

Original Article

A 6-year retrospective study of bloodstream *Salmonella* infection and antibiotic susceptibility of *Salmonella enterica* serovar Typhi and Paratyphi in a tertiary care hospital in Dhaka, Bangladesh



Hafsa Afroz ^{a, *}, Md. Manjur Hossain ^{a, b}, Md. Fakruddin ^c

^a Department of Microbiology, Primeasia University, Dhaka, Bangladesh

^b Medical Officer (MCH-FP), Bhaluka Upazila Health Complex, Bhaluka, Mymensingh, Bangladesh

^c Institute of Food Science and Technology, Bangladesh Council of Scientific and Industrial Research, Dhaka, Bangladesh

ARTICLE INFO

Article history:

Received 5 February 2014

Received in revised form

26 April 2014

Accepted 6 May 2014

Keywords:

Antibiotics

Bloodstream infections

Salmonella

Susceptibility

ABSTRACT

Objectives: Bloodstream infections (BSI) are a serious cause of morbidity and mortality worldwide. Emerging antimicrobial drug resistance among bacterial pathogens causing BSI can limit therapeutic options and complicate patient management. This retrospective study was conducted to determine trends in *Salmonella* BSI and antibiotic susceptibility patterns over 6 years (2008–2013) in a tertiary care hospital in Dhaka, Bangladesh.

Methods: A total of 3584 blood samples were collected from patients with clinically diagnosed enteric fever at Dhaka Medical College Hospital, Dhaka from January 2008 to December 2013. Isolates of *Salmonella enterica* serovars Typhi and Paratyphi were identified by standard microbiological and biochemical procedures.

Results: A total of 168 isolates of *S. enterica* serovar Typhi and 160 isolates of *S. enterica* serovar Paratyphi were found. The average prevalence rate of *Salmonella* in the blood was 9.15%. Young patients, neonates, and elderly individuals were more prone to *Salmonella* infection than other patients, and females were more susceptible to *Salmonella* septicemia than males. Among *Salmonella* spp. isolates, 20.92% were multidrug resistant and showed high resistance against amoxicillin, trimethoprim–sulfamethoxazole, ciprofloxacin, nalidixic acid, and chloramphenicol. Resistance rates to cefipime, cefixime, and ceftriaxone are increasing slowly. Among *Salmonella* spp. isolates, 57.01% showed extended-spectrum β -lactamase production capability.

Conclusion: Specific antibiotic utilization strategies such as antibiotic restriction, combination therapy and usage according to standard antimicrobial susceptibility testing may help decrease or prevent the emergence of resistance and incidence of BSI.

Copyright © 2014, Buddhist Compassion Relief Tzu Chi Foundation. Published by Elsevier Taiwan LLC. All rights reserved.

1. Introduction

Salmonella is an enteropathogenic microorganism that causes infection accompanied by different clinical manifestations, most commonly gastroenteritis and fever [1]. *Salmonella* bloodstream infections (BSI) represent a major health problem worldwide but particularly in developing countries such as Bangladesh [2–5]. Each

year, there are 12–33 million cases of typhoid fever worldwide. BSI cause significant morbidity and mortality worldwide and are among the most common health care-associated infections [6]. Microorganisms present in circulating blood, whether continuously or intermittently, are a threat to every organ in the body. Illnesses associated with BSI range from self-limiting infections to life-threatening sepsis that requires rapid and aggressive antimicrobial treatment [7].

Treatment of *Salmonella* infection has become challenging because of emerging antibiotic resistance to first-line antibiotics such as chloramphenicol, ampicillin, sulphamethoxazole-trimethoprim, and, more recently, the fluoroquinolones [8]. The

Conflicts of interest: none.

* Corresponding author. Department of Microbiology, Faculty of Sciences, Primeasia University, 9, Banani, Dhaka 1213, Bangladesh.

E-mail address: hafsa.afroz@gmail.com (H. Afroz).

<http://dx.doi.org/10.1016/j.tcmj.2014.05.006>

1016-3190/Copyright © 2014, Buddhist Compassion Relief Tzu Chi Foundation. Published by Elsevier Taiwan LLC. All rights reserved.

emergence of multidrug resistant (MDR) *Salmonella* strains with resistance to fluoroquinolones and third-generation cephalosporins is a serious problem that results in severe limitation of the possibilities for effective treatment of human infections [9,10]. The appearance of MDR *Salmonella enterica* serovar Typhi (SEST) has resulted in a pressing need to test newer antimicrobials, develop their dose regimens for the treatment of typhoid fever [11], and find the mechanism by which they acquire resistance [12].

Nowadays, bacterial drug resistance is an important problem. Because of the wide variations in this resistance, the results of studies and reports in one region or in one period of time are not necessarily true for other regions or periods of time [13]. Drug resistance is related to a series of social, environmental, and technological changes. Because of constantly evolving antimicrobial resistant patterns, there is need for constant antimicrobial sensitivity surveillance [14]. The determination of antibiotic sensitivity patterns at periodic intervals is mandatory in each region for clinicians to be aware of emerging pathogens that pose a threat to the community, provide safe and effective empirical therapies, develop rational prescribing practices and policy decisions in a hospital and finally assess the effectiveness of all [15]. Appropriate surveillance by monitoring antimicrobial drug susceptibility trends is a prerequisite to implementing rational measures to tackle the resistance problem [16].

The aim of our study was to assess the prevalence of *Salmonella* serotypes in a tertiary care hospital in Dhaka, Bangladesh. We determined the predominant serotypes and resistance profiles of *Salmonella* spp. strains isolated from patients over a period of 6 years (2008–2013) at a hospital that receives patients from different parts of the country.

2. Materials and methods

2.1. Duration and place of study

This study was conducted on 3584 samples of blood collected from patients with clinically diagnosed enteric fever at Dhaka Medical College Hospital, Dhaka from January 2008 to December 2013. Blood samples were collected from patients suspected of having septicemia and typhoid fever admitted to Dhaka Medical College Hospital. The age of the patients in this study ranged from 2 years to 61 years. The population under study included both male and female patients. With the permission of the hospital authority and institutional ethical review committee, informed consent was obtained from each participant. In the case of young patients (<20 years), consent was obtained from parents/legal guardians.

2.2. Collection of blood samples

The skin at the venipuncture site of the patient was first cleaned with 95% alcohol. A 10 mL sample of blood was drawn into a 10 mL disposable pyrogen free syringe. A 5 mL sample of blood was inoculated into a blood culture bottle containing 45 mL of brain–heart infusion broth. These bottles were immediately transported to the laboratory [17].

2.3. Isolation of *S. enterica* serovars

Blood cultures bottles were incubated aerobically at 37°C for 1 week. These bottles were examined daily throughout the week of incubation. When growth appeared on any of the medium, a Gram stain film was made. If Gram-negative bacilli were detected, the culture from the blood culture bottle was inoculated onto a blood agar, xylose lysine deoxycholate agar, and a MacConkey's agar plate [10].

2.4. Biochemical identification of serovars

The API 20E identification system was used for biomedical identification of SEST and *Salmonella enterica* serovar Paratyphi (SESP). The system consists of a plastic strip with 20 microtubes containing dehydrated substrate of orthonitrophenyl-galactopyranoside. The incubation box was prepared by putting 5 mL of sterile water into the honeycombed wells of the tray to create a humid chamber. The strip was then placed in the tray. A single isolated colony of suspected *Salmonella* was picked up from MacConkey's plate. It was emulsified in sterile saline to achieve a homogenous bacterial suspension. With a sterile pipette, the tubes and cupules of citrate, Voges–Proskauer and gelatin were filled with bacterial suspension. The remaining tubes and cupules were filled with bacterial suspension. An anaerobic environment was created in the arginine dihydrolase, lysine decarboxylase, ornithine decarboxylase, urease, and hydrogen sulfide tests by overlaying with mineral oil. The box was closed and incubated at 37°C for 24 hours. A MacConkey agar plate was inoculated with the same homogenous bacterial suspension to check the purity of the bacterial suspension and incubated at 37°C for 24 hours.

2.5. Serological identification of SEST and SESP

Anti-*Salmonella* agglutinating sera contain SEST and SESP A, SESP B, SESP C, and SESP Vi from BioMérieux (Marcy l'Étoile, France) were used. The Kauffmann and White scheme was followed for serological confirmation of SEST and SESP. One drop of agglutinating serum was placed on a clean glass slide. One colony of the test strain of *Salmonella* was picked up with a loop from the MacConkey agar plate. This bacterial culture and agglutinating serum were mixed slowly with a sterile stick. When fully mixed, the slide was rotated for 5–10 seconds. The agglutination was examined by the naked eye. Positive and negative controls were tested in a similar way on the same slide [18].

2.6. Antibiotic susceptibility testing

All the *Salmonella* spp. (328) strains were tested for antibiotic resistance by the standard agar disc diffusion technique [19] on Mueller–Hinton agar (HiMedia Laboratories Pvt. Ltd., Mumbai, India) using commercial discs (Oxoid, Basingstoke, Hampshire, UK). The following antibiotics with the disc strength in parentheses were used: amoxicillin (10 µg), ciprofloxacin (5 µg), cefipime (30 µg), ceftriaxone (30 µg), cefixime (5 µg), chloramphenicol (50 µg), meropenem (10 µg), trimethoprim–sulfamethoxazole (25 µg), and nalidixic acid (30 µg). A control strain of *Escherichia coli* ATCC 25922 was included in each plate. Antimicrobial breakpoints and interpretations were taken from standards of the Clinical and Laboratory Standards Institute [20]. Isolates resistant to three or more drugs were classified as MDR.

2.7. Detection of extended-spectrum β-lactamase by the double disc diffusion method

Positive (*Klebsiella pneumoniae* ATCC 700603) and negative (*E. coli* ATCC 25922) control strains were inoculated onto Muller–Hinton agar. An amoxicillin–clavulanic acid (20 mg and 10 mg) disc was placed on the center of the plate. Cefazidime (30 mg), ceftriaxone (30 mg), cefotaxime (30 mg), and aztreonam (30 mg) discs were placed peripherally away from the amoxicillin–clavulanic acid disc. After 24 hours of incubation at 37°C, band formation between the amoxicillin clavulanic acid disc and any other disc was considered extended-spectrum β-lactamase (ESBL) positive. The ESBL positive strains were further subjected to

phenotypic confirmatory tests using sensitivity discs, which contained third-generation cephalosporins both with and without clavulanic acid. The discs used included cefotaxime (30 mg), cefotaxime and clavulanic acid (30 mg and 10 mg), ceftazidime (30 mg), ceftazidime (30 mg and 10 mg), aztreonam (10 mg), and aztreonam and clavulanic acid (30 mg and 10 mg). The differences in the zones of inhibition caused by the cephalosporins alone and those combined with clavulanic acid were recorded and, if the difference was 5 mm or more, the strains were confirmed as ESBL-producing strains [21].

3. Results

3.1. Patient information

A total of 3584 patient blood samples were collected from 2008–2013. Of these 1465 (40.87%) were from male patients and 2119 (59.13%) were from females. The age distribution showed that young children, neonates, and elderly patients were almost equally susceptible to *Salmonella* infection in the blood. It is likely that their immune systems are weaker than healthy adults and thus they are prone to septicemia. The highest percentage of all patients with clinically diagnosed enteric fever were in the 20–35 year age group (29.19%), followed by the 36–50 year age group (26.62%) (Table 1). Treatment histories of all enteric fever patients showed that the highest percentage were from the gynecology department (26.4%) followed by medicine (19.89%), pediatrics (13.53%), surgery (8.34%), and outpatient (17.91%) departments (Table 1). The age, sex, and department of patients with *Salmonella* spp. in the bloodstream are also shown in Table 1.

3.2. Isolation and biochemical and serological identification of *Salmonella* spp.

A total of 328 samples of *Salmonella* were isolated and identified biochemically from 3584 blood samples. All the isolates showed negative results in the ortho-nitrophenyl- β -galactoside, arginine dihydrolase, citrate, urease, tryptophane deaminase, indole, Voges–Proskauer, gelatine, inositol, saccharose, and amylose tests, and positive results in the lysine decarboxylase, ornithine decarboxylase, urease, hydrogen sulfide H₂S, glucose, mannose, sorbose, rhamnose, melibiose, and arabinose tests. In serology, 168 isolates agglutinated with SEST polyvalent antisera and 160 isolates with SESP polyvalent antisera, confirming their identity.

Table 1
Age, sex, and treatment distribution of total patients and bloodstream *Salmonella* positive patients.

Parameter	No. of patients (%)	No. of <i>Salmonella</i> positive patients (%)
Sex		
Male	1465 (40.87)	150 (45.73)
Female	2119 (59.13)	178 (54.25)
Age group, y		
<20	861 (24.02)	83 (25.30)
20–35	1046 (29.19)	102 (31.1)
36–50	954 (26.62)	79 (24.09)
>50	723 (20.17)	64 (19.51)
Treatment department		
Pediatric	485 (13.53)	51 (15.54)
Medicine	713 (19.89)	61 (18.59)
Surgery	299 (8.34)	23 (7.01)
Obstetric–gynecology	946 (26.4)	77 (23.48)
External	642 (17.91)	116 (35.36)
Total	3584	328

3.3. Rates of SEST and SESP isolated from blood cultures

Distribution of illness by month and *Salmonella* prevalence are shown in Table 2. *Salmonella* spp. were isolated throughout the year, but the prevalence was comparatively low in the first half (January–June) of the year. The prevalence showed a peak during July, August, and September (Table 2).

The prevalence of *Salmonella* spp. from 2008 to 2013 showed a gradual increase although the prevalence in 2010 (8.65%) and 2011 (8.18%) was slightly lower than in 2012 (9.2%) and 2013 (11.41%; Fig. 1). Overall prevalence of *Salmonella* spp. in blood samples from 2008–2013 was 9.15%.

In 2008, there were fewer SEST isolates than SESP (Fig. 2), but from 2009–2013, an increasing pattern of SEST isolates was observed. In 2013, there were more SEST isolates ($n = 39$) than SESP ($n = 33$).

3.4. Sensitivity/resistance of *Salmonella* isolates to antimicrobial compounds

Antibiotic resistance of isolated *Salmonella* spp. against the nine antibiotics used increased each year from 2008–2013. Resistance to amoxicillin was 37.5% in 2008, 41.29% in 2009, 37.29% in 2010, 35.29% in 2011, 37.28% in 2012, and 43.1% in 2013. Resistance rates for other antibiotics in the same years were as follows: cefipime 13.75%, 15.5%, 14.17%, 11.17%, 10.16%, and 16.34%; cefixime 7.5%, 10%, 8.5%, 7.48%, 8.47%, and 11.2%; ceftriaxone 4.75%, 4.75%, 5.75%, 8.78%, 6.77%, and 9.1%; trimethoprim–sulfamethoxazole 31.5%, 34.5%, 29%, 25.73%, 23.72%, and 33.65%; ciprofloxacin 25.75%, 28%, 25.5%, 21.43%, 25.42%, and 26.4%; nalidixic acid 75.6%, 77.5%, 76%, 77.67%, 79.66%, and 79.9%; and chloramphenicol 24%, 25.5%, 27.5%, 25.73%, 23.72%, and 31.35% in 2013. All the isolates were sensitive to meropenem from 2008–2013 (Fig. 3).

Comparison of antibiotic resistance showed relatively higher resistance in *S. paratyphi* isolates than *S. typhi* (Figs. 4 and 5). Both groups of organism showed higher resistance to amoxicillin, trimethoprim–sulfamethoxazole, ciprofloxacin, nalidixic acid, and chloramphenicol than to other antibiotics. Resistance to fluoroquinolones such as cefipime, cefixime, and ceftriaxone increased over the time studied. No resistance was observed against meropenem.

3.5. MDR *Salmonella* patterns in blood cultures

MDR was found in 20.96% of *Salmonella* spp. isolates in total. MDR rates in 2008 were 22.56%; in 2009, 19.14%; in 2010, 22.1%; in 2011, 18.41%; in 2012, 16.25%; and 27.31% in 2013 (Fig. 6).

The distribution of MDR *Salmonella* spp. in blood cultures by month is shown in Table 3.

3.6. ESBL production

ESBL production was found in 57.01% of all *Salmonella* spp. isolates, 54.17% of SEST isolates, and 60.625% of SESP isolates (Fig. 7).

4. Discussion

Typhoid fever caused by SEST and SESP is one of the most common infections in Bangladesh [22]. Strains of SEST and SESP resistant to commonly used antibiotics such as chloramphenicol, amoxicillin, trimethoprim–sulfamethoxazole, and ciprofloxacin are emerging in many parts of the world including Bangladesh [23]. Emerging antimicrobial drug resistance among bacterial pathogens causing BSI can limit therapeutic options and complicate patient management. The epidemiology of invasive bloodstream

Table 2
Month-wise distribution of illness and organisms during 2008–2013.

Year	Parameter	Month												Total
		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	
2008	Febrile Illness	19	29	27	46	39	45	77	91	55	29	19	23	499
	<i>Salmonella</i> spp.	2	2	2	3	2	3	8	11	5	3	2	3	46
	SEST	0	1	1	1	0	1	4	6	2	2	1	1	20
	SESP	2	1	1	2	2	2	4	5	3	1	1	2	26
2009	Febrile Illness	21	32	29	45	39	55	88	97	55	33	37	21	552
	<i>Salmonella</i> spp.	0	3	2	3	2	3	9	12	5	3	2	3	47
	SEST	0	1	1	1	0	1	6	8	4	2	1	0	25
	SESP	0	2	1	2	2	2	3	4	1	1	1	3	22
2010	Febrile Illness	45	33	21	35	29	45	99	105	65	40	47	19	583
	<i>Salmonella</i> spp.	3	0	2	2	4	3	11	13	7	3	2	3	53
	SEST	1	0	1	1	0	1	8	8	2	2	0	1	25
	SESP	2	0	1	1	4	2	3	5	5	1	2	2	28
2011	Febrile Illness	29	31	41	45	32	48	103	98	75	40	55	21	618
	<i>Salmonella</i> spp.	6	2	3	2	0	1	15	9	6	3	2	2	51
	SEST	2	0	1	1	0	0	9	6	2	1	0	0	22
	SESP	4	2	2	1	0	1	6	3	4	2	2	2	29
2012	Febrile Illness	37	31	45	29	44	48	104	103	88	40	52	23	644
	<i>Salmonella</i> spp.	7	2	3	2	4	0	17	9	7	3	2	3	59
	SEST	1	0	1	1	0	0	15	6	2	2	0	1	29
	SESP	6	2	2	1	4	0	2	3	5	1	2	2	30
2013	Febrile Illness	41	44	36	28	48	58	86	105	99	112	107	94	858
	<i>Salmonella</i> spp.	8	5	6	4	7	7	9	15	12	17	14	15	119
	SEST	2	3	2	1	3	2	4	5	5	7	6	8	48
	SESP	6	2	4	3	4	5	5	10	7	10	8	7	71

SESP = *Salmonella enterica* serovars Typhi; SEST = *Salmonella enterica* serovar Paratyphi.

pathogens has changed dramatically over the years [24]. The changes in the incidence and epidemiology of infecting organisms have also brought about an increase in resistance to many antibiotic compounds, resulting in a reduction in therapeutic options [25].

Septicemia is one of the most severe invasive bacterial infections and surveillance of antibiotic susceptibility of the organisms isolated from blood cultures is an important method of obtaining information on resistance patterns at the regional and national level. Because of variations in the susceptibility patterns of *Salmonella* species from different geographical areas, constant monitoring is important to provide suitable guidelines for successful treatment.

This study was carried out to show the antibiotic susceptibility patterns of *Salmonella* strains (SEST and SESP) isolated from the blood of typhoid patients in a tertiary care hospital in Dhaka, Bangladesh. About 9.15% of the total samples were positive for *Salmonella* spp. The prevalence increased gradually from 2008 to 2013 in accordance with other studies [26,27]. SEST (168 samples) was more prevalent than SESP (160 samples). *Salmonella* infection occurred throughout the year but the highest prevalence was found in July–December.

Neonates and young (age 2–15 years) and elderly persons (age 46–60 years) were more susceptible to *Salmonella* infection, probably because of their weaker immune systems. Healthy adults are less susceptible to BSI with *Salmonella*. Females had more

infections than males and the same pattern was observed in *Salmonella* spp., SEST, and SESP infections.

A high percentage of the isolates showed resistance to first line (amoxicillin, chloramphenicol, trimethoprim–sulfamethoxazole) and second line drugs (nalidixic acid and ciprofloxacin). Resistance to cephalosporins such as cefipime, cefixime, and ceftriaxone tended to increase during this period. No resistance was observed against meropenem. Many researchers around the world have reported increased resistance of *Salmonella* spp. against nalidixic acid [28,29] and a dramatic increase in nalidixic acid-resistant isolates was observed in this study.

Several previous studies reported bloodstream *Salmonella* spp. in patients from Bangladesh. In one study [23], 66% of patients were *Salmonella* spp. positive and one third of the isolated *S. typhi* were MDR. The isolates were most resistant to amoxicillin, cotrimoxazole, and chloramphenicol. In another study [30], among 304 of 385 (79%) isolated *Salmonella* spp. were *S. typhi* and 81 (21%) were *S. paratyphi*. About 40% of the *S. typhi* isolates were resistant to ampicillin, chloramphenicol, and co-trimoxazole compared with only 1.8% of SESP. All SEST and SESP A were sensitive to ceftriaxone [31]. Twelve MDR *Salmonella* isolates from hospital waste were resistant to ciprofloxacin, ampicillin, amoxicillin, and penicillin. The

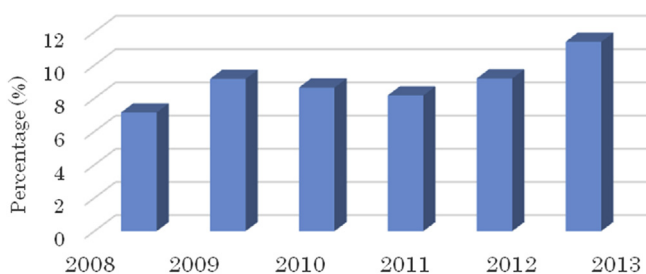


Fig. 1. Prevalence of *Salmonella* spp. in blood, 2008–2013.

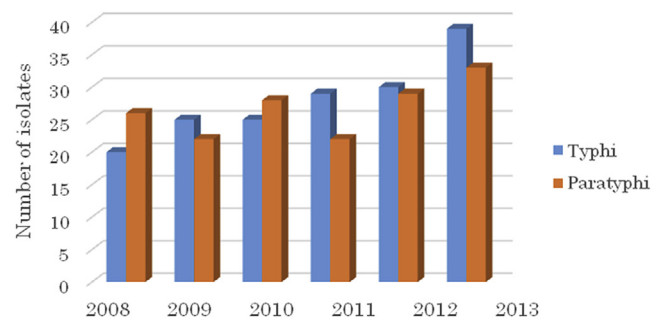


Fig. 2. Comparative prevalence of *Salmonella enterica* serovar Typhi and *Salmonella enterica* serovar Paratyphi in blood, 2008–2009.

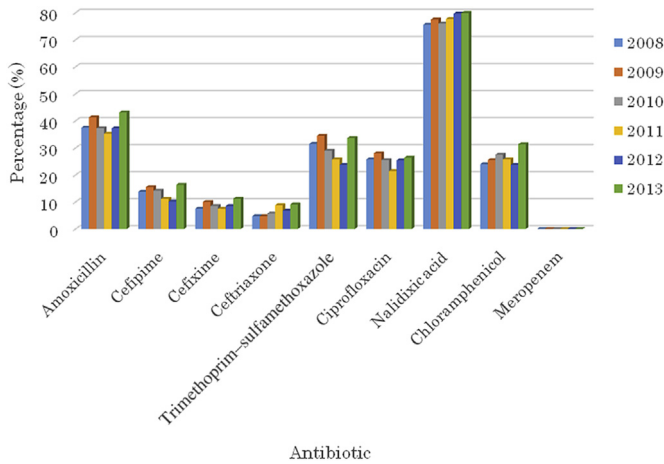


Fig. 3. Antibiotic resistance pattern of isolated *Salmonella* spp., 2008–2009.

presence of MDR *Salmonella* in hospital waste indicates BSI of patients with *Salmonella*. In another study, 943 SEST were isolated from patients with typhoid fever and >50% of isolates were resistant to ampicillin, co-trimoxazole, and chloramphenicol, and >90% of isolates were resistant to nalidixic acid. Resistance to ciprofloxacin was very low [32]. Similar results were also found in another study [33] where resistance was higher to ampicillin, cotrimoxazole, and chloramphenicol and all isolates were sensitive to ceftriaxone and ceftazidime.

Most of the previous studies in Bangladesh on bloodstream *Salmonella* spp. did not report detection of MDR *Salmonella* but in this study, 20.92% of isolates were MDR. From 2008 to 2012, MDR isolates decreased but in 2013 a sudden rise in the percentage of MDR isolates was observed (Fig. 6). The distribution of MDR isolates by month showed a higher prevalence from July to October each year (Table 2), which is in accordance with the higher prevalence of *Salmonella* spp. from July to December each year in this study (Table 3). In one study [29], MDR *Salmonella* spp. prevalence was 37%, which is higher than in the present study. Mohanty et al [34] also reported an increasing pattern of MDR *Salmonella* spp. in BSI.

In this study, ESBL production was observed in 57.01% of all *Salmonella* spp. isolates, 54.17% of SEST isolates and 60.625% of SESP isolates (Fig. 7). ESBL production was higher in this study than in some previous studies. Irajian et al [35] reported ESBL production in 2% of SESP. This indicates an increasing trend of ESBL production in bloodstream *Salmonella* spp. isolates in Bangladesh. ESBL *Salmonella* spp. in a hospital setting is a challenge because of possible spread of ESBL to other opportunistic pathogens and because of the limited therapeutic options against them.

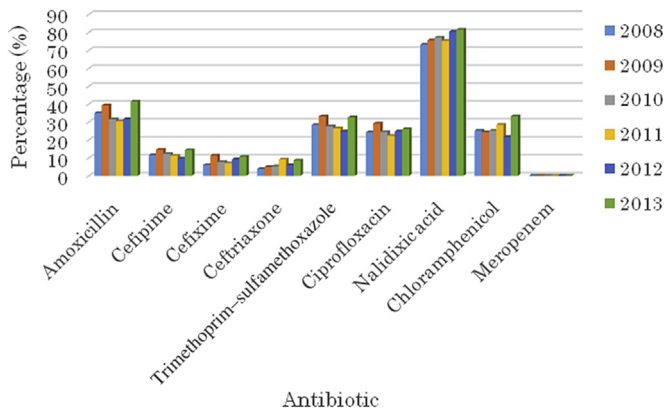


Fig. 4. Antibiotic resistance of *Salmonella enterica* serovar Typhi, 2008–2013.

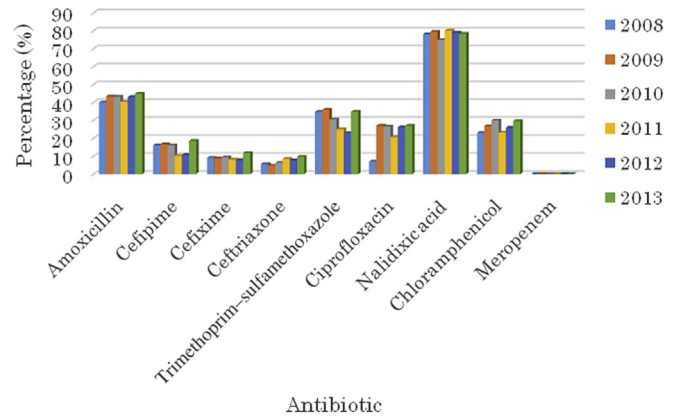


Fig. 5. Antibiotic resistance of *Salmonella enterica* serovar Paratyphi, 2008–2013.



Fig. 6. Multidrug resistant *Salmonella* spp. in blood, 2008–2013.

This study in conjunction with previous studies warns about the increasing prevalence of *Salmonella* BSI in a wide group of patients and their increased resistance to first line and second line drugs of choice. Although the mortality rate linked to salmonellosis is low, its high prevalence has significant economic, epidemiological, and health implications. Our data underscore the need for annual antimicrobial resistance surveillance reports, which can provide valuable insight into resistance trends at a particular medical facility to assist in the appropriate choice of empiric therapy.

Accurate prevalence rates and antibiotic resistant patterns of bloodstream *Salmonella* spp. in Bangladesh cannot be ascertained because of a lack of epidemiological surveillance systems at all levels of government (federal, state, and local), and the presence of other diseases considered to be of higher priority [11].

Table 3
Multidrug resistant *Salmonella* pattern in blood culture, 2008–2013.

Month	Multidrug resistance, %					
	2008	2009	2010	2011	2012	2013
January	0	50	25	16.67	14.286	16.45
February	50	0	0	0	0	11.32
March	33.333	0	0	0	0	25
April	0	0	50	50	50	0
May	0	33.333	33.333	33.33	25	33.33
June	25	0	0	0	0	33.33
July	30	23.077	13.333	14.286	11.765	25
August	28.571	25	22.22	22.222	22.222	25
September	40	33.333	40	40	28.571	0
October	33.33	50	50	50	13.333	0
November	0	0	0	0	0	33.33
December	25	25	25	0	0	25
Average	22.1	19.97	21.57	18.87	15.43	27.58

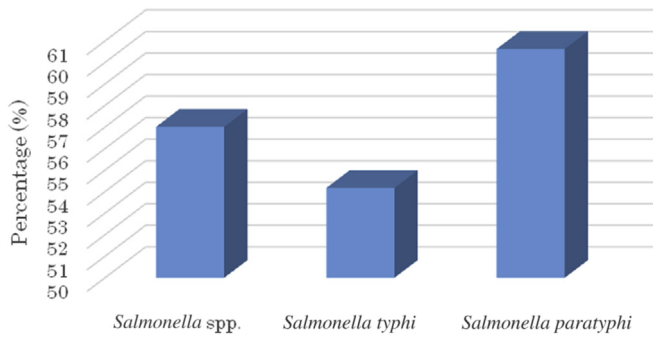


Fig. 7. Prevalence of extended-spectrum β -lactamase *Salmonella* spp. in blood, 2008–2013.

The selective pressure of unrestricted antimicrobial usage has probably contributed to the genesis of resistant SEST [36]. In Dhaka, antimicrobials are available from chemist shops without legal prescriptions. This encourages patients to buy antimicrobials over the counter and use them without consulting a doctor. Appropriate surveillance by monitoring antimicrobial drug susceptibility trends is a prerequisite to implementing rational measures to tackle the resistance problem. Continued surveillance of antimicrobial susceptibility patterns and study of MDR in *Salmonella* spp. in different parts of the country will help in updating knowledge about the proper antibiotics for therapeutic cure.

5. Conclusion

This study provided much needed information and warns about the increasing prevalence of MDR SEST and SESP causing BSI in Bangladesh. The rise in antibiotic resistance in blood isolates emphasizes the importance of sound hospital infection control, rational prescribing policies, and the need for new antimicrobial drugs and vaccines. Our data underscore the need for annual antimicrobial resistance surveillance reports, which can provide valuable insight into resistance trends at a particular medical facility to assist in the appropriate choice of empiric therapy.

References

- Islam MN, Rahman ME, Rouf MA, Islam MN, Khaleque MA, Siddika M, et al. Efficacy of azithromycin in the treatment of childhood typhoid fever. *Mymensingh Med J* 2007;16:149–53.
- Hoque SS, Alam AN, Islam MR, Khan MR. Recent advances in the treatment of typhoid: with special emphasis on multidrug resistant *Salmonella* Typhi in Bangladesh. *Bangladesh J Child Health* 1992;16:15–9.
- Bhattacharya SS, Das U. Occurrence of *Salmonella* Typhi infection in Rourkela, Orissa. *Indian J Med Res* 2000;111:75–6.
- Coovadia YM, Gathiram V, Bhamjee A, Garratt RM, Mlisana K, Pillay N, et al. An outbreak of multi-resistant *Salmonella* typhi in South Africa. *Quart J Med* 1992;82:91–100.
- Gautam V, Gupta NK, Chaudhary U, Arora DR. Sensitivity pattern of *Salmonella* serotypes in Northern India. *Braz J Infect Dis* 2002;6:281–7.
- Khan MR, Hoque SS. Emergence of multi-drug resistant *Salmonella* Typhi: a need for therapeutic reappraisal. *Bangladesh J Child Health* 1992;16:1–3.
- Akiniyemi KO, Oshundare YO, Oyeyinka OG, Coker AO. A retrospective study of community-acquired *Salmonella* infections in patients attending public hospitals in Lagos, Nigeria. *J Infect Dev Ctries* 2012;5:387–95.
- Aggarwal A, Vij AS, Oberoi A. A three-year retrospective study on the prevalence, drug susceptibility pattern, and phage types of *Salmonella enterica* subspecies Typhi and paratyphi in Christian Medical College and Hospital, Ludhiana, Punjab. *JACM* 2007;8:32–5.
- Albert MJ, Haider K, Nahar S, Kibriya AK, Hossain MA. Multiresistant *Salmonella* Typhi in Bangladesh. *J Antimicrob Chemother* 1991;27:554–5.
- Saha SK, Saha SK. Antibiotic resistance of *Salmonella* Typhi in Bangladesh. *J Antimicrob Chemother* 1994;33:190–1.
- Afroz H, Hossain MM, Fakruddin M, Hossain MA, Khan ZUM, Datta S. Prevalence and antibiotic susceptibility patterns of bloodstream *Salmonella* infections in a tertiary care hospital, Dhaka. *J Med Sci* 2013;13:360–6.
- Akter L, Hassan M, Ahmed Z. Present status and antibiotic sensitivity pattern of *Salmonella* Typhi and *S. Paratyphi* in different age group hospitalized patients in Dhaka City, Bangladesh. *IOSR J Pharm Biol Sci* 2012;4:27–30.
- Rahman M, Siddique AK, Shoma S, Rashid H, Salam MA, Ahmed QS, et al. Emergence of multidrug-resistant *Salmonella enterica* serotype Typhi with decreased ciprofloxacin susceptibility in Bangladesh. *Epidemiol Infect* 2005;134:433–8.
- Afroz S, Ilias M, Islam M, Saha SK. Prevalence of ciprofloxacin and nalidixic acid resistant *Salmonella enterica* serovar Typhi in Bangladesh. *Bangladesh J Microbiol* 2011;28:7–11.
- Shahriar M, Kabir S. Status Of antibiotic resistant *Salmonella* Typhi strains from clinical isolates in Dhaka. *Dhaka Univ J Biol Sci* 2010;19:207–9.
- Dimitrov TS, Panigrahi D, Emara M, Al-Nakkas A, Awni F, Passadilla R. Incidence of bloodstream infections in a speciality hospital in Kuwait: 8-year experience. *Med Princ Pract* 2005;14:417–21.
- Saha SK, Talukder SY, Islam M, Saha S. A highly ceftriaxone-resistant *Salmonella* typhi in Bangladesh. *Pediatr Infect Dis J* 1999;18:387.
- Morshed MG, Khan WA, Khan HZ, Akbar MS. Multiple drug resistant *Salmonella* typhi in Bangladesh (letter). *J Diarrhoeal Des Res* 1986;4:24.
- Bauer AW, Kirby WM, Sherris JC, Turck M. Antibiotic susceptibility testing by a standardized single disc method. *Am J Clin Path* 1966;45:493–6.
- CLSI. Performance standards for antimicrobial disk susceptibility tests. 9th Informational Supplement, CLSI document M2-A9. Wayne, PA: CLSI; 2006.
- Kumar MS, Lakshmi V, Rajagopalan R. Occurrence of extended spectrum beta-lactamases among *Enterobacteriaceae* spp. isolated at a tertiary care institute. *Ind J Med Microb* 2006;24:208e11.
- Rahman M, Ahmad A, Shoma S. Decline in epidemic multidrug-resistant *Salmonella* Typhi is not associated with increased incidence of antibiotic-susceptible strains in Bangladesh. *Epidemiol Infect* 2002;129:29–34.
- Alam AS, Zaman S, Chaiti F, Sheikh N, Kundu GK. A reappraisal of clinical characteristics of typhoid fever. *Bangladesh J Child Health* 2010;34:80–5.
- Benschop J, Hazelton ML, Stevenson MA, Dahl J, Morris RS, French NP. Descriptive spatial epidemiology of subclinical *Salmonella* infection in finisher pig herds: application of a novel method of spatially adaptive smoothing. *Vet Res* 2008;39:2.
- Boni-Cissé C, Meité S, Faye-Ketté H, Houedanou C, Timité-Konan M, Kalpi C, et al. Serotypes and antibiotypes of *Salmonella* isolated at the University Teaching Hospital of Yopougon, Abidjan, Cote d'Ivoire from 2005 to 2009. *J Microbiol Antimicrob* 2012;4:40–4.
- Pourakbari B, Sadr A, Ashtiani MT, Mamishi S, Dehghani M, Mahmoudi S, et al. Five-year evaluation of the antimicrobial susceptibility patterns of bacteria causing bloodstream infections in Iran. *J Infect Dev Ctries* 2012;6:120–5.
- Vlieghe E, Phe T, De Smet B, Veng CH, Kham C, Sar D, et al. Increase in *Salmonella enterica* serovar Paratyphi A infections in Phnom Penh, Cambodia, January 2011 to August 2013. *Euro Surveill* 2013;18. pii 20592.
- Muthu G, Suresh A, Sumathy G, Srivani R. Studies on antimicrobial susceptibility pattern of *Salmonella* isolates from Chennai, India. *Int J Pharm Bio Sci* 2011;2:435–42.
- Dimitrov T, Udo EE, Albaksami O, Al-Shehab S, Kilani A, Shehab M, et al. Clinical and microbiological investigations of typhoid fever in an infectious disease hospital in Kuwait. *J Med Microbiol* 2007;56:538–44.
- Shadia K, Borhan SB, Hasin H, Rahman S, Sultana S, Barai L, et al. Trends of antibiotic susceptibility of *Salmonella Enterica* serovar Typhi and Paratyphi in an urban hospital of Dhaka City over 6 years period. *Ibrahim Med Coll J* 2011;5:42–5.
- Chowdhury AMMA, Anwar MN. Isolation and characterization of ciprofloxacin resistant *Salmonella* from the wastes of hospital patients. *Bangladesh J Microbiol* 2010;27:6–9.
- Mahmud ASM, Mahmud MN, Hakim MA. Reduced susceptibility to fluoroquinolone in *Salmonella* Typhi and some molecular characteristics of fluoroquinolone resistance in indigenous isolates. *Bangladesh J Microbiol* 2010;27:38–41.
- Sarker ABM, Saha SK, Islam M, Hossain MA. Reduced susceptibility to fluroquinolone and molecular analysis of ciprofloxacin resistance in *Salmonella* Typhi in Bangladesh. *Dhaka Univ J Biol Sci* 2010;19:137–44.
- Mohanty S, Renuka K, Sood S, Das BK, Kapil A. Antibiogram pattern and seasonality of *Salmonella* serotypes in a North Indian tertiary care hospital. *Epidemiol Infect* 2006;134:961–6.
- Irajian G, Ranjbar R, Moghadas AJ. Detection of extended spectrum beta lactamase producing *Salmonella* spp. and multidrug resistance pattern. *Iranian J Pathol* 2009;4:128–32.
- Mills-Robertson F, Addy ME, Mensah P, Crupper SS. Molecular characterization of antibiotic resistance in clinical *Salmonella* Typhi isolated in Ghana. *FEMS Microbiol Lett* 2002;215:249–53.