failure of treatment, and time taken to reduce fever, were removed from the research. Moreover, patients who departed from medical care without completing a minimum of two days of hospitalization, those who had positive blood culture but did not seek medical attention at either hospital, and those who failed to return for a follow-up visit in the clinic after confirmation of the blood culture test were eliminated. Out of 210 medical records diagnosed with typhoid, only 120 met the eligibility standards and were included in this analysis.

We employed a organized instrument in the English dialect to gather data from the medicinal archives. The instrument consisted of factors such as personal characteristics (age, sex), indications such as high temperature upon arrival at the hospital/clinic, results of blood culture and antibiotic susceptibility tests, duration in days until fever resolved, unfavorable outcomes (if any) of the illness, kind and length of antibiotic treatment, adverse reactions (if any), and unsuccessful treatment. The definition of treatment failure was specified as the recurrence of the illness within 30 days after concluding the therapy, or the emergence of complications while undergoing the treatment (such as septic shock, meningitis, hepatitis, or death or the need to extend the duration of antimicrobial therapy beyond 14 days for meropenem and 10 days for azithromycin.

Results

From a total of 120 records examined for this investigation. The majority (n = 90; 75%) of patients with XDR Typhoid received inpatient treatment. Slightly over half (n = 70; 58.33%) of the patients were male and the mean age was 10.0 years with a range of 5-30 years. The average temperature upon hospital admission was 38.5 ±0.89 (Range = 40.0–36.0) 0C.

Pyrexia (n = 120; 100%) and emesis (n = 80; 66.66%) were the prevailing symptoms manifested throughout the progression of the ailment, trailed by loose bowels (n=68 ; 56.66%), pain in Abdomen (n=60; 50.0%), and Headache (n=45; 37.5%).

Among the 120 cases of XDR Typhoid, n= 35 (29.16%) were managed exclusively with azithromycin, while 40 (33.33%) were solely administered meropenem. The remaining 45(37.5%) received a combination of both azithromycin and meropenem.

Table I: Showing Clinical Symptoms in XDR Typhoid Patients. (n=120)

Symptoms	Frequency	Percentage
Pyrexia	120	100%
Vomiting	80	66.66%
Loose Bowels	68	56.66%
Abdominal Pain	60	50.0%
Headache	45	37.5%

Table II: Demonstrating Treatment protocol and outcomes in XDR typhoid patients. (n=120)

No. of Patients	Treatment received	Recovered	Recurrence
35 (29.16%)	Azithromycin only	33 (94.28%)	02 (5.71%)
40(33.33%)	Meropenem only	40 (100%)	0
45 (37.5%)	Both Azithromycin+ Meropenem	41 (91.11%)	4 (8.88%)

All patients who received only meropenem were hospitalized. Meropenem was administered intravenously (IV) at a dose of 20-40mg/kg thrice daily. Azithromycin was administered via mouth at a dosage of 20mg per kilogram per day. Only 02(5.71%) instance of treatment ineffectiveness was observed among patients who received azithromycin, whereas 4 cases of treatment ineffectiveness were recorded for patients who were treated with the combination of azithromycin and meropenem. No instances of treatment ineffectiveness were seen in patients who were treated with meropenem.

Discussion

XDR (extensively drug-resistant) typhoid is a severe form of typhoid fever that is resistant to multiple antibiotics, making it difficult to treat. [14] The indications and medical portrayal of typhoid fever might appear comparable to those of other contagious illnesses. [15] Typical signs encompass pyrexia, Headache, constipation or loose bowels, and muscle aches; nearly 30% of sick persons describe coughing or stomach soreness.[16] Upholding a heightened degree of doubtfulness can be crucial in establishing the diagnosis. The public health authorities must carry out thorough interviews to identify plausible origins of infection, execute fecal testing of kinfolks who might be carriers, and take measures to forestall auxiliary transmission.[17,28] Antibacterial medicines abridge the incidence and mortality of typhoid fever, but the selection of antibiotics has been complexed by high frequencies of resistance to orthodox treatment agent.[18,19] The majority of strains obtained from affected individuals in the epidemic have shown sensitivity to azithromycin and carbapenems. [20]

Highly resistant Typhi infections have been documented in travelers to and from Pakistan around the world and within the United States. [21] Additionally, an unconnected group of Typhi infections that are resistant to ceftriaxone and linked to Iraq has been reported in both the United States and the United Kingdom. [13,22]

The swift spread of extensively drug-resistant (XDR) infections across the globe has necessitated a cautious reassessment of ceftriaxone as an empirical treatment.[23] The worldwide emergence of decreased susceptibility to azithromycin in Typhi has also been documented, with Pakistan being among the affected countries and it is also documented in our study. [24,25]

In our study All patients who received only meropenem were hospitalized. Meropenem was administered intravenously (IV) at a dose of 20-40mg/kg thrice daily.

Our research Subjects demonstrated satisfactory outcomes when administered with meropenem. Meropenem is a β-lactam antibiotic variant that has natural durability against ESBLs and exhibits an extensive range of effects. These aspects may account for the meropenem's eradication rate. Azithromycin was administered via mouth at a dosage of 20mg per kilogram per day. Only 02(5.71%) instance of treatment ineffectiveness was observed among patients who received azithromycin, whereas 4 cases of treatment ineffectiveness were recorded for patients who were treated with the combination of azithromycin and meropenem. In the cohort administered with a blend of meropenem and azithromycin, 4 instances of treatment inadequacy were observed. All four patients manifested systemic complications, and regrettably, one of them expired. The delayed arrival of the patients at the medical facility led to a less favorable clinical condition, which might have contributed to the unfortunate outcome. No instances of treatment ineffectiveness were seen in patients who were treated with meropenem

Hospital-based studies on XDR typhoid fever are crucial for understanding the clinical aspects of the disease and developing effective treatments.[26,27] It is essential to promote measures that prevent the spread of this deadly disease and to prioritize the development of new drugs and treatment options. [29]

Conclusion

The escalating antibiotic resistance in Salmonella enterica has rendered it a complex ailment to address. This could have severe ramifications, particularly in low-to-middle income nations where numerous individuals lack access to healthcare facilities and costly antimicrobials. Measures ought to be implemented to enhance antibiotic prescription protocols and establish consistent recommendations for the management of highly resistant strains of Salmonella enterica.

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