Original article

Antimicrobial sensitivity patterns of *Salmonella typhi* in children

Ali MK[1], Sultana S[2]

Abstract:

Background: Enteric fever is an important public health problem in developing countries including Bangladesh. A changing antibiotic sensitivity pattern of *Salmonella typhi* and emergence of resistance has increased to a great concern. ***Objective***: Aim of the study was to investigate the antibiotic sensitivity pattern of *Salmonella typhi*. ***Methods***: A total of 181 *Salmonella typhi* samples from 5 to 15 years age group were collected from blood culture during the period of October to December 2014 from IBN SINA Hospital, Dhaka, Bangladesh. Specimens from the blood culture were identified by standard procedures as needed. Antimicrobial susceptibility testing was performed by disk diffusion method according to 'The Clinical Laboratory Standard Institute' guidelines. ***Results***: Among the tested antibiotics, *S. typhi* was susceptible to ceftriaxone 100%, followed by cefixime and gentamicin 99.4%, ciprofloxacin 98.6%, cotrimoxazole 88.9%, azithromycin 88.4 % and least susceptible antibiotic was Ampicillin 62.5% and nalidixic acid 5%. ***Conclusion***: The antimicrobial sensitivity testing showed that the *Salmonella typhi* were highly sensitive (>88%) to most of the drugs used in this study, whereas nalidixic acid showed only 5% sensitivity. So this study indicates that ceftriaxone, cefixime, gentamicin and ciprofloxacin can be used as a first line therapy and nalidixic acid should be avoided for treatment.

Key words: multidrug resistant; typhoid fever

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Introduction:

Enteric fever is an important public health problem in many developing countries. [1] Enteric fever includes typhoid fever caused by S*almonella typhi* and paratyphoid fever by S*almonella paratyphi* A B C. Typhoid fever affects roughly 21.6 million people annually, resulting 216,500 death. [2] More than 90% of this morbidity and mortality occurred in Asia.[3] World Health Organization in 2008 report on typhoid fever annual incidence in five Asian countries among 5-15 years age group. The incidence varied from 24.2 and 29.3 in Vietnam and China to 180.3 in Indonesia and to 412.9 and 493.5 in Pakistan and India respectively. [4]

Enteric fever continues to be a major health problem despite the use of antibiotics and the development of newer antibacterial drugs. [5] If not treated properly, enteric fever carries a mortality rate of 30%, whilst appropriate antimicrobial treatment reduces the mortality rate to as low as 0.5%.[6] In cases of enteric fever, it is often necessary to commence treatment before the results of laboratory sensitivity testing.[7] Fluoroquinolone ciprofloxacin has become the first-line drug for treatment, since the widespread emergence of *S. typhi* isolates that are multi drug resistant (MDR) to the more traditional antimicrobial agents comprising chloramphenicol, ampicillin and trimethoprim sulphamethoxazole (cotrimoxazole).[8] *Salmonella typhi* has rapidly gained resistance to antibiotics like ampicillin, chloramphenicol and cotrimoxazole and also to previously efficacious drugs like ciprofloxacin.[9]

The incidence of multidrug resistant (MDR) *S. typhi* was reported to be as high as 60 per cent. [10]

A US-based study noted an increase in the number of MDR strains and nalidixic acid resistant *S. typhi* (NARST), although overall, the isolates were sensitive to ciprofloxacin and ceftriaxone.[11] Another study from Bangladesh reported a decrease in MDR isolates with no corresponding increase in

1. Md. Khoyber Ali, Associate Professor & Head, Dept of Paedilatrics, Ibn Sina Medical COllege, Bangladesh.

2. Shahin Sultana, Professor, Dept of Microbiology, Delta Medical College, Bangladesh.

Corresponds to: Md. Khoyber Ali, Associate Professor & Head, Dept of Paedilatrics, Ibn Sina Medical COllege, Bangladesh. **E-mail:** khoyberali1962@gmail.com

Table 1: Age distribution of patients

Age groups (years)	No	Percentage (%)
0-5	66	36
6-10	74	41
11-15	41	23
Total	181	100

Table 2: Sex distribution of patients

Sex	No	Percentage (%)
Male	109	60
Female	72	40
Total	181	100

Table 3: Antibiotics sensitivity patterns of *Salmonella typhi* (n=181)

Antibiotics	**Sensitive n (%)**	**Resistant n (%)**
Ceftriaxone	181 (100)	0 (00)
Chloramphenicol	159 (88)	22 (12)
Cefixime	180 (99.4)	1 (0.6)
Co-trimoxazole	161 (88.9)	20 (11.1)
Nalidixic acid	9 (5)	172 (95)
Ampicillin	113 (62.5)	68 (37.5)
Azithromycin	160 (88.4)	21 (11.6)
Ciprofloxacin	179 (98.6)	2 (1.4)
Gentamicin	180 (99.4)	1 (0.6)

sensitive strains.[12]

Due to the variation in the susceptibility patterns of *S. Typhi*, it is important to constantly monitor the susceptibility patterns of *Salmonella typhi* to commonly prescribed antibiotics and to prevent the emergence of multi drug resistance.

Material and methods:

The blood samples for culture were collected from patient's age group 0-15 years attending in IBN SINA Hospital, Dhanmondi, Dhaka, Bangladesh from March to June 2014. The specimens were Cultured and antibiotics susceptibility tests were performed according to standards microbiological techniques. Brain-Heart infusion (BHI) broth was used for culture. Subcultures into blood agar, Mac-Conkeys agar were done as per standard methods. Non-lactose fermenting colonies were identified by biochemical reactions and confirmed by group and type specific Salmonella antisera. Antimicrobial susceptibility was performed by Kirby- Bauer Disc- diffusion methods on Muller-Hinton agar plates. Antibiotics disc used in this study were Ceftriaxone, Chloramphenicol, cefixime, Co-trimoxazole, Nalidixic acid, Ampicillin, Azithromycin, Ciprofloxacin and Gentamicin. Interpretation was done in accordance with the National Committee for Clinical Laboratory Standardards (NCCL).

This Study was approved by ethics Committee of Ibn Sina Hospital.

Results:

Culture positive samples were collected from the IBN SINA Hospital from the period of March to June 2014. A total of 181 *S. typhi* were obtained by blood culture from the suspected cases of enteric fever. Isolates were from 5-15 years age group (Table 1) and both male (60%) and female (40%) children (Table 2) included. *Salmonella typhi* was 100% susceptible to ceftriaxone followed by cefixime and gentamicin 99.4%, ciprofloxacin 98.6%, cotrimoxazole 88.9%, azithromycin 88.4 %; and least susceptible antibiotic was Ampicillin 62.5% and nalidixic acid 5% (Table 3).

Discussion:

Enteric fever is a major public health problem in our country.[1] The highest prevalence rate was observed in adult whose age was between 21 to 30 years whereas the lowest incidence of typhoid fever was in between 51 to 60 years age.[13] Prompt institution of appropriate antimicrobial therapy can reduce the mortality and morbidity of this illness.[2] Since 1948, chloramphenicol had been the mainstay of treatment of enteric fever until 1972.[14] A study done by Sharma et al who showed that 92.7% isolates were susceptible to chloramphenicol.[15] This finding was near about similar to our finding where 88% isolates were susceptible to chloramphenicol. Ceftriaxone was 95.7 % sensitive to *Salmonella typhi* reported from Pakistan and Bangladesh.[16] Another study showed 100% sensitivity against ceftriaxone and gentamicin.[17] Above two findings were in agreement with the findings of our study where ceftriaxone showed 100% sensitive to *S. typhi*. This underlines the importance of this drug for treating MDR and ciprofloxacin resistance cases in this region.[13] Emphasis is laid on the sparing use of this drug. It should be used only if the first and second line antibiotics fail to evoke a satisfactory response or if the isolate is resistant to nalidixic acid. Krishnan et al observed that *S. typhi* was highly sensitive to chloramphenicol (86%), ampicillin (84%), and cotrimoxazole (88%).[18] In our study sensitivity pattern to chloramphenicol (88%), ampicillin (62.5%), cotrimoxazole (88.9). The treatment of typhoid fever was relatively simple till 1989 in Bangladesh like many other countries because all *S. typhi* were uniformly

susceptible to first line antibiotics like ampicillin, chloramphenicol and co-trimoxazole.[19] A few sporadic cases of typhoid fever caused by antibiotic resistance *S. typhi* were reported. All of the drugs are more than 60% sensitive except nalidixic acid which shows lowest sensitivity about 5%.[20] Nalidixic acid susceptibility has been validated as a screening test for reduced susceptibility to ciprofloxacin and nalidixic acid resistance is associated with a high MIC of ciprofloxacin which in turn is associated with treatment failure.[21] Any isolate that shows nalidixic acid resistance should be reported as intermediately susceptible to ciprofloxacin and the clinician advised to switch over to another antibiotic.[5]

Conclusion:

The findings of the present study indicated that the first line antibiotics like chloramphenicol, ampicillin, cotrimoxazole may still have a role in the treatment of typhoid fever. Also the usefulness of nalidixic acid as a screening test for detecting reduced susceptibility to ciprofloxacin. Thus susceptibility pattern of causative organisms must be studied especially of their hospital when choosing a treatment regimen.

Conflict of interest: None

References:

1. Vikas Gautam, Naveen KumarGupta, Uma Chaudhary, D.R.Arora. Sensitivity pattern of Salmonella serotypes in Northern India. Braz J Infect Dis. 2002; 6(6).
2. Raza S, Tamrakar R, Bhatt CP, Joshi SK. Antimicrobial susceptibility pattern of salmonella typhi and salmonella paratyphi A in a tertiary care hospital. J Nepal Health Conc. 2012; 10(22): 214-217.
3. Lucky H, Moehario, Enty Tjoa, Veronica N.K.D, Kalay, Angela Abidin. Antibiotic susceptibility pattern of salmonella typhi in Jakarta and surrounding areas. Medical journal of Indonesia. 2012; 21 (5).
4. Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. Bull world health organ. 2004; 82 (5): 346-53.
5. U. Madhulika, B.N. Harish, S.C. Pajra. Current pattern in antimicrobial susceptibility of salmonella typhi isolates in Pondicherry. Indian J Med. Res. 2004; 111-114.
6. Singhal, PK Gupta, P Kale, V Gautam, P Ray. Trends in antimicrobial susceptibility of salmonella typhi from North India. Indian Journal Med. Microbiol. 2014; 32 (2): 149-152.
7. Kam KM, Luey KY, Chiu AW, Law CP, Leung SF. Molecular characterization of Salmonella enterica Serotype Typhi isolates by pulsed-field gel electrophoresis in Hong Kong, 2000-2004. Foodborne pathog Dis. 2007 Spring;4(1):41-9.
8. Kenji Hirose, Kajumichi Tamura, Hiroko Sagara, Haruo Watanabe. Antibiotic susceptibilities of Salmonella enteric serovar typhi and S. enteric serovar paratyphi A isolated from patients in Japan. Antimicrob. Agents Chemother. 2001; 45 (3): 956-958.
9. Jesudason MV, John TJ. Plasmid mediated multidrug resistance *in* Salmonella typhi. Indian J Med Res. *1992;95:66-7.*
10. Sanghavi SK, Mane MP, Niphadkar KB. Multidrug resistance in salmonella serotypes. Indian journal of med.microbiol. 1999; 17: 88-90.
11. Rahman M, Ahmad A, Shoma S. Decline in epidemic of multidrug resistant Salmonella typhi is not associated with increased incidence of antibiotic susceptible strain in Bangladesh. Epidemiol Infect. 2002; 129(1): 29–34.
12. Threlfall EJ, Ward LR. Decreased susceptibility to ciprofloxacin in Salmonella enterica serotype typhi, United Kingdom. Emerg Infect Dis. 2001; 7: 448-50.
13. Lovely Akhter, Munir Hassan, Zakaria Ahmed. Present status and antibiotic sensitivity pattern of Salmonella typhi and S. paratyphi in different age group hospitalized patients in Dhaka city, Bangladesh. ISOR Journals of pharmacy and biological sciences. 2012; 4 (3): 27-30.
14. Sood S, Kapil A, Jain Y, KabraSK. Reemergence of chloramphenicol sensitivity Salmonella typhi. Lancet. 1999; 353: 1241-2.
15. Islam A, Butler T, Kabir I, Alam NH. Treatment of typhoid fever with ceftriaxone for 5 days or chloramphenicol for 14 days: a randomized clinical trial. Antimicrob Agents Chemother. 1993; 37: 1572-75.
16. Riaz Muhammad, Zafar Ali, Khalid Mehmood, Ziauddin, Abdur Rahman Afridi, Fazal Bari. Antibiotic sensitivity pattern of salmonella paratyphi in patients with enteric fever in a teaching hospital. J Postgrad Med Inst. 2013; 27(4):397-402.
17. Bernard Rowe, Linda R. Ward, E. John Threlfall. Multidrug-Resistant Salmonella typhi: A Worldwide Epidemic. Clinical Infectious Diseases. 1997; 24(Suppl 1):S106-9.
18. Ashwini Kumar, Vinay Pandit, Seema Shetty, Chythra R Rao, Sarjay Pattanshetty, Charmaine M Samarasinghe. Study of Clinical Profile and antibiotic sensitivity pattern in culture positive typhoid fever cases. Indian J community Med. 2012 Oct- Dec; 37 (4): 256-258.
19. Shyamapada Mandal, Manisha Deb Mandal, Nighith Kumar Pal. R-Factor in Salmonellaenterica serovar typhi: Transfer to and acquisition from Escherichia coli. Jpn, J. Infect. Dis. 2003; 56: 65-67.
20. Bhan MK, Bahi R, Bhatnagar S. Typhoid and paratyphoid fever. Lancet. 2005; 366(9487): 749-62.
21. Ray P, Sharma J, Mark RS, Garg RK. Predictive efficacy of nalidixic acid resistance as a marker of fluroquinolone resistance in Salmonella enteric var typhi. Indian J Med Res. 2006; 124(1): 105-8.