INTRODUCTION

Enteric fever is caused by typhoidal Salmonellae, including Salmonella enterica serovars typhi and paratyphi A, B, and C. The disease remains an important public health problem in developing countries, including Pakistan. Burden of disease is highest in the middle and low income countries. According to an estimate, 11.9 million cases were reported in 2010 from these countries, leading to 120,000 deaths.¹

Typhoid and paratyphoid fever due to multi-drug resistant (MDR) strains; those resistant to all first line anti-typhoidal drugs, namely, chloramphenicol, trimethoprim-sulfamethoxazole and ampicillin, is common in our part of the world. In Pakistan, the first MDR isolate of Salmonella typhi (S. typhi) was reported in 1987, and since then the number has been constantly on the rise, with as much as 80% of S. typhi and up to 44% paratyphi isolates being reported to be MDR in some regional studies.²⁻⁴ Fluoroquinolones emerged as an effective treatment option for MDR Salmonellae; however, cases of therapeutic failure became prevalent with widespread and injudicious use of these agents as well.⁵ Third generation cephalosporins like ceftriaxone are now commonly used for the treatment of MDR Salmonella infections. However, they have slower fever clearance times.⁶ The azalide antibiotic azithromycin has been shown to be a cost-effective alternative for treatment of MDR infections. A 5-7 day oral treatment leads to resolution of symptoms and generally low relapse rates.⁷⁻⁹

There is a need for constant surveillance of the ever changing antimicrobial susceptibility trends. This study was conducted to evaluate the current trend of antimicrobial susceptibility of typhoidal Salmonellae in patients presenting to a tertiary care hospital.

METHODOLOGY

The study was conducted in the Department of Microbiology, PNS Shifa Hospital, Karachi, from January 2014 to December 2015. The study protocol was approved by institutional ethical and research committee. This was descriptive cross-sectional study. Sampling was done by non-probability consecutive sampling technique. Blood samples for culture were received from outpatient department, emergency and medical wards of hospital. Brain-heart infusion (BHI) broth (Oxoid, UK) was used to collect the blood for culture. Five to eight mL of venous blood was collected aseptically using a disposable syringe and added to 50 mL of sterile Brain Heart

ABSTRACT

Objective: To determine the current trend of antimicrobial susceptibility of typhoidal Salmonellae.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: The study was carried out in the Department of Microbiology, PNS Shifa Hospital, Karachi, from January 2014 to December 2015.

Methodology: Blood culture samples received from the wards and outpatient departments were included. Isolates of Salmonella were dealt with standard microbiological procedures. The antimicrobial sensitivity against the typhoidal Salmonellae was determined using Kirby-Bauer disc diffusion method as per the guidelines of Clinical and Laboratory Standards Institute (2013).

Results: A total of 460 typhoidal Salmonellae were isolated; out of which 270 were Salmonella typhi and 190 were Salmonella paratyphi A. The percentage of MDR isolates of S. typhi was 57% and that of S. paratyphi A was 42%. None of the isolates were resistant to ceftriaxone, while sensitivity to ciprofloxacin (07% and 0% for S. typhi and S. paratyphi A, respectively) was very low.

Conclusion: There is high percentage of MDR isolates of typhoidal Salmonellae in our region. The antimicrobial sensitivity of typhoidal Salmonellae to conventional agent has not improved enough to recommend their empirical use. There is almost complete resistance to fluoroquinolones as well, leaving very limited available treatment options.

Infusion (BHI) broth from adults and 3 mL blood in 30 mL BHI from children. The top of the culture bottle was cleaned with alcohol immediately before the addition of blood. Blood culture bottles were incubated at 35 ±2°C in ambient air.

The subcultures were done on Blood agar and MacConkey agar (Oxoid, Basingstoke, UK) at 24 hours (h), 48 h, and 5th and 7th days of incubation. The isolates were identified using standard microbiological techniques, on the basis of colony morphology and biochemical tests using API 20E (Biomerieux, France).10 Serotyping was done using group and type specific antisera (Bio-Rad).

Antimicrobial susceptibility was determined by the Kirby-Bauer disc diffusion method on Muller-Hinton agar (Oxoid, UK). Antimicrobial discs used were: ampicillin (10 µg), ceftriaxone (30 µg), chloramphenicol (30 µg), ciprofloxacin (5 µg) and trimethoprim-sulfamethoxazole (1.25/23.75 µg disk). The Muller-Hinton agar plates were incubated aerobically at 35 ±2°C for 18-24 hours in ambient air. Salmonella ATCC 700931 and Salmonella paratyphi ATCC 9150 were used for QC of anti-sera, and E. clocl ATCC 25922 was used for QC of discs.

The interpretation of zone diameters was done according to clinical and laboratory standards institute (CLSI) guidelines (2013).11 The data was analyzed using SPSS 17.0. Descriptive statistics were used to calculate frequencies and percentages of the qualitative variables.

RESULTS

During the study period, a total of 460 Typhoidal Salmonellae were isolated; out of which, 270 (58.7%) were S. typhi and 190 (41.3%) were S. paratyphi A.

The antimicrobial susceptibility pattern of S. typhi and paratyphi A is given in Figure 1. A fair percentage of isolates was found sensitive to chloramphenicol and trimethoprim-sulfamethoxazole. None of the isolates were resistant to ceftriaxone, while resistance to ciprofloxacin (93% and 100%) and ampicillin (88% and 82%) was very high.

The percentage of MDR isolates of S. typhi was 57% (154) and that of S. paratyphi A was 42% (80).

DISCUSSION

Typhoid fever remains one of the most common infectious diseases in countries like Pakistan. The pitiable state of sanitary practices, insecure and unsafe sources of potable water supplies and inadequate surveillance of blood cultures of febrile patients are hurdles in management of such patients.

Our experience has revealed that S. typhi isolates outnumbered S. paratyphi isolates, but the frequency of isolation of paratyphi has significantly increased as documented in various studies.12,13 One of the probable reasons for rise in cases and isolation of S. paratyphi could be the use of V1 polysaccharide and live oral Ty21A vaccine, which provides protection against S. typhi but not against paratyphi. The percentage of MDR isolates was 57% and 42% for S. typhi and paratyphi A, respectively. This is concurrent with the findings from other regional studies.12,14,15 The most salient feature of antimicrobial susceptibilities of typhoidal Salmonellae isolated in this study was extremely low susceptibility to quinolones as evidenced by 7% and 0% susceptibility for S. typhi and S. paratyphi A, respectively. This is comparable with other regional studies. In a study done in Pakistan, during the years 2012-2013, it was found that only 11% of S. typhi and 16% of S. paratyphi A isolates were susceptible to quinolones.14 Likewise, another study from Rawalpindi, revealed that only 8% of S. typhi isolates were susceptible to quinolones.15 Qaiser et al. reported 72% resistance of typhoidal Salmonellae to quinolones.16 This clearly indicates that antimicrobial susceptibility of typhoidal Salmonellae against quinolones is continuously on the decline in Pakistan. Studies from Bangladesh and India also report similar findings.17,18 The gradual rise in quinoline resistant strains is likely due to injudicious use, over the counter availability, and comparatively low cost of this class of agents.

Susceptibility to ceftriaxone was 100% for both S. typhi and paratyphi A. Similar results with good susceptibilities were reported from studies done in Pakistan and neighboring countries.16-18 Nevertheless, these results should not make us complacent, as already we have seen the extended spectrum beta lactamases detected in typhoidal Salmonellae isolates from Philippines and India.19,20 In addition, there is a possible threat of plasmid mediated resistance gene transfer from ceftriaxone resistant non-typhoidal salmonellae, which have also been reported from different countries including Pakistan.21,22 While compiling this data, an outbreak of ceftriaxone resistant Salmonella typhi was reported from Hyderabad, Pakistan.23

In the past decade, there have been reports of reversal towards sensitivity to conventional anti-typhoid drugs.13,24 In the present study, a fair percentage of isolates were found sensitive to chloramphenicol and...
CONCLUSION

It is imperative that continuous surveillance of typhoidal Salmonellae is carried out. Current treatment options remain limited. Susceptibility to conventional antibiotics, especially chloramphenicol and trimethoprim-sulfamethoxazole, is improving but not enough to encourage their empirical use. A judicious use of the second line drugs is recommended along with implementation of primary prevention strategies including vaccination, provision of safe drinking water, and basic health education of the masses.

REFERENCES


