Research article

Emergence of Multi Drug Resistant Salmonella Typhi as Epidemic Among Lower Sindh Regions Patients of Pakistan

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Abstract

This study was aimed to determine the frequency of multidrug-resistant *Salmonella* Typhi (*S. Typhi*) among patients from lower region Sindh. This cross-sectional study was conducted at diagnostic and research laboratory, Hyderabad by evaluating cultures and sensitivity reports collected from different health care centers during one year period (November 2016 to November 2017). Total 92 patients were included in this study where most of patients were children with mean age of 6.2yrs and male population was predominant (63%). A detailed history and examination was done and blood culture reports were followed for sensitivity and resistance. Blood culture and sensitivity results showed resistance to ampicillin, cefixime, ceftriaxone, ciprofloxacin, and sulphamethoxazole/trimethoprim in 80.4%, 66.3%, 63%, 63% and 82.6%, in respectively. The highest sensitivity (89.1%) was recorded against meropenem. It was concluded that MDR salmonella infection is prevalent in Sindh, particularly in Hyderabad.

Key Words: Salmonella, Multidrug Resistance, MDR, Sindh, Enteric Fever

INRODUCTION

Typhoid fever remains as one of the major healthcare problems for this geographical location. It is one of those diseases which are diagnosed in areas where there is water contamination, poor hygiene and transmission of infection through feco-oral contamination from the affected person. It affects a large population and approx. 12-13 million cases are reported annually with high death toll of 1,90,000 people in the year 2010.[1] About 1% of the cases are fatal. Its occurrence is rare in developed countries, however it is endemic in developing countries especially in Africa and Asia.[2] Southeast Asian countries seem to be the worst affected with high population density living in poor sanitary conditions and unavailability of clean water. Lack of education and hygiene further complicates the problem causing sudden

outbreaks in such communities.[1, 3] These outbreaks can be attributed to contaminated food due to poor cooking practice in restaurants or food stalls failing to follow standard hygienic practice in kitchens, drinking or using water for washing and cooking especially contaminated with human or animal waste, infected poultry and eggs, from waste material of sick and or clinically unhealthy people especially involved in cooking.

Typhoid fever or enteric fever is caused by *Salmonella enterica typhi* (most commonly referred to as *Salmonella typhi*) Para typhi A, Para typhi B and Para typhi C.[4] Salmonella typhi is a motile, facultative gram-negative enteric bacillus, belonging to Enterobacteriaceae family. It has six subspecies and includes about 2500 serotypes.[5] Humans are the only known reservoir. It is a food borne pathogen. It is found in the intestinal tract of its host. Numerous strains of this particular organism have been isolated; characterized by variable metabolic characteristics, different levels of virulence, and possessing multi-drug resistance genes.[5] These genes then are responsible for complicating the treatment or resulting in failure causing death.

A complete blood count test (CBC) may show decreased count of white blood cells (leukopenia), decreased neutrophil count (neutropenia), with decreased eosinophil count and a relative increase in lymphocyte count. Diagnostic criteria other than complete blood count includes stool D/R or a bone marrow cultures.[4] Bone marrow culture is more superior since it has more bacterial concentration and therefore considered gold standard for the diagnosis of S. Typhi. The growth on blood culture is attained on MacConkey and Eosin methylene blue (EMB) agars. This bacterium is non- lactose fermenting therefore no gas is produced when it is grown in Triple Sugar Iron (TSI) media, thus differentiating it from other *Enterobacteriaceae*. Symptoms of the disease include high grade fever spikes which may persists for several days with bradycardia, malaise, abdominal pain and occasionally cough. Abdominal pain can also be associated with diarrhea.[5] Hepatosplenomegaly may also be present. Dehydration can be found due to which patient may become delirious (typhoid state). About one third of the patients' develop rose spots on lower chest and abdomen. Complications include intestinal perforation which is a surgical emergency; septicemia, diffuse peritonitis, Encephalitis, pneumonia and acute bronchitis, cholecystitis, endocarditis, and osteitis are the notable. Timely empirical treatment and proper management can be curative for majority of the patients. However morbidity and mortality is significantly increased due to the emergence of multi drug resistant strains in endemic regions such as Asia.[6] Prevention is the key in high risk areas. Emergence of newer outbreaks of typhoid fever in large numbers formed the basis of this study.

METHODS

This cross-sectional study was conducted from November 2016 to November 2017. The consent of the patients were obtained both written and informed, before the commencement of study. The patients were selected from different areas of Sindh province **(Figure 1)**. The study included patients who presented to the outpatient department of healthcare units with features of typhoid fever.

Those with positive test for malaria or with signs of other infections on examination, having positive urine analysis for infection or any other systemic finding raising suspicion for any other infection were excluded from the study. History and systemic examination findings were recorded in predesigned data sheet. Patient's blood samples were collected for complete blood count (CBC) and peripheral smear examination. Blood culture and sensitivity using was carried out on MacConkey's agar following standard procedures. Currently recommended and commonly prescribed antibiotics were tested for sensitivity. The empirical treatment for enteric fever was continued in patients until the culture and sensitivity results were available.

The regular follow up of patients was kept in routine for treatment response and improvement or deterioration of clinical symptoms. The data was clinically analyzed. Statistical analysis was performed on SPSS version 16.0 employing descriptive statistics.

RESULTS

A total of 92 patients were included in this study, with a male to female ratio of 1.7:1. Mean age of the patients was 6.24 years. The study patients were selected from different cities and districts of Sindh Province. Majority of patients belonged from Hyderabad City Majority of the affected cases (51.1%) belonged to middle income group. The most affected ethnic group in this study were Urdu speaking community (47.8%) (**Figure 2**). Among the study patients, 52.2% presented with high grade fever (**Figure 3**). It was found that 41.3% of the patients relied on metropolitan board supplied water, which was neither filtered nor boiled; 92.4% of the patients relied on homemade food for their daily needs. Hygiene status was satisfactory in 55.4% of the patients. There was no history of pet animals in 88% of the patients. All the patient samples were 100% positive for polyvalent antisera for O antigen. Blood culture and sensitivity results showed resistance to ampicillin, cefixime, ceftriaxone, ciprofloxacin, and sulphamethoxazole/trimethoprim in 83%, 66%, 66%, 90% and 83%, in respective order (Table 1). Meropenem and Azithromycin were found to be the most effective ones, with no resistance in any case.

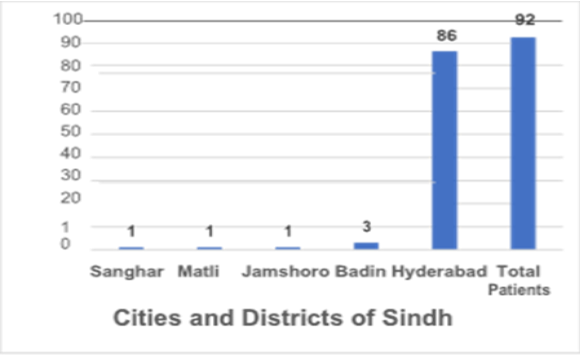

Figure 1. Frequency of Study Patients from different cities and districts of Sindh Province

Figure 2. Representation of different ethnicities Salmonella Typhi Infection

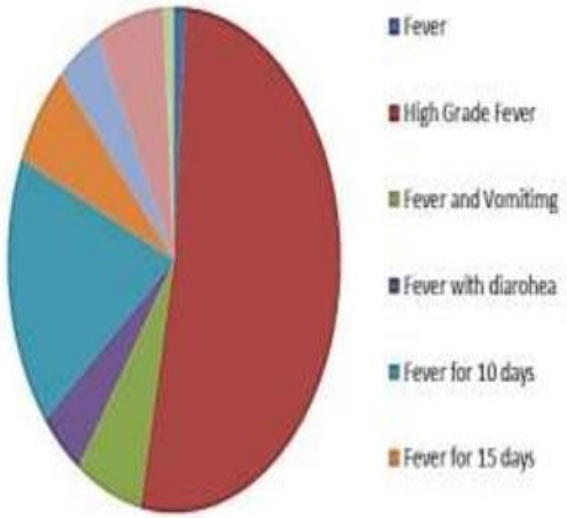

Figure 3. Distribution of fever found in patients with typhoid infection.

Table 1: Antimicrobial resistance of *S. typhi* isolated from blood cultures of cases included in the study

Antimicrobial agent	**Resistance rate %**
Ampicillin	83%
Trimet/Sulpha	83%
Chloramphenicol	83%
Ciprofloxacin	90%
Ceftriaxone	66%
Cefixime	66%
Meropenem	0
Azithromycin	0

Trimet/Sulpha, Trimethoprim/Sulphamethaoxazole

DISCUSSION

Multi drug resistance (MDR) salmonella typhi infection poses a worldwide threat. This disease is especially attributed to the developing countries including Asian and African countries; however, outbreaks have been reported in the developed world as well. Researchers worldwide have identified the MDR salmonella strains lineage, H58, being involved in Asian and African outbreaks and further studies are going on.[7, 8] This study reports MDR salmonella based on blood culture and sensitivity study and the resistant drug pattern is similar to an earlier study in Tajikistan India United states of America and Kenya.[7,10-13] Diagnosis of salmonella infection (typhoid fever) is important because of its complications and treatment challenges. In this particular study the number of patients was small, and most of the patients were children, there was an outbreak of a similar salmonella infection previously in Pakistan also.[14] Adults need to be included in further studies so that the sensitivity of drugs can also be studied. Patients from rural areas could not be included because the patient access was limited to tertiary care hospitals where all facilities are available for the diagnosis and treatment. Another limitation of this study is that those cases where blood cultures were negative for any growth of salmonella were excluded; however bone marrow cultures were not performed. We believe that a bigger study including patients enrolled from all over the country should be initiated. This would provide the complete spectrum of the disease and the status of MDR salmonella in Pakistan. We believe that a study should also be conducted for the identification of carriers of the disease and especially among workers involved in the food industry. Health departments of provincial and federal governments should lead prevention efforts and implementation of laws related to clean drinking water and healthy food practices.

Rational use of antibiotics, Proper education, creating awareness through print, broadcast and social media should be made, observing good sanitary hygiene and vaccination of the susceptible should be undertaken. The future research should be conducted to identify the MDR strains prevalent in this location and their genetic identification.

CONCLUSION

It was concluded that MDR salmonella infection is prevalent in Sindh. It is warranted that practice guidelines be developed to tackle this obvious threat.

Conflict of Interest: No conflict of Interest to be declared regarding publication of this paper.

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