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Comparative in vitro activity of tigecycline and other antimicrobial agents against *Shigella* species from Kuwait and the United Arab of Emirates

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Summary *Shigella* species isolated from stool samples of symptomatic patients of all age groups at the Mubarak Al Kabir Hospital and Infectious Diseases Hospital, Kuwait and Tawam Hospital, UAE during a 2-year period were investigated for their susceptibility to tigecycline and several other antibiotics by determining the minimum inhibitory concentrations (MICs) using the E test method. A total of 100 and 42 strains were collected from UAE and Kuwait, respectively. The extent of drug resistance in the *Shigella* spp. isolates from these two countries was analyzed by criteria recommended by the Clinical and Laboratory Standards Institute (CLSI). Amikacin, cefotaxime, cefuroxime, ciprofloxacin, imipenem, meropenem, piperacillin-tazobactam and tigecycline had excellent activities against all isolates from UAE and Kuwait with MIC_{90s} of 12, 0.094, 4, 0.012, 0.25, 0.032, 3 and 0.25 μg/ml and 4, 1, 4, 0.125, 0.38, 0.19, 3 and 0.25 μg/ml, respectively. Half of all isolates from both countries were resistant to ampicillin. None of the isolates in Kuwait was resistant to amoxicillin—clavulanic acid compared with 22% in UAE. Resistance to chloramphenicol was recorded in 50 and 36% of the isolates in Kuwait and UAE, respectively. The percentages of non-susceptibility to trimethoprim-sulfamethoxazole and tetracycline were very high in Kuwait and UAE (76% vs. 92% and 76% vs. 98%, respectively). Notably, one isolate, *S. flexneri*, from UAE had reduced susceptibility to ciprofloxacin (MIC, 0.25 μg/ml). Four (2.8%) of the isolates were ESBL producers by the E test ESBL method but could not be confirmed by PCR using primers for bla_{CTX-M}, bla_{SHV} and bla_{TEM}. In conclusion, *Shigella* spp. isolated from symptomatic patients in Kuwait and the UAE demonstrated high

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rates of resistance to the first-line antibiotics but very susceptible to the carbapenems, cephalosporins, fluoroquinolones and tigecycline. Tigecycline holds promise as a potential drug of choice for the therapy of severe shigellosis.

Introduction

Shigella species is an important public health problem throughout the world both in developing and developed countries. Shigellosis, the infection caused by *Shigella* spp., is regarded as a major cause of diarrhoea with high morbidity and mortality especially in children. *Shigella* infections can lead to mild self-limiting diarrhoea to severe dysentery. Complications are often seen in children, elderly, malnourished and immunosuppressed patients. Although conservative oral rehydration therapy may be adequate treatment for milder cases of infections caused by *Shigella* spp. other than *S. dysenteriae* type 1, antimicrobial chemotherapy is often required for treating shigellosis in general, and cases of *S. dysenteriae* type 1 in particular. However, since *S. dysenteriae* type 1 produces Shiga toxin, the use of antibiotics may become a dilemma. Effective and appropriate antimicrobial chemotherapy may reduce the duration of fecal excretion of the micro-organisms, reduce the duration of the illness and reduce the spread of the infection [1]. Ampicillin was the drug of choice until the mid-1980s when it was replaced by trimethoprim-sulfamethoxazole and nalidixic acid [2]. Antimicrobial resistance of *Shigella* spp. is increasing because of antimicrobial agents that are used widely in clinical medicine especially in developing countries [3,4]. Multi-drug resistant *Shigella* spp. have been reported including resistance to fluoroquinolones and the third-generation cephalosporins such as cefotaxime and ceftriaxone, in which antimicrobial therapy has become very limited [4,5]. Third-generation cephalosporins or ciprofloxacin are the main drugs used for treating invasive *Shigella* infection in Kuwait and UAE.

The aim of the present study is to evaluate the antimicrobial susceptibility of clinical isolates of *Shigella* spp. in Kuwait and UAE and determine the extent of resistance problem in the two countries.

Materials and methods

Bacterial strains

In Kuwait, *Shigella* spp. isolated from the stool samples of patients with acute diarrhoea were collected between April 2003 and March 2005 from Mubarak Al Kabir Hospital, Jabriya and Infectious Disease Hospital while in the UAE, *Shigella* spp. isolated from patients with similar symptoms attending Tawam Hospital, Al Ain were collected between January 2003 and December 2004. Only the *Shigella* spp. isolated from stool cultures were evaluated. There were no replicate strains in this study. The isolates were then stored at $-80\,^{\circ}C$ until used. Isolates from Kuwait were identified at the Clinical Microbiology Laboratory of Mubarak Al Kabir Hospital, Kuwait by standard methods using automated Vitek II system (BioMerieux, Marcy-l'Eoile, France) and those from UAE by API 20E (BioMerieux, France) in the Microbiology Laboratory of Tawam Hospital, Al Ain, UAE. The strains were identified to species levels using serological latex agglutination (Denka Seiken UK Ltd., Derbyshire, UK).

Antimicrobial susceptibility testing

The susceptibility testing was performed at the Anaerobe/Hospital Infection Laboratory, Department of Microbiology, Faculty of Medicine, Kuwait. All isolates were tested for their susceptibility to the following antibiotics: amikacin, ampicillin, amoxicillin—clavulanic acid, cefotaxime, ceftriaxone, cefuroxime, chloramphenicol, ciprofloxacin, gentamicin, imipenem, meropenem, piperacillin-tazobactam, tetracycline, tigecycline, and trimethoprim-sulfamethoxazole by determining the minimum inhibitory concentrations (MICs) using E test (AB Biodisk, Solna, Sweden). Breakpoints for antibiotics used to interpret the results of the *Shigella* spp. were according to the Clinical and Laboratory Standard Institute [6] except for tigecycline where the US Food and Drug Administration (FDA) breakpoint was applied (Tigacil package insert; Wyeth Pharmaceuticals Inc., Philadelphia, PA, USA). The antibiotic breakpoints used were as follows: amikacin $\leq 16\,\mu g/ml$, ampicillin $\leq 8\,\mu g/ml$, amoxicillin—clavulanic acid $\leq 8/4\,\mu g/ml$, cefotaxime $\leq 8\,\mu g/ml$, ceftriaxone $\leq 8\,\mu g/ml$, cefuroxime $\leq 8\,\mu g/ml$, chloramphenicol $\leq 8\,\mu g/ml$, ciprofloxacin $\leq 1\,\mu g/ml$, gentamicin $\leq 4\,\mu g/ml$, imipenem $\leq 4\,\mu g/ml$, meropenem $\leq 4\,\mu g/ml$, piperacillin-tazobactam $\leq 16/4\,\mu g/ml$, tetracycline $\leq 4\,\mu g/ml$, tigecycline $\leq 2\,\mu g/ml$

and trimethoprim-sulfamethoxazole ≤2 μg/ml. *Escherichia coli* ATCC 25922 was included in each run as quality control.

Detection of extended-spectrum β-lactamases (ESBL) production

Isolates inhibited by ≥1 μg/ml of cefotaxime (CTX) and ceftriaxone were investigated for ESBL production. For this phenotypic characterization, E test ESBL method using both ceftazidime (CAZ)/CAZ combined with clavulanic acid (CA) and CTX/CTX combined with CA strips (AB Biodisk, Solna, Sweden) was carried out according to the manufacturer's instructions. In-house ESBL-producing and ESBL-negative *E. coli* were included in the test runs as positive and negative controls, respectively.

Detection of resistance genes

Genotypic confirmation of ESBL-positive isolates was assessed by the PCR technique. Briefly, DNA extraction was carried out with the Nucleospin tissue Kit (Macherey-Nagel). PCR amplification was then carried out to detect the presence of bla_{CTX-M}, bla_{SHV} and bla_{TEM} using the following primers: for bla_{CTX-M}, MA-1 5′-SCS ATG TGC AGY ACC AGT AA-3′ and MA-2 5′-CCG CRA TAT GRT TGG TGG TG-3′, for bla_{SHV}, OS-5 5′-TTA TCT CCC TGT TAG CCA CC-3′ and OS-6 5′-GAT TTG CTG ATT TCG CTC GG-3′ and for bla_{TEM}, C 5′-TCG GGG AAA TGT GCG CG-3′ and D 5′-TGC TTA ATC AGT GAG GCA CC-3′ [7]. PCR was carried out as previously described [8].

Results

Bacterial isolates

A total of 142 *Shigella* isolates from fecal samples of patients with gastroenteritis, comprising 100 from UAE and 42 from Kuwait were studied. They were made up of 58 (58%) *S. flexneri*, 36 (36%) *S. sonnei*, 2 (2%) *S. dysenteriae*, 2 (2%) *S. boydii* and 2 (2%) *Shigella* spp. from UAE and those isolated from Kuwait were 32 (76.2%) *S. flexneri* and 10 (23.8%) *S. sonnei*. The overall predominant species was *S. flexneri* representing 90 (63.3%) of the total isolates, followed by *S. sonnei* 46 (32.4%) in both countries. Only 1.4% of the total isolates were *S. dysenteriae*.

Antimicrobial susceptibility

The susceptibility of *Shigella* spp. isolated from Kuwait and UAE is shown in Tables 1a and 1b. They are expressed as the concentration of antibiotics that inhibited 50% (MIC_{50}) and 90% (MIC_{90}) of the isolates. Of the 142 isolates, 71 (50%) from both Kuwait and UAE were resistant to ampicillin with MIC_{90} of >256 μg/ml. The *Shigella* spp. isolated from UAE were more resistant to tetracycline and trimethoprim-sulfamethoxazole than those from Kuwait. Among the UAE isolates, 98 (98%) and 92 (92%) were resistant to tetracycline and trimethoprim-sulfamethoxazole, respectively, compared to 32 (76.2%) and 32 (76.2%), respectively from Kuwait. The MIC_{90}s of tetracycline (128 μg/ml) and trimethoprim-sulfamethoxazole (>32 μg/ml) against UAE isolates were very high.

Table 1a The minimum inhibitory concentrations (MICs) of antimicrobials against clinical isolates of *Shigella* spp. from Kuwait.

Antibiotic (breakpoint, μg/ml)	Range	MIC_{50}	MIC_{90}	No (%) resistant
Amikacin (16)	1.5—4	1.5	4	0 (0)
Ampicillin (8)	0.5—>256	3	>256	21 (50)
Amoxicillin—CA (8/4)	1.5—6	3	6	0 (0)
Cefotaxime (8)	0.047—1	0.19	1	0 (0)
Ceftriaxone (8)	0.047—1	0.19	0.75	0 (0)
Cefuroxime (8)	0.75—4	1	4	0 (0)
Chloramphenicol (8)	1—>256	2	>256	21 (50)
Ciprofloxacin (1)	0.004—0.125	0.006	0.125	0 (0)
Gentamicin (4)	2—6	2	6	11 (26.2)
Imipenem (4)	0.023—0.38	0.125	0.38	0 (0)
Meropenem (4)	0.016—0.19	0.032	0.19	0 (0)
Piperacillin-taz (16/4)	0.38—3	1.5	3	0 (0)
Tetracycline (4)	1.5—192	96	128	32 (76.2)
Tigecycline (2	0.064—0.25	0.064	0.25	0 (0)
TRM-SXT (4)	0.19—>32	>32	>32	32 (76.2)

CA: clavulanic acid; Piperacillin-taz: piperacillin-tazobactam; TRM-SXT: trimethoprim-sulfamethoxazole.

Table 1b The MICs of antimicrobials against clinical isolates of *Shigella* spp. in UAE

Antibiotic (breakpoint, μg/ml)	Range	MIC_{50}	MIC_{90}	No (%) resistant
Amikacin (16)	2—16	4	12	0 (0)
Ampicillin (8)	1.5—>256	12	>256	50 (50)
Amoxicillin—CA (8/4)	1.5—16	2	12	22 (22)
Cefotaxime (8)	<0.016—2	0.032	0.094	0 (0)
Ceftriaxone (8)	0.032—1	0.19	0.094	0 (0)
Cefuroxime (8)	0.032—4	2	4	0 (0)
Chloramphenicol (8)	0.5—>256	4	>256	36 (36)
Ciprofloxacin (1)	0.003—0.25	0.008	0.012	0 (0)
Gentamicin (4)	1—6	3	4	6 (6)
Imipenem (4)	0.125—0.5	0.19	0.25	0 (0)
Meropenem (4)	0.016—0.047	0.023	0.032	0 (0)
Piperacillin-taz (16/4)	0.25—16	0.75	3	0 (0)
Tetracycline (4)	3—>256	96	128	98 (98)
Tigecycline (2)	0.047—0.5	0.064	0.25	0 (0)
TRM-SXT (4)	0.047—>32	>32	>32	92 (92)

CA: clavulanic acid; Piperacillin-taz: piperacillin-tazobactam; TRM-SXT: trimethoprim-sulfamethoxazole.

However, Kuwaiti isolates were more resistant to chloramphenicol and gentamicin than the UAE isolates. Among the Kuwaiti isolates, 21 (50%) and 11 (26.2%) were resistant to chloramphenicol and gentamicin, respectively compared with 36 (36%) and 6 (6%) of the UAE isolates. The MIC_{90} of chloramphenicol were each >256 μg/ml for both countries. None of the Kuwaiti isolates were resistant to amoxicillin—clavulanic acid, in contrast to 22 (22%) resistant isolates from the UAE.

However, all the isolates from both countries were fully susceptible to amikacin, cefotaxime, ceftriaxone, cefuroxime, imipenem, meropenem, piperacillin-tazobactam and tigecycline. The average MIC_{90}s for the Kuwaiti isolates were as follows: amikacin 4 μg/ml, cefotaxime 1 μg/ml, ceftriaxone 0.75 μg/ml, cefuroxime 4 μg/ml, ciprofloxacin 0.125 μg/ml, imipenem 0.38 μg/ml, meropenem 0.19 μg/ml, piperacillin-tazobactam 3 μg/ml and tigecycline 0.25 μg/ml; while for the UAE isolates they were 12 μg/ml, 0.094 μg/ml, 0.094 μg/ml, 4 μg/ml, 0.012 μg/ml, 0.25 μg/ml, 0.32 μg/ml, 3 μg/ml and 0.25 μg/ml, respectively.

All the isolates from Kuwait and the UAE were susceptible to ciprofloxacin with MIC range of 0.003—0.25 μg/ml, although only one isolate, *S. flexneri* serotype 3, from the UAE demonstrated reduced susceptibility with MIC 0.25 μg/ml.

Prevalence of multi-drug resistance

Of the 100 isolates from the UAE, 80 (80%) were resistant to two or more drugs, especially the first-line antibiotics and 39 (48.8%) were resistant to three or more antibiotics, i.e. multi-drug resistant isolates (MDR). The distribution of these multi-resistant isolates is shown in Table 2. According to the resistance pattern profiles, they were assigned into 10 groups of various combinations. The most common pattern among isolates from UAE was resistance to tetracycline and trimethoprim-sulfamethoxazole accounting for 47.5% of the resistant isolates, followed by resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole and tetracycline, i.e. 16.3%. A total of 75 (93.8%) isolates were

Table 2 Antibiotic resistance profile of the multi-resistant clinical isolates of *Shigella* spp. in UAE and Kuwait.

Antibiotic resistance pattern	No (%) of isolates	
	UAE ($n = 80$)	Kuwait ($n = 32$)
Amp, TRM-SXT	3 (3.8)	0 (0)
TRM-SXT, Tet	38 (47.5)	11 (34.4)
Amp, C, Tet	3 (3.8)	0 (0)
Amp,TRM-SXT, Tet	8 (10)	0 (0)
Amp, C, TRM-SXT, Tet	13 (16.7)	11 (34.4)
Amp, C, TRM-SXT, Amc, Tet	8 (10)	0 (0)
Amp, TRM-SXT, Amc, Tet	3 (3.8)	0 (0)
Amp, C, Amc, Tet	2 (2.5)	0 (0)
Amp, C, Gn, TRM-SXT, Amc, Tet	2 (2.5)	0 (0)
Amp, C, Gn, TRM-SXT, Tet	0 (0)	10 (31.3)

Amp: ampicillin; TRM-SXT: trimethoprim-sulfamethoxazole; Tet: tetracycline; C: chloramphenicol; Gn: gentamicin; Amc: amoxicillin—clavulanic acid.

resistant to trimethoprim-sulfamethoxazole and other drugs while 42 (52.5%) were resistant to ampicillin and other antibiotics. In contrast, 32 (76.2%) of the 42 isolates from Kuwait were resistant to two or more antibiotics of which 21 (65.6%) were resistant to three or more antibiotics. Three categories of resistance patterns emerged among the isolates; 11 (34.4%) each were resistant to trimethoprim-sulfamethoxazole/tetracycline and ampicillin/chloramphenicol/trimethoprim-sulfamethoxazole/tetracycline combinations while 10 (31.3%) were resistant to ampicillin/chloramphenicol/gentamicin/trimethoprim-sulfamethoxazole/tetracycline combination.

In the UAE, the MDR isolates among individual *Shigella* spp., were represented mainly by *S. flexneri* which accounted for 56 (70%) and *S. sonnei*, 24 (30%) while in Kuwait the proportion of MDR isolates that were *S. flexneri* was 32 (100%) and *S. sonnei* 0 (0%).

Prevalence of ESBL-producing *Shigella* isolates

Only 12 (8.5%) isolates were inhibited by $\geq$1 μg/ml of cefotaxime or ceftriaxone and these were investigated for ESBL production. Of these, 4 (33.3%) were positive for ESBL phenotypes by both of the E test ESBL methods (CTX/CTX + CA and CAZ/CAZ + CA). That is, 2.8% of the total isolates were ESBL producers. As shown in Table 3, they were 3 *S. flexneri* and 1 *S. sonnei*; all from the UAE collection. However, amplified PCR products of these isolates investigated for *bla* genes of ESBL were negative.

Discussion

S. dysenteriae, *S. flexneri*, *S. boydii* and *S. sonnei* are responsible for the disease known as shigellosis. In the 1990s, *S. flexneri* was the most common serogroup isolated in Kuwait accounting for 46% of all clinical isolates closely followed by *S. sonnei* (42%) [9]. Data from a surveillance study in the UAE between October 1999—September 2001 and January—May 2002, showed that *S. sonnei* was more common than *S. flexneri* with prevalence rates of 67% and 28%, respectively [10]. In the present study, there was a much higher prevalence of *S. flexneri* in Kuwait and UAE accounting for 76% and 58%, respectively while prevalence of *S. sonnei* has fallen considerably to 23% and 36%, respectively, over time. This is fairly similar to the prevalence data reported in other developing countries such as India [11], Turkey [12], Nigeria [13] and Eritrea [14]. In contrast, the situation in the developed countries, like USA, shows that *S. sonnei* is the most common isolates accounting for 80% of all *Shigella* spp. [15].

In this study, tigecycline demonstrated an excellent in vitro activity against all isolates from both countries. This is a new drug which has only recently been introduced for use in Kuwait and UAE. Other drugs with excellent in vitro activities include amikacin, cephalosporins, carbapenems and ciprofloxacin. However, the impact of overuse and misuse of antimicrobial agents in the therapy of diarrhoea or other infectious diseases have been an increase in antimicrobial resistance, which can be seen with the high resistance rates to the first-line drugs in this study. This finding is, no doubt, crucial in clinical practice, especially in the developing countries.

Table 3 Susceptibility of four ESBL-producing *Shigella* spp. to selected antibiotics.

Antimicrobial agents	Minimum inhibitory concentration (μg/ml)			
	S. flexneri No. 22	*S. sonnei* No. 37	*S. flexneri* No. 39	*S. flexneri* No. 41[a]
Amikacin	4	8	8	3
Ampicillin	>256	>256	>256	>256
Cefotaxime	1	2	2	1.5
Cefuroxime	1.5	3	3	2
Chloramphenicol	1	2	256	2
Ciprofloxacin	0.12	0.006	0.012	0.006
Gentamicin	3	6	2	4
TRM-SXT	>32	>32	>32	>32
Imipenem	0.125	0.25	0.25	0.19
Meropenem	0.016	0.047	0.032	0.032

TRM-SXT: trimethoprim-sulfamethoxazole.
[a] Serial number.

This study demonstrates that the resistance rate of Kuwait and UAE isolates to the first-line drugs has changed over the years since the first reports that came out of these countries [9,10]. For example, in Kuwait, there is an upward trend in the resistance rates to chloramphenicol, trimethoprim-sulfamethoxazole and gentamicin, whereas the resistance rates to ampicillin and amoxicillin—clavulanic acid appear to have declined slightly. In UAE, ampicillin and trimethoprim-sulfamethoxazole resistance in the previous study was 56.6% and 84.9%, respectively [10] but are 50% and 92% in this study. These levels of resistance to the first-line drugs are lower than that reported in China where the resistance rates to ampicillin, trimethoprim-sulfamethoxazole and gentamicin were 64.9%, 94.6% and 62.2% [16]. Streit et al. [17] have also reported very high level of ampicillin resistance among *Shigella* isolates in Latin America as 73.6%, and 76% in Europe, Israel and Turkey, which are much higher than the 50% rate observed in the current study in Kuwait and UAE. In 2003, a SENTRY antimicrobial surveillance program, reported that over 65% of isolates from Latin America and about 66% in Europe, Israel and Turkey, were resistant to trimethoprim-sulfamethoxazole [17], a finding much lower than the level of resistance among UAE isolates but slightly lower than that experienced in Kuwait. It is conceivable that this high level of resistance in Kuwait is probably due the frequent and uncontrolled use of this drug as a first-line choice for the treatment of many infections, including urinary tract infection, respiratory tract infections and some skin infections (personal observation). Although chloramphenicol has been banned for general use in Kuwait for over two decades there is an unacceptable high rate of chloramphenicol resistance among the isolates. Part of the explanation for this finding may lie in the fact that the majority of the isolates were from patients of South East Asian countries or from patients who have visited the region in recent times, where chloramphenicol resistant *Shigella* spp. are highly prevalent [3,18,19].

All isolates in Kuwait and UAE were susceptible to ciprofloxacin signalling the fact that ciprofloxacin can be used effectively for the treatment of shigellosis in adults in both countries. However, one *S. flexneri* serotype 3 with reduced susceptibility to ciprofloxacin (MIC, 0.25 μg/ml) was detected in UAE but the clinical significance of this finding is unclear at this moment although treatment failure of infections due to *Salmonella* strains with reduced susceptibility has been reported [20]. Whether or not similar treatment failure may occur in shigellosis caused by *Shigella* spp. with reduced susceptibility to ciprofloxacin is unknown. However, fluoroquinolone-resistant *Shigella* spp. remain rare although have recently been identified in *S. dysenteriae* isolates from some Asian countries like Bangladesh, India and Nepal [21—23], and strains with reduced susceptibility (MIC 0.25—1.0 μg/ml) have been reported in UK [24].

The susceptibility to the third-generation cephalosporins, e.g. cefotaxime and ceftriaxone, remains stable over time as demonstrated by their excellent activities against isolates from both countries in this study and in previous ones [9,10]. Other investigators have reported similar trends to ours [12,17]. Therefore, cefotaxime, or ceftriaxone, continues to be an important agent targeting these pathogens in Kuwait and UAE. However, it must be stated that although rare, cephalosporin-resistant *Shigella* spp. have been reported from several countries such as Argentina [25], Israel [26], Lebanon [27], China [16] and USA [28].

There was a very high level of tetracycline resistance among *Shigella* spp. isolated from both countries although with rates relatively lower in Kuwait than UAE (76.2% vs. 98%). One of the reports with higher rates than these came from isolates studied in Europe, Israel and Turkey (80%) [17]. Reports from other countries are considerably much lower than those demonstrated in ours, such as 52% in Latin America and 45% in the USA [15].

Resistance to the third-generation cephalosporins mediated by ESBL enzymes is a rare phenomenon although a few reports have appeared in the literature which suggested that this may be an emerging resistance problem in *Shigella* spp. For instance, CTX-M-type ESBL has been reported among *S. sonnei* isolates in Israel [26], China [16], Lebanon [27] and USA [28]. In the Republic of Korea, Kim et al. [5] found both the CTX-M-type and TEM-type ESBLs in 20 isolates of *S. sonnei*. In our present study, even though 2.8% of the isolates were phenotypically confirmed as ESBL-producers by the E test ESBL methods, this observation could not be verified at the molecular level by the range of PCR primers used. All the strains, although showed decreased susceptibility to extended-spectrum cephalosporins, were nonetheless inhibited by cefotaxime MICs in the susceptible range. Thus, although unlikely, they might have given false-positive results by the E test ESBL methods or perhaps other genes not included among the ones tested were responsible for the ESBL production.

In conclusion, treatment for shigellosis is critical in person with severe disease such as children

or immunosuppressed patient as well as patients infected by *S. dysenteriae*. At this time, the option, as a result of the data presented in this study, for the choice of the antimicrobial agents from the first-line panel for the treatment of shigellosis in Kuwait and UAE is very limited. Tigecycline, in this study, demonstrated excellent in vitro activity and thus holds promise for the therapy of shigellosis. The third-generation cephalosporins and fluoroquinolones can be effectively used to treat shigellosis in children and adults, respectively. However, continued monitoring of emerging resistance in *Shigella* spp. is important for the appropriate recommendations for antimicrobial chemotherapy.

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Conflict of interest statement

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