THE MICROBIAL SENSITIVITY AND DRUG RESISTANCE PATTERN OF PATIENTS SUFFERING FROM ENTERIC FEVER

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ABSTRACT

Introduction: Enteric fever (typhoid) is one of the most important and quite common bacterial infection in South Asia**.** About seven million people are affected each year in South Asia with about 75 000 deaths. Not only from Pakistan but also from the rest of the countries of Asia and throughout the world, increasing resistance of the organism is being reported, which we are also seeing in our day to day practice.

Objective: Objectives of this study were to determine the microbial sensitivity and drug resistance pattern of patients suffering from enteric fever

Material and methods: After getting approval from the hospital E&RC, all the patients above >14 years who presented with enteric fever, but had not used any antibiotics, were included in the study. Blood, collected from the patients, was sent for culture and sensitivity. All the data was collected on the purposefully predesigned performa.

Results: A total of 195 patients were included in the study, 66.2% were males and 34.9% were females. On sensitivity reports, 40.5% were resistant to ampicillin, 44.1% to carbapenem, 30.3% to co-trimoxazole, 48.7% to ciprofloxacin, 35.4% to cefixime, 35.9% to amikacin, 46.7% to ceftriaxone, 34.9% to polymyxin B, 49.2% to chloramphenicol and 55.4% to gentamicin.

Conclusion: Antibiotic resistance against commonly used antibiotics is significantly high in our patients with enteric fever.

Key words: Enteric Fever, antibiotics, resistance, sensitivity, salmonella typhi

INTRODUCTION

Enteric fever (typhoid) is one of the the most important and quite common bacterial infection in South Asia[1]. It is caused by Salmonella enterica serovars Typhi and Paratyphi A. Salmonella Typhi is the aetiological agent of almost 30% of community-acquired bacterial bloodstream infections in Asia[2,3] and 10% in Africa[4], whilst Salmonella Paratyphi A is an emerging pathogen in Asia, that causes up to 35% of all enteric fever episodes in India and Nepal and more than 60% in China[5,6]. Notably, paratyphoid fever is clinically indistinguishable from typhoid fever[5]. Despite good control of enteric fever in several parts of the world, it remains an important public health problem in South Asia[7].

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The estimated incidence is over 100 per 100 000 population and about seven million people are affected each year in South Asia with about 75 000 deaths[8], but because of limitations in population based surveillance systems and reliable diagnostic methods these figures may be underestimated[9]. Mortality is less than 1% if treatment is started before onset of complications, and increases to around 15% if treatment is started after onset of complications[10]. Enteric fever is confirmed by blood culture. However, this method has variable sensitivity depending on the duration of fever and prior antibiotic therapy. It is most sensitive in the early part of infection (within seven days). The rate falls with increasing duration of fever. The WHO currently recommends chloramphenicol, ampicillin, cotrimoxazole (trimethoprim-sulfamethoxazole), fluoroquinolones, third-generation cephalosporines (ceftriaxone, cefixime) and azithromycin for the treatment of enteric fever[11]. The first line drugs include chloramphenicol, ampicillin and cotrimoxazole (trimethoprim-sulfamethoxazole). Multidrug resistance refers to resistance to all the first line drugs while extended drug resistance refers to resistance to first line drugs plus

floroquinolones and ceftriaxone[12]. Widespread use and over the counter availability of fluoroquinolones has led to decreased susceptibility of organisms[13,14] across the subcontinent[15-17]. Recently from Pakistan Fluoroquinolone resistance has reported in nearly 90% of S Typhi and S Paratyphi isolates[18]. Subsequent resistance has been recorded for ampicillin, chloramphenicol, and co-trimoxazole, & near universal resistance to ciprofloxacin [19,20].

Because of increasing resistance of Salmonella Typhi to various commonly used antibiotics in our patients we wanted to determine the microbial sensitivity and drug resistance pattern of patients suffering from enteric fever. In this way we will be able to make a strategy as how to cope with this problem well in time. The data will be shared with the rest of the faculty members of our hospital and at provencial level for the benefits of patients suffering from or suspected to have enteric fever.

MATERIALS AND METHODS

This cross sectional study, was carried out in the department of Medicine, Khyber Teaching Hospital, Peshawar, from 1st November 2020 till sample size completed, after approval from hospitals ethical and research committee.. The sample size was 195 patients, using 45% proportion of S typhi sensitivity to gentamicin, 95% confidence level and 7% margin of error, using WHO software. Consecutive non probability sampling was done. Inclusion criterea was all patients of more than 14 years of age who presented with fever of more than 100 F (for at least 2 days) and positive culture for S Typhi. Exclusion criteria were patient having a localized infection, or other infections detected through clinical examination and history of use of antibiotics in last one month, as these conditions act as confounders and if included will introduce bias in the study results.

All patients meeting the inclusion criteria i.e. all patients with history of fever and having positive culture for S typhi were included in the study. The purpose and benefit of the study were explained to the patients and a written informed consent was obtained. All patients were worked up with detailed history and clinical examination and followed by routine investigations. From all the patients, a blood sample was collected under strict aseptic conditions and was sent to hospital laboratory for sensitivity testing against ciprofloxacin, ampicillin, chloramphenicol, cotrimaxazole, carbapenem, polymyxin B, gentamicin, amikacin, cefixime and ceftriaxome. All the above mentioned information including name, age, gender and address were recorded in a pre designed proforma. All the laboratory investigations were done under supervision of an expert pathologist having minimum of five years of experience.

Data collected on Proforma was analyzed in SSPS version 20. Mean + SD was calculated for quantitative variables like age. Percentage and frequencies were computed for categorical variables like gender, previous history of enteric fever, residence, and antibiotic sensitivity pattern for ciprofloxacin, ampicillin, chloramphenicol, co-trimaxazole, carbapenem, polymyxin B, gentamicin, amikacin, cefixime and ceftriaxome. Stratification of sensitivity were done with regards to age and gender using chi square test keeping p value of < 0.05 as significant. All results were presented in the form of table and graphs.

RESULTS

The study was conducted on 195 patients presenting with enteric fever due to salmonella typhi. The mean age of our patients was 34.1 years with a standard deviation of 8.8 years. Out of 195 patients, there were 66.2% were males and 34.9% were females. 65.1% were from urban residence (table 3) and 30.3% had history of typhoid fever in past .

Table 1 AGE-WISE DISTRIBUTION OF SAMPLE (n=195)

Age	Frequency	Percent
20-30 years	81	41.5 %
30-40 years	71	36.4 %
40-50 years	43	22.1
Total	195	100.00

Table 2 ANTIBIOTIC RESISTANCE (n = 195)

Antibiotic resistance	Frequency	Percent
Resistance to ampicillin	No 116	59.5
	Yes 79	40.5
Resistance to carbapenem	No 109	55.9
	Yes 86	44.1
Resistance to cotrimoxazole	No 136	69.7
	Yes 59	30.3
Resistance to ciprofloxacin	No 100	51.3
	Yes 95	48.7
Resistance to cefixime	No 126	64.6
	Yes 69	35.4
Resistance to Amikacin	No 125	64.1
	Yes 70	35.9
Resistance to ceftriaxone	No 104	53.3
	Yes 91	46.7
Resistance to polymyxin B	No 127	65.1
	Yes 68	34.9
Resistance to chloramphenicol	No 99	50.8
	Yes 96	49.2
Resistance to Gentamicin	No 87	44.6
	Yes 108	55.4

DISCUSSION

Although mortality has reduced due to good antibiotic treatment over the past few years, there are apprehensions that the morbidity and mortality may increase once again due to emerging antibiotic resistance, being reported from various parts of the world. it is still a cause of concern due to increasing antibiotic resistance. The mortality due to enteric fever depends on time taken to diagnose and institute appropriate antibiotic treatment. Enteric fever has been eliminated in industrialised countries by improving drinking water and sanitation; vaccination can also be deployed to reduce the burden of typhoid fever (there is no vaccine against S. Paratyphi A), but effective treatment is critical to reduce morbidity and mortality. Although enteric fever may affect both males and females, in our study there was slightly male predominance ie 66.2% patients were males. Similarly Iyer RN et al. Have also reported 53.2% males in their study[21], so in both of the studies males were more as compared to females. However the percentage was more in our patients as compared to patients of Iyer et al. Although no age is exempted but majority of the patients are young, as shown in a previous study in which 61.9% of the patients were young[21]. Similarly 77.9% of our patients were of the age group 20-40 years, though our figure is slightly higher.

In our study, antibiotic resistance was recorded in a range of 30.3% to 65.1% for commonly used antibiotics. On sensitivity reports show that 40.5% of strains were

resistant to ampicillin, 44.1% to carbapenem, 30.3% to co-trimoxazole, 48.7% to ciprofloxacin, 35.4% to cefixime, 35.9% to amikacin, 46.7% to ceftriaxone, 34.9% to polymyxin B, 49.2% to chloramphenicol and 55.4% to gentamicin (table 2).

Chatham-Stephens K et al. from the United States, have reported Salmonella species causing enteric fever, from 3538 blood cultures. Out of these, 65% were resistant to fluoroquinolones and 12% were MDR; 244 culture-positive patients had been to Pakistan, out of which 79% were fluoroquinolone-resistant and 50% were MDR[22], but in our study 48.7% were resistant to ciprofloxacin, much higher than our patients. In our study 46.7% of the strains were resistant to ceftriaxone but in a study published by by Iyer et al., 100% of strains were sensitive to ceftriaxone and azithromycin[21]. A study conducted in India showed that all the typhoidal strains of Salmonella were sensitive to ceftriaxone and azithromycin but only 3.6% were sensitive to ofloxacin[23]. In our study 40.5% of the strains were resistant to ampicillin but Laghari et al.[24] reported 81.6% and 100% ampicillin-sensitive Salmonella typhi and Salmonella paratyphi, respectively, from Jamshoro, Southern Pakistan that means only 18.4% resistance to ampicillin. In our patients 69.7% strains wre sensitive to co-trimoxazole but 96.4% sensitivity has been reported by Laghari et al. [24]. In our patients 44.1% strains were resistant to carbapenem ie only 55.9% were sensitive but Leghari et al has reported sensitivity to Imipenem in 87.8% Salmonella typhi. Azithromycin was sensitive in 94.6% to Salmonella typhi and 100% to Salmonella paratyphi A. The prevalence of MDR and XDR Salmonella typhi and Salmonella paratyphi was 2.6% and 0.9%[24]. Another study in Pakistan reported that the frequency of MDR Salmonella typhi was 76% and Salmonella paratyphi was 34%. The frequency of XDR Salmonella typhi was 48%[25] . Another study done in India reported that all the Salmonella typhi strains were sensitive to imipenem, and 97.67% of strains were sensitive to meropenem, 83% were sensitive to ampicillin-sulbactam, 91% were sensitive to ceftazidime, 90.6% were sensitive to ceftriaxone, 57.5% were sensitive to ciprofloxacin, and 57.5% were sensitive to cotrimoxazole. The MDR Salmonella typhi were present in 44% of the cases[26].

Inview of rising incidence of multidrug resistance, it is suggested that Carbapenems and azithromycin should not be prescribed routinely unless the strain is resistant to first-line drugs, ciprofloxacin, and ceftriaxone on the antibiotic susceptibility report, otherwise injudecious use of Carbapenems and azithromycin may result in development of resistance to these drugs as well.

CONCLUSION

Antibiotic resistance against commonly used antibiotics is significantly high in our patients suffering from enteric fever. However, our sample size was quite small, so we recommend more studies on larger scale as this will help to reduce the morbidity associated with enteric.

CONFLICT OF INTERESTS, FINANCIAL SUPPORTS, GRANTS: None to declare.

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