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The Drug Changing Sensitivity and Resistance Pattern of Different Antibiotics and their Minimum Inhibitory Concentration against *Salmonella*

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ABSTRACT

In the present study, MDRP shows that ampicillin, cotrimoxazole, gentamycin, tetracycline, were resistant. Whereas ceftriaxone with sulbactam, ciprofloxacin, ofloxacin was sensitive. The azithromycin and cefpodoxime were intermediate against *S. typhi.* The antibiotic susceptibility pattern of *S. typhi* during the period from Sep 2016 to June 2017and it was found that out of 676 the most sensitive antibiotics were ceftriaxone and sulbactam 90 (100%), ciprofloxacin 90 (100%) and ofloxacin 90 (100%) whereas the most resistant antibiotics were tetracycline 237 (87.77%) and amoxycillin 225 (83.33%). The change in sensitivity pattern during the period of Sep 2016 to June 2017, July 2016 to 1 April 2018 and May 2018 to Feb 2019 of the drug ceftriaxone and sulbactam, is 100%. The drug cefuroxime is 97.77%, 100 %, and 96.60%. The drug ciprofloxacin 100%, 100%, and 97.57%. The drug ofloxacin is 100%, 94.00%, and 92.23%. The drug amikacin 96.66%, 80.00%, and 50.48%. Out of 676 isolates of *S. typhi*, the MDR for two drug combination cotrimoxazole and nalidixic acid is 35 (5.17%).

Keywords: antibiotics resistance, antigens, Enteric fever, gastroenteritis, *Salmonella typhi*.

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INTRODUCTION

The global estimates for the burden of invasive *Salmonella* disease found that South-Central and East-Central Asia experienced the highest incidences of typhoid fever, with >100 cases per 100000 person-years of observation[1]. The incidence rates of typhoid fever in many of the Typhoid Fever Surveillance in Africa Program (TSAP) sites were equivalent to, or indeed greater than, incidences reported in parts of Asia in the early 2000s[1,2]. In the previous studies, it is shown that the incidence of typhoid fever in Ghana was substantially different between adjacent urban and rural areas[3]. In another study conducted on TSAP found that the substantial prevalence of drug resistance and multidrug-resistant strains of invasive *Salmonella* species circulating in sub-Saharan Africa[4]. There is a high prevalence of resistance to first-line antimicrobial agents was identified in both *S. typhi* and nontyphoidal *Salmonella* isolates in some locations. These data are largely reflective of other observations in further sites in Africa and Asia[5-8].

Typhoid is the 5th most common communicable disease in India. It is a major cause of absenteeism in schools and workplaces. Children constitute about 69% of hospitalized typhoid victims in India. Even sophisticated drugs are proving to be ineffective against resistant strains of typhoid bacteria. A retrospective hospital-based study at Safdarjang hospital-India was undertaken between January 1999 and December 2003 to estimate age-related epidemiological, clinical and microbiological characteristics in enteric fever cases, which showed that more than 24% of cases were in children up to 5 years of age [9]. In India, the disease is endemic in almost all parts of the country with periodic outbreaks of waterborne or foodborne diseases. In 1992, about 3,52, 980 cases with 735 deaths were reported. The number was 3,57, 452 cases and 888 deaths in 1993, whereas, in 1994, it declined to 2,78,451 cases and 304 deaths[10]. In hospital-based studies and outbreak reports from India indicate that enteric fever is a major public health problem in this country, with *S. typhi* the most common etiologic agent but with an apparently increasing number of cases due to *S. paratyphi* A[11].

The excessive antibiotic use causes an increased risk of infection with both drug-resistant and drug-sensitive serotypes of *S. typhi*[12]. The emergence of antimicrobial resistance in *Salmonella* strains is a serious health problem worldwide[13]. In the early 1960s, the first incidence of *Salmonella* resistance to a single antibiotic, namely chloramphenicol, was reported[14]. Since then, the frequency of isolation of *Salmonella* strains with resistance towards one or more antimicrobial agents has increased in many

countries, including the USA, the UK, and Saudi Arabia[15]. Antimicrobial agents such as ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole are used as the traditional first-line treatments for *Salmonella* infections. The *Salmonella* spp. are resistant towards these agents are referred to as multi-drug resistant (MDR). For many years, the phenotypic trait of MDR was widely distributed among *S. typhi* and at a lower rate, among *S. paratyphi*[16].

Africa and Asia are two continents with a high isolation frequency of *S. typhi* displaying MDR phenotype. In a surveillance study conducted in five Asian countries like India, Pakistan, Vietnam Indonesia, and China, among which the former three countries had higher rates of MDR isolates of *S. typhi* than Indonesia and China[17]. Other reports present similar data with a high rate of MDR isolates of *S. typhi i*n Pakistan, India, Nepal, and Vietnam, while in China and Indonesia have less incidence rate of MDR *S. typhi*[18]. With the emergence of resistance towards traditional antibiotics, fluoroquinolones and extended-spectrum cephalosporins have been introduced as the antimicrobial agents of choice in treating MDR *S. typhi*[19]. nalidixic acid resistance, which is used as an indicator of reduced susceptibility of ciprofloxacin and other fluoroquinolones, is displayed by isolates from Pakistan, India, and Vietnam, with high incidence rates of 59%, 57% and 44%, respectively[17]. As for NTS, the number of strains developing MDR phenotype has increased in many countries since the first emergence of MDR *S. typhimurium* DT104 strains in 1990[20]. NARMS presented data (from 1996–2007) which are more comprehensive, reporting the emergence of NTS isolates that are resistant to nalidixic acid and ceftriaxone. This phenomenon has raised concern among public health authorities regarding both clinical management and prevention of the infection[21]. A surveillance study on 135,000 clinical isolates of NTS was conducted in Europe from 2000 to 2004, and the data showed that 15% of the isolates displayed MDR phenotype and 20% of the isolates were resistant to nalidixic acid[22].

The emergence of *Salmonella* with antimicrobial resistance is mainly promoted by the use of antibiotics in animal feed to promote the growth of food animals and in veterinary medicine to treat bacterial infections in those animals[23]. This poses a high risk of zoonotic disease with the transmission of MDR *Salmonella* strains from animals to humans *via* the ingestion of food or water contaminated with the animal feces with direct contact or the consumption of infected food of animals[24]. Moreover, MDR *Salmonella* strains were found in some exotic pet animals such as tortoises and turtles as well as their water environment and this could result in a higher risk of zoonotic infections in humans through direct contact with these animals[25,26]. The quinolones and third-generation cephalosporins have been the antibiotics of choice in treating infections with MDR *Salmonella*[27]. Epidemiological studies show that MDR *Salmonella* strains cause more severe or prolonged syndromes than susceptible strains implying that the MDR strains are more virulent than the susceptible ones[28]. Data shows that patients infected with MDR *Salmonella* strains are more ill and septic at the onset of the disease and the illness is typically accompanied by high fever, enlargement of the spleen, liver and abdominal swelling[29].

MATERIALS AND METHODS

Collection, processing of samples

The samples from males, females, and children with the age group between 5 to 80 years were collected for epidemiological investigations from Kashmir. A total of 676 samples were collected from various patients from hospitals and clinical laboratories.

Antibiotic susceptibility testing by Kirby-Bauer disc diffusion method

The cultures of *S. typhi* were prepared in broth medium. Inoculate the plate with the cultures by swabbing the entire surface of the plate. Then rotate the plate 45 and 90 degrees and using the same swab, streak the plate again. The lid was replaced and the swab was discarded. Then repeat the procedure for a new plate. Allow the plates to dry for 5 minutes. Now use the sterile forceps and transfer different antibiotic discs to all the plate. Then label the plates and incubate at 37°C for 24 hrs. After incubation, the plates are examined and the diameter of zones of inhibition was measured.

The Minimum inhibitory concentration (MIC) Method

The minimum inhibitory concentration (MIC), which is the lowest concentration that still inhibits the growth of a particular organism can be determined using serial dilution methods. This procedure establishes the concentration of an antibiotic that is effective in preventing the growth of the pathogen and gives an indication of the dosage of that antibiotic that should be effective in controlling the infection in the patient.

- Sterility checked peptone water was inoculated with 2-5 morphologically similar colonies of *Salmonella* isolate. The broth was incubated at 37°C and turbidity matched to 0.5 Mac Farland standard.
- The drug with different concentration was prepared in Mueller-Hinton media and was sterilized and cooled to 50°C. Then the antibiotic suspension was added to each agar containing tube to get a fixed concentration of 0.25 µg/ml, 1 µg/ml and 2 µg/ml. These drugs containing agar tubes were poured into Petri dishes and allowed to solidify and then incubate at 37°C.
- The grid was made on the drug-containing Mueller-Hinton agar and spot inoculation of each isolate was made separately. The ATCC *E. coli* (25922) was used as a control plate.
- The plates were incubated aerobically in an upright position at 37°C for 24 hours.
- The drug-containing plate was examined for growth/no growth of the inoculated *Salmonella* isolates. The minimum concentration of different antibiotics inhibiting the growth of test strain (s) was recorded as the MIC of different antibiotics.

RESULT AND DISCUSSION

Antibiotic sensitivity

The result of the in vitro antibiotic sensitivity test showed that isolates of *S. typhi* were generally resistant to antibiotics like chloramphenicol, ampicillin, tetracycline, cotrimoxazole, gentamycin, nalidixic acid (Table 1). The intermediate antibiotics were azithromycin and cefpodoxime whereas antibiotics such as ceftriaxone+salbactum, ciprofloxacin and ofloxacin were sensitive to *S. typhi*. In the present study, MDRP shows that ampicillin, co-trimoxazole, gentamycin, tetracycline, were resistant whereas ceftriaxone with sulbactam, ciprofloxacin and cefpodoxime were also sensitive against *S. typhi* (Table 1).

Table 1. Drug sensitivity pattern of *S. typhi* against various antibiotics.

S. No	Antibiotics	Zone of inhibition (mm)	Sensitivity (S), Intermediate (I), Resistant (R)
1	Ampicillin	0	R
2	Chloramphenicol	7.2	R
3	Cotrimoxazole	0	R
4	Gentamycin	0	R
5	Tetracycline	0	R
6	Azithromycin	10.0	I
7	Ceftriaxone+ Salbactum	16.6	S
8	Ciprofloxacin	14.8	S
9	Cefpodoxime	10.2	I
10	Nalidixic acid	0	R
11	Ofloxacin	12.8	S

S=Sensitivity, I=Intermediate, R=Resistant

The fluoroquinolones (ofloxacin, ciprofloxacin) are widely regarded as optimal for the treatment of typhoid fever in adults[30]. They are relatively inexpensive, well tolerated and more rapidly and reliably effective than the former first-line drugs, viz. chloramphenicol, ampicillin, amoxicillin, and trimethoprim-sulfamethoxazole (Table 2). The majority of isolates are still sensitive. The fluoroquinolones attain excellent tissue penetration and kill *S. typhi* in its intracellular stationary stage in monocytes/macrophages and achieve higher active drug levels in the gall bladder than other drugs. They produce a rapid therapeutic response within three to five days and very low rates of post-treatment carriage[31,32].

Table 2. Antibiotic susceptibility pattern of *S. paratyphi* A by disc diffusion method (N=178)

S. No.	Antibiotic	Sensitive n (%)	Intermediate n (%)	Resistant n (%)
1	Ampicillin	71.2(40)	1.78(1)	105.02(59)
2	Amoxycillin & Clavulinic acid	150.41(84.5)	3.56(2)	24.03(13.5)
3	Ceftriaxone & Salbactum	178(100)	0	0
4	Chloramphenicol	165.896(93.2)	2.136(1.2)	9.968(5.6)
5	Ciprofloxacin	178(100)	0	0(0)
6	Co-trimoxazole	64.792(36.4)	0	113.208(63.6)
7	Amikacin	178(100)	0	0
8	Nalidixic acid	1.78(1)	0	176.22(99)

There is no evidence of the superiority of any particular fluoroquinolone. The nalidixic acid and norfloxacin do not achieve adequate blood concentrations after oral administration and should not be used. No evidence of toxicity and impact on growth has been described in children with typhoid who have received ciprofloxacin[33]. For nalidixic-acid-sensitive *S. typhi*, seven-day regimens have proved highly effective. Courses of treatment of three and five days have also proved highly effective against nalidixic-acid-sensitive strains. For nalidixic-acid-resistant infections, a minimum of seven days of treatment at the maximum permitted dosage is necessary and 10-14 days are usually required (Table 3).

Table 3. Antibiotic susceptibility pattern of *S. typhi* by disc diffusion method (N=235)

S. No.	Antibiotic	Sensitive n (%)	Intermediate n (%)	Resistant n (%)
1	Ampicillin	123.37(52.5)	4.7(2)	106.92(55.5)
2	Amoxycillin & Clavulinic acid	211.5(90)	2.35(1)	21.15(9)
3	Ceftriaxone & Salbactum	235(100)	0	0
4	Chloramphenicol	206.8(88)	7.05(3)	21.15(9)
5	Ciprofloxacin	235(100)	0	0
6	Co-trimoxazole	70.5(30)	4.7(2)	159.8(68)
7	Amikacin	235(100)	0	0
8	Nalidixic acid	(0)	0	235(100)

The recent emergence of resistance to fluoroquinolones, however, suggests that their widespread and indiscriminate use in primary care settings should be restricted. In areas of the world where the fluoroquinolones are not available or not registered for public health use and where the bacterium is still fully sensitive to traditional first-line drugs (chloramphenicol, amoxicillin or trimethoprim-sulfamethoxazole), these remain appropriate for the treatment of typhoid fever. They are inexpensive, widely available and rarely associated with side-effects.

Antibiotic susceptibility pattern of *S. typhi*

The sensitivity and resistant pattern of *S. typhi* for the period of Sep 2016 to June 2017, July 2016 to 1 April 2018 and May 2018 to Feb 2019 are represented in Table 4, 5 and 6 respectively. Antibiotic susceptibility pattern of *S. typhi* during the period Sep 2016 to June 2017 is given in table 4. Out of 676, the most sensitive antibiotics were ceftriaxone & sulbactam 90 (100%), ciprofloxacin 90 (100%) and ofloxacin 90 (100%) whereas the most resistant antibiotics were tetracycline 237 (87.77%) and amoxycillin 225 (83.33%). Antibiotic susceptibility pattern of *S. typhi* during the period of July 2016 to 1 April 2018 is given in table 5. Out of 676, the most sensitive antibiotics were ceftriaxone & sulbactam was 100 (100%), cefuroxime 100 (100%) and ciprofloxacin 100 (100%) whereas the most resistant antibiotics were cotrimoxazole 184 (92.00%) and tetracycline 176 (88.00%). Antibiotic susceptibility pattern of *S. typhi* during the period of May 2018 to Feb 2019 is given in table 6. Out of 676, the most sensitive antibiotics were ceftriaxone & sulbactam was 95 (100%), cefuroxime 92 (96.84%) and ciprofloxacin 93 (97.89%) whereas the most resistant antibiotics were amikacin 102 (49.51%) and cotrimoxazole 189 (91.74%).

Table 4. Antibiotic susceptibility pattern of *S. typhi* during the period Sep 2016 to June 2017

S. No.	Antibiotics	Sensitivity (%) n = 270	Resistant (%) N = 270
1	Ampicillin	60 (22.22)	210 (77.77)
2	Chloramphenicol	90 (33.33)	180 (66.66)
3	Cotrimoxazole	39 (14.44)	221 (85.55)
4	Tetracycline	33 (12.22)	237 (87.77)
5	Ceftriaxone & Salbactum	270 (100)	00 (00)
6	Cefuroxime	264 (97.77)	6 (2.22)
7	Ciprofloxacin	270 (100)	00 (00)
8	Ofloxacin	270(100)	00(00)
9	Nalidixic acid	60 (22.22)	210 (77.77)
10	Amikacin	261 (96.66)	9 (3.33)
11	Gentamycin	42 (15.55)	218 (84.44)
12	Amoxycillin	45 (16.66)	225 (83.33)

Table 5. Antibiotic susceptibility pattern of *S. typhi* during the period 1st July 2017 to 1 April 2018

S. No.	Antibiotics	Sensitivity (%) n = 200	Resistant (%) N = 200
1	Ampicillin	44 (22.0)	156 (78.0)
2	Chloramphenicol	62 (31.00)	138 (69.00)
3	Cotrimoxazole	16 (8.00)	184 (92.00)
4	Tetracycline	24 (12.00)	176 (88.00)
5	Ceftriaxone & Salbactum	200(100)	00(00)
6	Cefuroxime	200(100)	00 (00)
7	Ciprofloxacin	200(100)	00 (00)
8	Ofloxacin	188 (94.00)	12 (6.00)
9	Nalidixic acid	30 (15.0)	170 (85.0)
10	Amikacin	160 (80.00)	40 (20.00)
11	Gentamycin	36 (18.00)	164 (82.00)
12	Amoxycillin	44 (22.00)	156 (78.00)

Table 6. Antibiotic susceptibility pattern of *S. typhi* during the period May 2018 to Feb 2019

S. No.	Antibiotics	Sensitivity (%) n = 206	Resistant (%) N = 206
1	Ampicillin	48 (23.30)	178 (76.69)
2	Chloramphenicol	56 (27.18)	150 (72.81)
3	cotrimoxazole	17 (8.25)	189 (91.74)
4	Tetracycline	23 (11.16)	183 (88.83)
5	Ceftriaxone &Salbactum	206 (100)	00 (00)
6	Cefuroxime	199 (96.60)	7 (3.39)
7	Ciprofloxacin	201 (97.57)	5 (2.48)
8	Ofloxacin	190 (92.23)	16 (7.76)
9	Nalidixic acid	26 (12.62)	180 (87.37)
10	Amikacin	104 (50.48)	102 (49.51)
11	Gentamycin	36 (17.47)	170 (82.52)
12	Amoxycillin	35 (16.99)	171 (83.00)

Changing in sensitivity pattern of *S. typhi*

The sensitivity of *S. typhi* isolates during the period of Sep 2016 to June 2017, July 2016 to 1 April 2018 and May 2018 to Feb 2019 are shown in Table 7. The change in sensitivity pattern during the period of Sep 2016 to June 2017, July 2016 to 1 April 2018 and May 2018 to Feb 2019 of the drug Ceftriaxone and Salbactum, is 100%. The drug Cefuroxime is 97.77%, 100 %, and 96.60%. The drug Ciprofloxacin 100%, 100%, and 97.57%. The drug Ofloxacin is 100%, 94.00%, and 92.23%. The drug Amikacin 96.66%, 80.00%, and 50.48%.

Table 7. Changing in sensitivity pattern of *S. typhi* from Sep 2016 to June 2017, July 2016 to 1 April 2018 and May 2018 to Feb 2019

S. No.	Antibiotics	Sep 2016 to June 2017 n= 90 %	1st July 2017 to 1 April 2018 n= 100%	May 2018 to Feb 2019 n=95 %
1	Ampicillin	60 (22.22)	44 (22.0)	48 (23.30)
2	Chloramphenicol	90 (33.33)	62 (31.00)	56 (27.18)
3	Cotrimoxazole	39 (14.44)	16 (8.00)	17 (8.25)
4	Tetracycline	33 (12.22)	24 (12.00)	23 (11.16)
5	Ceftriaxone & Salbactum	270 (100)	200(100)	206 (100)
6	Cefuroxime	264 (97.77)	200(100)	199 (96.60)
7	Ciprofloxacin	270 (100)	200(100)	201 (97.57)
8	Ofloxacin	270(100)	188 (94.00)	190 (92.23)
9	Nalidixic acid	60 (22.22)	30 (15.0)	26 (12.62)
10	Amikacin	261 (96.66)	160 (80.00)	104 (50.48)
11	Gentamycin	42 (15.55)	36 (18.00)	36 (17.47)
12	Amoxycillin	45 (16.66)	44 (22.00)	35 (16.99)

Changing in the resistant pattern of *S. typhi*

The resistant pattern of *S. typhi* isolates during the period of Sep 2016 to June 2017, July 2016 to 1 April 2018 and May 2018 to Feb 2019 are shown in Table 8. The change in a resistant pattern during the period of Sep 2016 to June 2017, July 2016 to 1 April 2018 and May 2018 to Feb 2019 of the drug ampicillin is 77.77%, 78.0%, and 76.69%. The drug tetracycline is 87.77%, 88.00%, and 88.83%. The drug cotrimoxazole is 85.55%, 92.00%, and 91.74%. The drug amoxycillin is 83.33%, 78.00%, and 83.00%

Table 8. Changing in the resistant pattern of *S. typhi* from Sep 2016 to June 2017, July 2016 to 1 April 2018 and May 2018 to Feb 2019

S. No.	Antibiotics	Sep 2016 to June 2017, n= 90 %	1st July 2017 to 1 April 201 n= 100%	May 2018 to Feb 2019, n=95 %
1	Ampicillin	210 (77.77)	156 (78.0)	178 (76.69)
2	Chloramphenicol	180 (66.66)	138 (69.00)	150 (72.81)
3	Cotrimoxazole	221 (85.55)	184 (92.00)	189 (91.74)
4	Tetracycline	237 (87.77)	176 (88.00)	183 (88.83)
5	Ceftriaxone & Salbactum	00 (00)	00(00)	00 (00)
6	Cefuroxime	6 (2.22)	00 (00)	7 (3.39)
7	Ciprofloxacin	00 (00)	00 (00)	5 (2.48)
8	Ofloxacin	00(00)	12 (6.00)	16 (7.76)
9	Nalidixic acid	210 (77.77)	170 (85.0)	180 (87.37)
10	Amikacin	9 (3.33)	40 (20.00)	102 (49.51)
11	Gentamycin	218 (84.44)	164 (82.00)	170 (82.52)
12	Amoxycillin	225 (83.33)	156 (78.00)	171 (83.00)

Multidrug resistance (MDR) Strains

The isolate showing drug resistance to more than three antibiotics is considered as multidrug resistant. The usual pattern of multidrug resistance of *S. typhi* shows the resistance of the combination of drugs like ampicillin, chloramphenicol and Tetracycline, and also a combination of drugs like ampicillin, chloramphenicol, and cotrimoxazole. The multidrug resistance of *S. typhi* during the period of three years, from Sep 2016 to Feb 2019 is shown in Table 9.

Out of 676 isolates of *S. typhi*, the MDR for two drug combination cotrimoxazole and nalidixic acid is 35 (5.17%). In three-drug combination ampicillin, cotrimoxazole and nalidixic acid is 58 (8.57%). In four-drug combination ampicillin, cotrimoxazole, Nalidixic acid, and gentamycin is 53 (7.84%). Five drug combination cotrimoxazole, tetracycline, nalidixic acid ampicillin, and amoxycillin is 115 (17.01%). In six drug combination cotrimoxazole, tetracycline, nalidixic acid, ampicillin, chloramphenicol, and amoxycillin is 219 (32.39%).

Table 9. Multidrug resistance of *S. typhi* for the period of Sep 2016 to June 2017, July 2016 to 1 April 2018 and May 2018 to Feb 2019.

S. No.	MDR Pattern	Antibiotics	Resistant strains (%) n= 676
1	Two drugs	Cotrimaxazole and Nalidixic acid	35 (5.17)
2	Three drugs	Ampicillin, Cotrimaxazole and Nalidixic acid	58 (8.57)
3	Four drugs	Ampicillin, Cotrimaxazole, Nalidixic acid and Gentamycin	53 (7.84)
2	Five drugs	Cotrimaxazole, Tetracycline, Nalidixic acid, Ampicillin and Amoxycillin	115 (17.01)
3	Six drugs	Cotrimaxazole, Tetracycline, Nalidixic acid, Ampicillin, Chloramphenicol and Amoxycillin	219 (32.39)
4	Seven drugs	Ampicillin, Chloramphenicol, Cotrimaxazole, Tetracycline, Nalidixic acid, Amoxycillin and Amikacin	113 (16.71)
5	Eight drugs	Ampicillin, Chloramphenicol, Cotrimaxazole, Ciprofloxacin, Ofloxacin, Nalidixic acid, Amikacin and Amoxycillin	62 (9.17)
6	Nine drugs	Ampicillin, Chloramphenicol, Cotrimaxazole, Tetracycline, Ciprofloxacin, Ofloxacin, Amikacin, Gentamycin and Amoxycillin	40 (5.91)

Minimum Inhibitory Concentration (MIC)

The MIC range MIC_{50} and MIC_{90} of all twelve drugs ampicillin, chloramphenicol, cotrimoxazole, tetracycline, ceftriaxone, cefuroxime, ciprofloxacin, ofloxacin, nalidixic acid, amikacin, gentamycin, and amoxycillin are represented in table 10. The MIC range of all 12 drugs used against the reprehensive strain of *S.typhi*. This result indicates the lowest and highest MIC values. MIC_{50} and MIC_{90} values were recorded in case of more than 50% and more than 90% of the total strains inhibited by the drugs at a particular concentration. For ampicillin MIC_{50} is 64.0 and MIC_{90} > 256.0. For chloramphenicol MIC_{50} is 16.0 and MIC_{90} > 256.0. For cotrimoxazole MIC_{50} is 32.0 and MIC_{90} 128.0.

Table 10. MIC range, MIC_{50} and MIC_{90} of drugs against *S. typhi*

S. No.	Antibiotics	MIC range	MIC_{50}	MIC_{90}
1	Ampicillin	16.0 to 256.0	64.0	> 256.0
2	Chloramphenicol	8.0 to 256.0	16.0	> 256.0
3	Cotrimaxazole	8.0 to 256.0	32.0	128.0
4	Tetracycline	32.0 to 256.0	64.0	> 256.0
5	Ceftriaxone	0.125 to 1.0	0.25	1.0
6	Cefuroxime	0.125 to 1.0	4.0	8.0
7	Ciprofloxacin	2.0 to 64.0	2.0	8.0
8	Ofloxacin	2.0 to 256.0	8.0	128.0
9	Nalidixic acid	64 to 156.0	64.0	256.0
10	Amikacin	4.0 to 128.0	8.0	128.0
11	Gentamycin	2.0 to 256	4.0	256.0
12	Amoxycillin	8 to 64	8.0	256.0

More than 90% of patients can be managed at home with oral antibiotics, reliable care and close medical follow-up for complications or failure to respond to therapy[34]. However, patients with persistent vomiting, severe , and abdominal distension may require hospitalization and parenteral antibiotic therapy. The efficacy availability and cost are important criteria for the selection of first-line antibiotics to be used in developing countries[35,36]. It should be noted that however, therapeutic strategies for children e.g. the choice of antibiotics, the dosage regimen and the duration of therapy may differ from those for adults.

The *S. typhi*, particularly the multidrug-resistant (MDR) strain is relatively ubiquitous and is the cause of many community endemic and epidemic typhoid fever infections[35,36]. The MDR strain of *S. typhi* is of concern not only because of its resistance to available antibiotics resulting in high death rate but also because of its potential for epidemic outbreaks, which may be difficult to manage. The consequence of such an outbreak will no doubt be devastating especially in developing countries where health facilities are often inadequate.

CONCLUSION

The result of this study has further accentuated the growing concern about the presence and spread of multidrug-resistant *S. typhi* thereby underscoring the need for the rational application of antibiotics and other necessary interventions that will help to control the menace of antibiotic resistance. They were, however, sensitive to ofloxacin even though these two antibiotics are no longer used for the treatment of typhoid fever on account of adverse reactions. The result of this study indicates that chloramphenicol and ofloxacin have proved to be active against these isolates even though they were resistant to the commonly prescribed drugs. This observation showed that an organism that is previously resistant to a particular antibiotic may become susceptible if treatment with the antibiotic is suspended for a long time. What has been reported earlier is interesting because of its obvious implication for public health management. However, more studies are recommended in this regard.

Conflict of interest

The authors declare no conflict of interest

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