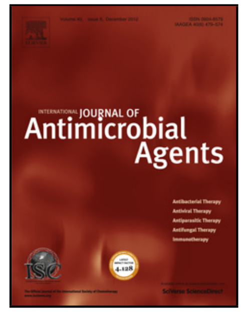
Accepted Manuscript



Title: In vitro activity of tigecycline and comparators against Gram-positive and Gram-negative isolates collected from the Middle East and Africa between 2004 and 2011

Author: Souha Kanj Andrew Whitelaw Michael J. Dowzicky

PII: S0924-8579(13)00368-3
DOI: http://dx.doi.org/doi:10.1016/j.ijantimicag.2013.10.011
Reference: ANTAGE 4215

To appear in: *International Journal of Antimicrobial Agents*

Received date: 2-6-2013
Revised date: 18-9-2013
Accepted date: 16-10-2013

Please cite this article as: Kanj S, Whitelaw A, Dowzicky MJ, In vitro activity of tigecycline and comparators against Gram-positive and Gram-negative isolates collected from the Middle East and Africa between 2004 and 2011, *International Journal of Antimicrobial Agents* (2013), http://dx.doi.org/10.1016/j.ijantimicag.2013.10.011

In vitro activity of tigecycline and comparators against Gram-positive and Gram-negative isolates collected from the Middle East and Africa between 2004 and 2011

Souha Kanj [a,*], Andrew Whitelaw [b,c], Michael J. Dowzicky [d]

[a] *Department of Internal Medicine, Division of Infectious Diseases, American University of Beirut Medical Center, P.O. Box 11-0236, Riad El-Solh 1107 2020, Beirut, Lebanon*

[b] *Division of Medical Microbiology, Faculty of Health Sciences, University of Stellenbosch, Cape Town, South Africa*

[c] *National Health Laboratory Service, Tygerberg Hospital, Cape Town, South Africa*

[d] *Pfizer Inc., Collegeville, PA 19426, USA*

ARTICLE INFO

Article history:

Received 2 June 2013

Accepted 16 October 2013

1

Keywords:

Tigecycline

Antimicrobial susceptibility

Gram-positive

Gram-negative

Middle East

Africa

* Corresponding author. Tel.: +961 1 350 000; fax: +961 1 370 814.

ABSTRACT

The Tigecycline Evaluation and Surveillance Trial (T.E.S.T.) was established in 2004 to monitor longitudinal changes in bacterial susceptibility to numerous antimicrobial agents, specifically tigecycline. In this study, susceptibility among Gram-positive and Gram-negative isolates between 2004 and 2011 from the Middle East and Africa was examined. Antimicrobial susceptibilities were determined using Clinical and Laboratory Standards Institute (CLSI) interpretive criteria, and minimum inhibitory concentrations (MICs) were determined by broth microdilution methods. US Food and Drug Administration (FDA)-approved breakpoints were used for tigecycline. In total, 2967 Gram-positive and 6322 Gram-negative isolates were examined from 33 participating centres. All *Staphylococcus aureus* isolates, including meticillin-resistant *S. aureus*, were susceptible to tigecycline, linezolid and vancomycin. Vancomycin, linezolid, tigecycline and levofloxacin were highly active (>97.6% susceptibility) against *Streptococcus pneumoniae*, including penicillin-non-susceptible strains. All *Enterococcus faecium* isolates were susceptible to tigecycline and linezolid, including 32 vancomycin-resistant isolates. Extended-spectrum β-lactamases were produced by 16.6% of *Escherichia coli* and 32.9% of *Klebsiella pneumoniae*. More than 95% of *E. coli* and *Enterobacter* spp. were susceptible to amikacin, tigecycline, imipenem and meropenem. The most active agents against *Pseudomonas aeruginosa* and *Acinetobacter baumannii* were amikacin (88.0% susceptible) and minocycline (64.2% susceptible), respectively; the MIC_{90} (MIC required to inhibit 90% of the isolates) of tigecycline against *A. baumannii* was low at 2 mg/L. Tigecycline and carbapenem agents were highly active against most Gram-negative pathogens. Tigecycline, linezolid and vancomycin showed good activity against most Gram-positive pathogens from the Middle East and Africa.

1. Introduction

Antimicrobial resistance has been reported to all major groups of antibiotics and is a cause of global concern. Resistance has appeared in the Middle East and Africa over the past decade (e.g. carbapenem-resistant *Acinetobacter baumannii* in Lebanon [1] and extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* in South Africa [2]). Antimicrobial surveillance is critical for monitoring emerging trends in antimicrobial resistance and for guiding clinicians to appropriate empirical antimicrobial therapy.

Tigecycline, a broad-spectrum antimicrobial agent, is licensed for the treatment of complicated skin and intra-abdominal infections (as well as community-acquired bacterial pneumonia in the USA) [3]. The Tigecycline Evaluation and Surveillance Trial (T.E.S.T.) is a global surveillance study designed to monitor bacterial susceptibility to tigecycline and comparator antimicrobial agents. We report on the activity of tigecycline and comparators against Gram-positive and Gram-negative pathogens from the Middle East and Africa between 2004 and 2011. This paper updates some of the data presented by Bertrand and Dowzicky [4], who examined antimicrobial susceptibility among Gram-negative isolates from North America, Europe, the Asia-Pacific Rim, Latin America, the Middle East and Africa collected as part of T.E.S.T. between 2004 and 2009.

2. Materials and methods

2.1. Isolate collection

Isolates were collected from 33 centres in the Middle East and Africa between 2004 and 2011 (Israel, 10 centres, 2005–2011; Jordan, 1 centre, 2009–2011; Lebanon, 1 centre, 2006–2007; Mauritius, 1 centre, 2009; Namibia, 1 centre, 2008–2009; Oman, 1 centre, 2006–2007; Pakistan, 3 centres, 2004–2006; Saudi Arabia, 3 centres, 2009 and 2011; and South Africa, 12 centres, 2004–2009 and 2011).

Each centre was expected to contribute at least 65 Gram-positive and 135 Gram-negative isolates annually, including 15 *Streptococcus pneumoniae*, 15 *Enterococcus* spp., 25 *Staphylococcus aureus*, 10 *Streptococcus agalactiae*, 15 *Haemophilus influenzae*, 15 *Acinetobacter* spp., 25 *E. coli*, 25 *Enterobacter* spp., 20 *Pseudomonas aeruginosa*, 10 *Serratia* spp. and 25 *Klebsiella* spp. isolates. All isolates were to be collected consecutively and considered clinically significant as determined by local criteria. They could be of nosocomial or community origin. Only one isolate was permitted per patient; isolate inclusion was independent of patient age, sex, previous medical history and/or previous antimicrobial use.

2.2. Susceptibility testing

Minimum inhibitory concentrations (MICs) were determined locally based on broth microdilution methodology as described by the Clinical and Laboratory Standards Institute (CLSI) [5] using Sensititre® plates (TREK Diagnostic Systems, East Grinstead, UK) or MicroScan® panels

(Siemens, Sacramento, CA). The test panel for Gram-positive pathogens included amoxicillin/clavulanic acid (AMC), ampicillin, ceftriaxone, imipenem (MicroScan® only), levofloxacin, linezolid, meropenem (Sensititre® only), minocycline, penicillin, piperacillin/tazobactam (TZP), tigecycline and vancomycin. Gram-negative isolates were tested against amikacin, AMC, ampicillin, cefepime, ceftazidime, ceftriaxone, imipenem, levofloxacin, meropenem, minocycline, TZP and tigecycline. As a result of stability issues, imipenem was replaced by meropenem in 2006; MicroScan® panels were replaced by Sensititre® plates that same year. MIC determinations were carried out using cation-adjusted Mueller–Hinton broth (*Streptococcus* spp. were cultured in Mueller–Hinton broth supplemented with lysed horse blood). In 2008, the test panel for *S. pneumoniae* was extended to include azithromycin, clarithromycin, clindamycin and erythromycin; this means that some isolates were tested retrospectively.

Laboratories International for Microbiology Studies, a division of International Health Management Associates, Inc. (IHMA, Schaumburg, IL), was responsible for isolate collection and transport as well as the management of a centralised T.E.S.T. database; IHMA's role in T.E.S.T. has been described in detail elsewhere [6].

Antimicrobial susceptibility was determined using interpretive criteria as described by the CLSI [7]; non-meningeal oral breakpoints have been applied to *S. pneumoniae*. US Food and Drug Administration (FDA)-approved breakpoints were used for tigecycline, as provided in the tigecycline package insert [3]. Statistically significant changes in susceptibility were identified using the Cochran–Armitage test for trend.

2.3. Extended-spectrum β-lactamase testing

ESBL production was examined among *E. coli* and *Klebsiella* spp. according to CLSI guidelines [6,7].

3. Results

In total, 2967 Gram-positive and 6322 Gram-negative isolates were collected in the Middle East and Africa between 2004 and 2011 (Tables 1 and 2). Isolates were submitted from 33 centres in nine countries; most isolates originated from Israel (52.9%) or South Africa (28.4%).

3.1. Gram-positive isolates

All 1216 isolates of *S. aureus* were susceptible to linezolid, tigecycline and vancomycin; susceptibility to minocycline was also high at 96.4% (Table 1a). Overall, 27.8% of *S. aureus* isolates were meticillin-resistant *S. aureus* (MRSA), with a rate of almost 50% noted from Mauritius (Table 3). MRSA prevalence was low in Namibia, Pakistan and Oman, ranging from 12.5% to 13.8%; in the remaining countries, the MRSA incidence ranged from 23.8% to 45.8%. Only 18.6% of MRSA isolates were susceptible to levofloxacin (Table 1a); among all meticillin-susceptible *S. aureus* isolates, levofloxacin susceptibility decreased significantly ($P < 0.05$) from 100% in 2004 to 94.9% in 2010 before increasing to 98.0% in 2011 (only 51 isolates were available in 2011; data not shown).

Streptococcus pneumoniae (*n* = 598) were highly susceptible (≥97.6%) to vancomycin, linezolid, tigecycline and levofloxacin, including penicillin-non-susceptible isolates (Table 1a). Macrolide susceptibility was lowest in Jordan (Table 1b), which also showed the highest rates of penicillin-non-susceptible *S. pneumoniae* (Table 3). *Streptococcus agalactiae* (*n* = 465) were highly susceptible to vancomycin, penicillin, meropenem, linezolid, ceftriaxone and ampicillin (each 100%), levofloxacin (98.5%) and tigecycline (94.2%). However, only 16.1% of isolates were susceptible to minocycline (Table 1a).

Among *Enterococcus faecalis* (*n* = 565), ≥99.5% susceptibility was observed for ampicillin, linezolid, penicillin, tigecycline and vancomycin (Table 1a); levofloxacin and minocycline susceptibilities were 56.3% and 26.9%, respectively. A single vancomycin-resistant *E. faecalis* isolate was collected in Israel. Susceptibility rates were lower among *Enterococcus faecium* (*n* = 123) than *E. faecalis*, although 100% susceptibility was reported for linezolid and tigecycline (Table 1a). Twenty-six percent of *E. faecium* isolates were vancomycin-resistant (Tables 1a and 3).

3.2. Gram-negative isolates

Enterobacter spp. (*n* = 1137) showed high (≥95%) susceptibility to amikacin, imipenem, meropenem and tigecycline; <5% of isolates were susceptible to AMC or ampicillin (Table 2a).

Escherichia coli (*n* = 1238) were highly susceptible (≥96.5%) to tigecycline, amikacin, imipenem and meropenem (Table 2a); a single tigecycline-non-susceptible isolate was collected from Jordan. ESBL production was noted among 16.6% of *E. coli* (Table 3) but had little effect on the activity of tigecycline, amikacin and the carbapenems (Tables 2a). Levofloxacin susceptibility ranged from 33.3% in Jordan to 91.3% in Namibia. Low susceptibility rates were noted in Jordan (Table 2a), likely due to higher numbers of ESBL-producing coliforms there (62.5%) (Table 3). ESBL production in *E. coli* was lowest in Lebanon (0.0%), South Africa (3.7%) and Namibia (4.3%) (Table 3).

Klebsiella pneumoniae (*n* = 1105) were highly susceptible to imipenem (96.6%), tigecycline (93.4%) and amikacin (91.0%). Levofloxacin susceptibility ranged from 56.3% in Israel to 100% in Namibia and Oman (Table 2a). ESBLs were produced by 32.9% of isolates (Table 3) but did not impact the activity of imipenem or amikacin; tigecycline susceptibility decreased to 88.7% (Table 2a). ESBL production was lowest in Oman (4.2%) and Namibia (13.0%) (Table 3). Among *Klebsiella oxytoca* isolates (*n* = 121), ≥93.7% were susceptible to amikacin, tigecycline and meropenem (Table 2a).

Among *Serratia marcescens* isolates (*n* = 444), high susceptibility (≥94.1%) was observed for meropenem, amikacin, cefepime, TZP, imipenem, tigecycline and levofloxacin (Table 2a); *S. marcescens* is intrinsically resistant to AMC and ampicillin.

Amikacin was highly active against *P. aeruginosa* (*n* = 975; 88.0% susceptible); low susceptibility to several antimicrobials was observed in Pakistan (Table 2). The most active agent against *A. baumannii* (*n* = 664) was minocycline (64.2% susceptible) (Table 2a). A low tigecycline

MIC_{90} (MIC required to inhibit 90% of the isolates) (2 mg/L) was recorded for *A. baumannii*. Overall susceptibility was low in Pakistan (Table 2). Among non-*A. baumannii Acinetobacter* spp. (*n* = 33), 84.8% and 66.7% of isolates were susceptible to minocycline and meropenem, respectively; an MIC_{90} of 1 mg/L for tigecycline to non-*A. baumannii* was observed.

Haemophilus influenzae (*n* = 605) were highly susceptible (≥97.9%) to most agents on the T.E.S.T. panel (Table 2a). β-Lactamase-positive *H. influenzae* were rare in most countries (<10 in Jordan, Lebanon, Mauritius, Oman, Pakistan and Saudi Arabia).

3.3. Changes in susceptibility

Significant (*P* < 0.01) changes in susceptibility were examined only in Israel and South Africa owing to insufficient isolate numbers from other countries. In Israel, significant decreases in minocycline susceptibility were noted among *A. baumannii* (95.8% in 2006 to 55.0% in 2010; *P* < 0.0001), *Enterobacter* spp. (82.6% in 2006 to 59.4% in 2010; *P* < 0.001) and *S. pneumoniae* (92.6% in 2006 to 47.7% in 2010; *P* < 0.0001). A significant decrease in tigecycline susceptibility was noted among *S. marcescens* (100% in 2006 to 82.4% in 2010; *P* < 0.01). A significant increase in meropenem susceptibility occurred among *E. coli*: 77.6% of isolates were susceptible in 2007 (*n* = 98), increasing to 100% in 2009 (*n* = 207) and 2010 (*n* = 176) (*P* < 0.0001) [100% susceptibility was also recorded in 2005 and 2006, but isolate numbers were considerably lower (*n* = 9 and 39, respectively)]. In South Africa, a significant decrease in susceptibility was noted among *A. baumannii* to TZP (52.9% in 2005 to 27.1% in 2006; *P* < 0.01), although isolate numbers were low (≤6) between 2007 and 2011 (data not shown).

4. Discussion

Staphylococcus aureus and enterococci susceptibility rates resemble reports from other recent studies. *Staphylococcus aureus* susceptibility to tigecycline, linezolid and vancomycin was 100% in the current study. These results corroborate findings in a recent report from Lebanon [8], although vancomycin-resistant *S. aureus* isolates have been reported in the region [9]. Salem-Bekhit et al. [10] reported 3.9% vancomycin resistance among 206 clinical isolates of enterococci collected in Saudi Arabia between 2009 and 2012. These results resemble those given here, as 33 (4.8%) vancomycin-resistant enterococci (32 *E. faecium* and 1 *E. faecalis*) were seen from the Middle East and Africa in the current study; 16 enterococci were collected from Saudi Arabia, of which 1 single isolate (6.3%) was vancomycin-resistant.

T.E.S.T. intensive care unit (ICU) isolates from the Middle East and Africa between 2004 and 2009 have previously been described [4]. *Acinetobacter baumannii* isolates were 7–17% less susceptible to cefepime, ceftazidime, meropenem and TZP compared with the 2004–2011 interval, likely due in part to the 2004–2009 data containing only ICU isolates, which are generally more resistant than non-ICU isolates. These changes may also be due to changes in participating centres that occur in surveillance studies.

Although not indicated for the treatment of infections caused by *Acinetobacter* spp., tigecycline is often regarded as a viable treatment option for multidrug-resistant *Acinetobacter* infections [11]. The Enterobacteriaceae susceptibility breakpoint (≤2 mg/L) is often used for tigecycline in the absence of CLSI tigecycline susceptibility breakpoints. An MIC_{90} of 2 mg/L was recorded for tigecycline against *Acinetobacter* in the current study. Low tigecycline resistance in Lebanon (0% resistant, 2% intermediate) and Kuwait (13.6% resistant) reflected good activity against *Acinetobacter* reported in the current study [8,12].

Previous studies have reported 100% tigecycline susceptibility among *E. coli* isolates from Lebanon and Oman, including ESBL-producers [12,13]. Only one single (0.1%) non-susceptible *E. coli* isolate from Jordan was reported in the current study. No *E. coli* ESBL production was observed from Lebanon, possibly due to sampling error: in comparison, another recent study demonstrated ESBL production among *E. coli* of 30% in a tertiary care centre in Lebanon in 2011 [8]. Two imipenem-non-susceptible isolates of *K. pneumoniae* were collected in the current study, one of which was resistant to tigecycline. Meropenem resistance occurred among 103 isolates (77 from Israel, 22 from South Africa, 2 from Saudi Arabia and 1 each from Pakistan and Mauritius); of these, 2 (1.9%) were also resistant to tigecycline (data not shown). Araj et al. [8] also reported good results for tigecycline among ESBL-positive *K. pneumoniae* isolates collected in Lebanon, with only 3% tigecycline-resistant and 16% intermediate.

Sader et al. have recently published susceptibility results for tigecycline against more than 22 000 clinical bacteria collected worldwide as a part of the SENTRY study in 2011 [14]; the tigecycline results presented here for the Middle East and Africa broadly agree with these global results. *Staphylococcus aureus*, *Enterococcus* spp., *S. pneumoniae* and *E. coli* from the Middle East/Africa were each within 1% of global results (all above 99% susceptible), whilst *Acinetobacter* shared an MIC_{90} of 2 mg/L in both studies. *Enterobacter* and *Klebsiella* susceptibility to tigecycline were slightly lower in Middle East/Africa than globally. *Enterobacter* spp. susceptibility was 95.5% in Middle East/Africa compared with 98.6% globally, whilst *K. pneumoniae* and *K. oxytoca* were 93.4% and 96.7% susceptible, respectively, in the current study, whilst 98.6% of *Klebsiella* spp. were susceptible to tigecycline worldwide.

Tigecycline resistance mechanisms have recently been summarised by Linkevicius et al. [15]. Resistance–nodulation–division (RND) efflux pumps are used by several bacteria [*Acinetobacter* spp., *Enterobacter cloacae*, *E. coli*, *K. pneumoniae*, *Morganella* spp. (AcrAB), *Proteus* spp. (AcrAB), *Providencia* spp., *P. aeruginosa* (MexXY–OprM) and *Salmonella enterica*] to reduce susceptibility to tigecycline. Efflux pumps are also responsible for tigecycline resistance among *Burkholderia* spp., whilst overexpression of multidrug and toxin extrusion (MATE) family efflux pumps (MepA) may reduce tigecycline susceptibility among *S. aureus* isolates. Although still uncommon, resistance to those agents commonly used against multidrug-resistant pathogens, such as tigecycline and colistin, has occurred in some regions [11]. Molecular resistance mechanisms are not identified as part of T.E.S.T.

Tigecycline retains in vitro activity against a wide range of organisms collected from the Middle East and Africa. The results presented highlight the importance of newer antimicrobial agents such as tigecycline, which do not share cross-resistance with other commonly used antibacterial drugs [3]. The question of whether the in vitro activity of tigecycline corresponds to clinical efficacy is unclear. Tigecycline may offer an addition to the limited armamentarium available for the management of infections caused by increasingly resistant pathogens.

Acknowledgments: The authors thank the many T.E.S.T. investigators and laboratories for their participation in this study, and IHMA staff for co-ordination of T.E.S.T. Dr Rod Taylor (Micron Research Ltd., Chatteris, UK) provided editorial assistance, which was funded by Pfizer Inc. Micron Research Ltd. also provided data management services, which were funded by Pfizer Inc.

Funding: T.E.S.T. is funded by Pfizer Inc.

Competing interests: SK has presented conference proceedings on behalf of AstraZeneca, Biologix, MSD and Pfizer; MJD is an employee of Pfizer, Inc. AW declares no competing interests.

Ethical approval: Not required.

References

[1] Zarrilli R, Vitale D, Di Popolo A, Bagattini M, Daoud Z, Khan AU, et al. A plasmid-borne *bla*$_{OXA-58}$ gene confers imipenem resistance to *Acinetobacter baumannii* isolates from a Lebanese hospital. Antimicrob Agents Chemother 2008;52:4115–20.

[2] Brink AJ, Botha RF, Poswa X, Senekal M, Badal RE, Grolman DC, et al. Antimicrobial susceptibility of Gram-negative pathogens isolated from patients with complicated intra-abdominal infections in South African hospitals (SMART Study 2004–2009): impact of the new carbapenem breakpoints. Surg Infect (Larchmt) 2012;13:43–9.

[3] Pfizer Inc. (Wyeth Pharmaceuticals Inc.). *Tygacil® product insert*. Philadelphia, PA: Pfizer Inc.; January 2011. http://www.pfizerpro.com/hcp/tygacil [accessed 6 November 2013].

[4] Bertrand X, Dowzicky MJ. Antimicrobial susceptibility among Gram-negative isolates collected from intensive care units in North America, Europe, the Asia-Pacific Rim, Latin America, the Middle East, and Africa between 2004 and 2009 as part of the Tigecycline Evaluation and Surveillance Trial. Clin Ther 2012;34:124–37.

[5] Clinical and Laboratory Standards Institute. *Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard*. 8th ed. Document M7-A8. Wayne, PA: CLSI; 2009.

[6] Balode A, Punda-Polić V, Dowzicky MJ. Antimicrobial susceptibility of Gram-negative and Gram-positive bacteria collected from countries in Eastern Europe: results from the Tigecycline Evaluation and Surveillance Trial (T.E.S.T.) 2004–2010. Int J Antimicrob Agents 2013;41:527–35.

[7] Clinical and Laboratory Standards Institute. *Performance standards for antimicrobial susceptibility testing: twenty-third informational supplement*. Document M100-S23. Wayne, PA: CLSI; 2013.

[8] Araj GF, Avedissian AZ, Ayyash NS, Bey HA, El Asmar RG, Hammoud RZ, et al. A reflection on bacterial resistance to antimicrobial agents at a major tertiary care center in Lebanon over a decade. J Med Liban 2012;60:125–35.

[9] Taj Y, Abdullah FE, Kazmi SU. Current pattern of antibiotic resistance in *Staphylococcus aureus* clinical isolates and the emergence of vancomycin resistance. J Coll Physicians Surg Pak 2010;20:728–32.

[10] Salem-Bekhit MM, Moussa IM, Muharram MM, Alanazy FK, Hefni HM. Prevalence and antimicrobial resistance pattern of multidrug-resistant enterococci isolated from clinical specimens. Indian J Med Microbiol 2012;30:44–51.

[11] Shin JA, Chang YS, Kim HJ, Kim SK, Chang J, Ahn CM, et al. Clinical outcomes of tigecycline in the treatment of multidrug-resistant *Acinetobacter baumannii* infection. Yonsei Med J 2012;53:974–84.

[12] Araj GF, Ibrahim GY. Tigecycline in vitro activity against commonly encountered multidrug-resistant Gram-negative pathogens in a Middle Eastern country. Diagn Microbiol Infect Dis 2008;62:411–5.

[13] Al-Yaqoubi M, Elhag K. Susceptibilities of common bacterial isolates from Oman to old and new antibiotics. Oman Med J 2008;23:173–8.

[14] Sader HS, Flamm RK, Jones RN. Tigecycline activity tested against antimicrobial resistant surveillance subsets of clinical bacteria collected worldwide (2011). Diagn Microbiol Infect Dis 2013;76:217–21.

[15] Linkevicius M, Sandegren L, Andersson DI. Mechanisms and fitness costs of tigecycline resistance in *Escherichia coli*. Antimicrob Chemother 2013 Jul 9 [Epub ahead of print].

Table 1a

MIC_{90} values (in mg/L) and percent antimicrobial susceptibility (%S) among Gram-positive isolates (including resistant phenotypes) collected in the Middle East and Africa between 2004 and 2011 [a,b]

	N	AMC		AMP		CRO		IPM		LVX		LZD		MEM		MIN		PEN		TZP		TIG	
		MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S
Staphylococcus aureus																							
Israel	631	≥16	71.8	≥32	11.3	≥128	70.8	–	–	16	68.8	4	100	≥32 (*n* = 631)	76.7	0.5	98.1	≥16	9.8	≥32	74.3	0.5	100
Jordan	29	8	69.0	≥32	3.4	≥128	65.5	–	–	4	89.7	4	100	8 (*n* = 29)	89.7	0.5	96.6	≥16	3.4	≥32	82.8	0.25	100
Lebanon	25	8	88.0	≥32	8.0	64	84.0	0.25 (*n* = 25)	96.0	0.25	92.0	2	100	–	–	≤0.25	100	≥16	8.0	8	96.0	0.25	100
Mauritius	24	≥16	58.3	≥32	12.5	≥128	54.2	–	–	8	66.7	4	100	≥32 (*n* = 24)	66.7	8	62.5	≥16	12.5	≥32	62.5	0.25	100
Namibia	24	8	87.5	≥32	8.3	16	87.5	–	–	0.5	91.7	2	100	4 (*n* = 24)	91.7	≤0.25	100	≥16	8.3	8	91.7	0.25	100
Oman	29	4	93.1	≥32	10.3	16	89.7	–	–	0.5	100	2	100	0.5 (*n* = 29)	100	≤0.25	100	≥16	10.3	4	100	0.12	100
Pakistan	62	8	88.7	≥32	8.1	64	85.5	1 (*n* = 46)	93.5	8	83.9	4	100	≥32 (*n* = 16)	81.3	1	95.2	≥16	6.5	16	88.7	0.5	100

Saudi Arabia	42	≥16	76.2	≥32	4.8	≥128	76.2	–	–	8	78.6	2	100	≥32 (*n* = 42)	78.6	≤0.25	95.2	≥16	4.8	≥32	78.6	0.25	100
South Africa	350	≥16	77.7	≥32	7.1	≥128	76.3	≥32 (*n* = 106)	74.5	8	79.1	2	100	≥32 (*n* = 244)	84.0	4	95.1	≥16	6.6	≥32	78.9	0.25	100
All countries	1216	≥16	75.3	≥32	9.4	≥128	73.9	≥32 (*n* = 177)	82.5	16	75.0	4	100	≥32 (*n* = 1039)	79.7	1	96.4	≥16	8.4	≥32	77.9	0.25	100
Meticillin-resistant *S. aureus*																							
Israel	190	≥16	6.3	≥32	0.0	≥128	6.8	–	–	≥64	8.4	4	100	≥32 (*n* = 190)	22.6	0.5	96.3	≥16	0.0	≥32	14.7	0.25	100
Jordan	9	–	[0]	–	[0]	–	[0]	–	–	–	[7]	–	[9]	– (*n* = 9)	[6]	–	[8]	–	[0]	–	[4]	–	[9]
Lebanon	8	–	[5]	–	[0]	–	[4]	–	[7]	–	[6]	–	[8]	–	–	–	[8]	–	[0]	–	[7]	–	[8]
Mauritius	11	≥16	9.1	≥32	0.0	≥128	0.0	–	–	8	27.3	4	100	≥32 (*n* = 11)	27.3	≥16	27.3	≥16	0.0	≥32	18.2	0.5	100
Namibia	3	–	[0]	–	[0]	–	[0]	–	–	–	[1]	–	[3]	– (*n* = 3)	[1]	–	[3]	–	[0]	–	[1]	–	[3]
Oman	4	–	[2]	–	[0]	–	[1]	–	–	–	[4]	–	[4]	– (*n* = 4)	[4]	–	[4]	–	[0]	–	[4]	–	[4]
Pakistan	8	–	[1]	–	[0]	–	[0]	–	[2]	–	[0]	–	[8]	– (*n* = 3)	[0]	–	[5]	–	[0]	–	[1]	–	[8]

Saudi Arabia	10	≥16	0.0	≥32	0.0	≥128	0.0	–	–	16	10.0	2	100	≥32 (*n* = 10)	10	8	80.0	≥16	0.0	≥32	10.0	0.25	100
South Africa	95	≥16	17.9	≥32	0.0	≥128	16.8	≥32 (*n* = 44)	38.6	8	26.3	2	100	≥32 (*n* = 51)	23.5	8	84.2	≥16	0.0	≥32	22.1	0.5	100
All countries	338	≥16	11.2	≥32	0.0	≥128	10.1	≥32 (*n* = 57)	45.6	32	18.6	2	100	≥32 (*n* = 281)	24.9	8	89.3	≥16	0.0	≥32	20.4	0.5	100
Streptococcus pneumoniae																							
Israel	336	2	92.0	4	NA	1	92.3	–	–	1	97.3	1	100	1 (*n* = 336)	75.9	≥16	59.2	2	51.8	4	NA	0.03	99.7
Jordan	14	4	50.0	8	NA	2	78.6	–	–	2	100	1	100	1 (*n* = 14)	21.4	≥16	28.6	4	7.1	8	NA	0.03	100
Mauritius	9	–	[7]	–	NA	–	[7]	–	–	–	[9]	–	[9]	– (*n* = 9)	[4]	–	[0]	–	[2]	–	NA	–	[9]
Oman	15	1	100	2	NA	1	100	–	–	1	100	1	100	0.5 (*n* = 15)	73.3	2	93.3	2	53.3	2	NA	0.03	100
Pakistan	32	0.12	100	0.25	NA	0.25	100	0.25 (*n* = 15)	86.7	1	93.8	1	100	≤0.12 (*n* = 17)	100	8	50.0	0.25	62.5	≤0.25	NA	0.06	100
Saudi Arabia	18	2	94.4	4	NA	2	83.3	–	–	1	100	1	100	0.5 (*n* = 18)	55.6	≥16	44.4	4	22.2	4	NA	0.06	94.4
South Africa	174	4	85.6	4	NA	1	97.1	0.5 (*n* = 50)	52.0	1	100	1	99.4	1 (*n* = 124)	63.7	4	82.8	2	31.6	4	NA	0.03	98.3

All countries	598	4	89.6	4	NA	1	93.5	0.5 (*n* = 65)	60.0	1	98.2	1	99.8	1 (*n* = 533)	71.1	8	64.4	2	44.1	4	NA	0.03	99.2
Penicillin-non-susceptible *S. pneumoniae* [c]																							
Israel	162	4	83.3	4	NA	2	84.0	–	–	2	95.1	1	100	1 (*n* = 162)	50.0	≥16	52.5	4	0.0	4	NA	0.03	100
Jordan	13	4	46.2	8	NA	2	76.9	–	–	2	100	1	100	1 (*n* = 13)	15.4	≥16	30.8	4	0.0	8	NA	0.03	100
Mauritius	7	–	[5]	–	NA	–	[5]	–	–	–	[7]	–	[7]	– (*n* = 7)	[2]	–	[0]	–	[0]	–	NA	–	[7]
Oman	7	–	[7]	–	NA	–	[7]	–	–	–	[7]	–	[7]	– (*n* = 7)	[3]	–	[6]	–	[0]	–	NA	–	[7]
Pakistan	12	0.25	100	0.5	NA	0.25	100	– (*n* = 5)	[3]	0.5	100	1	100	– (*n* = 7)	[7]	≥16	33.3	0.5	0.0	0.5	NA	0.06	100
Saudi Arabia	14	2	92.9	4	NA	2	78.6	–	–	1	100	1	100	0.5 (*n* = 14)	42.9	≥16	35.7	4	0.0	4	NA	0.03	92.9
South Africa	119	4	79.0	4	NA	1	95.8	0.5 (*n* = 36)	33.3	1	100	1	99.2	1 (*n* = 83)	45.8	8	77.3	4	0.0	4	NA	0.06	98.3
All countries	334	4	81.4	4	NA	2	88.3	0.5 (*n* = 41)	36.6	1	97.6	1	99.7	1 (*n* = 293)	47.4	≥16	58.7	4	0.0	4	NA	0.03	99.1
Streptococcus agalactiae																							
Israel	255	0.12	NA	0.12	100	0.12	100	–	–	1	97.3	1	100	≤0.12 (*n* = 255)	100	≥16	20.0	0.12	100	0.5	NA	0.12	100

Jordan	15	0.12	NA	0.12	100	0.25	100	–	–	1	100	2	100	0.5 (*n* = 15)	100	≥16	26.7	0.12	100	0.5	NA	0.5	66.7
Lebanon	10	0.12	NA	0.12	100	0.12	100	≤0.12 (*n* = 10)	NA	1	100	1	100	–	–	≥16	30.0	0.12	100	≥32	NA	2	0
Mauritius	9	–	NA	–	[9]	–	[9]	–	–	–	[9]	–	[9]	– (*n* = 9)	[9]	–	[0]	–	[9]	–	NA	–	[9]
Namibia	5	–	NA	–	[5]	–	[5]	–	–	–	[5]	–	[5]	– (*n* = 5)	[5]	–	[0]	–	[5]	–	NA	–	[5]
Oman	8	–	NA	–	[8]	–	[8]	–	–	–	[8]	–	[8]	– (*n* = 8)	[8]	–	[1]	–	[8]	–	NA	–	[8]
Pakistan	24	0.12	NA	0.12	100	0.12	100	0.25 (*n* = 15)	NA	1	100	1	100	– (*n* = 9)	[9]	≥16	8.3	0.12	100	≤0.25	NA	0.06	100
Saudi Arabia	16	0.12	NA	0.12	100	0.12	100	–	–	1	100	1	100	≤0.12 (*n* = 16)	100	≥16	18.8	≤0.06	100	≤0.25	NA	0.5	68.8
South Africa	123	0.12	NA	0.12	100	0.12	100	0.5 (*n* = 41)	NA	1	100	1	100	≤0.12 (*n* = 82)	100	≥16	8.9	0.12	100	≤0.25	NA	0.12	94.3
All countries	465	0.12	NA	0.12	100	0.12	100	0.25 (*n* = 66)	NA	1	98.5	1	100	≤0.12 (*n* = 399)	100	≥16	16.1	0.12	100	0.5	NA	0.12	94.2
Enterococcus faecalis																							
Israel	284	1	NA	2	99.6	≥128	NA	–	–	≥64	52.8	2	100	8 (*n* = 284)	NA	≥16	27.1	4	99.6	8	NA	0.25	99.6

Jordan	28	1	NA	2	100	≥128	NA	–	–	≥64	53.6	2	100	8 (*n* = 28)	NA	≥16	28.6	4	100	8	NA	0.25	100
Mauritius	9	–	NA	–	[9]	–	NA	–	–	–	[1]	–	[9]	– (*n* = 9)	NA	–	[1]	–	[9]	–	NA	–	[9]
Namibia	13	1	NA	1	100	≥128	NA	–	–	32	76.9	2	100	8 (*n* = 13)	NA	≥16	38.5	4	100	8	NA	0.25	100
Oman	15	0.5	NA	1	100	≥128	NA	–	–	32	66.7	2	100	4 (*n* = 15)	NA	8	40.0	2	100	4	NA	0.12	100
Pakistan	23	2	NA	2	100	≥128	NA	2 (*n* = 11)	NA	≥64	43.5	2	100	≥32 (*n* = 12)	NA	8	17.4	8	100	16	NA	0.12	100
Saudi Arabia	8	–	NA	–	[8]	–	NA	–	–	–	[4]	–	[8]	– (*n* = 8)	NA	–	[2]	–	[8]	–	NA	–	[8]
South Africa	185	1	NA	1	100	≥128	NA	4 (*n* = 54)	NA	≥64	63.8	2	99.5	8 (*n* = 131)	NA	≥16	26.5	4	100	4	NA	0.12	100
All countries	565	1	NA	2	99.8	≥128	NA	4 (*n* = 65)	NA	≥64	56.3	2	99.8	8 (*n* = 500)	NA	≥16	26.9	4	99.8	8	NA	0.25	99.8
Enterococcus faecium																							
Israel	79	≥16	NA	≥32	22.8	≥128	NA	–	–	≥64	16.5	2	100	≥32 (*n* = 79)	NA	≥16	51.9	≥16	26.6	≥32	NA	0.25	100
Jordan	5	–	NA	–	[2]	–	NA	–	–	–	[1]	–	[5]	– (*n* = 5)	NA	–	[4]	–	[1]	–	NA	–	[5]
Mauritius	3	–	NA	–	[1]	–	NA	–	–	–	[1]		[3]	– (*n* = 3)	NA	–	[3]	–	[1]	–	NA	–	[3]

Oman	1	–	NA	–	[0]	–	NA	–	–	–	[0]		[1]	– (*n* = 1)	NA	–	[1]	–	[0]	–	NA	–	[1]
Pakistan	13	≥16	NA	≥32	7.7	≥128	NA	– (*n* = 9)	NA	≥64	15.4	2	100	– (*n* = 4)	NA	≥16	38.5	≥16	7.7	≥32	NA	0.12	100
Saudi Arabia	8	–	NA	–	[2]	–	NA	–	–	–	[1]	–	[8]	– (*n* = 8)	NA	–	[5]	–	[0]	–	NA	–	[8]
South Africa	14	≥16	NA	≥32	28.6	≥128	NA	– (*n* = 6)	NA	≥64	35.7	2	100	– (*n* = 8)	NA	≥16	21.4	≥16	28.6	≥32	NA	0.12	100
All countries	123	≥16	NA	≥32	22.8	≥128	NA	≥32 (*n* = 15)	NA	≥64	18.7	2	100	≥32 (*n* = 108)	NA	≥16	50.4	≥16	22.8	≥32	NA	0.25	100
Vancomycin-resistant *E. faecium*																							
Israel	27	≥16	NA	≥32	3.7	≥128	NA	–	NA	≥64	3.7	2	100	≥32 (*n* = 27)	NA	≥16	55.6	≥16	7.4	≥32	NA	0.25	100
Oman	1	–	NA	–	[0]	–	NA	–	NA	–	[0]	–	[1]	– (*n* = 1)	NA	–	[1]	–	[0]	–	NA	–	[1]
Pakistan	3	–	NA	–	[0]	–	NA	– (*n* = 3)	NA	–	[0]	–	[3]	–	NA	–	[2]	–	[0]	–	NA	–	[3]
Saudi Arabia	1	–	NA	–	[0]	–	NA	–	NA	–	[0]	–	[1]	– (*n* = 1)	NA	–	[1]	–	[0]	–	NA	–	[1]
All countries	32	≥16	NA	≥32	3.1	≥128	NA	– (*n* = 3)	NA	≥64	3.1	2	100	≥32 (*n* = 29)	NA	≥16	59.4	≥16	6.3	≥32	NA	0.25	100

Table 1b

MIC_{90} (in mg/L) and percent antimicrobial susceptibility (%S) for macrolides and clindamycin against isolates of *Streptococcus pneumoniae* (including penicillin-resistant isolates) collected in the Middle East and Africa between 2004 and 2011

	N	AZM		CLR		ERY		CLI	
		MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S
S. pneumoniae									
Israel	321	64	76.3	64	76.0	64	76.0	≥128	87.9
Jordan	14	64	28.6	64	28.6	64	28.6	64	78.6
Mauritius	9	–	[4]	–	[4]	–	[4]	–	[4]
Oman	9	–	[7]	–	[7]	–	[7]	–	[8]
Pakistan	26	64	61.5	≥128	61.5	≥128	61.5	≥128	80.8
Saudi Arabia	15	64	46.7	64	46.7	64	46.7	≥128	73.3
South Africa	147	≥128	66.7	≥128	66.7	≥128	66.7	≥128	72.8
All countries	541	64	70.4	64	70.2	64	70.2	≥128	82.1
Penicillin-non-susceptible *S. pneumoniae* [c]									
Israel	154	64	61.0	64	60.4	64	60.4	≥128	81.2
Jordan	13	64	30.8	64	30.8	64	30.8	64	76.9
Mauritius	7	–	[2]	–	[2]	–	[2]	–	[2]
Oman	4	–	[2]	–	[2]	–	[2]	–	[3]
Pakistan	11	64	36.4	64	36.4	64	36.4	≥128	72.7
Saudi Arabia	12	64	33.3	64	33.3	64	33.3	≥128	66.7

South Africa	105	≥128	54.3	≥128	54.3	≥128	54.3	≥128	62.9
All countries	306	≥128	54.6	≥128	54.2	≥128	54.2	≥128	72.5

MIC_{90}, minimum inhibitory concentration required to inhibit 90% of the isolates; AMC, amoxicillin/clavulanic acid; AMP, ampicillin; CRO, ceftriaxone; IPM, imipenem; LVX, levofloxacin; MEM, meropenem; MIN, minocycline; PEN, penicillin; TZP, piperacillin/tazobactam; TIG, tigecycline; VAN, vancomycin; NA, not applicable.

[a] MIC_{90} and %S are not presented where $n < 10$; instead, the number of susceptible isolates is given in square brackets.

[b] Only countries from which resistant phenotypes have been collected are listed. A single isolate of vancomycin-resistant *E. faecalis* was collected (in Israel) so is not listed here.

[c] Penicillin-intermediate + penicillin-resistant.

Table 2a

MIC_{90} (in mg/L) and percent antimicrobial susceptibility (%S) among Gram-negative isolates (including resistant phenotypes) collected in the Middle East and Africa between 2004 and 2011 [a,b]

	N	AMK		AMC		AMP		FEP		CRO		IPM		LVX		MEM		MIN		TZP		TIG	
		MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S
Enterobacter spp.																							
Israel	611	2	99.3	≥64	2.3	≥64	3.4	8	94.4	64	61.5	–	–	2	90.2	0.12 (*n* = 611)	97.2	16	59.7	64	75.1	2	94.8
Jordan	45	4	97.8	≥64	0.0	≥64	2.2	32	80.0	≥128	62.2	–	–	8	82.2	0.25 (*n* = 45)	100	16	46.7	128	80.0	1	97.8
Lebanon	18	4	100	≥64	5.6	≥64	5.6	8	100	≥128	77.8	1 (*n* = 18)	94.4	0.06	100	–	–	4	100	64	83.3	1	100
Mauritius	10	16	90.0	≥64	0.0	≥64	0.0	≥64	60.0	≥128	10.0	–	–	1	90.0	0.5 (*n* = 10)	90.0	≥32	20.0	≥256	60.0	1	100
Namibia	10	1	100	≥64	10.0	≥64	0.0	1	100	64	80.0	–	–	0.25	100	0.12 (*n* = 10)	100	8	70.0	32	80.0	1	100

Oman	23	2	100	≥64	4.3	≥64	0.0	16	87.0	≥128	78.3	–	–	8	87.0	0.12 (*n* = 23)	95.7	4	91.3	32	87.0	1	100
Pakistan	45	8	91.1	≥64	4.4	≥64	0.0	≥64	57.8	≥128	33.3	1 (*n* = 44)	97.7	≥16	80.0	– (*n* = 1)	[1]	≥32	60.0	≥256	73.3	1	97.8
Saudi Arabia	49	8	98.0	≥64	4.1	≥64	0.0	16	87.8	≥128	69.4	–	–	1	93.9	0.25 (*n* = 49)	100	16	61.2	128	75.5	1	93.9
South Africa	326	8	96.0	≥64	8.3	≥64	3.1	8	90.2	≥128	69.3	1 (*n* = 100)	98.0	4	88.3	0.5 (*n* = 226)	93.8	≥32	79.4	64	82.8	2	95.7
All countries	1137	4	97.9	≥64	4.2	≥64	2.9	8	90.6	≥128	63.3	1 (*n* = 162)	97.5	4	89.3	0.25 (*n* = 975)	96.6	16	66.0	64	77.7	2	95.5
Escherichia coli																							
Israel	651	8	98.8	32	58.5	≥64	22.4	16	87.1	≥128	68.5	–	–	≥16	58.5	≤0.06 (*n* = 651)	96.5	16	65.1	16	92.0	1	100

Jordan	48	8	100	32	45.8	≥64	4.2	≥64	52.1	≥128	37.5	–	–	≥16	33.3	0.12 (*n* = 48)	100	≥32	54.2	≥256	79.2	0.5	97.9
Lebanon	27	8	100	16	44.4	≥64	22.2	32	74.1	≥128	63.0	0.5 (*n* = 27)	100	≥16	55.6	–	–	16	70.4	16	96.3	0.25	100
Mauritius	17	16	100	16	64.7	≥64	23.5	≥64	64.7	≥128	64.7	–	–	≥16	58.8	0.25 (*n* = 17)	100	16	70.6	64	70.6	0.5	100
Namibia	23	4	100	16	47.8	≥64	4.3	1	95.7	8	87.0	–	–	1	91.3	≤0.06 (*n* = 23)	100	≥32	47.8	64	87.0	0.5	100
Oman	26	4	100	16	65.4	≥64	30.8	16	84.6	≥128	76.9	–	–	8	61.5	≤0.06 (*n* = 26)	100	16	73.1	8	92.3	0.25	100
Pakistan	72	8	95.8	≥64	47.2	≥64	13.9	≥64	63.9	≥128	50.0	0.5 (*n* = 72)	100	≥16	37.5	–	–	16	66.7	32	87.5	0.5	100
Saudi Arabia	48	8	95.8	32	64.6	≥64	29.2	≥64	68.8	≥128	66.7	–	–	≥16	58.3	≤0.06 (*n* = 48)	100	16	64.6	64	83.3	0.25	100

South Africa	326	4	99.1	32	63.5	≥64	23.0	8	93.9	8	86.2	0.5 (*n* = 122)	97.5	≥16	76.1	≤0.06 (*n* = 204)	95.6	16	66.9	32	89.9	0.5	100
All countries	1238	8	98.7	32	58.6	≥64	21.5	32	85.0	≥128	71.2	0.5 (*n* = 221)	98.6	≥16	61.6	≤0.06 (*n* = 1017)	96.9	16	65.3	16	90.1	0.5	99.9
ESBL-positive *E. coli*																							
Israel	113	16	96.5	≥64	23.9	≥64	0.0	≥64	42.5	≥128	0.9	–	–	≥16	15.0	0.25 (*n* = 113)	92.9	≥32	56.6	128	79.6	1	100
Jordan	30	8	100	≥64	36.7	≥64	0.0	≥64	23.3	≥128	0.0	–	–	≥16	30.0	0.12 (*n* = 30)	100	≥32	56.7	128	80.0	0.5	96.7
Mauritius	6	–	[6]	–	[1]	–	[0]	–	[0]	–	[0]	–	–	–	[0]	– (*n* = 6)	[6]	–	[4]	–	[1]	–	[6]
Namibia	1	–	[1]	–	[1]	–	[0]	–	[1]	–	[0]	–	–	–	[1]	– (*n* = 1)	[1]	–	[0]	–	[1]	–	[1]
Oman	6	–	[6]	–	[1]	–	[0]	–	[2]	–	[0]	–	–	–	[2]	– (*n* = 6)	[6]	–	[4]	–	[6]	–	[6]

Pakistan	22	8	95.5	≥64	18.2	≥64	4.5	≥64	22.7	≥128	0.0	0.25 (*n* = 22)	100	≥16	4.5			≥32	50.0	16	90.9	0.5	100
Saudi Arabia	15	8	93.3	32	46.7	≥64	0.0	≥64	6.7	≥128	0.0	–	–	≥16	13.3	≤0.06 (*n* = 15)	100	≥32	53.3	128	73.3	0.25	100
South Africa	12	8	100	32	25.0	≥64	0.0	≥64	41.7	≥128	0.0	– (*n* = 4)	[4]	≥16	41.7	– (*n* = 8)	[8]	16	58.3	32	75.0	0.5	100
All countries	205	8	97.1	≥64	26.8	≥64	0.5	≥64	33.7	≥128	0.5	0.25 (*n* = 26)	100	≥16	18.0	0.12 (*n* = 179)	95.5	≥32	56.1	128	79.0	1	99.5
Klebsiella pneumoniae																							
Israel	586	32	89.8	≥64	49.7	≥64	0.9	≥64	66.2	≥128	52.9	–	–	≥16	56.3	≥32 (*n* = 586)	86.2	≥32	50.5	≥256	64.3	2	92.7
Jordan	47	8	95.7	16	57.4	≥64	2.1	≥64	68.1	≥128	55.3	–	–	4	80.9	0.25 (*n* = 47)	100	8	68.1	16	91.5	1	93.6
Mauritius	7	–	[6]	–	[1]	–	[0]	–	[1]	–	[1]	–	–	–	[2]	– (*n* = 7)	[6]	–	[1]	–	[2]	–	[6]

Namibia	23	2	100	16	60.9	≥64	0.0	16	87.0	≥128	69.6	–	–	0.5	100	≤0.06 (*n* = 23)	100	≥32	69.6	64	82.6	1	100
Oman	24	2	100	8	91.7	≥64	0.0	≤0.5	100	≤0.06	95.8	–	–	0.06	100	≤0.06 (*n* = 24)	100	4	91.7	2	100	0.5	100
Pakistan	62	≥128	79.0	≥64	41.9	≥64	0.0	≥64	50.0	≥128	37.1	0.5 (*n* = 60)	100	8	82.3	– (*n* = 2)	[1]	16	62.9	64	82.3	2	93.5
Saudi Arabia	47	16	93.6	32	63.8	≥64	2.1	≥64	59.6	≥128	57.4	–	–	≥16	80.9	0.12 (*n* = 47)	93.6	≥32	66.0	≥256	76.6	2	95.7
South Africa	309	16	93.5	≥64	51.8	≥64	1.6	≥64	62.1	≥128	45.3	1 (*n* = 114)	94.7	≥16	69.6	8 (*n* = 195)	88.2	≥32	63.8	≥256	75.1	2	93.5
All countries	1105	16	91.0	≥64	51.7	≥64	1.1	≥64	64.8	≥128	51.2	1 (*n* = 174)	96.6	≥16	65.2	8 (*n* = 931)	88.3	≥32	57.4	≥256	71.0	2	93.4
ESBL-positive *K. pneumoniae*																							

Israel	151	16	90.7	≥64	9.9	≥64	0.0	≥64	26.5	≥128	0.7	–	–	≥16	31.1	0.25 (*n* = 151)	93.4	≥32	34.4	≥256	41.7	4	84.8
Jordan	21	8	90.5	32	19.0	≥64	0.0	≥64	28.6	≥128	0.0	–	–	4	66.7	0.25 (*n* = 21)	100	8	61.9	32	85.7	4	85.7
Namibia	3	–	[3]	–	[0]	–	[0]	–	[2]	–	[0]	–	–	–	[3]	– (*n* = 3)	[3]	–	[1]	–	[1]	–	[3]
Oman	1	–	[1]	–	[0]	–	[0]	–	[1]	–	[0]	–	–	–	[1]	– (*n* = 1)	[1]	–	[1]	–	[1]	–	[1]
Pakistan	33	≥128	63.6	≥64	15.2	≥64	0.0	≥64	24.2	≥128	0.0	0.5 (*n* = 33)	100	8	78.8	–	–	≥32	48.5	≥256	72.7	2	93.9
Saudi Arabia	20	16	90.0	32	30.0	≥64	0.0	≥64	10.0	≥128	5.0	–	–	≥16	60.0	0.12 (*n* = 20)	90.0	≥32	45.0	≥256	55.0	2	90.0
South Africa	135	16	92.6	≥64	21.5	≥64	0.0	≥64	32.6	≥128	1.5	1 (*n* = 46)	95.7	≥16	46.7	16 (*n* = 89)	84.3	≥32	54.1	≥256	60.0	2	91.9
All countries	364	32	89.0	≥64	16.2	≥64	0.0	≥64	28.3	≥128	1.1	1 (*n* = 79)	97.5	≥16	45.6	0.5 (*n* = 285)	90.9	≥32	45.3	≥256	54.7	4	88.7

Klebsiella oxytoca																							
Israel	54	4	94.4	≥64	81.5	≥64	0.0	16	88.9	64	79.6	–	–	8	77.8	2 (*n* = 54)	88.9	16	85.2	≥256	83.3	1	98.1
Jordan	1	–	[1]	–	[0]	–	[0]	–	[1]	–	[1]	–	–	–	[1]	– (*n* = 1)	[1]	–	[1]	–	[1]	–	[1]
Mauritius	4	–	[4]	–	[3]	–	[1]	–	[3]	–	[3]	–	–	–	[3]	– (*n* = 4)	[4]	–	[3]	–	[3]	–	[4]
Namibia	2	–	[2]	–	[2]	–	[0]	–	[2]	–	[2]	–	–	–	[2]	– (*n* = 2)	[2]	–	[1]	–	[2]	–	[2]
Oman	2	–	[2]	–	[2]	–	[0]	–	[2]	–	[2]	–	–	–	[2]	– (*n* = 2)	[2]	–	[2]	–	[2]	–	[2]
Pakistan	13	≥128	84.6	≥64	38.5	≥64	0.0	32	61.5	≥128	38.5	8 (*n* = 12)	83.3	8	84.6	– (*n* = 1)	[1]	16	69.2	64	84.6	1	92.3
Saudi Arabia	1	–	[1]	–	[0]	–	[0]	–	[0]	–	[0]	–	–	–	[0]	– (*n* = 1)	[1]	–	[0]	–	[0]	–	[0]
South Africa	44	4	100	16	79.5	≥64	0.0	4	90.9	16	81.8	2 (*n* = 14)	78.6	0.5	93.2	≤0.06 (*n* = 30)	100	16	81.8	16	90.9	1	97.7

All countries	121	8	95.9	≥64	75.2	≥64	0.8	16	86.0	≥128	76.0	8 (*n* = 26)	80.8	8	84.3	0.12 (*n* = 95)	93.7	16	81.0	64	86.0	1	96.7
Serratia marcescens																							
Israel	243	4	98.4	≥64	2.5	≥64	1.7	2	97.5	8	81.1	–	–	1	93.4	0.25 (*n* = 243)	98.8	16	51.0	8	96.3	2	91.8
Jordan	17	16	94.1	≥64	5.9	≥64	0.0	16	88.2	64	76.5	–	–	1	100	0.12 (*n* = 17)	100	16	23.5	8	100	2	94.1
Mauritius	6	–	[6]	–	[0]	–	[0]	–	[6]	–	[5]	–	–	–	[6]	– (*n* = 6)	[6]	–	[2]	–	[6]	–	[6]
Oman	3	–	[3]	–	[0]	–	[0]	–	[3]	–	[2]	–	–	–	[3]	– (*n* = 3)	[3]	–	[3]	–	[3]	–	[3]
Pakistan	24	≥128	83.3	≥64	4.2	≥64	0.0	≥64	83.3	≥128	50.0	1 (*n* = 23)	95.7	8	79.2	– (*n* = 1)	[1]	8	87.5	16	91.7	2	95.8
Saudi Arabia	18	4	100	≥64	0.0	≥64	0.0	4	94.4	32	66.7	–	–	0.5	100	0.12 (*n* = 18)	94.4	8	61.1	≥256	72.2	2	94.4

South Africa	133	4	99.2	≥64	8.3	≥64	5.3	2	96.2	8	78.9	1 (*n* = 41)	95.1	1	96.2	0.12 (*n* = 92)	98.9	8	87.2	8	97.7	2	99.2
All countries	444	4	97.7	≥64	4.3	≥64	2.5	2	95.9	16	77.9	1 (*n* = 64)	95.3	1	94.1	0.12 (*n* = 380)	98.7	8	63.3	8	95.7	2	94.6
Pseudomonas aeruginosa																							
Israel	498	16	90.8	≥64	NA	≥64	NA	16	79.9	≥128	NA	–	–	≥16	64.7	16 (*n* = 498)	75.9	≥32	NA	128	67.3	16	NA
Jordan	39	64	87.2	≥64	NA	≥64	NA	32	82.1	≥128	NA	–	–	≥16	64.1	16 (*n* = 39)	74.4	≥32	NA	64	79.5	≥32	NA
Lebanon	19	8	100	≥64	NA	≥64	NA	≥64	68.4	≥128	NA	8 (*n* = 19)	78.9	≥16	68.4	–	–	≥32	NA	128	68.4	≥32	NA
Mauritius	8	–	[4]	–	NA	–	NA	–	[6]	–	NA	–	–	–	[3]	– (*n* = 8)	[4]	–	NA	–	[7]	–	NA
Namibia	22	16	95.5	≥64	NA	≥64	NA	16	86.4	≥128	NA	–	–	4	81.8	1 (*n* = 22)	100	≥32	NA	16	95.5	16	NA
Oman	20	4	90.0	≥64	NA	≥64	NA	16	85.0	≥128	NA	–	–	≥16	80.0	16 (*n* = 20)	80.0	≥32	NA	32	80.0	≥32	NA

Pakistan	60	≥128	76.7	≥64	NA	≥64	NA	≥64	66.7	≥128	NA	8 (*n* = 59)	74.6	≥16	60.0	– (*n* = 1)	[1]	≥32	NA	128	66.7	16	NA
Saudi Arabia	38	64	84.2	≥64	NA	≥64	NA	≥64	73.7	≥128	NA	–	–	≥16	73.7	8 (*n* = 38)	81.6	≥32	NA	≥256	71.1	16	NA
South Africa	271	32	85.6	≥64	NA	≥64	NA	32	77.9	≥128	NA	8 (*n* = 94)	77.7	≥16	65.3	≥32 (*n* = 177)	71.2	≥32	NA	128	80.4	≥32	NA
All countries	975	32	88.0	≥64	NA	≥64	NA	32	78.4	≥128	NA	8 (*n* = 172)	76.7	≥16	65.4	16 (*n* = 803)	75.6	≥32	NA	128	72.6	≥32	NA
Acinetobacter baumannii																							
Israel	342	≥128	25.1	≥64	NA	≥64	NA	≥64	26.6	≥128	8.5	–	–	≥16	21.6	≥32 (*n* = 342)	32.2	8	61.7	≥256	16.7	2	NA
Jordan	20	≥128	45.0	≥64	NA	≥64	NA	≥64	25.0	≥128	0.0	–	–	≥16	40.0	≥32 (*n* = 20)	30.0	8	75.0	≥256	25.0	2	NA
Mauritius	9	–	[6]	–	NA	–	NA	–	[1]	–	[0]	–	–	–	[1]	– (*n* = 9)	[4]	–	[7]	–	[1]	–	NA

Namibia	7	–	[7]	–	NA	–	NA	–	[7]	–	[3]	–	–	–	[7]	– (*n* = 7)	[7]	–	[7]	–	[6]	–	NA
Oman	17	8	94.1	≥64	NA	≥64	NA	32	82.4	≥128	41.2	–	–	4	70.6	2 (*n* = 17)	100	4	100	128	82.4	0.5	NA
Pakistan	40	≥128	20.0	≥64	NA	≥64	NA	≥64	12.5	≥128	5.0	≥32 (*n* = 40)	20.0	≥16	17.5	–	–	4	92.5	≥256	12.5	1	NA
Saudi Arabia	30	≥128	43.3	≥64	NA	≥64	NA	≥64	16.7	≥128	3.3	–	–	≥16	30.0	≥32 (*n* = 30)	20.0	8	80.0	≥256	13.3	1	NA
South Africa	199	≥128	39.2	≥64	NA	≥64	NA	≥64	24.6	≥128	15.1	≥32 (*n* = 75)	68.0	≥16	33.2	≥32 (*n* = 124)	25.8	16	54.3	≥256	28.1	1	NA
All countries	664	≥128	33.6	≥64	NA	≥64	NA	≥64	26.7	≥128	10.8	≥32 (*n* = 115)	51.3	≥16	27.7	≥32 (*n* = 549)	33.2	16	64.2	≥256	22.3	2	NA
Non-*baumannii Acinetobacter* spp.																							
Israel	11	64	63.6	≥64	NA	≥64	NA	≥64	72.7	≥128	63.6	–	–	8	54.5	≥32 (*n* = 11)	72.7	8	81.8	≥256	72.7	2	NA

Lebanon	14	≥128	7.1	≥64	NA	≥64	NA	≥64	0.0	≥128	0.0	≥32 (*n* = 14)	21.4	≥16	0.0	–	–	8	85.7	≥256	0.0	1	NA
Pakistan	1	–	[1]	–	NA	–	NA	–	[1]	–	[1]	– (*n* = 1)	[1]	–	[1]	–	–	–	[1	–	[1]	–	NA
South Africa	7	–	[4]	–	NA	–	NA	–	[5]	–	[4]	–	–	–	[4]	– (*n* = 7)	[4]	–	[6]	–	[5]	–	NA
All countries	33	≥128	39.4	≥64	NA	≥64	NA	≥64	42.4	≥128	36.4	≥32 (*n* = 15)	26.7	≥16	33.3	≥32 (*n* = 18)	66.7	8	84.8	≥256	42.4	1	NA
Haemophilus influenzae																							
Israel	331	8	NA	2	100	32	78.2	≤0.5	100	≤0.06	100	–	–	0.03	100	0.25 (*n* = 331)	100	2	97.6	≤0.06	100	0.25	100
Jordan	15	8	NA	2	100	32	80.0	≤0.5	100	≤0.06	100	–	–	0.06	100	0.25 (*n* = 15)	100	1	100	≤0.06	100	0.25	100
Lebanon	16	4	NA	2	100	≥64	81.3	≤0.5	100	≤0.06	100	1 (*n* = 16)	100	0.015	100	–	–	≤0.5	100	≤0.06	100	0.5	87.5

Mauritius	1	–	NA	–	[1]	–	[0]	–	[1]	–	[1]	–	–	–	[1]	– (*n* = 1)	[1]	–	[1]	–	[1]	–	[1]
Oman	14	8	NA	1	100	8	78.6	≤0.5	100	≤0.06	100	–	–	0.015	100	0.12 (*n* = 14)	100	≤0.5	92.9	≤0.06	100	0.25	100
Pakistan	29	8	NA	0.5	100	32	89.7	≤0.5	100	≤0.06	100	1 (*n* = 29)	100	0.5	100	–	–	2	93.1	≤0.06	100	0.25	100
Saudi Arabia	23	4	NA	2	100	32	73.9	≤0.5	100	≤0.06	100	–	–	0.015	100	≤0.06 (*n* = 23)	100	1	100	≤0.06	100	0.25	100
South Africa	176	8	NA	1	100	1	90.3	≤0.5	100	≤0.06	100	1 (*n* = 46)	100	0.03	100	0.25 (*n* = 130)	100	1	98.9	≤0.06	99.4	0.25	100
All countries	605	8	NA	1	100	16	82.1	≤0.5	100	≤0.06	100	1 (*n* = 91)	100	0.03	100	0.25 (*n* = 514)	100	1	97.9	≤0.06	99.8	0.25	99.7
β-Lactamase-positive *H. influenzae*																							
Israel	69	8	NA	2	100	≥64	0.0	≤0.5	100	≤0.06	100	–	–	0.03	100	0.12 (*n* = 69)	100	2	97.1	≤0.06	100	0.25	100

Jordan	3	–	NA	–	[3]	–	[0]	–	[3]	–	[3]	–	–	–	[3]	– (*n* = 3)	[3]	–	[3]	–	[3]	–	[3]
Lebanon	3	–	NA	–	[3]	–	[0]	–	[3]	–	[3]	– (*n* = 3)	[3]	–	[3]	–	–	–	[3]	–	[3]	–	[2]
Mauritius	1	–	NA	–	[1]	–	[0]	–	[1]	–	[1]	–	–	–	[1]	– (*n* = 1)	[1]	–	[1]	–	[1]	–	[1]
Oman	3	–	NA	–	[3]	–	[0]	–	[3]	–	[3]	–	–	–	[3]	– (*n* = 3)	[3]	–	[3]	–	[3]	–	[3]
Pakistan	3	–	NA	–	[3]	–	[0]	–	[3]	–	[3]	– (*n* = 3)	[3]	–	[3]	–	–	–	[3]	–	[3]	–	[3]
Saudi Arabia	6	–	NA	–	[6]	–	[0]	–	[6]	–	[6]	–	–	–	[6]	– (*n* = 6)	[6]	–	[6]	–	[6]	–	[6]
South Africa	13	8	NA	4	100	≥64	0.0	≤0.5	100	≤0.06	100	– (*n* = 4)	[4]	0.015	100	– (*n* = 9)	[9]	1	100	≤0.06	100	0.25	100
All countries	101	8	NA	2	100	≥64	0.0	≤0.5	100	≤0.06	100	1 (*n* = 10)	100	0.03	100	0.12 (*n* = 91)	100	2	98.0	≤0.06	100	0.25	99.0

Table 2b

MIC_{90} (in mg/L) and percent antimicrobial susceptibility (%S) for ceftazidime against isolates of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* collected in the Middle East and Africa between 2004 and 2011

	N	MIC_{90}	%S
P. aeruginosa			
Israel	498	32	71.1
Jordan	39	32	82.1
Lebanon	19	≥64	73.7
Mauritius	8	–	[5]
Namibia	22	16	81.8
Oman	20	16	80.0
Pakistan	60	≥64	65.0
Saudi Arabia	38	32	76.3
South Africa	271	16	84.9
All countries	975	32	75.6
A. baumannii			
Israel	342	≥64	17.5
Jordan	20	≥64	30.0
Mauritius	9	–	[1]
Namibia	7	–	[7]
Oman	17	≥64	82.4
Pakistan	40	≥64	7.5
Saudi Arabia	30	≥64	20.0
South Africa	199	≥64	25.6
All countries	664	≥64	22.3

MIC_{90}, minimum inhibitory concentration required to inhibit 90% of the isolates; AMK, amikacin; AMC, amoxicillin/clavulanic acid; AMP, ampicillin; FEP, cefepime; CRO, ceftriaxone; IPM, imipenem; LVX, levofloxacin; MEM, meropenem; MIN, minocycline;

TZP, piperacillin/tazobactam; TIG, tigecycline; ESBL, extended-spectrum β-lactamase; NA, not applicable.

[a] MIC_{90} and %S are not presented where $n < 10$; instead, the number of susceptible isolates is given in square brackets.

[b] Only countries from which resistant phenotypes have been collected are listed. Only seven ESBL-positive *K. oxytoca* isolates were collected (one in Saudi Arabia, two in Israel and four in South Africa) so are not listed here.

Table 3

Prevalence of total and resistance phenotypes among isolates collected in the Middle East and Africa between 2004 and 2011

Organism	Country	Total *N*	% with resistance phenotype (*n*) [a]
Gram-positive isolates			
Meticillin-resistant *Staphylococcus aureus*	Israel	631	30.1 (190)
	Jordan	29	31.0 (9)
	Lebanon	25	32.0 (8)
	Mauritius	24	45.8 (11)
	Namibia	24	12.5 (3)
	Oman	29	13.8 (4)
	Pakistan	62	12.9 (8)
	Saudi Arabia	42	23.8 (10)
	South Africa	350	27.1 (95)
	Middle East/Africa	1216	27.8 (338)
Penicillin-resistant *Streptococcus pneumoniae*	Israel	336	19.9 (67)
	Jordan	14	71.4 (10)
	Mauritius	9	– (7)
	Oman	15	20.0 (3)
	Pakistan	32	0.0 (0)
	Saudi Arabia	18	33.3 (6)
	South Africa	174	25.9 (45)
	Middle East/Africa	598	23.1 (138)
Penicillin-non-susceptible *S. pneumoniae*	Israel	336	48.2 (162)
	Jordan	14	92.9 (13)

	Mauritius	9	– (7)
	Oman	15	46.7 (7)
	Pakistan	32	37.5 (12)
	Saudi Arabia	18	77.8 (14)
	South Africa	174	68.4 (119)
	Middle East/Africa	598	55.9 (334)
Vancomycin-resistant *Enterococcus faecium*	Israel	79	34.2 (27)
	Jordan	5	– (0)
	Mauritius	3	– (0)
	Oman	1	– (1)
	Pakistan	13	23.1 (3)
	Saudi Arabia	8	– (1)
	South Africa	14	0.0 (0)
	Middle East/Africa	123	26.0 (32)
Gram-negative isolates			
ESBL-positive *Escherichia coli*	Israel	651	17.4 (113)
	Jordan	48	62.5 (30)
	Lebanon	27	0.0 (0)
	Mauritius	17	35.3 (6)
	Namibia	23	4.3 (1)
	Oman	26	23.1 (6)
	Pakistan	72	30.6 (22)
	Saudi Arabia	48	31.3 (15)
	South Africa	326	3.7 (12)
	Middle East/Africa	1238	16.6 (205)
ESBL-positive *Klebsiella pneumoniae*	Israel	586	25.8 (151)
	Jordan	47	44.7 (21)

	Mauritius	7	– (0)
	Namibia	23	13.0 (3)
	Oman	24	4.2 (1)
	Pakistan	62	53.2 (33)
	Saudi Arabia	47	42.6 (20)
	South Africa	309	43.7 (135)
	Middle East/Africa	1105	32.9 (364)
BL-positive *Haemophilus influenzae*	Israel	331	20.8 (69)
	Jordan	15	20.0 (3)
	Lebanon	16	18.8 (3)
	Mauritius	1	– (1)
	Oman	14	21.4 (3)
	Pakistan	29	10.3 (3)
	Saudi Arabia	23	26.1 (6)
	South Africa	176	7.4 (13)
	Middle East/Africa	605	16.7 (101)

ESBL, extended-spectrum β-lactamase; BL, β-lactamase.

[a] % prevalence is not presented where $N < 10$.

A single isolate of vancomycin-resistant *Enterococcus faecalis* was collected (in Israel) so is not listed here. Only seven ESBL-positive *Klebsiella oxytoca* isolates were collected (one in Saudi Arabia, two in Israel and four in South Africa) so are not listed here.

No isolates of penicillin-non-susceptible *S. pneumoniae* or vancomycin-resistant *E. faecium* were reported in Lebanon or Namibia; no ESBL-positive *K. pneumoniae* were recorded in Lebanon; and no BL-positive *H. influenzae* were collected from Namibia.