ORIGINAL ARTICLE

Changing Trends of Antibiotic Susceptibility Pattern of *Salmonella typhi* and *paratyphi* in recent isolates

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Abstract:

Due to lack of proper sanitation measures and clean water typhoid and paratyphoid fever is prevalent in developing counties like Bangladesh. Increasing number of cases of antibiotic resistance as well as multi-drug resistance have been reported in Indian sub-continent. A total of 120 patients selected for this study on the basis of clinical diagnosis. Among them salmonella typhi and paratyphi were isolated in 54 cases by blood culture. Among the isolates 100% sensitivity was present to third generation cephalosporines, gentamycine and carbapenems. Resistance to conventional antibiotics like chloramphenicol, ampicillin, amoxycillin, cotrimoxazole were decreasing which was encouraging. Multi-drug resistant salmonella strains were found in 11.11% cases. S. typhi and paratyphi isolates were highly sensitive to not commonly used antibiotics like gentamycine, ceftazidim and carbapenems. So a careful consideration should be taken before deciding the antibiotic for treatment of enteric fever patients in order to prevent the emergence of antibiotic resistance.

Introduction:

Typhoid fever caused by salmonella enterica serovar Typhi (S. typhi) is a common and occasionally fatal disease, [prevalent mainly in the developing countries including Bangladesh due to lack of pure drinking water and sanitation measures. Roughly 21.6 million people are affected by typhoid annually resulting in 216,500 deaths occurring in Asia[1,2]. In Bangladesh it is an epidemic problem and also in other countries of Indian subcontinent. Antimicrobials are the mainstay of therapy for typhoid patients. Despite the use of newly developed antibiotics, enteric fever such as typhoid and paratyphoid caused by multi-drug resistant bacterial strains are of major health problems in Bangladesh[3]. In early 1970s, emergence of plasmid mediated resistance to chloramphenicol was reported and its effectiveness as first line drug decreased gradually by outbreaks in countries like Mexico and India. In the next five years outbreaks by resistant strains occurred in Vietnam, Indonesia, Korea, Chile and Bangladesh[4]. Salmonella typhi is now rapidly developing resistance to

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ciprofloxacin and other quinolone along with other conventional antibiotics are being reported in different parts of the world and emerged as new challenges to treatment of typhoid fever[5,6]. The intensive use of first-line antibiotics such as ampicillin, chloramphenicol, and cotrimoxazole have lead to the emergence and global spread of multi-drug resistant (MDR) S. typhi strains[7]. The frequent use of fluoroquinolones have lead to rapid increase in reduced susceptibility of S. typhi to these antibiotics. MDR S. typhi with reduced ciprofloxacin susceptibility has become common in Africa and South and South-east Asia[8,9]. Chien-Shun, Tsai-Ling, Dac C, Haruo W, Jung K, Pei-Jen 2004 have shown[10] that majority of S. typhi isolates from Bangladesh and Vietnam are MDR and are genetically closely related, 40% of isolates from Bangladesh are ciprofloxacin resistant.

Materials and method:

The study was done in medicine department of Holy Family Red Crescent Medical College Hospital (Dhaka, Bangladesh) during the period of 2017 and 2018. 120 adult patients were selected from both admitted and OPD cases on the basis of clinical diagnosis as enteric fever and those who did not take any antibiotic. Blood for culture and sensitivity along CBC, widal test and others were advised to do before starting antibiotic. 18 antibiotics were tested to see sensitivity though not all were applied to each sample because culture sensitivity were done at different laboratories by their own choice of the patients.

Results:

Among 120 patients blood culture was positive in 54 cases. 41 (75.9%)patients had S. typhi and 13(24.1%) patients had S. paratyphi 'A' isolates. Most of the patients were in the age group 12-30 years. Only 16.7% was above the age 30 years.

Table I: Distribution of the patients according to age (n=54)

Age (years)	Frequency (n)	Percentage (%)
12-20	23	42.6
21-30	22	40.7
>30	9	16.7
Total	54	100.0

Table II: Distribution of organisms among the patients (n=54)

Organism	Frequency (n)	Percentage (%)
Salmonella Typhi	41	75.9
Salmonella Paratyphi 'A'	13	24.1

Among the 18 applied antibiotics 100% sensitivity was in cephalosporins – cefepime, cefixime, ceftazidime, ceftriaxone, cefuroxime; gentamycine,carbapenems. Next sensitivity was found in levofloxacin 96.7%, ciprofloxacin 85.0%, chloramphenicol 85.7%. Amoxycillin was sensitive to 66.7% and azithromycin 56.8% . Heighest resistance was found in amoxyclav 50.0% then amoxicillin 33.3%. Resistance pattern of azithromycin was found in 16.2% of S. typhi but in paratyphi A it was 38.5%. Multi-drug resistance (Resistant to chloramphenicol, ampicillin and cotrimoxazole) was 11.11% cases.

Discussion:

The occurence of antibiotic resistance in third world countries takes place due to poor access to doctors which eventually encourages the unacceptable practice of selling antibiotics to the patients directly by the pharmacists11. Risk factors frequently associated with the development of antibiotic resistance include excessive or indiscriminate use of antibiotics,

Table III: Sensitivity and resistance pattern of antibiotics (n=54)

		Salmonella paratyphi 'A' (n=13)	Salmonella Typhi (n=41)
Amoxycillin	Sensitive	2(100.0)	4 (66.7)
	Resistant	0 (0.0)	2 (33.3)
Amoxyclav	Sensitive	1 (100.0)	2 (50.0)
	Resistant	0 (0.0)	2 (50.0)
Ampicillin	Sensitive	9 (81.8)	17 (58.6)
	Resistant	2 (18.2)	12 (41.4)
Azithromycin	Sensitive	2 (15.4)	21 (56.8)
	Resistant	5 (38.5)	6 (16.2)
	Intermediate	6 (46.2)	10 (27.0)
Cefepime	Sensitive	9 (100.0)	13 (100.0)
Cefixime	Sensitive	10 (100.0)	30 (100.0)
	Resistant	0 (0.0)	0 (0.0)
Ceftazidime	Sensitive	11 (100.0)	32 (100.0)
Ceftriaxone	Sensitive	13 (100.0)	39 (100.0)
	Resistant	0 (0.0)	0 (0.0)
Cefuroxime	Sensitive	1 (50.0)	8 (100.0)
	Resistant	1 (50.0)	0 (0.0)
Cephalexin	Sensitive	1 (100.0)	2 (66.7)
	Resistant	0 (0.0)	1 (33.3)
Cephradin	Sensitive	7 (100.0)	13 (86.7)
	Resistant	0 (0.0)	1 (6.7)
	Intermediate	0 (0.0)	1 (6.7)
Chloramphenicol	Sensitive	9 (75.0)	30 (85.7)
	Resistant	3 (25.0)	5 (14.3)
Ciprofloxacin	Sensitive	11 (91.7)	34 (85.0)
	Resistant	1 (8.3)	1 (2.5)
	Intermediate	0 (0.0)	5 (12.5)
Cotrimoxazole	Sensitive	9 (75.0)	30 (76.9)
	Resistant	3 (25.0)	9 (23.1)
Gentamycin	Sensitive	4 (100.0)	22 (100.0)
Imipenem	Sensitive	2 (100.0)	13 (100.0)
Levofloxacin	Sensitive	10 (100.0)	29 (96.7)
	Resistant	0 (0.0)	0 (0.0)
	Intermediate	0 (0.0)	1 (3.3)
Meropenem	Sensitive	3 (100.0)	16 (100.0)
Moxifloxacin	Sensitive	6 (100.0)	10 (33.3)
	Resistant	0 (0.0)	1 (8.3)
	Intermediate	0 (0.0)	1 (8.3)
Nalidixic Acid	Sensitive	12 (100.0)	27 (90.0)
	Resistant	0 (0.0)	3 (10.0)
Netilmicin	Sensitive	4 (100.0)	13 (100.0)
Ofloxacin	Sensitive	1 (100.0)	1 (100.0)

In this study we have seen that susceptibility of salmonella typhi and paratyphi to common antibiotics are increasing. 100% sensitivity was present in third generation cephalosporins and carbapenems and even to gentamycin. Shesh RP, Sujit B, Chandra BP, Gopal N 2017 have shown in their study14 reversal of drug resistance pattern of S. typhi was quite obvious. Another study by Rather et. Al 2013 conducted in Kashmir India15 reported 100% sensitivity against gentamycin and 91.67% sensitivity for amikacin and ciprofloxacin. In our study ciprofloxacin sensitivity was present in 85% of S. typhi and 91.7% of S. paratyphi. In this study even increase of chloramphenicol sensitivity was observed, 85.7% in S. typhi and 75.0% in S. paratyphi. Agarwal KS et. al in 1998 have shown16 in India a resurgence in chloramphenicol susceptibility in S. typhi strain in their study. In this study MDR salmonella strain was found in 11.11% isolates. In a study done by Shesh RP, Sujit B, Chandra BP, Gopal N14 2017 MDR Typhi isolates was detected in 25.6%.

This is likely that the use of more effective antibiotics could have caused a decrease in the circulation of resistant strains. On the basis of above observations it may be suggested that conventional antibiotics e.g. co-trimoxazole, ampicillin, chloramphenicol should be prescribed at least in combination for the treatment of typhoid fever and third generation cephalosporins and carbapenems may be kept on hold for use in future.

Conclusion:

It was intriguing to observe that there was significant come back of conventional anti-typhoid antibiotics with resistance rate of amoxicillin 33.3%, ampicillin 41.4%, chloramphenicol 14.3% and cotrimoxazole 23.1%. On the basis of present findings, we may suggest that combination of any of the two above conventional drugs may be prescribed empirically in the therapy of enteric fever patients.

Limitations of the study – It was a very small scale study. A large scale study will be more informative in the changing trends of antibiotic susceptibility pattern of typhoid fever.

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