EXTENDED SPECTRUM BETA LACTAMASE PRODUCING CEPHALOSPORIN RESISTANT *SALMONELLA* TYPHI, A CASE REPORT FROM KARACHI, PAKISTAN

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ABSTRACT

Typhoid fever and paratyphoid fever are systemic illnesses caused by *Salmonella enterica* serotypes Typhi and Paratyphi, respectively, and manifest with continuous high-grade fever and abdominal symptoms. Due to MDR (resistant to ampicillin, chloramphenicol, cotrimoxazole) strains and increasing resistance to fluoroquinolones treatment of enteric fever has been complicated in various regions including Southeast Asia (endemic area). Third generation cephalosporins have been used as treatment of choice for past couple of years. We report a case of typhoid fever caused by Salmonella Typhi which was MDR, resistant not only to ciprofloxacin but also to third generation cephalosporins. The patient was treated with intravenous administration of a carbapenem/ Meropenem.

Keywords: Ceftriaxone, Multidrug-resistant typhoid, Salmonella Typhi.

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INTRODUCTION

Typhoid fever is both common and infectious disease endemic in various parts of Southeast Asia [1] associated with high morbidity and mortality, therefore requiring a suitable antimicrobial therapy for better outcome. Increasing drug resistance is posing a major problem in the treatment of typhoid fever. Cephalosporins became the mainstay of treatment after resistance to fluoroquinolones in addition to multidrug resistance [2]. Rising MICs to Cephalosporins and production of Extended Spectrum Beta lactamases (ESBLs) by *Salmonella* enteric a serovar Typhi is noticeable. ESBLs are encoded by genes on plasmids and renders resistance to cephalosporins. It has also been found in different organisms of the family enterobacteriaceae and may be carried on to other members of family, making them resistant to cephalosporins. Spread of these resistant organisms is quite alarming as treatment options for typhoid fever will be very narrowed. We report a case of typhoid fever due to Salmonella enteric a serovar Typhi which was resistant to all the first line antibiotics, fluoroquinolones and third generation cephalosporin. The patient had to be treated with meropenem, a carbapenem drug which is not generally recommended for the treatment of typhoid fever.

CASE REPORT

This patient is 22 years of age presented at PNS Shifa hospital with 10 days history of fever. It was continuous, high grade associated with headache, fatigue and abdominal pain. There were no rigors and chills. It was not relieved by the medication. There was no history of diarrhea or constipation. On examination, he was febrile (102ºF), unwell and mildly dehydrated. His abdomen was tender, liver was palpable 4 cm below right costal margin and spleen was palpable 3 cm below the left costal margin. Bowel sounds were present. He had bradycardia (Pulse 56 beats/min). Complete blood picture revealed haemoglobin of 8.7 g/dl and total leukocyte count $3.3x10^9$/L. Liver function tests and other serological markers for acute viral hepatitis were normal. Urinalysis and stool examination revealed no abnormality. Ultrasound of abdomen showed both hepatomegaly and splenomegaly with multiple enlarged mesenteric lymph nodes. His past history was unremarkable. He was provisionally diagnosed as a case of Enteric fever. Paired blood and stool samples were collected for culture and the patient was put on injection ceftriaxone 2 gram intravenously at stat dose and then 1gram intravenous twice daily. The fever did not settle till 5th post admission day. On 5th day blood culture showed the growth of multidrug resistant (ampicillin, cotrimoxazole, chloramphenicol) Salmonella Typhi. The isolate was an ESBL producer and was also resistant to ciprofloxacin, azithromycin and ceftriaxone, sensitive only to meropenem. Keeping in view the sensitivity report, patient was started on Injectable Meropenem 1 gram 8 hourly. He continued to have high grade fever (>39ºC) for 48 hours. His general condition and appetite started improving. Repeat blood and stool culture were negative.

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Keeping in view the high resistance of the isolate, the treatment (Injection Meropenem) was continued for 7 more days. The patient was successfully managed with inj meropenem and was discharged from hospital on 14th day of admission without any complain

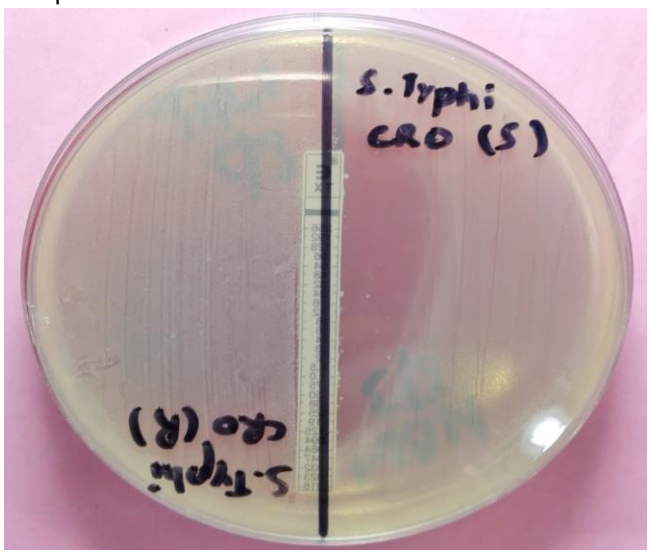

Figure-1: MIC of isolate (sensitive control and isolate) by Estrip method.

DISCUSSION

Treatment options for enteric fever have been limited especially after the emergence of MDR strains which are resistant to ampicillin, trimethoprim-sulfamethoxazole, and chloramphenicol. These strains are prevalent worldwide now including Southeast Asia and China as well. In addition, the increased resistance to fluoroquinolones is also an evolving challenge [1-3]. The resistance to 3rd generation cephalosporins has also been reported from many countries including Pakistan [4]. Sarika Jain *et al* carried out a study on 344 strains of Salmonella and resistance to 3rd generation cephalosporin was observed in 7(2%) strains of Salmonella Typhi [5].

In Bangladesh MDR isolates account for majority of Salmonella Typhi [6]. Prevalence of MDR strains varies from country to country in Middle East and Central Asia [7]. Genome sequencing has identified H58 strain as a predominant MDR Salmonella Typhi strain, throughout Asia and Africa [8].

In 2010 and 2012 a single cephalosporin resistant strain ESBL was isolated from Japan and Bangladesh respectively.6 Amna *et al*. carried out a study in Faisalabad, Pakistan on 30 isolates of Salmonella Typhi showed emerging resistance to cephalosporins, but no ESBL producing strain was found [9]. Farah Naz *et al* revealed the sensitivity data of 4,323 positive isolates of Salmonella Typhi and Salmonella Paratyphi A isolated during the three-year period. The majority of isolates were Salmonella Typhi (59.6%). the incidence of multidrug-resistant (MDR) Salmonella Typhi was from 64.8%-66.0%. Ceftriaxone-resistant Salmonella Typhi were isolated in two children [10].

The high resistance to first line antimicrobials, fluoroquinolones and resistance to third generation cephalosporins is really alarming as we will be left with no option but to switch over carbapenems and tigecycline for the empirical treatment of typhoid. This will have serious connotations in countries where typhoid is endemic.

AUTHORS CONTRIBUTION

Sana Yousuf: Research work, sample collection, analysis and writeup.

Faisal Hanif & Saddam Hussain: Literature review and writeup.

Saman Nadeem: Data Collection.

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