

Original Article

Typhoidal Salmonella in Holy Family Red Crescent Medical College Hospital, Dhaka, Bangladesh

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Abstract

Enteric fever is still an important public health problem in many developing countries like Bangladesh. A changing antibiotic susceptibility pattern of *Salmonella typhi* and *Salmonella paratyphi A* and emergence of multidrug resistance has increased to a greater concern. The present study was undertaken to find out the rate of isolation of *Salmonella* from Blood samples and to compare the changing patterns of drug resistance at Holy Family Hospital and Medical College and Hospital over a two year study period from January 2013 to December 2014. During the period January 2013 to December 2013, total 31 *Salmonella* were isolated (14% of blood isolates) in which *Salmonella typhi* were 27 and *Salmonella paratyphi* were 4. Again, during the period January 2014 to December 2014, total 27 *Salmonella* were isolated (10% of blood isolates) in which *Salmonella typhi* were 23 and *Salmonella paratyphi* were 4. The rate of isolation of *S. typhi* was noted higher among pediatric group when compared to adult group in both study periods. The sensitivity of cotrimoxazole and chloramphenicol was increased which were (80-88)% & (79-93)% respectively in 2 year study period. Nalidixic acid resistant *Salmonella typhi*(NARST) was 88-89% and all of NARST showing good sensitivity to ciprofloxacin. In our study period, Azythromycin resistance rate is increasing from 30-35%. All the isolates were fully susceptible to 3rd generation of cephalosporin in both study periods. The rate of Multi drug resistant(MDR) was (6.5- 7.4)%; which was low in 2 year period. The policy of empirical treatment of enteric fever needs to be rationalized and newer generation antibiotics should be restricted only for multi-resistant cases of enteric fever.

Key words: Bangladesh, Nalidixic acid resistant, *Salmonella typhi*.

Introduction:

Enteric fever is a global health problem. According to recently revised global estimate, it infects around 21.6 million people each year which kills 226,500 people each year. The disease is endemic in the Indian subcontinents, Southeast Asia, South and Central America and Africa.¹ Bangladesh is endemic for enteric fever as other south Asian countries. Studies conducted in Bangladesh by ICDDR,B showed an incidence of approximately 2000 per 100000 per year.²

Drug resistance in typhoid fever is considered as one of the important factors in the morbidity and mortality of the disease. In 1948 chloramphenicol was started for the treatment of typhoid fever.³ But in 1972, chloramphenicol-resistant typhoid fever became a major problem. Several outbreaks occurred in Mexico, India, Vietnam, Thailand, Korea and Peru. In 1989 *Salmonella typhi* developed

resistance simultaneously to all the first line drugs (ampicillin, cotrimoxazole, chloramphenicol) due to indiscriminate use of these drugs and acquisition of plasmid mediated R factor. Resistance toward 3 first-line drugs are referred as MDR.⁴ Then in early 1990s, fluoroquinolones (ciprofloxacin or ofloxacin) was started as the drug of choice for the treatment of enteric fever.⁵ But within 3 years NARST appear & 2002-2005 ciprofloxacin were totally resistance.^{6,7}

Third generations of cephalosporins are now used for treatment of enteric fever. However, there were sporadic reports of ESBL production reported in salmonella from Bangladesh, India and Germany. Thus treatment options are getting limited.^{8,9,10} This situation highlights the need of continued surveillance for changing antibiotic sensitivity and resistance profile of *Salmonella* spp. over time so that physicians can choose the right antibiotic and prevent misuse of valuable drugs. So, we tried to compile the available data related to blood culture reports positive for salmonellae from the patients of HFRMCH from 2013 to 2014 to find out the rate of isolation of *Salmonella* from Blood samples, to see the antibiotic sensitivities of the bacteria against the commonly used drugs and to compare the changing patterns of drug resistance during these years.

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Material and Methods:

This study was done during January, 2013 to December 2014 at Holy Family Red Crescent Medical College Hospital. During these 2 years 3834 blood culture samples received from the patients of HFRCMCH were analyzed. All laboratory works were performed in the department of Microbiology and Immunology in HFRCMCH. Under aseptic precautions, 5ml of blood was inoculated into bottles containing 50 ml of tryptone soya broth (for adult) and 3ml blood into 27ml medium (for children). Hence, 1:10 times dilution is done. After inoculation of samples the bottles were incubated at 370 C upto 72 hours. Each day, those were observed for turbidity and sub-culture on Blood, Mac conkey's and chocolate agar plates. Typical colonies were enumerated, selected and examined further for Biochemical test. Antimicrobial susceptibility test was done by the Disc diffusion method (Kirby-Bauer technique) using Muller Hilton agar.

Result:

During the period January 2013 - December 2013, total 1742 blood culture samples were enrolled. Number of organisms isolated were 218(12%) & out of which 31 was salmonellae which is (14%) of blood isolates. Among the Salmonellae positive cases, 19 were male & 12 were female with a ratio of 1.58:1. During the period January 2014 - December 2014, total 2092 blood culture samples were enrolled. Number of organisms were isolated 257(12%) & out of which, 27 was salmonellae which is (10%) of blood isolates. Among the Salmonellae positive cases, 15 were male & 12 were female with a ratio of 1.25:1. Rate of isolation of Salmonellae typhi in relation to two different age groups are shown in table-1. The rate of isolation of S. typhi was noted higher 17(54.8%) & 17 (63%) among pediatric group when compared to adult group 14 (45.2%) & 10 (37%) in 2013 and 2014 year respectively. S. typhi was found in 27 cases followed by 4 cases of S paratyphi A in the period of January 2013-December 2013 (Figure-1). S. typhi was found in 23 cases followed by 4 cases of S paratyphi A in the period of January 2014- December 2014 (Figure-1). During the period January 2013- December 2013, sensitivity was found 12% for ampicillin, 88% for cotrimoxazole, 93% for chloramphenicol, 92% for ciprofloxacin, 100% for cefixime, 100% for ceftriaxone and 71% for azithromycin (Table-2). During this period 6.5% cases were MDR and 89% cases were NARST. During the period January 2014- December 2014, sensitivity was found 33% for ampicillin, 80% for cotrimoxazole, 78% for chloramphenicol, 96% for ciprofloxacin, 100% for cefixime, 100% for ceftriaxone and 65% for azithromycin (Table-2). During this period 7.4% cases were MDR and 88 % cases were NARST.

Table-1: Rate of isolation of Salmonella in relation to age groups

Age group	No of isolates in 2013	No of isolates in 2014
Paediatric group (Upto 15 years)	17 (54.8)	17 (63)
Adult group (above 15 years)	14 (45.2)	10 (37)
Total	31	27

Figure within parentheses indicate percentage

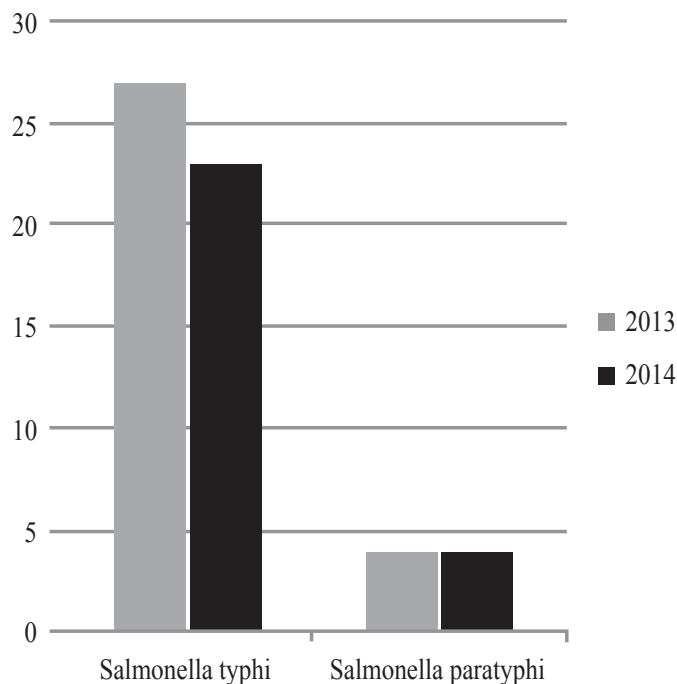


Fig-1: Distribution of isolated organisms

Table-2 Antimicrobial sensitivity pattern in enteric fever

January 20013- December 2013			January 2014 – December 2014		
Antibiotics	Sensitivity%	Resistant%	Antibiotics	Sensitivity%	Resistant%
Cotrimoxazole (n=25)	22 (88)	3(12)	Cotrimoxazole (n=25)	20(80)	5(20)
Ampicillin (n=25)	3(12)	22(88)	Ampicillin (n=21)	7(33.3)	14(66.7)
Chloramphenicol (n=16)	15(93)	1(7)	Chloramphenicol (n=14)	11(78.6)	3(21.4)
Ciprofloxacin (n=27)	25(92)	2(8)	Ciprofloxacin (n=26)	25(96.2)	1(3.8)
Azythromycin (n=28)	20(71.48)	11(39.3)	Azythromycin (n=20)	13(65)	7(35)
Ceftriaxzone (n=25)	25(100)	0 (0)	Ceftriaxzone (n=20)	20(100)	0(0)
Cefixime (n=25)	25(100)	0(0)	Cefixime (21)	21(100)	0(0)
Nalid (n=28)	3(11)	25(89)	Nalid (n=25)	3(12)	22(88)

Discussion

Enteric fever is still a significant public health problem in many developing countries, involving huge health care costs, high morbidity and economic loss. The disease is endemic in Bangladesh, where there is a high incidence in children. Children are affected mostly between 5-12 years.¹¹ In a study of Hasan *et al* noted the rate of isolation of *S. typhi* was higher (17.54%) among pediatric group when compared to adult group (13.95%).¹² In our study, we also found similar findings. In our study causative organism of enteric fever were predominantly *S. typhi* followed by *S. paratyphi* which was correlated with study of Begum *et al*.¹³ However, Shirakawa *et al* found their study *S. paratyphi* was the commonest cause of typhoid fever.¹⁴

Out break of typhoid fever, resistant to various drugs, have been reported from different parts of the world^{15, 16} as well as in Bangladesh.^{17, 18} But recent studies from different parts of the subcontinent have shown that there is a change in the drug resistance of salmonellae. In 1990, in various studies the rate of MDR was high.⁴ However, after the increasing use of ciprofloxacin MDR strain now drastically decreased. In present study MDR is about 6.5% and the susceptibility of cotrimoxazole and chloramphenicol remained good over both study periods. One study done previously in our Holy Family lab also showed good susceptibility to these two drugs.¹⁹ High susceptibility to chloramphenicol, cotrimoxazole and ampicillin were also reported from several parts of India such as Bangaluru, Chennai, Chandigarh, Central west and northern India.²⁰ In Bangladesh, study done by Begum *et al*¹³ revealed increased sensitivity to chloramphenicol, ampicillin and cotrimoxazole over the 2 year study periods. Probably, clinicians are not using amoxicillin, cotrimoxazole and chloramphenicol very frequently in this region and drug resistance strains have been eliminated. So, the re-emergence of increased sensitivity of cotrimoxazole and chloramphenicol to salmonella should be considered and we may think about antibiotic recycling.

In present study NARST was 88-89% and all of NARST showing good sensitivity to ciprofloxacin. However, Neopane *et al*,²¹ found that ciprofloxacin which showed good sensitivity in vitro was not effective in vivo if the isolates was nalidixic acid resistant. They advised to using nalidixic acid sensitivity testing for deciding treatment with fluoroquinolones as the isolates that are Nalidixic acid resistance may not show response in vivo with fluoroquinolone even through the strain is sensitive to it in vitro. World Health Organization(WHO) recommended that azithromycin or 3rd generation of cephalosporin or a 10-14 day course of high-dose fluoroquinolones for the treatment of

nalidixic acid resistant typhoid (NART).¹³ In western country studies, azythromycin showed higher bacteriological cure and negligible relapse rate.²² But in various Indo-Pak-Bangla studies they have documented clinical non-response to azythromycin.^{23,13} In our study its resistance rate is increasing from 30-35%.

So, dependence is now on 3rd generation of cephalosporin. In this study, all the isolates were fully susceptible to this group of drug in both period which correlates with the study of Arora *et al*.²⁴ But from 2008-2010 there were sporadic reports of ESBL production in salmonella from Bangladesh, India and Germany.^{8,9,10} So emphasis has to be laid on the sparing use of the drug to prevent the occurrence of resistance to ceftriaxone.

Conclusion:

As the MDR was decreasing and sensitivity of Cotrimoxazole and chloramphenicol to Salmonella were increasing, it should be considered in using it as first line therapy. Hence, antibiotic susceptibility testing is required in different parts of the country to know the sensitivity pattern among enteric fever pathogens, which will be helpful for clinicians for rational prescribing.

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