

Original article:

Current Pattern in Antimicrobial Susceptibility in Enteric Fever In A Private Medical College

Arafat MY¹, Sobur MA², Haq MA³, Islam MN⁴

Abstract

Background and objectives: Enteric fever continues to be an important health problem in Bangladesh. Emerging drug resistance adds magnitude to this problem. Only surveillance studies can help form guidelines for therapy under such a situation. The present study was undertaken to determine the current pattern in antimicrobial susceptibility of enteric fever cases in a private medical college and to find out the incidence of multidrug resistant (MDR) cases.

Study design: Hospital based observational study.

DOI: <http://dx.doi.org/10.3329/bjms.v13i1.17440>

Bangladesh Journal of Medical Science Vol. 13 No. 01 January '14 Page 67-69

Study setting and period: Medicine units of Ibn Sina Medical College hospital from october'11 to august'12.

Source of materials/participants: Fever cases with clinical diagnosis of enteric fever and positive blood culture, attending the outpatient and admitted at hospital were included in the study. Susceptibility of the isolates to commonly available antibiotics were recorded. Treatment and responses were followed up.

Results: 100 adult patients with fever had positive blood cultures were included in the study. Majority of patients were 19 – 30 yr olds (63%). Susceptibility of the isolates were tested against 14 available antibiotics. Ceftriaxone was sensitive in 99% cases followed by ciprofloxacin (96%), Gentamycin (96%) and cefixime (91%). A declining trend in sensitivity to Azithromycin (61%) was

observed. Resurgence of chloramphenicol (81%) and cotrimoxazole (75%) sensitivity was noted. In 98 cases sensitivity to all three (amoxicillin, co-trimoxazole and chloramphenicol) were tested. 13 cases were found resistant to all the three drugs (13/98=13.2%). These MDR cases were sensitive to ceftriaxone (100%), cefixime (100%), azithromycin (100%), gentamycin(94%)and ciprofloxacin (88%).

Conclusion: Antibiotic sensitivity pattern showed a trend with onset of emerging resistance to azithromycin (ceftriaxone vs azithromycin z value = 7.63; P value =0.001 (Significant) and azithromycin vs ciprofloxacin Z value = 6.66; P value =0.001 (Significant). Multidrug resistant cases present showed reduced susceptibility to gentamycin. Sensitivity of these drugs must be preserved through constant surveillance and use only under a protocol.

Introduction:

Enteric fever is a major cause of morbidity in Bangladesh and other developing countries. The worldwide incidence of enteric fever is estimated to be approximately 22 million cases annually with 7 million cases occurring in south east Asia alone, for more than 200,000 deaths annually.¹ Brooks *et al.* reported an overall IR of 3.9/1000 person-years in an urban slum in Bangladesh.² The reasons for high

prevalence of enteric fever pathogens in Dhaka (and indeed all over Bangladesh) include poor hygienic standards, low socioeconomic status of a large part of the population and lack of clean water supply to most localities. The development of resistance to first line antibiotics in enteric fever pathogens poses an additional threat of increased morbidity and mortality.³⁻⁵ By the end of 1990s, Salmonella enterica developed resistance simultaneously to all first line

1. Dr. Md. Yasir Arafat, Registrar, Department of medicine, Ibn Sina Medical College
2. Prof. Md. Abdus Sobur, head of the department, Department of medicine, Ibn Sina Medical College
3. Dr. Md. Azizul Haq, Associate professor, Department of medicine, Ibn Sina Medical College
4. Dr. Md. Nazrul Islam, Registrar, Department of medicine, Ibn Sina Medical College

Corresponds to: Dr. Md. Yasir Arafat, Registrar, Department of medicine, Ibn Sina Medical College, E-mail: yasirarafatdr@yahoo.com

drugs like chloramphenicol, cotrimoxazole and ampicillin. The appearance of fluoroquinolone-resistant strains of *S. typhi* represents a new obstacle for clinicians in endemic area. Full resistance to fluoroquinolones (MIC >1 mcg/mL) in both *S. typhi* and *S. paratyphi* is less common but increasing worldwide. A compilation of studies showed rates of fully quinolone-resistant organisms ranged from 0 to 13 percent.⁶ Treatment options for multi-drug resistant (MDR) and quinolone-resistant isolates include parenteral ceftriaxone, oral cefixime, and oral azithromycin. There have also been sporadic reports of high-level resistance to ceftriaxone in *S. typhi* and *S. paratyphi*.⁷ Experience with azithromycin appears better than fluoroquinolone drugs in populations that included participants with drug-resistant strains.⁸ Multidrug resistant (MDR) cases are emerging rapidly in many countries. Only by monitoring this variation in the susceptibility pattern through constant surveillance studies can suitable guidelines be formed for treatment.

Table 1: Patient profile

| | |
|--|-------|
| Total number of patients (n=Blood culture positive patients) | 100 |
| Male | 55 |
| Female | 45 |
| Male: female | 1.2:1 |

Table 2: Age distribution

| Age group (years) | 12-18 | 19-30 | 31-40 | 41-59 | >60 |
|--------------------|-------|-------|-------|-------|-----|
| Number of patients | 11 | 63 | 12 | 5 | 1 |
| Percentage% | 17 | 63 | 13 | 6 | 1 |

Methods: Total 100 patients of both the sex 55 males and 45 females of adult patient, with a clinical diagnosis of enteric fever were selected for the study. Blood sample for culture were collected by vein puncture with disposable syringe from patients attending Ibn Sina Medical College and Hospital, Dhaka, Bangladesh During the period from Oct 2011 to Aug 2012. All *Salmonella typhi* positive cases were included in the study.

Results: Fifty five of the 100 study patients were male and forty five were female. Majority of the patient (63%) presented in the age group of 19-30, which was comparable to the other study.⁹ Seventy one of the 100 study patients (71%) were positive for

Table 3: Drug susceptibility profile (n = 100)

| Sl.no | Antibiotics | Sensitive% | Partially sensitive% | Resistant% |
|-------|-----------------|------------|----------------------|------------|
| 1 | Ceftriaxone | 99 | - | 1 |
| 7 | Ciprofloxacin | 96 | - | 3 |
| 9 | Gentamycin | 96 | - | - |
| 2 | Cefixime | 91 | 6 | 2 |
| 3 | Chloramphenicol | 81 | - | 17 |
| 4 | Cotrimoxazole | 75 | 2 | 21 |
| 6 | Azithromycin | 61 | 21 | 10 |
| 5 | Ampicillin | 14 | 2 | 84 |
| 10 | Ceftazidime | 2 | - | 3 |
| 8 | Nalidixic acid | 1 | - | 97 |
| 11 | Cefuroxime | 1 | - | 2 |
| 13 | Fusidic acid | 1 | - | - |
| 14 | Netilmycin | 1 | - | - |
| 12 | Erythromycin | - | - | 1 |

Salmonella typhi while the rest had *Salmonella paratyphi A*. Table-3 shows the drug sensitivity patterns of different antibiotics. Ceftriaxone was the highest (98%) sensitive drug in this study followed by ciprofloxacin (96%) and gentamycin (96%). 13 cases was resistant to amoxicillin, co-trimoxazole and chloramphenicol. Ceftriaxone, Cefixime and Azithromycin was 100% sensitive in multidrug resistant cases.

Table 4. Multidrug Resistant Cases(n= 13)

| | |
|---|----|
| Number of cases in which sensitivity was tested to all three drugs (ampicillin, co-trimoxazole and chloramphenicol) | 98 |
| Number of cases resistant to all three drugs | 13 |

Table 5: Drug Susceptibility Profile of Multidrug Resistant Cases (n=13)

| Sl.no | Antibiotics | Sensitive % | Partially sensitive % | Resistant % |
|-------|----------------|-------------|-----------------------|-------------|
| 1 | Ceftriaxone | 100 | - | - |
| 2 | Cefixime | 100 | - | - |
| 3 | Azithromycin | 100 | - | - |
| 4 | Ciprofloxacin | 88 | - | 12 |
| 5 | Gentamycin | 94 | - | 6 |
| 6 | Nalidixic acid | - | - | 100 |

Discussion: Change in antimicrobial sensitivity pattern of *Salmonella typhi* occurs frequently.¹⁰ So, knowledge about current pattern in susceptibility is useful for guiding therapy.¹¹

Drug susceptibility: In the present study Ceftriaxone was sensitive in 99% cases followed by ciprofloxacin (96%) and Gentamycin (96%). A declining trend in sensitivity to Azithromycin (61%) was observed (ceftriaxone vs azithromycin z value = 7.63; P value =0.001 (Significant) and azithromycin vs ciprofloxacin Z value = 6.66; P value =0.001 (Significant). Chloramphenicol resurgence of sensitivity (81%) was noted similar to earlier reports.^{12,13} Drugs like Ceftriaxone, Cefixime, ciprofloxacin and the aminoglycosides which con-

continue to be sensitive (>90%) need to be used under a protocol to prevent emergence of resistance.

Multidrug resistance: Drug resistance,¹⁴ including MDR, is a recognized problem in enteric fever treatment. First reported from Mexico¹⁵ MDR Salmonella typhi rapidly appeared worldwide. In the present study 13.2% isolates were resistant to ampicillin, cotrimoxazole and chloramphenicol among those tested for all those three drugs. Various incidences of resistance to those drugs ranging from 22-82.5% have been reported¹⁶. In our study all MDR cases responded well to ceftriaxone, cefixime and azithromycin (100%), but ciprofloxacin was found resistant in 12% cases. Hospital based studies like the present one poorly reflect the true drug sensitivity pattern in the community acquired enteric fever. The study of an outbreak¹⁶ depicts the pattern in an

isolated instance. Only controlled field trials¹⁶ represent the resistance situation of drugs prevalent in the community. Periodic therapeutic reappraisal should be done in the referral centers. Studies like on the plasmid transfers or mutations responsible for reduced susceptibility to drugs¹⁷ would help future management of multidrug resistance.

Conclusion

Antibiotic sensitivity pattern in enteric fever cases in adult was studied. A trend with beginning of emerging resistance to azithromycin was observed. Cefixime sensitivity had begun to decline. Multidrug resistant cases were present which showed reduced sensitivity to ciprofloxacin. It is urgent to preserve the sensitivity of these antibiotics. Continued surveillance and a protocol for their use are necessary for preventing resistance.

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