Antimicrobial susceptibility patterns of selected bacteraemic isolates from South African public sector hospitals, 2010

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We report on antimicrobial susceptibility surveillance data for six key bloodstream pathogens *(Escherichia coli, Klebsiella pneumoniae, Enterobacter* spp., *Pseudomonas aeruginosa, Acinetobacter baumannii* and *Staphylococcus aureus*) identified in public sector hospitals in South Africa during 2010. Major findings include the accelerated emergence of carbapenem resistance among *K. pneumoniae* and *Enterobacter* species, with overall susceptibility rates of 98% and 96% for ertapenem, and above 99% for meropenem and imipenem. Levels of resistance among *P. aeruginosa* and *A. baumannii* remain high in all centres, with few changes since 2009. Large decreases in piperacillin-tazobactam susceptibility rates were noted at three institutions, probably related to methodological issues. *S. aureus* remains a major pathogen countrywide, with between 30-60% of isolates resistant to cloxacillin [methicillin-resistant *S. aureus* (MRSA)]. Ongoing surveillance for antimicrobial resistance is vital, and the use of a centralised data extraction system may aid in this.

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Introduction

Regular surveillance of local antimicrobial susceptibility patterns is recommended, as it can provide information on new, or changing, patterns of resistance, and may be useful in informing clinician prescribing and choice of empiric therapy. The South African Society for Clinical Microbiology is a voluntary professional association, which is continuing the antimicrobial surveillance activities previously carried out by the National Antibiotic Surveillance Forum (NASF), and its predecessor organisations. Previous reports on bloodstream isolates identified in public sector laboratories, documented, among other findings, the markedly greater resistance in *Klebsiella pneumoniae,* compared to *Escherichia coli*, as well as a general upward trend in resistance in these two organisms between 2001-2004.[1] A report from 2007 suggested stabilisation of resistance levels, but figures from 2009 revealed increasing resistance to ciprofloxacin, and increased levels of extended-spectrum beta-lactamase (ESBL) production in *K. pneumoniae,* as well as high levels of methicillin-resistant *Staphylococcus aureus* (MRSA).[2,3] Reports from South African private sector laboratories have highlighted similar concerns with MRSA and ESBL producers, as well as high levels of resistance in *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.[4] Here we report on antimicrobial susceptibility surveillance data for six key bloodstream pathogens identified in public sector hospitals in South Africa during the 12 months between January-December 2010.

Methodology

Antimicrobial susceptibility testing was carried out on site by accredited National Health Laboratory Service (NHLS) laboratories. The following laboratories, located in different cities, participated in antimicrobial surveillance in 2010: Chris Hani Baragwanath (Johannesburg), Charlotte Maxeke Johannesburg Academic (Johannesburg), Steve Biko Academic (Pretoria), Universitas (Bloemfontein), Groote Schuur (Cape Town), Tygerberg (Cape Town), and Green Point NHLS laboratory (Cape Town).

Laboratories used a variety of testing methodologies (see Table I), and interpreted results according to the contemporary 2010 Clinical and Laboratory Standards Institute (CLSI) criteria.[5] Data on final authorised results were transferred to the NHLS centralised data repository, Central Data Warehouse

Table I: Methods of antimicrobial susceptibility testing utilised by participating laboratories, for selected organisms, isolated from blood culture

Organism group	Participating laboratories						
	NHLS, Chris Hani Baragwanath	NHLS, Charlotte Maxeke Johannesburg Academic	NHLS, Steve Biko Academic	NHLS, Universitas	NHLS, Groote Schuur	NHLS, Tygerberg	NHLS, Green Point
Gram-negative bacilli	MicroScan®	MicroScan®	Vitek 2®	Disc diffusion	Vitek 2®	Vitek 2®	Vitek 2®
Staphylococcus aureus	Disc diffusion, Etest®	Disc diffusion Etest®, MicroScan®	Vitek 2®, Etest®	Disc diffusion	Disc diffusion, Etest®	Disc diffusion, Etest®	Disc diffusion

Vitek®: BioMérieux, North Carolina. MicroScan®: Dade Behring Inc, California

(CDW). Data for specified organisms, isolated from bloodstream infections, were extracted by computer programme from CDW on a quarterly, and annual, basis. Subsequently, the data extracts were reviewed by local pathologists to ensure consistency with local experience.

Guidelines on reporting of cumulative AST data were followed, in that susceptibility test results were omitted if a laboratory reported < 30 isolates per annum, or if selective testing was performed. For these reasons, 2010 data from Dr George Mukhari were excluded, as were data from Green Point NHLS laboratory for ESBL and carbapenem susceptibility testing, and for *P. aeruginosa* and *A. baumannii*.[6] However, because of computer software limitations, it was not possible to exclude duplicate isolates as recommended by the guidelines.[6] Results are reported as percentage susceptible, with 95% confidence intervals calculated by the Clopper-Pearson method.[6] Categorical data were analysed using a chi-square test. Specific data on ESBL production were not reliably reported, and hence ESBL production was inferred if *E.coli* and *K. pneumoniae* isolates were reported as resistant to cefepime. Since this inference is unreliable in *Enterobacter* spp., ESBL production is not reported for these isolates, but simply cefepime susceptibility rates.

Antimicrobial susceptibility results were reported for the following six organisms: *E. coli*, *K. pneumoniae*, *Enterobacter* spp., *P. aeruginosa, A. baumannii* and *S. aureus*. Community-acquired meningeal, respiratory, or diarrhoeal pathogens, that

Table II: Susceptibility of *Escherichia coli* isolated from blood to selected antimicrobial agents at 7 participating laboratories, South Africa, 2010.

Participating laboratories	Antimicrobial agent						
	Gentamicin-susceptible, n/N (%) (95% CI)	**Amikacin-susceptible, n/N (%) (95% CI)**	**Ciprofloxacin-susceptible, n/N (%) (95% CI)**	**ESBL producer, n/N (%) (95% CI)**	**Ertapenem-susceptible, n/N (%) (95% CI)**	**Imipenem-susceptible, n/N (%) (95% CI)**	**Meropenem-susceptible, n/N (%) (95% CI)**
NHLS Chris Hani Baragwanath	370/465 (80) (76-83)	450/463 (97) (95-98)	384/463 (83) (79-86)	79/463 (17) (14-21)	462/463 (100) (99-100)	463/463 (100) (99-100)	462/463 (100) (99-100)
NHLS Charlotte Maxeke Johannesburg Academic	222/261 (85) (80-89)	252/261 (97) (94-98)	219/264 (83) (78-87)	31/262 (12) (8-16)	264/264 (100) (99-100)	262/262 (100) (99-100)	260/260 (100) (99-100)
NHLS Steve Biko Academic	218/270 (81) (76-85)	183/250 (73) (67-79)	162/241 (67) (61-73)	64/252 (25) (20-31)	213/213 (100) (98-100)	243/243 (100) (98-100)	242/242 (100) (98-100)
NHLS Universitas	59/67 (88) (78-95)	57/61 (93) (84-98)	56/67 (84) (73-92)	2/62 (3) (0-11)	63/63 (100) (94-100)	61/61 (100) (91-100)	41/41 (100) (94-100)
NHLS Groote Schuur	190/231 (82) (77-87)	194/217 (89) (85-93)	182/223 (82) (76-86)	34/217 (16) (11-21)	217/217 (100) (98-100)	217/217 (100) (98-100)	217/217 (100) (98-100)
NHLS Tygerberg	101/118 (86) (78-91)	97/118 (82) (74-89)	107/116 (92) (86-96)	13/116 (11) (6-18)	114/114 (100) (97-100)	116/116 (100) (97-100)	116/116 (100) (97-100)
NHLS Green Point	107/124 (86) (79-92)	101/111 (91) (84-96)	115/125 (92) (86-96)				
Total	**1 267/1 536 (82)**	**1 334/1 481 (90)**	**1 225/1 499 (82)**	**225/1 375 (16)**	**1 344/1 345 (100)**	**1 373/1 373 (100)**	**1 349/1 350 (100)**

n = number susceptible, N = number tested, % = percentage susceptible, 95% CI = 95% confidence interval

were previously included in NASF surveillance reports, were excluded as national surveillance data are reported regularly by the Group for Enteric, Respiratory and Meningeal disease Surveillance in South Africa (GERMS-SA).[7] The choice of antibiotics to be reported was determined by members of the NASF in 2009. The following criteria influenced their decisions: the antibiotic was included in routine susceptibility testing panels in most, if not all, laboratories; and the antibiotic was available in South Africa, and considered by local clinicians to be therapeutically useful.

Results

The antimicrobial susceptibilities of specified organisms are listed in Tables II-VII and Figures 1-6.

Escherichia coli

The susceptibility of *E.coli* isolates (see Table II, Figure 1) ranged from 80-88% for gentamicin, 82-97% for amikacin, and 82-92% for ciprofloxacin. However, these figures exclude results from Steve Biko Academic (Pretoria) where strains appear to be consistently less susceptible, with only 81% susceptible to gentamicin, 73% susceptible to amikacin, and 67% susceptible to ciprofloxacin. Similarly, 25% of Steve Biko Academic *E.coli* strains produce ESBLs, which confer resistance to broad-spectrum cephalosporins, compared to only 3-17% of strains from the other six laboratories. Minimal carbapenem resistance was reported among *E. coli,* with a single isolate from Chris Hani Baragwanath that was resistant to ertapenem and meropenem.

Klebsiella pneumoniae

Thirty to fifty-one per cent of *K. pneumoniae* isolates were susceptible to gentamicin (see Table III, Figure 2), and 49-79% were susceptible to ciprofloxacin. Susceptibility to amikacin ranged from 66-98%, while 55-74% of all strains produced ESBLs. Six of seven laboratories reported resistance to carbapenems. Ertapenem susceptibility rates ranged from 96-99%, and imipenem or meropenem susceptibility rates from 98-100%.

Enterobacter species

Reported susceptibility rates among *Enterobacter* spp. ranged from 55-87% for gentamicin (see Table IV, Figure 3), 84-93% for amikacin, and 75-92% for ciprofloxacin. Cefepime susceptibility varied from 58-86%. While no resistance to meropenem or imipenem was reported, susceptibility rates for ertapenem were 91-99%.

Pseudomonas aeruginosa

High levels of resistance to the various antipseudomonal antibiotics were reported from all laboratories, with no single antibiotic agent attaining more than 65% susceptibility countrywide (see Table V, Figure 4). Patterns of susceptibility

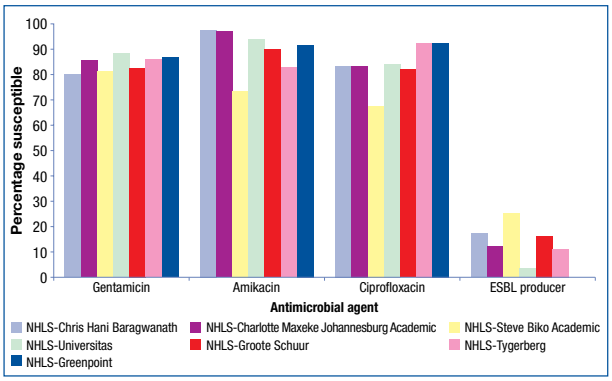

Figure 1: Susceptibility of *Escherichia coli* isolated from blood to selected antimicrobial agents at seven participating laboratories, South Africa, 2010

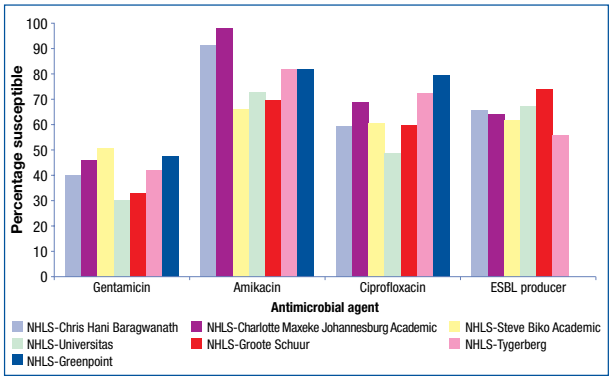

Figure 2: Susceptibiity of *Klebsiella pneumoniae* isolated from blood to selected antimicrobial agents at seven participating laboratories, South Africa, 2010

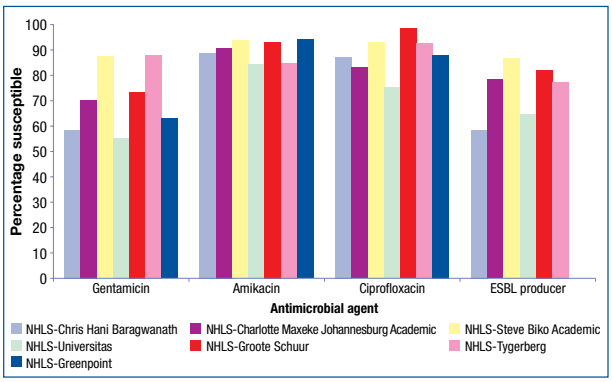

Figure 3: Susceptibility of *Enterobacter* species isolated from blood to selected antimicrobial agents at seven participating laboratories, South Africa, 2010

varied considerably between different laboratories, with the highest levels of carbapenem resistance occurring in the Western Cape (55% susceptibility to imipenem and 55% and 67% susceptibility to meropenem, at Groote Schuur and Tygerberg, respectively). Extreme differences in piperacillin-tazobactam susceptibility rates were noted (from 1-80%).

Acinetobacter baumannii

High levels of resistance to all antibiotics were reported from all laboratories, though the number of isolates varied considerably (see Table VI, Figure 5).

Table III: Susceptibility of *Klebsiella pneumoniae* isolated from blood to selected antimicrobial agents at seven participating laboratories, South Africa, 2010.

Participating laboratories	Antimicrobial agent						
	Gentamicin-susceptible, n/N (%) (95% CI)	Amikacin-susceptible, n/N (%) (95% CI)	Ciprofloxacin-susceptible, n/N (%) (95% CI)	ESBL producer, n/N (%) (95% CI)	Ertapenem-susceptible, n/N (%) (95% CI)	Imipenem-susceptible, n/N (%) (95% CI)	Meropenem-susceptible, n/N (%) (95% CI)
NHLS Chris Hani Baragwanath	199/498 (40) (36-44)	455/497 (92) (89-94)	296/498 (59) (55-64)	169/498 (34) (30-38)	485/498 (97) (96-99)	495/498 (99) (98-100)	497/498 (100) (99-100)
NHLS Charlotte Maxeke Johannesburg Academic	138/301 (46) (40-52)	298/305 (98) (95-99)	208/304 (68) (63-74)	109/304 (36) (30-42)	295/302 (98) (95-99)	302/304 (99) (98-100)	303/304 (100) (98-100)
NHLS Steve Biko Academic	256/504 (51) (46-55)	316/477 (66) (62-70)	273/450 (61) (56-65)	184/488 (38) (33-42)	441/445 (99) (98-100)	483/484 (100) (99-100)	485/485 (100) (99-100)
NHLS Universitas	33/111 (30) (21-39)	79/109 (72) (63-81)	54/11 (49) (39-58)	36/110 (33) (24-42)	109/110 (99) (95-100)	111/111 (100) (97-100)	88/90 (98) (92-100)
NHLS Groote Schuur	84/256 (33) (27-39)	177/254 (70) (64-75)	151/254 (59) (53-66)	67/254 (26) (21-32)	245/254 (96) (93-98)	251/253 (99) (97-100)	252/253 (100) (98-100)
NHLS Tygerberg	81/194 (42) (35-49)	158/194 (81) (75-87)	140/193 (73) (66-79)	86/194 (44) (37-52)	193/193 (100) (98-100)	194/194 (100) (98-100)	194/194 (100) (98-100)
NHLS Green Point	57/120 (48)	96/118 (81)	95/120 (79)				
Total	**848/1 984 (43)**	**1 579/1 954 (81)**	**1 217/1 930 (63)**	**656/1 861 (35)**	**1 835/1 869 (98)**	**1 902/1 910 (100)**	**1 884/1 890 (100)**

n = number susceptible, N = number tested, % = percentage susceptible, 95% CI = 95% confidence interval

Table IV: Susceptibility of *Enterobacter* species isolated from blood to selected antimicrobial agents at seven participating laboratories, South Africa, 2010.

Participating laboratories	Antimicrobial agent						
	Gentamicin-susceptible, n/N (%) (95% CI)	Amikacin-susceptible, n/N (%) (95% CI)	Ciprofloxacin-susceptible, n/N (%) (95% CI)	ESBL producer, n/N (%) (95% CI)	Ertapenem-susceptible, n/N (%) (95% CI)	Imipenem-susceptible, n/N (%) (95% CI)	Meropenem-susceptible, n/N (%) (95% CI)
NHLS Chris Hani Baragwanath	128/220 (58) (51-65)	193/218 (89) (84-92)	190/219 (87) (82-91)	128/220 (58) (51-65)	202/221 (91) (87-95)	221/222 (100) (98-100)	220/221 (100) (98-100)
NHLS Charlotte Maxeke Johannesburg Academic	79/113 (70) (61-78)	102/113 (90) (83-95)	93/113 (82) (74-89)	88/113 (78) (69-85)	110/112 (98) (94-100)	113/113 (100) (97-100)	112/112 (100) (97-100)
NHLS Steve Biko Academic	226/260 (87) (82-91)	238/255 (93) (90-96)	222/240 (93) (88-95)	222/257 (86) (82-90)	209/213 (98) (95-99)	259/259 (100) (99-100)	261/261 (100) (99-100)
NHLS Universitas	22/40 (55) (38-71)	31/37 (84) (68-94)	30/40 (75) (59-87)	25/39 (64) (47-79)	34/35 (97) (85-100)	37/37 (100) (91-100)	23/23 (100) (85-100)
NHLS Groote Schuur	59/81 (73) (62-82)	75/81 (93) (85-97)	79/81 (98) (91-100)	66/81 (81) (71-89)	80/81 (99) (93-100)	81/81 (100) (96-100)	81/81 (100) (96-100)
NHLS Tygerberg	34/39 (87) (73-96)	32/38 (84) (69-94)	26/29 (92) (79-98)	30/39 (77) (61-89)	37/38 (97) (86-100)	39/39 (100) (91-100)	39/39 (100) (91-100)
NHLS Green Point	10/16 (63) (35-85)	14/15 (93) (68-100)	14/16 (88) (62-98)				
Total	**558/769 (73)**	**685/757 (90)**	**664/748 (89)**	**562/752 (75)**	**679/709 (96)**	**759/760 (100)**	**745/746 (100)**

n = number susceptible, N = number tested, % = percentage susceptible, 95% CI = 95% confidence interval

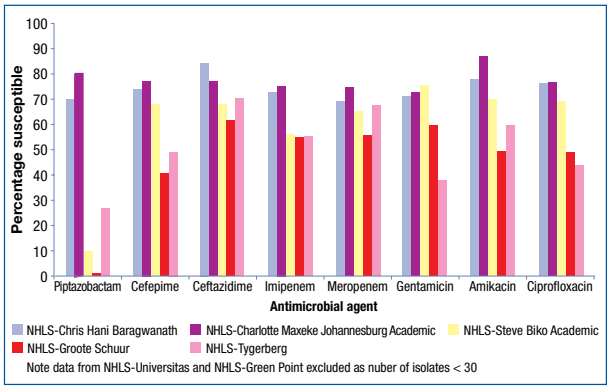

Figure 4: Susceptibility of *Pseudomonas aeruginosa* isolated from blood to selected antimicrobial agents at seven participating laboratories, South Africa, 2010

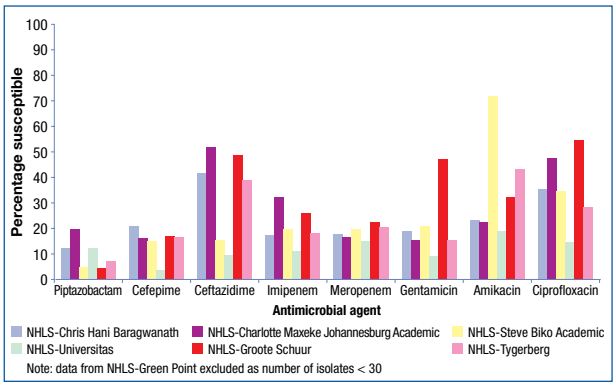

Figure 5: Susceptibility of *Acinetobacter baumannii* isolated from blood to selected antimicrobial agents at seven participating laboratories, South Africa, 2010

Staphylococcus aureus

Between 41-76% of *S. aureus* isolates were susceptible to cloxacillin (see Table VII, Figure 6), while susceptibility to erythromycin and clindamycin was slightly higher, ranging from 41-83%, and from 55-85% respectively. *S. aureus* was one of the most common bloodstream pathogens, and constituted the largest number of isolates for any single organism at three out of seven laboratories, while in the remaining four sites, it was matched only by *K. pneumoniae* (in three laboratories) or *K. pneumoniae* and *E.coli* (in one laboratory).

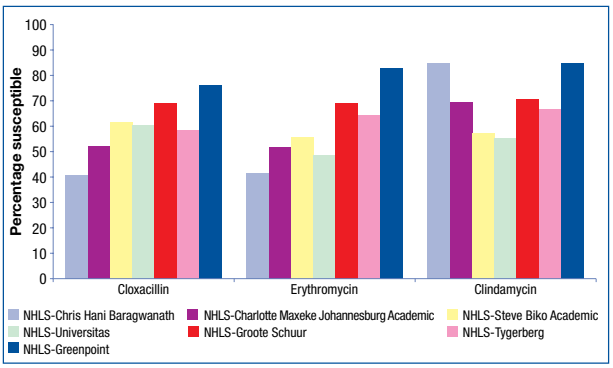

Figure 6: Susceptibility of *Straphylococcus aureus* isolated from blood to selected antimicrobial agents at seven participating laboratories, South Africa, 2010

Discussion

During 2010, 8 494 bloodstream isolates of *E. coli*, *K. pneumoniae*, *Enterobacter* spp., *P. aeruginosa, A. baumannii* and *S. aureus* were detected at seven participating laboratories, in three provinces of South Africa. The participating laboratories, with the exception of Green Point NHLS, are based at academic centres,

Table V: Susceptibility of *Pseudomonas aeruginosa* isolated from blood to selected antimicrobial agents at seven participating laboratories, South Africa, 2010

Participating laboratories	Antimicrobial agen							
	Piperacillin-tazobactam-susceptible, n/N (%) (95% CI[d])	Cefepime-susceptible, n/N (%) (95% CI)	Ceftazidime-susceptible, n/N (%) (95% CI)	Imipenem-susceptible, n/N (%) (95% CI)	Meropenem-susceptible, n/N (%) (95% CI)	Gentamicin-susceptible, n/N (%) (95% CI)	Amikacin-susceptible, n/N (%) (95% CI)	Ciprofloxacin-susceptible n/N (%) (95% CI)
NHLS Chris Hani Baragwanath	144/207 (70) (63-75)	153/207 (74) (67-80)	174/207 (84) (78-89)	149/205 (73) (66-79)	141/204 (69) (62-75)	147/207 (71) (64-77)	159/205 (78) (71-83)	157/206 (76) (70-82)
NHLS Charlotte Maxeke Johannesburg Academic	126/157 (70) (63-76)	120/156 (77) (70-83)	120/156 (77) (70-83)	116/155 (75) (67-81)	116/156 (74) (67-81)	111/153 (73) (65-79)	130/150 (87) (80-92)	118/154 (77) (69-83)
NHLS Steve Biko Academic	17/168 (10) (6-16)	111/164 (68) (60-75)	127/187 (68) (61-75)	93/166 (56) (48-64)	108/166 (65) (57-72)	142/188 (76) (69-81)	116/166 (70) (62-77)	101/147 (69) (61-76)
NHLS Groote Schuur	1/104 (1) (0-5)	36/88 (41) (31-52)	64/104 (62) (51-71)	48/88 (55) (44-65)	46/83 (55) (44-66)	62/104 (60) (50-69)	45/91 (49) (39-60)	50/103 (49) (39-59)
NHLS Tygerberg	13/49 (27) (15-41)	24/49 (29) (34-64)	35/50 (70) (55-82)	27/49 (55) (40-69)	33/49 (67) (52-80)	19/50 (38) (25-53)	29/49 (59) (44-73)	21/48 (44) (29-59)
Total	**320/709 (45)**	**468/694 (67)**	**542/731 (74)**	**449/680 (66)**	**455/669 (68)**	**507/736 (69)**	**504/690 (73)**	**475/690 (69)**

Note: Data from NHLS Universitas and Green Point, excluded, as the number of isolates was < 30.
n = number susceptible, N = number tested, % = percentage susceptible, 95% CI = 95% confidence interval

Table VI: Susceptibility of *Acinetobacter baumannii* isolated from blood to selected antimicrobial agents at 7 participating laboratories, South Africa, 2010

Participating laboratories	Antimicrobial agent							
	Piperacillin-tazobactam-susceptible, n/N (%) (95% CI)	Cefepime-susceptible, n/N (%) (95% CI)	Ceftazidime-susceptible, n/N (%) (95% CI)	Imipenem-susceptible, n/N (%) (95% CI)	Meropenem-susceptible, n/N (%) (95% CI)	Gentamicin-susceptible, n/N (%) (95% CI)	Amikacin-susceptible, n/N (%) (95% CI)	Ciprofloxacin-susceptible n/N (%) (95% CI)
NHLS Chris Hani Baragwanath	55/441 (12) (10-16)	95/450 (21) (17-25)	189/451 (42) (37-47)	78/442 (18) (14-22)	80/447 (18) (14-22)	85/450 (19) (15-23)	105/449 (23) (20-28)	160/449 (36) (31-40)
NHLS Charlotte Maxeke Johannesburg Academic	8/41 (20) (9-35)	20/123 (16) (10-24)	64/124 (52) (42-61)	13/40 (33) (19-49)	20/120 (17) (10-25)	19/121 (16) (10-23)	27/120 (23) (15-31)	59/125 (47) (38-56)
NHLS Steve Biko Academic	12/236 (5) (3-9)	36/235 (15) (11-21)	37/238 (16) (11-21)	48/240 (20) (15-26)	48/240 (20) (15-26)	51/239 (21) (16-27)	166/231 (72) (66-78)	75/217 (35) (28-41)
NHLS Universitas	4/32 (13) (4-29)	2/53 (4) (-13)	5/51 (10) (3-21)	6/52 (12) (4-23)	4/26 (15) (4-35)	5/53 (9) (3-21)	10/53 (19) (9-32)	8/53 (15) (7-28)
NHLS Groote Schuur	10/220 (5) (2-8)	34-199 (17) (12-23)	110/226 (49) (42-55)	59/226 (26) (21-32)	48/213 (23) (17-29)	107/226 (47) (41-54)	64/198 (47) (41-54)	64/198 (32) (26-39)
NHLS Tygerberg	9/120 (8) (3-14)	20/119 (17) (11-25)	46/118 (39) (30-48)	22/120 (18) (12-26)	22/108 (20) (13-29)	19/120 (16) (10-24)	49/113 (43) (34-53)	34/120 (28) (20-37)
Total	**101/1 100 (9)**	**221/1 199 (18)**	**459/1 228 (37)**	**232/1 131 (21)**	**229/1 165 (20)**	**302/1 229 (25)**	**440/1 184 (37)**	**475/1 210 (39)**

Note: Data from NHLS, Green Point, excluded, as the number of isolates was < 30.
n = number susceptible, N = number tested, % = percentage susceptible, 95% CI = 95% confidence interval

and they service predominantly, though not exclusively, tertiary referral hospital populations. Green Point laboratory serves predominantly primary level hospitals, and this is reflected in both the smaller numbers of the typical intensive care unit pathogens (*P. aeruginosa* and *A. baumannii* isolated) as well as in the lower levels of resistance reported, for example 76% of Green Point *S. aureus* isolates were susceptible to cloxacillin.

The bloodstream isolates included in this report reflect a mixture of both community- and hospital-acquired infections, and the relative proportions may influence the antimicrobial susceptibility profiles. Thus *E. coli* bacteraemia, which frequently originates from the normal enteric flora in conditions such as community-acquired urinary tract infections or acute abdominal sepsis, may show higher levels of susceptibility than *K. pneumoniae*, a predominantly hospital-acquired pathogen. The very varied antimicrobial susceptibility profiles of *P. aeruginosa* from different laboratories probably reflects local nosocomial spread of endemic strains.

Compared to 2009, levels of resistance to gentamicin, amikacin, ciprofloxacin and cephalosporins, among *E. coli*, *K. pneumoniae* and *Enterobacter* spp., remained generally unchanged, apart from decreasing susceptibility reported from Steve Biko Academic. This decrease in susceptibility requires further investigation, to determine whether it represents a genuine increase in resistance, or whether it is an artifact, due to changes in laboratory techniques or catchment population. Nonetheless, the reported low levels of susceptibility, particularly to ciprofloxacin (67%), are reason for concern.

However, the major change noted in 2010 was the increased resistance to carbapenems among *K. pneumoniae* and *Enterobacter* species. Resistance to carbapenems was first noted in 2009, but is now far more widespread, with low levels of resistance reported from all laboratories. Resistance is greater for ertapenem, than imipenem or meropenem. Unfortunately, neither the minimum inhibitory concentration (MIC) values for these isolates, nor the mechanisms of carbapenem resistance, were available for reporting. While a combination of either ESBL or intrinsic AmpC-type cephalosporinase production, plus decreased permeability, is the most likely cause of carbapenem resistance, the presence of carbapenemases, such as New Delhi metallo-beta-lactamase-1 (NDM-1), detected in Gauteng in 2011, or others, cannot be excluded.[8-11] The impact of increasing carbapenem resistance, particularly in *K. pneumoniae,* is likely to be severe, as this organism is a common, multi-resistant, nosocomial pathogen, and there are few alternative treatment options available.

The levels of resistance to multiple antibiotics among *P. aeruginosa* and *A. baumannii* remain high in all laboratories,

Table VII: Susceptibility of *Staphylococcus aureus* isolated from blood to selected antimicrobial agents at seven participating laboratories, South Africa, 2010

Participating laboratories	Antimicrobial agent		
	Cloxacillin-susceptible, n/N (%) (95% CI)	Erythromycin-susceptible, n/N (%) (95% CI)	Clindamycin-susceptible, n/N (%) (95% CI)
NHLS Chris Hani Baragwanath	310/757 (41) (37-45)	311/750 (41) (38-45)	639/750 (85) (82-88)
NHLS Charlotte Maxeke Johannesburg Academic	163/312 (52) (47-58)	160/308 (52) (46-58)	217/311 (70) (64-75)
NHLS Steve Biko Academic	306/498 (61) (57-66)	228/409 (56) (51-61)	235/410 (57) (52-62)
NHLS Universitas	46/76 (61) (49-72)	36/74 (49) (37-61)	42/76 (55) (43-67)
NHLS Groote Schuur	214/309 (69) (64-74)	212/306 (69) (64-74)	217/307 (71) (65-76)
NHLS Tygerberg	100/170 (59) (51-66)	109/169 (64) (57-72)	113/169 (67) (59-74)
NHLS Green Point	90/118 (75) (68-84)	97/117 (83) (75-89)	100/117 (85) (78-91)
Total	**1 229/2 240 (55)**	**1 153/2 140 (54)**	**1 563/2 140 (73)**

n = number susceptible, N = number tested, % = percentage susceptible, 95% CI = 95% confidence interval

with few changes since 2009. However, at Steve Biko Academic, there were significant increases in susceptibility of *P. aeruginosa* to gentamicin, ciprofloxacin, cefepime, ceftazidime and meropenem in 2010 (p-value < 0.05). There was no significant change in imipenem susceptibility rates. The reasons for these changes are unknown, but it could possibly be due to decreased transmission of highly resistant hospital-acquired strains. Conversely, decreased rates of susceptibility were seen for gentamicin at Tygerberg and Charlotte Maxeke Johannesburg Academic laboratories (p-value < 0.05).

Large decreases in piperacillin-tazobactam susceptibility rates were noted at three institutions, with reductions from 60% to10% at Steve Biko Academic, from 40% to 1% at Groote Schuur, and from 43% to 27% at Tygerberg. All three laboratories perform antimicrobial susceptibility testing with the Vitek 2® system, an automated system, previously noted to have a high rate of false susceptibility results for testing of *P. aeruginosa* against piperacillin-tazobactam.[12] The dramatic increase in piperacillin-tazobactam resistance suggests that the system's Advanced Expert System may have been changed in 2010 to minimise false susceptibility reporting, but that this also had the effect of artificially inflating resistance rates. The Vitek 2® system is currently being reformulated to permit more accurate determination of piperacillin-tazobactam susceptibility in future.

The clinical significance of *A. baumannii* bacteraemia is more difficult to interpret, as on occasions, the presence of these low-virulence organisms may reflect contamination with colonising skin flora. Colistin susceptibility of *A. baumannii* is not reported here, partly because of problems with testing method standardisation. However, this important therapeutic antibiotic will be included in future surveillance.

S. aureus remains a major pathogen countrywide, with between 30-60% of isolates resistant to cloxacillin (MRSA). These figures are in agreement with the GERMS-SA data from sentinel site surveillance, which revealed MRSA bloodstream infection rates of between 41-46% for 2010.[7]

Limitations

While these national laboratory-based surveillance data provide valuable information, they are, in common with all laboratory-based surveillance data, subject to certain clinical and technical limitations. The major clinical limitation is the fact that the probability of detecting a bloodstream pathogen depends on the test request practices of clinicians. Thus the numbers and proportions of resistant or susceptible organisms may vary, depending on whether clinicians in different institutions are more or less likely to take blood cultures in particular clinical scenarios. In addition, laboratory surveillance data on their own cannot distinguish between community-acquired and hospital-acquired infections, and hence clinicians should be wary of direct extrapolation of these data to clinical practice. Other limitations are the retrospective nature of the data collection, delays in reporting, and lack of clinical correlation, although it can be assumed that the vast majority of bloodstream pathogens reported here are significant.

In addition, certain technical limitations may affect the presented data. Since it was not possible to retest all isolates at a central laboratory, the susceptibility data are completely dependent on the accuracy of laboratory practices in the participating institutions. Different laboratories utilise different testing systems (see Table I), and there may also be differences in interpretation of certain borderline results. However, all laboratories are fully accredited and maintain high standards, as evidenced by participation in ongoing external quality-assurance programmes.

At the data collection level, extraction of data via CDW can eliminate potential variations in data collation that might occur when this is performed at local laboratory level. However, centralised data extraction also highlights differences in reporting practices between laboratories, for example use of different codes to report the same organism. While attempts have been made to correct such differences, undetected errors may still occur.

Most importantly, at this stage, CDW data extraction methods were not able to exclude duplicate isolates, a recommended

practice, because it minimises bias due to over-representation of those patients who are cultured most frequently. Since patients who have multiple isolates included are more likely to harbour resistant pathogens, the 2010 data may overstate resistance rates.

Conclusion

Despite these limitations, we conclude that antimicrobial resistance in key pathogens is high, and that the threat of increasing resistance, particularly with regard to carbapenems, is real. Ongoing surveillance is essential, but data extraction methods need to be further refined, specifically to exclude duplicate isolates. Centralised data extraction is a valuable tool, because the standardised data it generates have the potential to facilitate further analysis of trends in antimicrobial resistance in a more timeous manner. Ideally antimicrobial resistance surveillance should be linked to increased capacity for further studies on highly resistant organisms, while studies that differentiate between community-acquired and hospital-acquired infections are also highly desirable.

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