

Antimicrobial resistance surveillance in the South African private sector report for 2016

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Aim: The relevance of surveillance for antimicrobial resistance is increasingly recognised in the light of a global action plan to combat resistance. This report presents antimicrobial susceptibility testing on ESKAPE pathogens from private sector laboratories in South Africa for 2016.

Methods: Antimicrobial susceptibility testing (AST) performed on ESKAPE organisms (*Enterococcus faecium*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter cloacae* and *Escherichia coli*) isolated from blood cultures at four private pathology laboratories in 2016 were analysed. Analysis and reporting of data were done via a uniform platform created by the NICD for national AST data.

Results: AST were reported on 9 029 ESKAPE organisms including 58% Enterobacteriaceae, 28% Gram-positive bacteria and 14% Gram-negative bacteria and drug-bug combination was performed following the Global Antimicrobial Surveillance System (GLASS) guidelines by the World Health Organization.

Conclusions: The most important resistance to address is a high level of ESBL in Enterobacteriaceae, which necessitates the use of carbapenems for treatment. Resistance to carbapenems is recorded in this report but not confirmation of genes by genotypic methods. During this period, no increase in vancomycin-resistant Enterococci was observed.

Keywords: antimicrobial resistance, surveillance, ESKAPE organisms

Introduction

Over the last 20 years, antimicrobial resistance (AMR) has reached a pandemic level.¹ According to estimates by the US Centres for Disease Control and Prevention, each year more than two million people are infected with antimicrobial-resistant microorganisms of whom 23 000 die due to these infections.¹ The Global Report on Surveillance by the World Health Organization indicated that AMR is on the increase in Africa.² However, accurate and reliable data are limited and as a result the true extent of the problem is unknown.² Here we report on a select group of bacteria that not only cause healthcare-associated infections, but also effectively 'escape' the effects of antimicrobial agents. This group of bacteria is known by the acronym, ESKAPE.³ The aim of this report was to describe the spectrum of ESKAPE pathogens (*Enterococcus faecium*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter cloacae* and *Escherichia coli*) together with their antimicrobial susceptibility testing (AST) patterns identified from private-sector laboratories across South Africa.

Methods

Secondary data analysis was conducted on ESKAPE isolates identified from four accredited private sector pathology laboratories (Ampath, Lancet Laboratories, PathCare and Vermaak

and Partners) located in all nine provinces in South Africa, from January to December 2016. The study population was all patients who had a blood culture submitted to a private laboratory. We could not distinguish hospital-associated infections from community-associated infections as admission data were not available at the time of analysis. Positive blood cultures with any one of the ESKAPE organisms isolated were included in the analysis. A 21-day de-duplication rule was applied to all positive blood cultures. AST and interpretation of results were performed according to Clinical and Laboratory Standards Institute (CLSI) 2016 guidelines.⁴ AST results were categorised based on categorical data, i.e. susceptible (S) and non-susceptible, including intermediate (I) and resistant (R). Reporting of susceptibility patterns for drug-bug combinations was performed based on the Global Antimicrobial Surveillance System (GLASS) manual.⁵ No patient demographic or clinical data were available. AST data for specified ESKAPE isolates were extracted from a secure web-based electronic platform created by the Surveillance Information Management Unit (SIMU) at the National Institute for Communicable Diseases (NICD). These data are available on the AMR dashboard from the NICD website accessible at <http://www.nicd.ac.za>. Absolute frequencies, percentages, bar charts and tables were used to describe the data.

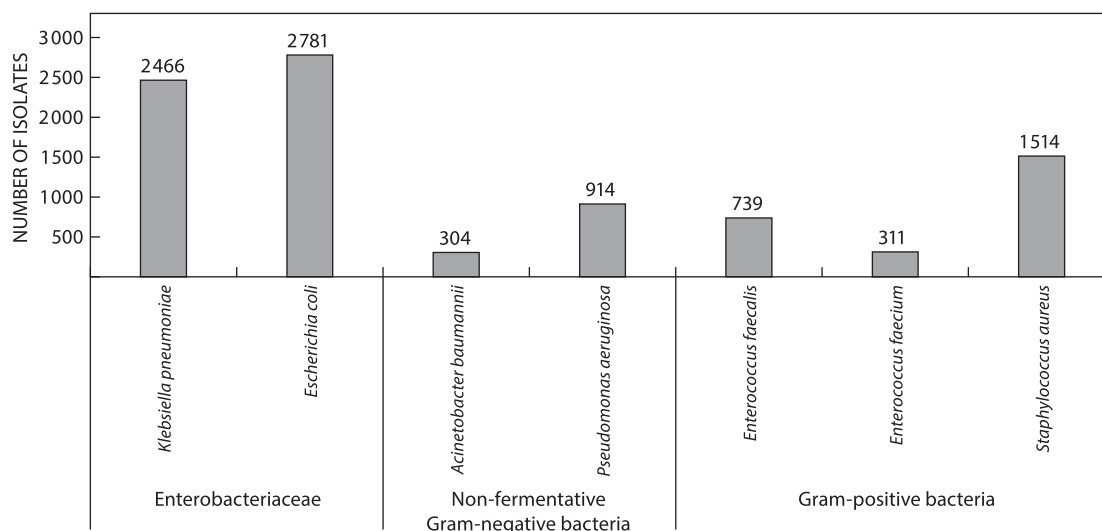


Figure 1: Number of ESKAPE isolates identified from blood cultures, January to December 2016.

Results

For the purpose of this report, ESKAPE pathogen profiles were categorised as Enterobacteriaceae (*Klebsiella pneumoniae* and *Escherichia coli*), non-fermentative Gram-negative bacteria (*Acinetobacter baumannii* and *Pseudomonas aeruginosa*) and Gram-positive bacteria (*Enterococcus faecalis*, *Enterococcus faecium* and *Staphylococcus aureus*). Of the 9 029 blood cultures that grew ESKAPE organisms, 58% (5 247) were Enterobacteriaceae, 28% ($n = 2 564$) were Gram-positive bacteria and 14% ($n = 1218$) were non-fermentative Gram-negative bacteria. Of the seven ESKAPE organisms, *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus* were the three organisms most commonly isolated from blood cultures (Figure 1).

Enterobacteriaceae

Klebsiella pneumoniae

Forty-three per cent and 20% of *K. pneumoniae* isolates were non-susceptible to the aminoglycosides, gentamicin and amikacin, respectively. Forty-one per cent and 25% of isolates were non-susceptible to the quinolones, ciprofloxacin and levofloxacin, respectively. Non-susceptibility to the third-generation cephalosporins, cefotaxime/ceftriaxone and ceftazidime, was from 55% to 57%, while non-susceptibility to the fourth-generation cephalosporin, cefepime, was 56%. Fifty-seven per cent of isolates were non-susceptible to the beta-lactam + beta-lactamase inhibitor, piperacillin/tazobactam. Less than 10% of isolates were non-susceptible to the carbapenems: imipenem, meropenem and doripenem, but 15% were non-susceptible to ertapenem (Table 1).

Escherichia coli

Fifteen per cent and 6% of *E. coli* isolates were non-susceptible to the aminoglycosides, gentamicin and amikacin, respectively. Thirty-one per cent and 25% of isolates were non-susceptible to the quinolones, ciprofloxacin and levofloxacin, respectively. Non-susceptibility to the third-generation cephalosporins, cefotaxime/ceftriaxone and ceftazidime, was from 18% to 19%, while non-susceptibility to the fourth-generation cephalosporin, cefepime was 18%. Twenty per cent of isolates were non-susceptible to the beta-lactam + beta-lactamase inhibitor, piperacillin/tazobactam. Less than 1% of isolates were non-susceptible to the carbapenems: imipenem, meropenem, ertapenem and doripenem, respectively (Table 1).

Non-fermentative Gram-negative bacteria

Acinetobacter baumannii

Forty-seven per cent and 37% of *A. baumannii* isolates were non-susceptible to the aminoglycosides, gentamicin and amikacin, respectively. Non-susceptibility to the carbapenems, imipenem and meropenem, were from 54% to 56%, while non-susceptibility to doripenem was observed in 53% of the isolates. Susceptibility patterns for tetracycline and minocycline were not reported; however, 10% of isolates were non-susceptible to tigecycline (Table 2).

Pseudomonas aeruginosa

Less than 30% of *P. aeruginosa* isolates were non-susceptible to the third-generation cephalosporin, ceftazidime, and the fourth-generation cephalosporin, cefepime. Non-susceptibility to the carbapenems, meropenem and imipenem, was 36% and 38%, while non-susceptibility to doripenem was observed in 32% of the isolates. Thirty-six per cent of isolates were non-susceptible to the beta-lactam + beta-lactamase inhibitor, piperacillin/tazobactam (Table 2).

Gram-positive bacteria

Enterococcus species

Enterococcus faecalis. Twenty-five per cent of *E. faecalis* isolates were non-susceptible to penicillin/ampicillin. Less than 1% of isolates were non-susceptible to the glycopeptides, teicoplanin and vancomycin, respectively. Less than 1% of isolates were non-susceptible to the oxazolidinone, linezolid (Table 3).

Enterococcus faecium. A high proportion of *E. faecium* isolates (92%) were non-susceptible to penicillin/ampicillin. Four per cent and 5% of isolates were non-susceptible to the glycopeptides, teicoplanin and vancomycin, respectively. Low levels of non-susceptibility were observed in 2% of isolates to the oxazolidinone, linezolid (Table 3).

Staphylococcus aureus. Twenty-six per cent of *S. aureus* isolates were non-susceptible to cloxacillin and could be classified as methicillin-resistant *S. aureus* (MRSA) (Table 4).

Discussion

Almost the same number of ESKAPE pathogens were isolated from blood cultures in public sector, 10 952 compared with

Table 1: Antimicrobial susceptibility patterns of Enterobacteriaceae isolated from blood cultures reported from four private groups in South Africa, January 1, 2016 to December 31, 2016

Antimicrobial agent	<i>Klebsiella pneumoniae</i> complex					<i>Escherichia coli</i>				
	Number of isolates tested	Non-susceptible		Susceptible		Number of isolates tested	Non-susceptible		Susceptible	
		n	%	n	%		n	%	n	%
Amikacin	2 444	480	19.6	1964	80.4	2 781	183	6.6	2598	93.4
Amoxicillin-clavulanic acid	2 450	1475	60.2	975	39.8	2 780	835	30.0	1945	70.0
Ampicillin/amoxicillin	–	–	–	–	–	1 998	1569	78.5	425	21.3
Cefepime	2 435	1365	56.1	1070	43.9	2 778	495	17.8	2283	82.2
Cefotaxime/ceftriaxone	2 442	1390	56.9	1052	43.1	2 777	524	18.9	2253	81.1
Ceftazidime	1 760	971	55.2	789	44.8	2 148	393	18.3	1755	81.7
Ciprofloxacin	2 068	837	40.5	1231	59.5	1 997	619	31.0	1378	69.0
Cotrimoxazole	1 853	1064	57.4	789	42.6	1 746	1089	62.4	657	37.6
Doripenem	2 376	191	8.0	2185	92.0	2 753	5	0.2	2748	99.8
Ertapenem	2 419	363	15.0	2056	85.0	2 779	10	0.4	2769	99.6
Gentamicin	2 442	1037	42.5	1405	57.5	2 779	411	14.8	2368	85.2
Imipenem	2 410	235	9.8	2175	90.2	2 777	5	0.2	2772	99.8
Levofloxacin	509	127	25.0	382	75.0	792	199	25.1	593	74.9
Meropenem	2 431	225	9.3	2206	90.7	2 780	3	0.1	2777	99.9
Piperacillin/tazobactam	2 443	1393	57.0	1050	43.0	2 774	562	20.3	2212	79.7

Abbreviations: number of isolates (n), percentage (%), not reported (–).

Colistin was not reported as no reference method was applied at private-sector laboratories.

9 029 from private laboratories (unpublished data) in 2016. In the private sector 56% of *K. pneumoniae* isolates ($n = 2\,466$) were resistant to third and fourth generation cephalosporins compared with 65% ($n = 2\,783$) in the public sector (unpublished data). Of the total number of *E. coli* isolates ($n = 2\,781$), 18% showed non-susceptibility to third and fourth generation cephalosporins in the private sector compared with 28% of *E. coli* isolates ($n = 1850$) in the public sector, while 30% were non-susceptible to ciprofloxacin in both sectors.

Regarding non-fermentative Gram-negative bacteria, 56% of *A. baumannii* isolates ($n = 304$) were non-susceptible to carbapenems in the private sector while 80% ($n = 2318$) in the public sector.

P. aeruginosa isolates showed similar susceptibility patterns in both public and private sectors.

Gram-positive organisms showed very stable susceptibility patterns and no vancomycin-resistant Enterococci outbreaks were

Table 2: Antimicrobial susceptibility patterns of non-fermenters isolated from blood cultures reported from four private groups in South Africa, January 1, 2016 to December 31, 2016

Antimicrobial agent	<i>Acinetobacter baumannii</i>					<i>Pseudomonas aeruginosa</i>				
	Number of isolates tested	Non-susceptible		Susceptible		Number of isolates tested	Non-susceptible		Susceptible	
		n	%	n	%		n	%	n	%
Amikacin	288	106	36.8	182	63.2	–	–	–	–	–
Cefepime	–	–	–	–	–	908	256	28.2	652	71.8
Ceftazidime	–	–	–	–	–	892	235	26.3	657	73.7
Doripenem	257	137	53.3	120	46.7	883	282	31.9	601	68.1
Gentamicin	303	142	46.9	161	53.1	–	–	–	–	–
Imipenem	304	165	54.3	139	45.7	911	344	37.8	567	62.2
Meropenem	304	171	56.3	133	43.8	912	324	35.5	588	64.5
Piperacillin/tazobactam	–	–	–	–	–	902	320	35.5	582	64.5
Tigecycline	212	22	10.4	190	89.6	–	–	–	–	–

Abbreviations: number of isolates (n), percentage (%), not reported (–).

Colistin was not reported as no reference method was applied at private-sector laboratories.

Table 3: Antimicrobial susceptibility patterns of enterococci species isolated from blood cultures reported from four private groups in South Africa, January 1, 2016 to December 31, 2016

Antimicrobial agent	<i>Enterococcus faecalis</i>					<i>Enterococcus faecium</i>				
	Number of isolates tested	Non-susceptible		Susceptible		Number of isolates tested	Non-susceptible		Susceptible	
		n	%	n	%		n	%	n	%
Daptomycin	168	N/A	N/A	168	100.0	65	N/A	N/A	63	96.9
Linezolid	511	3	0.6	508	99.4	215	5	2.3	210	97.7
Penicillin/ampicillin	88	22	25.0	66	75.0	38	35	92.1	3	7.9
Teicoplanin	695	3	0.4	692	99.6	295	12	4.1	283	95.9
Vancomycin	726	2	0.3	724	99.7	309	14	4.5	295	95.5

Abbreviations: number of isolates (n), percentage (%).

Table 4: Antimicrobial susceptibility patterns of *Staphylococcus aureus* isolated from blood cultures reported from four private groups in South Africa, January 1, 2016 to December 31, 2016

Antimicrobial agent	<i>Staphylococcus aureus</i>				
	Number of isolates tested	Non-susceptible		Susceptible	
		n	%	n	%
Cloxacillin	1 283	333	26.0	950	74.0

Abbreviations: number of isolates (n), percentage (%).

noted during this period. MRSA was identified in 30% of *S. aureus* isolates (n = 2 338) from the public sector and 26% isolates (n = 1283) in the private sector.

Limitations

In this report, not all private laboratories were included (only the four largest private groups). Another limitation is the different practices employed by private laboratories, which may influence specimen submission practices and the testing and reporting of results. For instance, in this report we observed that for each of the ESKAPE pathogens, the number of isolates tested for the various antimicrobial agents was different. We have not been able to report on colistin AST due to changed methodology by the CLSI and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) in 2017. Data in this report represents a snapshot over only one year, thus long-term data are required for trend analysis.

Conclusions

K. pneumoniae and *E. coli* remained the commonest blood culture pathogens in the private sector for 2016. More than 50% of *K. pneumoniae* isolates and more than 15% of *E. coli* isolates were non-susceptible to the third- and fourth-generation cephalosporins, which is of concern. Carbapenem resistance among non-fermentative Gram-negative bacteria is alarming. Less than 50% of *A. baumannii* isolates were susceptible to carbapenems. From all *P. aeruginosa* isolates, 65% were susceptible to piperacillin/tazobactam. On a positive note, 75% of *E. faecalis* isolates were susceptible to penicillin/ampicillin with less than 1% showing non-susceptibility to the glycopeptides. However, as expected, only 8% of *E. faecium* isolates were susceptible to

penicillin/ampicillin with less than 5% showing non-susceptibility to the glycopeptides. The prevalence of vancomycin resistance was higher among *E. faecium* isolates compared with *E. faecalis* isolates. Approximately one-quarter of all *S. aureus* bacteraemia was caused by MRSA. This report represents national data and it should be stressed that local and/or institutional level data should be utilised to help direct empiric treatment guidelines.

Disclaimer

Data are reported as received through the SIMU. No demographic, epidemiological, clinical or molecular data were available to distinguish between healthcare-associated and community-associated infections. CHARM is not responsible for testing or reporting results at patient level.

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