Antimicrobial susceptibilities and ESBL production rates of *Salmonella* and *Shigella* strains in Turkey

Acute bacterial diarrhea is an important cause of morbidity and public health concern in Turkey, especially in children [1]. To determine the antibiotic susceptibility patterns and extended-spectrum β-lactamase (ESBL) activity, we evaluated consecutive strains of *Salmonella* and *Shigella* spp. isolated from community-acquired infections from three different centers in Ankara, Turkey.

In vitro antibiotic susceptibilities of *Shigella* (117) and *Salmonella* (84) strains were determined by disc diffusion method, according to the instructions of the NCCLS [2]. Production of ESBL was determined by double disc synergy and inhibitor-potentiated disc diffusion tests. The distribution of strains were 81 (41%) *Sh. sonnei*, 32 (16%) *Sh. flexneri*, three (1%) *Sh. dysenteriae*, one (1%) *Sh. boydii*, 45 (22%) *Salmonella* group B (26 *Sal. typhimurium*), 31 (15%) *Salmonella* group D (21 *Sal. typhi*), seven (3%) group C and one (1%) *Salmonella* group A (Tables 1 and 2).

A multi-resistance pattern was seen most frequently in *Sh. flexneri* and *Sal. typhimurium* strains. All *Shigella* and *Salmonella* strains were susceptible to ciprofloxacin and imipenem. We detected ESBL activity in four *Sal. typhimurium* strains and, to the best of our knowledge, this is the first report of ESBL-producing *Salmonella* strains from community-acquired infections in our country.

First-line antibiotics such as ampicillin, trimethoprim-sulfamethoxazole (TMP-SMX) and chloramphenicol have alarming resistance rates, and occur world-wide [2–6]. ESBL production was first identified in 1984, fron nosocomial *Salmonella* strains [7]. This enzyme was thought to spread among other *Enterobactericeae* species, resulting in widespread ESBL production [8,9]. Also, the PER-1 enzyme has been previously isolated among hospital-acquired *Sal. typhimurium* strains in Turkey, creating further awareness of the clinical and environmental implications [5].

In this study, 11 of 32 (35.4%) *Sh. flexneri*, three of 81 (3.7%) *Sh. sonnei* and one *Sh. dysanteriae* isolates had multi-resistant patterns, but no ESBL activity was determined in any. Five of 84 *Salmonella* isolates (6%) were also found to be multi-resistant, all *Sal. typhimurium* including four with ESBL activity. ESBL-producing strains showed *in vitro* resistance to ampicillin, ceftriaxone, ceftazidim, cefotaxime and aztreonam. No fluoroquinolone or imipenem resistance was found in any strains, including ESBL-producing strains.

Increasing resistance to commonly used antimicrobial agents in *Shigella* and *Salmonella* species has become a major public health concern world-wide [10]. Among *Shigella* strains, plasmid-borne resistance against first-line antibiotics such as ampicillin, choramphenicol and tetracycline have been reported globally [11]. In *Sh. flexneri*, high antibiotic resistance rates, multi-resistant patterns and plasmid-associated β-lactamase production are more frequent [3,11,12]. In this study, *Sh. sonnei* was the most frequently isolated species, but higher antibiotic resistance rates and multi-resistant patterns were found in *Sh. flexneri* strains; these findings are in close accordance with other studies carried out in our country [1,4,11]. Even higher resistance rates were found in *Sal. typhimurium* strains. The highest rate of ampicillin resistance was detected in non-typhi *Salmonella* group D, although evaluation of these results is rather difficult due to the very small number of strains used in our study.

Chloramphenicol has been used as a first antimicrobial agent in *Sal. typhi* infection for many years, and the first epidemic with chloramphenicol resistance was reported in 1972, in Mexico [6,13]. This resistance encoded via plasmids and frequently occurred together with streptomycin, sulfonamides and tetracycline resistance [11]. Since 1989, infections with multi-resistant strains have been reported in many countries, especially Pakistan and India [6].

In a Turkish study published in 1994, no *Sal. typhi* strains were reported resistant to ampicillin, TMP/SMX and chlor-

Table 1 The distribution of *Shigella* strains and their antibiotic susceptibility results

	Sh. sonnei **(*n* = 81)** **Number susceptible (%)**	***Sh. flexneri*** **(*n* = 32)** **Number susceptible (%)**	***Sh. dysenteriae*** **(*n* = 3)**	***Sh. boydi*** **(*n* = 1)**
Ampicillin	71 (88)	5 (16)	1	1
TMP/SMX	46 (57)	17 (53)	2	1
Chloramphenicol	76 (93)	11 (34)	2	1
Ciprofloxacin	81 (100)	32 (100)	3	1
Ceftriaxone	81 (100)	32 (100)	3	1
Imipenem	81 (100)	32 (100)	3	1

Table 2 The antimicrobial susceptibilities and ESBL production of *Salmonella* isolates

	Sal. typhimurium **(*n* = 26)** **Number (%)**	**Group B[a]** **(*n* = 19)** **Number (%)**	**Group C** **(*n* = 7)** **Number**	**Group D[b]** **(*n* = 10)** **Number (%)**	***Sal. typhi*** **(*n* = 21)** **Number (%)**
Ampicillin	16(62)	16(84)	7	2(20)	19(87)
TMP/SMX	23(88)	19(100)	7	10(100)	20(93)
Chloamphenicol	16(62)	16(84)	6	10(100)	20(93)
Ciprofloxacin	26(100)	19(100)	7	10(100)	21(100)
Ceftriaxone	22(85)	19(100)	7	10(100)	21(100)
Imipenem	26(100)	19(100)	7	10(100)	21(100)
ESBL	4(15)	0(0)	8	0(0)	0(0)

[a]Except *Sal. typhimurium* strains; [b]Except *Sal. typhi* strains.

amphenicol. However, in a recent study carried out by the same investigators, 16% of *Sal. typhi* strains were found to be multi-resistant to all three antibiotics [4,14]. In our study, ampicillin, chloramphenicol and TMP/SMX resistance of *Sal. typhi* strains was detected in 13%, 7% and 7% of strains, respectively, and we consider that there is a growing resistance problem in *Salmonella* strains in Turkey. Fluoroquinolone resistance was not found in any of our *Salmonella* strains, although quinolone resistance has been reported in developing countries [6]. Our study raises concerns about ESBL in community-originated *Sal. typhimurium* strains, one of the most frequently isolated serotypes among human salmonellosis.

In conclusion, ampicillin, choramphenicol and TMP/SMX are no longer empiric treatment alternatives for acute diarrheal infections acquired in Turkey and it is believed that early determination and closer epidemiologic observation would have a significant impact on the prevention of expansion of new resistance forms.

D. Kiliç[*],
N. Tulek,
G. Tuncer,
L. Doganci and
A. Willke
[*]Kirikkale University Medical School,
Infectious Diseases and Clinical
Bacteriology Department, DE Gol Cad 39/6,
Besevler/Ankara,
Turkey
Tel: +90 312 2157924
E-mail: kilic@ato.org.tr

REFERENCES

1. Doğanci L, Baylan O, Albay A, Gün H. Bacterial pathogens in childhood diarrhea in Turkey. *Ped Infect Dis J* 1997; 16: 1097–9.
2. NCCLS. *Performance Standards for Antimicrobial Disk Susceptibility.* 1998; 18: M2–A6.
3. Willke A, Altay G, Tulunay FC, Ertugrul N. Comparative *in vitro* activity of four new quinolones and eight other antibiotics against *V. cholerae and Shigella* spp. *Selected Proceedings from the International Congress for Infectious Diseases.* Rio de Janeiro, Brazil, April 17–21, 1998 (Poster Presentation).
4. Wilke A, Arman D, Çokca F *et al*. Resistance of *Salmonella and Shigella* in Turkey. *Clin Microbiol Infect Dis* 1999; 5: 588–90.
5. Vahaboğlu H, Dodanl| Ş, Eroğlu C *et al*. Characterization of multiple-antibiotic-resistant Salmonella typhimurium strains: molecular epidemiology of PER-1-producing isolates and evidence for nosocomial plasmid exchange by a clone. *J Clin Microbiol* 1996; 34: 2942–6.
6. Rowe B, Ward LR, Threlfall EJ. Multidrug-resistant Salmonella typhi: a worldwide epidemic. *Clin Infect Dis* 1997; 24 (Suppl. 1): S106–9.
7. Morosini MI, Canton R, Martinez-Beltran J *et al*. New extended-spectrum TEM-type β-lactamase from Salmonella enterica subsp enterica isolated in a nosocomial outbreak. *Antimicrob Agents Chemother* 1995; 39: 458–61.
8. Gaillot O, Clément C, Simonet M, Philippon A. Novel transferable β-lactam resistance with cephalosporinase characteristics in *Salmonella enteritidis*. *J Antimicrob Chemother* 1997; 39: 85–7.
9. Bradford PA, Yang Y, Sahm D, Grope I, Gardovska D, Storch G. CTX-M-5, a novel cefotaxime-hydrolysing β-lactamase from outbreak of *Salmonella typhimurium* in Latvia. *Antimicrob Agents Chemother* 1998; 42: 1980–4.
10. Mandell GL, Bennett JE, Dolin R, Dupont HL. *Shigella species (bacillary dysentery). Principles and practice of infectious diseases*. Philadelphia: Churchill Livingstone, 2000; 2363–8.
11. Ceyhan M, Akan Ö, Kanra G, Ecevit Z, Seçmeer G, Berkman E. Changing patterns of the prevalence of different *Shigella* species and their antibiotic susceptibilities in Ankara. *Turkey J Diarrhoeal Dis Res* 1996; 14: 187–9.
12. Bauernfeind A, Casellas JM, Goldberg M *et al*. A new plasmidic cefotaximase from patients infected with *Salmonella typhimurium*. *Infection* 1992; 20: 48–53.
13. Centers for Disease Control. Typhoid fever – Mexico. *Morb Mortal Wkl Rep* 1972; 21: 177–8.
14. Arman D, Willke A, Tural D. *In vitro* activity of eight antibiotics against *Salmonella and Shigella* species. *Eur J Epidemiol* 1994; 10: 345–7.