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Original Article

Recent Sensitivity Pattern of *Salmonella typhi* in a Tertiary Care Hospital

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ABSTRACT

Salmonella typhi is the main cause of the enteric fever in Homo sapiens. The topic of the concern now a day is the emerging multidrug resistance. It causes the disease of intestinal tract known as enteric fever, while *Salmonella paratyphi* cause the paratyphoid fever. This infection is waterborne and foodborne. Approximately 12 – 33 million people suffered from the typhoid fever annually around the globe. **Objective:** The aim of the study was to evaluate the sensitivity patterns of *Salmonella typhi* and *Salmonella paratyphi*. It is a retrospective study, conducted at the Medicine Department of Sahara Medical College, Narowal and Rawalpindi Medical University, Rawalpindi. **Methods:** The blood sample of 306 patients visiting the teaching hospital of our institute were collected. The samples were tested to evaluate the antimicrobial sensitivity. The Kirby-Bauer disc diffusion method was used. The E-test was leveraged for obtaining MIC of ciprofloxacin, while agar dilution method was utilized for obtaining MIC of azithromycin. **Results:** The samples were collected from patients. Out of the 306 sample, 177 samples were of *S. paratyphi* and other 127 were of *S. typhi*. 56% sample showed the sensitivity to ciprofloxacin antibiotic, while 281 samples showed sensitivity to nalidixic antibody. According to the MIC criteria 94% sample isolate were susceptible to ciprofloxacin and 46% to azithromycin. While 31% sample were resistant to it. 90% of the samples were susceptible to ampicillin while other 95% to trimoxazole. **Conclusion:** The co-trimoxazole and ampicillin care highly suggested for the management of the enteric fever. Ciprofloxacin resistance cannot be accurately measured by Nalidixic acid resistance screening. The samples also showcased emerging resistance against azithromycin.

INTRODUCTION

The *Salmonella typhi* cause the disease of intestinal tract known as enteric fever, while *Salmonella paratyphi* causes the paratyphoid fever. This infection is waterborne and foodborne. The major risk factor associated with enteric fever is the consumption of the street food [1, 2]. The approximately 12 – 33 million people effected from the typhoid fever globally. It is most commonly observed in the adults of age 18 – 35 years. It is commonly transmitted through contaminated food and impure water. The usage of the untreated sewage for crop fertilization is another source promoting the transmission of typhoid. The low vaccination rates with excessive use of antibiotics in Pakistani people is adding to the increasing resistance of Salmonella. The excessive use of antibiotics in the farm animals is also an associated factor. This eventually results in development of the antibiotic resistance genes. Annually, around 250,000 deaths are reported because of typhoid fever. While the 5.4 million cases of paratyphoid are reported around the globe. The higher incidence of enteric fever is observed in the summer season. It most commonly affects the male candidate [3, 4]. As the male candidate has the more exposure to outdoor and street food rather than the female candidate in Pakistan. The highest cases of *S. typhi* are observed in the cities like Hyderabad and

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Karachi. Out of all the reported cases the 80% of the death cases are observed in the Asia region. Due to poor sanitations and impure drinking water, this disease is a huge burden for the developing countries. It is a major health issue in Pakistan also. Moreover, it has led to an increased number of mortality and morbidity cases in Pakistan, decreasing the quality of life. 30% mortality rates are associated with typhoid fever. Intestinal perforation has also been observed in many cases. The extensive cases of drug resistance are observed in different regions of Pakistan [5, 6]. Chloramphenicol remained the treatment of first choice for many physicians. But the *Salmonella enterica* have evolved multidrug resistance to chloramphenicol, ampicillin, and co-trimoxazole. It is used as standard for comparison to the other antimicrobials. The first line of treatment for the enteric fever are chloramphenicol, ampicillin, and co-trimoxazole. The multidrug resistance against *Salmonella* was first time reported in 1980. The use of foloroquinolone has increased the resistance of *Salmonella* against nalidixic acid. The extensive drug resistance outbreak was observed in Pakistan from 2016 – 2017. This has eventually increased the treatment cost and physicians are running out of treatment options [7, 8]. Different outbreaks because of evolving multi-drug resistance have been reported in the literature. This evolving drug resistance is posing major problems to clinicians and microbiologists. In Pakistan the *S. enterica* isolates with reduced susceptibility to fluoroquinolone has also observed [9]. The sensitivity of the ampicillin, chloramphenicol, and co-trimoxazole for *S. typhi* range between 90-100%. The limited and inadequate knowledge about the *S. typhi* sensitivity and susceptibility patterns in Pakistan is available. A number of bacteria develop resistance against various antibiotics, consecutive monitoring of the effect of these antibiotics is needed. Therefore, the effects of different antimicrobial are continuously studied for *S. typhi*. For the management of the enteric fever the knowledge of the *Salmonella* antibiotics and anti-biogram is required. The aim of this study is to evaluate the antibiotic sensitivity of *S. typhi* and *S. paratyphi* [10]. The main purpose of this research work was to evaluate the sensitivity of *Salmonella* to various antibiotics so that the treatment of the patients can be made possible with the more effective antibiotics with greater sensitivity and those antibiotics should avoid against which the bacteria developing resistance.

METHODS

The blood sample isolate of 306 patients who visited the Teaching Hospital of our institute, were collected. The duration of the study was from December 2021 to May 2022. The ethical and review committee of the hospital approved the study. BACTEC 9240 automated system was used for the processing of the blood sample. The commercial antimicrobial disks were used to determine the susceptibility pattern of antimicrobials. 30µg of nalidixic ceftriaxone and cholaramphenicol while 15µg of azithromycin was used. 10µg of ampicillin, 1.35/23.75µg of co-trimoxazole, and 5µg of ciprofloxacin was used. The Clinical and Laboratory Standard Institute (CLSI) provided with the guidelines. The guidelines of Kirby-Bauer disc diffusion method were used to perform the tests. According to inclusion criteria, the patients who were diagnosed with any other disease other than enteric fever were excluded from the study. For determining MIC quantity of ciprofloxacin, its concentration was reduced from 0.5µg/ml to 0.0625µg/ml. The transitional reaction of the antibiotics with isolates were observed. The E-test was used to determine the Minimum Inhibitory Concentration (MIC) of ciprofloxacin. It is most preferable method with better results. For quality control the Escherichia coli strain was used. The agar dilution method was used for obtaining MIC of azithromycin.

RESULTS

In the given experiment 306 samples were studied, among them, S. typhi samples were 177 and S. paratyphi samples were 127. Of all the isolated specimens, 56% of the samples show sensitivity to the antibiotic ciprofloxacin with a minimum concentration of about 0.26mg/ml. while on the other hand, 281 of the isolated samples were sensitive to the antibiotic nalidaxic acid. From the nalidaxic acid sensitive samples, some of the sample specimens (about 264) were vulnerable to the ciprofloxacin with a concentration of less than 0.6mg/ml. Some of the samples like 249 samples were tested against the antibiotic azithromycin, and 114 of them were vulnerable to the antibiotic while 77 of the specimens show resistance to the given antibiotic by showing proliferation. In this test, 52 samples show the transitional reaction to the antibiotic test. The total of 306 samples show sensitivity to the antibiotic chloramphenicol, and ceftriaxone while 275 samples were sensitive to the ampicillin antibiotic. For the drug co-trimoxiazol, 94 % sensitivity was observed. Here in the given table sensitivity patterns of all the available antibiotics are mentioned for the proper understanding of antibiotic vulnerability and sensitivity.

Antibiotics	Sample specimens	Sensitivity of the isolates	Percentage
Chloramphenicol	306	306	95%
Cotrimoxazole	306	291	100%
Ciprofloxacin	306	166	8%
Ampicillin	306	275	54%
Nalidaxic acid	306	25	90%
Ceftriaxone	306	306	100%

Table 1: Sensitivity of antibiotics against samples

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DISCUSSION

In our population, enteric fever is a major health issue. Several studies have been done for the isolation and treatment of S. typhi. In our study, the effect of various antibiotics was studied against S. typhi. In this study, samples were collected, among these samples, 57% of the samples were of S. typhi, and 43% samples were of S. paratyphi [11]. In the previous years, various studies have been done for the antibiotic ciprofloxacin again S. typhi. For the ciprofloxacin, nalidixic acid is considered an effective marker, which highlights the resistance of the ciprofloxacin. For the validation of this fact, different studies have been reported, to find out the resistance of nalidixic acid against various strains and the usage of ciprofloxacin in those cases [12, 13]. The sample specimens used in our study showed a reduced vulnerability to the ciprofloxacin, about 13 % of the population showed such behaviour when less than 0.6mg/ml of the concentration was used. When further testing has been done, it was predicted that 93% of the population show resistance to the nalidixic acid as well as to the ciprofloxacin. The prescribed method to the ciprofloxacin is Kirby Bauer disc, but it is not a much more efficient method. For the estimation of MIC of ciprofloxacin, E test is the most recommended method [14, 15]. However, a number of bacteria may develop resistance against various antibiotics, therefore there is a need for the consecutive monitoring of the effect of these antibiotics. Therefore, azithromycin and ciprofloxacin effects are continuously studied for the S. typhi. The invasion of the bacterial specie increase, when microbes develop resistance against various antibiotics [16]. From the very start of this disease, the gold standard method for the treatment of typhoid was the use of chloramphenicol. This antibiotic drug was used for a number of many other diseases at this time. This antibiotic was used against those diseases, which were caused by some bacteria. When such patients were treated with chloramphenicol, the death rate was very much reduced from 21% to 1.0%. The time limit of the infection was also reduced from 13 – 26 days to 4 – 6 days. However, by the consecutive use of these antibiotics, different microbes start to develop resistance against various diseases like microbes as well as the severity of the disease was also affected due to the development of resistance [17, 18]. Different kinds of issues emerge with the development of resistance to antibiotics like a high rate of relapse, the toxicity of bone marrow, and an increased death rate. The issues due to antibiotic resistance were mostly developed in developing countries. Then other effective drugs were introduced like ampicillin and co-trimoxazole. At this time, three antibiotics were used for the treatment of typhoid i.e. ampicillin, chloramphenicol, and co-trimoxazole. All of these three antibiotics show a different level of sensitivity against salmonella specie. About 100% to 95% sensitivity was shown by these three antibiotics. These effective antibiotic drugs are used for the treatment of enteric fever in our population [19]. Further studies were conducted on the other antibiotics to find out the more available options of treatment. Then new antibiotic azithromycin was tested in animal models and then it was further studied in clinical trials. The spores of the S. Typhi show resistance against these antibiotics, then all the sample specimens were tested for the ceftriaxone antibiotic. The results were quite controversial as some of the specimens showcased resistance against S. Typhi, but some show sensitivity against these antibiotics. Multiple other studies groups were also doing the same experimentation. Their all samples showed sensitivity against ceftriaxone. Therefore, a proper conclusion cannot be drawn about the effects of this antibiotic drug because of the varying results of the two research groups. The possible reason for the different results may be due to the handling issues or the other contaminations [20, 21]. Due to the difference in results, our research also shows some limitations or may give the chances of false results, because in this study testing of various antibiotics was not completely analysed at clinical level trials. In our population quinolone is an effective drug although it develops resistance under in vitro conditions. The ceftriaxone was also linked with the resolution of long lasting fever, but under in vitro conditions, it shows sensitivity [22].

CONCLUSION

From the above research, it is concluded that for the proper clarification of the vulnerability of various drugs like quinolone which is required in the enteric fever case, while on the other hand, another antibiotic nalidixic acids show resistance against S. Typhi. The resistance to azithromycin is originating. But the antibiotics, co trimoxazole, ampicillin, and chloramphenicol are useful for oral treatment of this disease. For the effective treatment of typhoid, ceftriaxone is the most effective drug available.

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