

Antimicrobial susceptibility of *Salmonella* in New Zealand, 2017-2019

Hospital and community laboratories are requested to refer all *Salmonella* isolated from human salmonellosis cases to ESR for serotyping and laboratory-based surveillance of this disease.¹ *Salmonella* from other non-human sources, including food, animal and environmental sources, are also referred to ESR for typing.

This report describes the antimicrobial susceptibility of:

- (i) a sample (approximately 20%) of non-typhoidal *Salmonella* from 2019 only,
- (ii) all internationally recognised multidrug-resistant *Salmonella* referred between 2017 and 2019, and
- (iii) all typhoidal *Salmonella* referred between 2017 and 2019.

Until 2016 a sample of non-typhoidal *Salmonella* from New Zealand underwent susceptibility testing every year. From 2017 a sample of non-typhoidal *Salmonella* have been tested every third year, so no data is available for isolates from 2017 and 2018. The internationally multidrug-resistant *Salmonella* tested were *S. enterica* serovar 4,[5],12:i:- and *Salmonella* Typhimurium phage types DT12, DT104, DT120, DT193 and U302.

Between 2017-2019, antimicrobial susceptibility was determined by the European Committee on Antimicrobial Susceptibility (EUCAST) disc diffusion method.² Ampicillin, amoxicillin-clavulanate, cefotaxime, ceftazidime, chloramphenicol, ciprofloxacin, co-trimoxazole and gentamicin results were interpreted using EUCAST breakpoints, current for the year the isolate was received at ESR.^{3,4,5} Ciprofloxacin testing was performed using a 5 µg pefloxacin disc to predict ciprofloxacin susceptibility and which detects low-level ciprofloxacin resistance more reliably than testing with a ciprofloxacin disc, as recommended by EUCAST. Azithromycin, streptomycin, sulphonamide and tetracycline zone diameters were interpreted using Clinical and Laboratory Standards Institute (CLSI) breakpoints, current for the year the isolate was received at ESR,^{6,7,8} as there are no EUCAST breakpoints for these antibiotics. All cefotaxime- or ceftazidime-resistant isolates were further tested for the production of extended-spectrum β-lactamase (ESBL) using the combination disc test.⁸ Any cefotaxime- or ceftazidime-resistant isolates that were found to be ceftazidime-resistant were also tested by PCR for plasmid-mediated AmpC β-lactamase genes.⁹ Multidrug resistance was defined as resistance to ≥3 antibiotic classes.¹⁰ Overseas travel history for human salmonellosis cases was obtained from information reported in the EpiSurv notifiable disease database, supplemented with any additional travel information received when the isolate from the case was referred to ESR.

Non-typhoidal Salmonella

In 2019, the antimicrobial susceptibility of every fifth non-typhoidal *Salmonella* received at ESR was tested. This sample of 400 isolates represented approximately 20% of all non-typhoidal samples referred. It contained 225 isolates from human sources and 175 isolates from non-human sources, including isolates from food, animal, and environmental sources. A total of 85 serovars were represented in the sample, with the most common serovars being *Salmonella* Bovismorbificans (74 isolates), *Salmonella* Brandenburg (34), *S. Typhimurium* phage type 108/170 (22), *S. Typhimurium* phage type 101 (21) and *Salmonella enterica* serovar 4,[5],12:i:- (20).

Antimicrobial resistance in the sample of 400 non-typhoidal *Salmonella* is shown in Table 1, with data for each of the 11 antimicrobials tested as well as multidrug resistance. Resistance remains relatively low, with 91.0% fully susceptible to all 11 antimicrobials (89.3% of human isolates and 93.1% of non-human isolates).

Table 1. Antimicrobial resistance among non-typhoidal *Salmonella*, 2019

| Antimicrobial | Percent resistant | | | P value ¹ |
|---|-------------------------|------------------------------|----------------------------------|----------------------|
| | All isolates n = 400 | Human isolates n = 225 | Non-human isolates n = 175 | |
| Ampicillin | 3.5 | 6.2 | 0.0 | <0.001 |
| Amoxicillin-clavulanate | 1.5 | 2.7 | 0.0 | 0.038 |
| Cefotaxime | 0.3 | 0.4 | 0.0 | 1.000 |
| Ceftazidime | 0.3 | 0.4 | 0.0 | 1.000 |
| Chloramphenicol | 1.0 | 1.8 | 0.0 | 0.135 |
| Ciprofloxacin ² | 3.8 | 6.7 | 0.0 | <0.001 |
| Co-trimoxazole | 1.8 | 2.7 | 0.6 | 0.142 |
| Gentamicin | 0.5 | 0.9 | 0.0 | 0.507 |
| Streptomycin | 2.8 | 4.4 | 0.6 | 0.027 |
| Sulphonamides | 3.5 | 5.8 | 0.6 | 0.050 |
| Tetracycline | 6.5 | 6.2 | 6.9 | 0.840 |
| Multiresistant to ≥ 3 antimicrobials ³ | 3.5 | 6.2 | 0.0 | <0.001 |

1 Significance of any difference in resistance between human and non-human isolates based on chi-square test or Fisher's Exact test as appropriate.

2 Ciprofloxacin susceptibility was inferred from the results of pefloxacin 5 µg disc testing.

3 Seven of the 14 multiresistant isolates belonged to recognised multiresistant clones. All were *S. enterica* serovar 4,[5],12:i:-.

Salmonella from human sources were significantly ($p < 0.05$) more resistant to ampicillin, amoxicillin-clavulanate, ciprofloxacin, streptomycin and sulphonamides than *Salmonella* from non-human sources (Table 1), which was independent of a history of overseas travel. One 2019 isolate was ESBL positive, but no isolates with AmpC were identified. 3.8% of the *Salmonella* tested were categorised as ciprofloxacin-resistant (6.7% from human sources and 0.0% from other sources).

Table 2 shows a comparison of resistance among isolates from salmonellosis cases reported to have recently travelled overseas with isolates from cases for whom no recent overseas travel was reported. *Salmonella* from people who had travelled were not significantly more resistant or multidrug resistant, except ciprofloxacin resistance which was significantly ($p < 0.05$) more common in isolates from cases who had recent overseas travel.

Table 2. Antimicrobial resistance among non-typhoidal *Salmonella* from cases who had travelled overseas compared with non-travellers, 2019

| Antimicrobial | Percent resistant | | P value ¹ |
|---|--|---|----------------------|
| | Cases who had travelled overseas n = 62 | Cases who had not travelled overseas n = 163 | |
| Ampicillin | 6.5 | 6.1 | 1.000 |
| Amoxicillin-clavulanate | 1.6 | 3.1 | 1.000 |
| Cefotaxime | 1.6 | 0.0 | 0.276 |
| Ceftazidime | 1.6 | 0.0 | 0.276 |
| Chloramphenicol | 3.2 | 1.2 | 0.304 |
| Ciprofloxacin ² | 14.5 | 3.7 | 0.007 |
| Co-trimoxazole | 3.2 | 2.5 | 0.668 |
| Gentamicin | 0.0 | 1.2 | 1.000 |
| Streptomycin | 4.8 | 4.3 | 1.000 |
| Sulphonamides | 6.5 | 5.5 | 0.757 |
| Tetracycline | 8.1 | 5.5 | 0.539 |
| Multiresistant to ≥ 3 antimicrobials | 8.1 | 5.5 | 0.539 |

- 1 Significance of any difference in resistance between cases that had or had not travelled overseas based on chi-square test or Fisher's Exact test as appropriate.
- 2 Ciprofloxacin susceptibility was inferred from the results of pefloxacin 5 µg disc testing.

Trends in resistance among non-typhoidal *Salmonella* from human cases since 2011 are shown in Figure 1. Since 2011 there has been a significant decrease ($p < 0.05$) in resistance for ampicillin, streptomycin, sulphonamides, and tetracycline. Since 2011 there has been a significant increase ($p < 0.05$) in resistance for amoxicillin-clavulanate and ciprofloxacin. The increase in amoxicillin-clavulanate resistance may be related to a change from the CLSI to EUCAST standard, which was introduced in 2016. The increase in ciprofloxacin resistance may be partially attributable to the change in test methods from 2016, as the use of the surrogate pefloxacin disc detects more low-level ciprofloxacin resistance than testing with ciprofloxacin itself.

Figure 1. Resistance among non-typhoidal *Salmonella* from human cases, 2011 - 2019

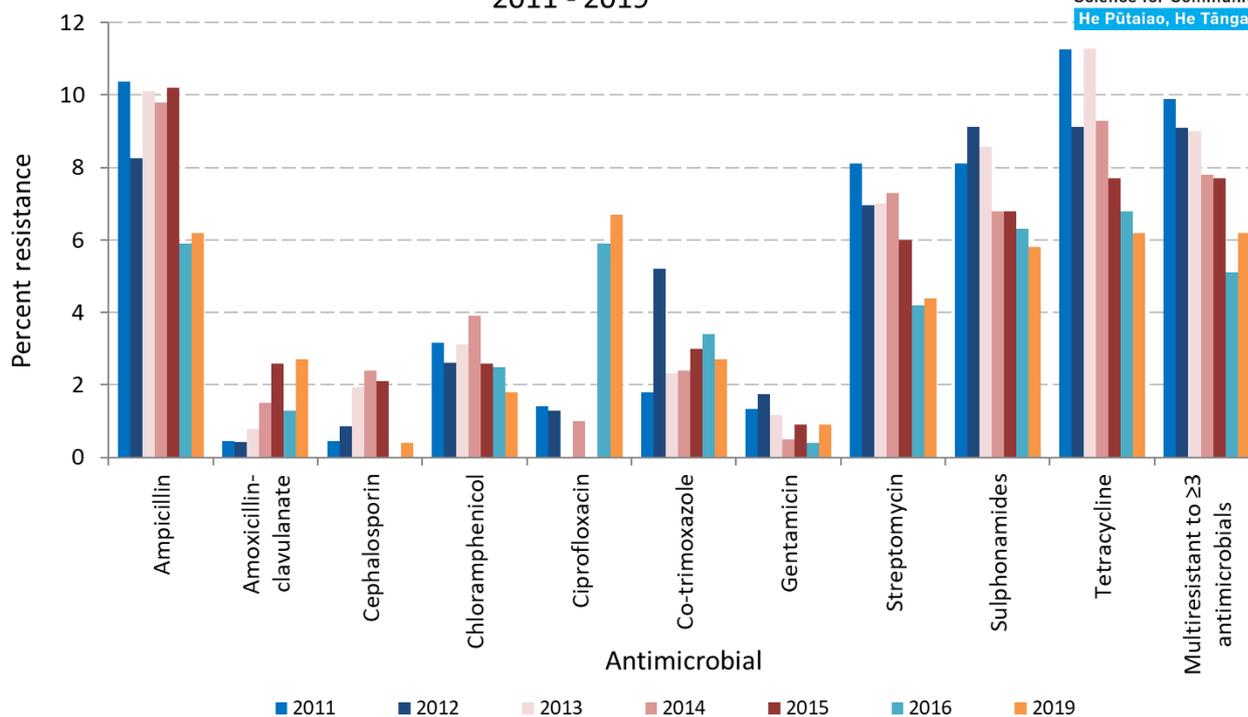


Figure footnotes:

1. National susceptibility data for non-typhoidal *Salmonella* was not collected in 2017 and 2018.
2. The ciprofloxacin resistance rates for the years 2011 to 2015 are based on ciprofloxacin disc susceptibility testing and the current CLSI breakpoints. The rates for 2016 and 2019 are based on testing with the surrogate pefloxacin disc and EUCAST breakpoints. Testing with a pefloxacin disc is more likely to detect low-level ciprofloxacin resistance than ciprofloxacin disc susceptibility testing. This change in test procedures is likely to account for the apparent increase in ciprofloxacin resistance from 2016.
3. The cephalosporin resistance rates for the years 2011 to 2016 are based on cephalothin (1st generation cephalosporin) disc susceptibility testing. The rates for 2019 are based on cefotaxime and ceftazidime (3rd generation cephalosporin) disc susceptibility testing. This change in test procedure may be responsible for the apparent decrease in cephalosporin resistance.

Internationally recognised multidrug-resistant Salmonella

From 2017-2019, several isolates belonging to internationally recognised multidrug-resistant *Salmonella* clones were identified (Table 3). These clones were *S. enterica* serovar 4,[5],12:i:- and the *S. Typhimurium* phage types DT12, DT104, DT120, DT193 and U302. The most common multidrug-resistant *Salmonella* identified in New Zealand between 2017-2019 were *S. enterica* serovar 4,[5],12:i:-. This monophasic variant of *S. Typhimurium* is typically multiresistant to ampicillin, streptomycin, sulphonamides and tetracycline.¹¹ *S. Typhimurium* phage types DT12, DT104, DT193 and U302 are characterised by resistance to ampicillin, chloramphenicol, streptomycin, sulphonamides, and tetracycline.^{12,13,14}

Table 3. *Salmonella* belonging to internationally recognised multidrug-resistant clones, 2017-2019

| Serotype/Phage type | Total | | | Multiresistant to ≥3 antimicrobials | | |
|---|-------|------|------|-------------------------------------|------|------|
| | 2017 | 2018 | 2019 | 2017 | 2018 | 2019 |
| <i>S. enterica</i> serovar 4,[5],12:i:- | 36 | 26 | 57 | 29 | 23 | 41 |
| <i>S. Typhimurium</i> phage type DT12 | 9 | 0 | 8 | 0 | 0 | 2 |
| <i>S. Typhimurium</i> phage type DT104 | 0 | 0 | 0 | 0 | 0 | 0 |
| <i>S. Typhimurium</i> phage type DT120 | 4 | 3 | 3 | 3 | 3 | 1 |
| <i>S. Typhimurium</i> phage type DT193 | 25 | 7 | 12 | 3 | 3 | 7 |
| <i>S. Typhimurium</i> phage type U302 | 1 | 1 | 0 | 0 | 0 | 0 |

Multidrug-resistant *Salmonella* in 2019

S. enterica serovar 4,[5],12:i:- was the third most common serovar in New Zealand in 2019.¹⁵ The antimicrobial susceptibility of 57 isolates was tested, 56 from human salmonellosis cases. Most (71.9%) were multidrug resistant. Twenty-nine multidrug resistant isolates had the resistance pattern typical of this serovar, with 19 isolates also ciprofloxacin resistant. All four ESBL-producers were multidrug resistant and three had the resistance pattern typical of this serovar. Travel history was reported for all 41 multidrug-resistant cases. Of these, 21 had recently travelled overseas, with travel to Europe (1) or Asia (20 total: Cambodia (1), China (2), Hong Kong (1), Indonesia (1), Malaysia (2), Philippines (2), Taiwan (1), Thailand (4), Viet Nam (1), and multiple Asian countries (5)). Twenty-one (21/41, 51%) had reported no overseas travel.

There were 12 isolates of *S. Typhimurium* phage type DT193. Four non-human and three human isolates were fully susceptible (7/12, 58%). Three human isolates were resistant to tetracycline only and two human isolates were resistant to both the folate pathway inhibitors and tetracycline.

Eight isolates of *S. Typhimurium* phage type DT12 were identified. Five non-human isolates and one human isolate were fully susceptible (6/8, 75%). One human isolate was resistant to tetracycline only, and two were multiresistant. The multiresistant isolates were from a patient who had travelled to China and a patient who had no recent travel history.

There were three isolates of *S. Typhimurium* phage type DT120 identified. Two human isolates were fully susceptible. One, from a patient with no reported travel history, was multidrug resistant.

Multidrug-resistant *Salmonella* in 2018

In 2018 there were 26 *S. enterica* serovar 4,[5],12:i:- isolates, with 25 from human salmonellosis cases. Most (88.5%) were multidrug resistant, 18 of which had the resistance pattern typical of this serovar. Nine *S. enterica* serovar 4,[5],12:i:- isolates were ciprofloxacin-resistant, with seven of these having the resistance pattern typical of this serovar. Travel history was reported for 22 of the 23 multidrug-resistant cases. Of these 18 had recently travelled overseas, with travel to Europe (1) or Asia (17 total: China (1), Hong Kong (2), Indonesia (3), Philippines (1), Thailand (5), Viet Nam (3) and multiple Asian countries (2)). Four had no recent travel history.

There were seven isolates of *S. Typhimurium* phage type DT193. Four fully susceptible isolates were from animal sources, one fully susceptible isolate was from a human case, one was resistant to ciprofloxacin and tetracycline and one, from a case who had travelled to Cambodia, was multiresistant.

There were three isolates of *S. Typhimurium* phage type DT120. One was fully susceptible, one was resistant to gentamicin and ciprofloxacin, and the third isolate, from a patient who had travelled to Indonesia, was multidrug resistant.

There was one isolate of *S. Typhimurium* phage type U302, which was multiresistant and from a case who had recently travelled to the Middle East and Europe.

Multidrug-resistant *Salmonella* in 2017

In 2017 there were 36 *S. enterica* serovar 4,[5],12:i:- isolates, and all were from human salmonellosis cases. Of these 29 (80.6 %) were multidrug resistant, 24 of which had the resistance pattern typical of this serovar (i.e., resistant to at least ampicillin, streptomycin, sulphonamides and tetracycline). The resistance pattern of eight of the multidrug-resistant isolates also included pefloxacin resistance. Travel history was reported for 25 of the 29 multidrug-resistant cases, 19 of whom had recently travelled overseas: Europe (1) or Asia (18 total: Cambodia (1), China (1), Hong Kong (1), Indonesia (1), Philippines (3), Taiwan (1), Thailand (4), Viet Nam (2), and multiple or unknown Asian countries (4)).

Twenty-five isolates of *S. Typhimurium* phage type DT193 were identified. Fifteen non-human isolates and six human isolates were fully susceptible. One human isolate, from a patient with no travel history, was resistant to the folate pathway inhibitors and tetracycline. Three human isolates were multidrug resistant, one from a patient that had visited Thailand and the other with unknown travel history.

There were nine *S. Typhimurium* phage type DT12 identified. All isolates were fully susceptible, with six non-human isolate and one human isolate.

There were four isolates of *S. Typhimurium* phage type DT120. Three human isolates were multidrug resistant and one non-human isolate was fully susceptible. Two of the human isolates were from patients who had recent travel to Viet Nam, and the third isolate was from a patient with no recent overseas travel.

One isolate of *S. Typhimurium* phage type U302 was identified, which was fully susceptible.

Typhoidal Salmonella

Internationally the effectiveness of antimicrobial treatment for typhoidal *Salmonella* is threatened by the emergence and expansion of antibiotic resistant strains. Multidrug-resistant isolates are prevalent in parts of Asia and Africa, which continue to be areas where antimicrobial resistance develops and subsequently spreads internationally.¹⁶ In the 1980's resistance to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole were detected, leading to a shift to fluoroquinolones as the primary treatment option. Fluoroquinolone resistance is now common internationally, leaving third generation cephalosporins, azithromycin and carbapenems as possible treatment options for typhoidal *Salmonella*. While isolates resistant to third-generation cephalosporins or azithromycin have also been reported, reports of carbapenem resistance in *Salmonella* remain rare.¹⁶ The propensity for resistant strains to develop, spread and expand, means that the ongoing availability of antimicrobial treatment for typhoidal *Salmonella* cannot be guaranteed.

Resistance among the typhoidal *Salmonella* isolates in New Zealand between 2017 and 2019 is shown in Table 4. Ciprofloxacin resistance increased in *Salmonella* Typhi isolates from 36.8% in 2017 to 48.1% in 2019. Most ciprofloxacin-resistant isolates were isolated from patients who had recently travelled to the Indian subcontinent. In 2019 travel history was known for 24 of the 25 patients with ciprofloxacin-resistant isolates. They had travelled to the Indian subcontinent (20), other parts of Asia (2) and the Pacific region (2). In 2018 all patients with ciprofloxacin-resistant isolates had travelled to the Indian subcontinent. In 2017 travel history was known for 18 of the 21 patients with ciprofloxacin-resistant isolates. They had travelled to the Indian subcontinent (16), South East Asia (1) and Europe (1). Due to the emergence of ciprofloxacin non-susceptibility among *S. Typhi* in the Indian subcontinent and Southeast Asia, azithromycin is now the recommended treatment for typhoid fever. No azithromycin resistance was detected among the *S. Typhi* from 2017-2019.

Ten *S. Typhi* isolates from 2017-2019 were multidrug resistant. Eight isolates were from cases that reported travel to the Indian subcontinent, one from a case that reported travel to Cambodia, and one from a case that reported travel to both Taiwan and Australia. Nine multidrug resistant isolates had similar patterns of resistance (to ampicillin, chloramphenicol, co-trimoxazole, streptomycin and sulphonamides) and eight of these isolates were also resistant to ciprofloxacin.

None of the *S. Paratyphi* A or *S. Paratyphi* B from 2017-2019 were multidrug resistant, however, a high proportion of *S. Paratyphi* A were ciprofloxacin resistant (Table 4).

Most cases of non-typhoidal *Salmonella* do not require antimicrobial treatment. However, given the current international rates of resistance, third generation cephalosporins remain an appropriate empiric choice treatment for invasive infections and typhoid fever, whilst ciprofloxacin should be avoided until susceptibility testing results are known.

Table 4. Antimicrobial resistance among *S. Typhi* and *S. Paratyphi*, 2017-2019

| Antimicrobial | Percent (number) resistant | | | | | | | | |
|--|----------------------------|----------------|----------------------|-----------------------|----------------|----------------|------------------------------------|---------------|---------------|
| | <i>S. Typhi</i> | | | <i>S. Paratyphi A</i> | | | <i>S. Paratyphi B</i> ¹ | | |
| | 2017 n = 57 | 2018 n = 52 | 2019 n = 52 | 2017 n = 22 | 2018 n = 18 | 2019 n = 12 | 2017 n = 1 | 2018 n = 1 | 2019 n = 5 |
| Ampicillin | 1.8 (1) | 3.9 (2) | 11.5 (6) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0 (0) | 0 (0) | 0.0 (0) |
| Amoxicillin-clavulanate | 1.8 (1) | 3.9 (2) | 3.9 (2) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Azithromycin | 0.0 (0) | 0.0 (0) | 0.0 (0) | _2 | _2 | _2 | _2 | _2 | _2 |
| Cefotaxime | 0.0 (0) | 0.0 (0) | 1.9 (1) ³ | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Ceftazidime | 0.0 (0) | 0.0 (0) | 1.9 (1) ³ | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Chloramphenicol | 1.8 (1) | 3.9 (2) | 11.5 (6) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Ciprofloxacin ⁴ | 36.8 (21) | 46.2 (24) | 48.1 (25) | 40.9 (9) | 83.3 (15) | 100.0 (12) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Co-trimoxazole | 1.8 (1) | 5.8 (3) | 11.5 (6) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Gentamicin | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Streptomycin | 5.3 (3) | 11.5 (6) | 15.4 (8) | 0.0 (0) | 5.6 (1) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Sulphonamides | 1.8 (1) | 5.8 (3) | 11.5 (6) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Tetracycline | 0.0 (0) | 1.9 (1) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) |
| Multiresistant to ≥3 antimicrobials | 1.8 (1) | 5.8 (3) | 11.5 (6) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) | 0.0 (0) |

1 *S. Paratyphi B* var *Java* isolates are not included with the *S. Paratyphi* isolates, as they are no longer considered to belong to the typhoidal *Salmonella*.

2 There are no CLSI azithromycin interpretive standards for *S. Paratyphi*.

3 One isolate was resistant to both cefotaxime and ceftazidime. The isolate was ESBL positive.

4 Ciprofloxacin susceptibility was inferred from the results of pefloxacin 5 µg disc testing

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