ANTIMICROBIAL RESISTANCE SURVEILLANCE FROM SENTINEL PUBLIC HOSPITALS, SOUTH AFRICA, 2014

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Introduction

Antimicrobial resistance (AMR) is a key public health concern that threatens effective treatment of severe infections, both locally and globally. Surveillance is conducted to determine the extent and pattern of resistance amongst the most important pathogens causing infections in humans.[1] Integrated data on resistance in bacteria are obtained from electronic reports generated by public laboratories in South Africa. The objectives of the AMR surveillance programme are to determine the number of cases reported from selected hospitals by month for selected pathogens and to describe antimicrobial susceptibility to the most important treatment regimens by pathogen and by hospital.

Methods

All data for this report were sourced from the National Health Laboratory Service (NHLS) Corporate Data Warehouse (CDW). This is a national repository for laboratories serving all public health hospitals in South Africa and contains archived data from two laboratory information systems (LISs), either DISA or TrakCare.[2]

Bloodstream infections over the period January-December 2014 were extracted for the following pathogens: *Acinetobacter baumannii* complex, *Enterobacter cloacae* complex, *Escherichia coli, Enterococcus faecalis, Enterococcus faecium, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Staphylococcus aureus.* Routine electronic data were collected from sentinel sites (mostly tertiary academic hospitals) (table 1).

Due to two different LISs, each with its own coding system for organisms and antibiotics, as well as a lack of standardisation across NHLS laboratories on how data were captured, extensive cleaning and recoding of data was necessary. Cleaning of the data involved creating unique patient identifiers, which enabled de-duplication and the generation of patient-level data.

Antimicrobial susceptibility reporting was based on Clinical Laboratory Standards Institute (CLSI) guidelines.[3] The various laboratory methods used included Microscan, Vitek, E test and disk diffusion. Vancomycin resistance is not reported for *Staphylococcus aureus* due to the lack of confirmatory test methods (pending agreement with the South African Society for Clinical Microbiology (SASCM)). Data were omitted for those sites that tested fewer than 30 organisms for a particular antibiotic.

Table 1: Hospitals participating in antimicrobial resistance surveillance by province, South Africa, and their characteristics.

Hospital Site	Province	Academic Hospital	No of beds
Charlotte Maxeke Johannesburg Academic Hospital (CMJAH)	Gauteng	Yes	1088
Chris Hani Baragwanath Hospital (CHBH)	Gauteng	Yes	3200
Dr George Mukhari Hospital (DGMH)	Gauteng	Yes	1200
Grey's Hospital (GH)	KwaZulu-Natal	Yes	530
Groote Schuur Hospital (GSH)	Western Cape	Yes	893
Helen Joseph Hospital (HJH)	Gauteng	Yes	700
Inkosi Albert Luthuli Central Hospital (IALCH)	KwaZulu-Natal	Yes	846
King Edward VIII Hospital (KEH)	KwaZulu-Natal	Yes	922
Mahatma Gandhi Hospital (MGH)*	KwaZulu-Natal	No	350
Nelson Mandela Academic Hospital/Mthatha Tertiary (NMAH)	Eastern Cape	Yes	520
RK Khan Hospital (RKKH)	KwaZulu-Natal	No	543
Steve Biko Academic Hospital (SBAH)	Gauteng	Yes	832
Tygerberg Hospital (TH)	Western Cape	Yes	1310
Universitas Hospital (UH)	Free State	Yes	650

Results

Data for bloodstream infections and antimicrobial susceptibility tests are summarised for *Acinetobacter baumannii* complex (figure 1), *Enterobacter cloacae* complex (figure 2), *Enterococcus faecalis* (figure 3), *Enterococcus faecium* (figure 4), *Escherichia coli (*figure 5*), Klebsiella pneumoniae* (figure 6), *Pseudomonas aeruginosa* (figure 7) and *Staphylococcus aureus* (figure 8). For each organism, the total number of cases, as well as their susceptibility profiles and percentage susceptibility to selected antimicrobial agents by site were analysed (figures 1-8).

***Acinetobacter baumannii* complex**

Acinetobacter baumannii was resistant to most of the antimicrobial agents tested. This is due to its ability to harbour multiple mechanisms of resistance, such as the loss of outer membrane porins resulting in reduced permeability, efflux systems, *ampC* β-lactamases and others. The proportions of isolates resistant to imipenem, cefepime and ceftazidime were high at 77%, 79% and 75% respectively, whereas resistance proportions were 67% to ciprofloxacin, 43% to amikacin and 51% to tobramycin. Resistance to colistin was estimated to be 5%. Resistance to most agents have not changed in comparison with the previous year, except for the increase in resistance to tobramycin and colistin. AST testing and breakpoints for colistin are lacking and these results should be treated with caution.

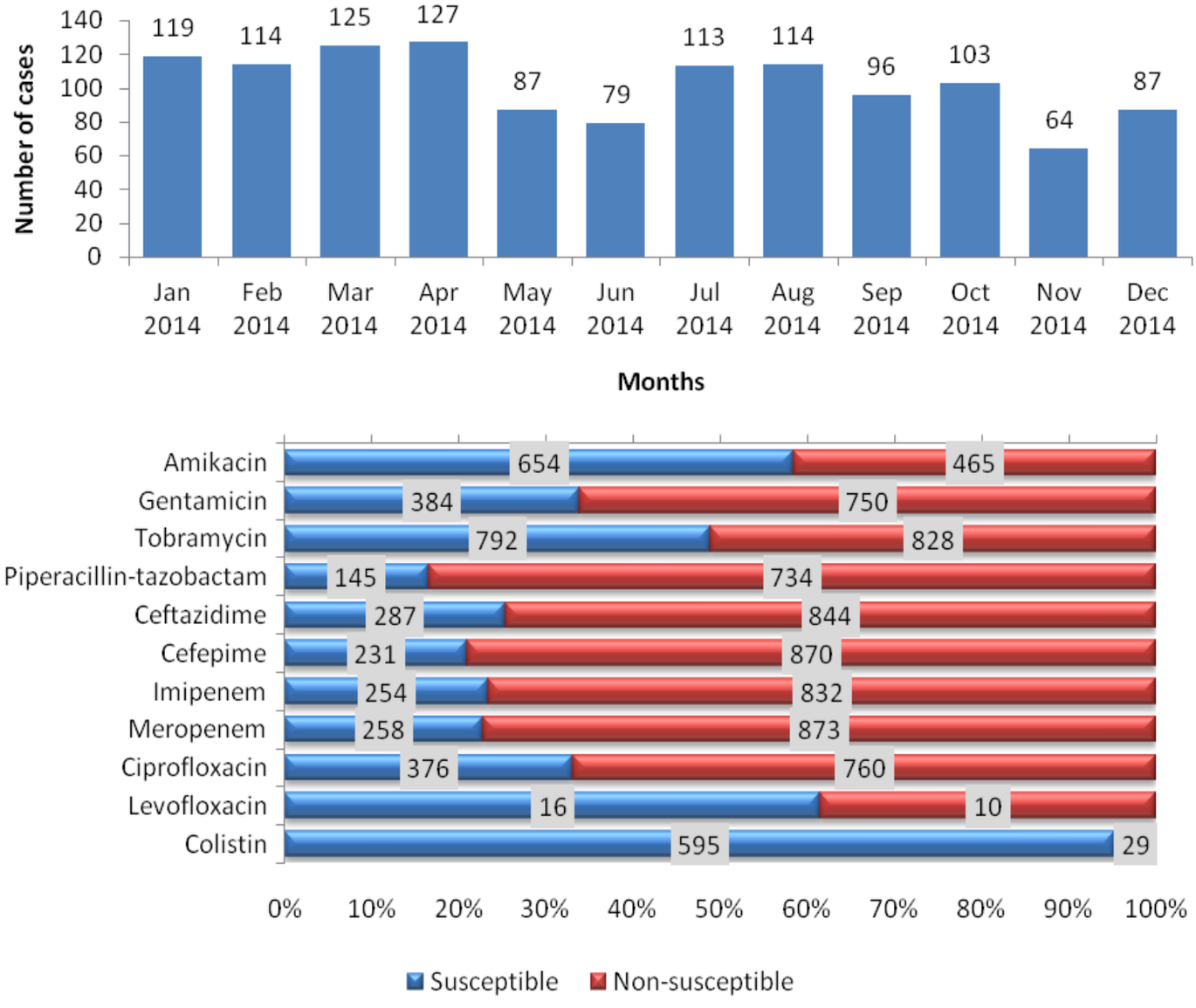


Figure 1: *Acinetobacter baumannii* cases by month, and numbers and percentages of susceptible and resistant *A. baumannii* complex isolates from blood cultures at public-sector sentinel sites, 2014. Total number of isolates analyzed =1228.

***Enterobacter cloacae* complex**

The high level of *Enterobacter cloacae* complex isolates resistant to ertapenem (12%) should be taken with reservation (refer to the limitations discussed earlier), although resistance to imipenem and meropenem has remained stable (2%). Resistance to cefepime (35%) is indicative of *ampC* β-lactamase hyper-production in combination with porin loss, which may confer resistance to cephalosporins.

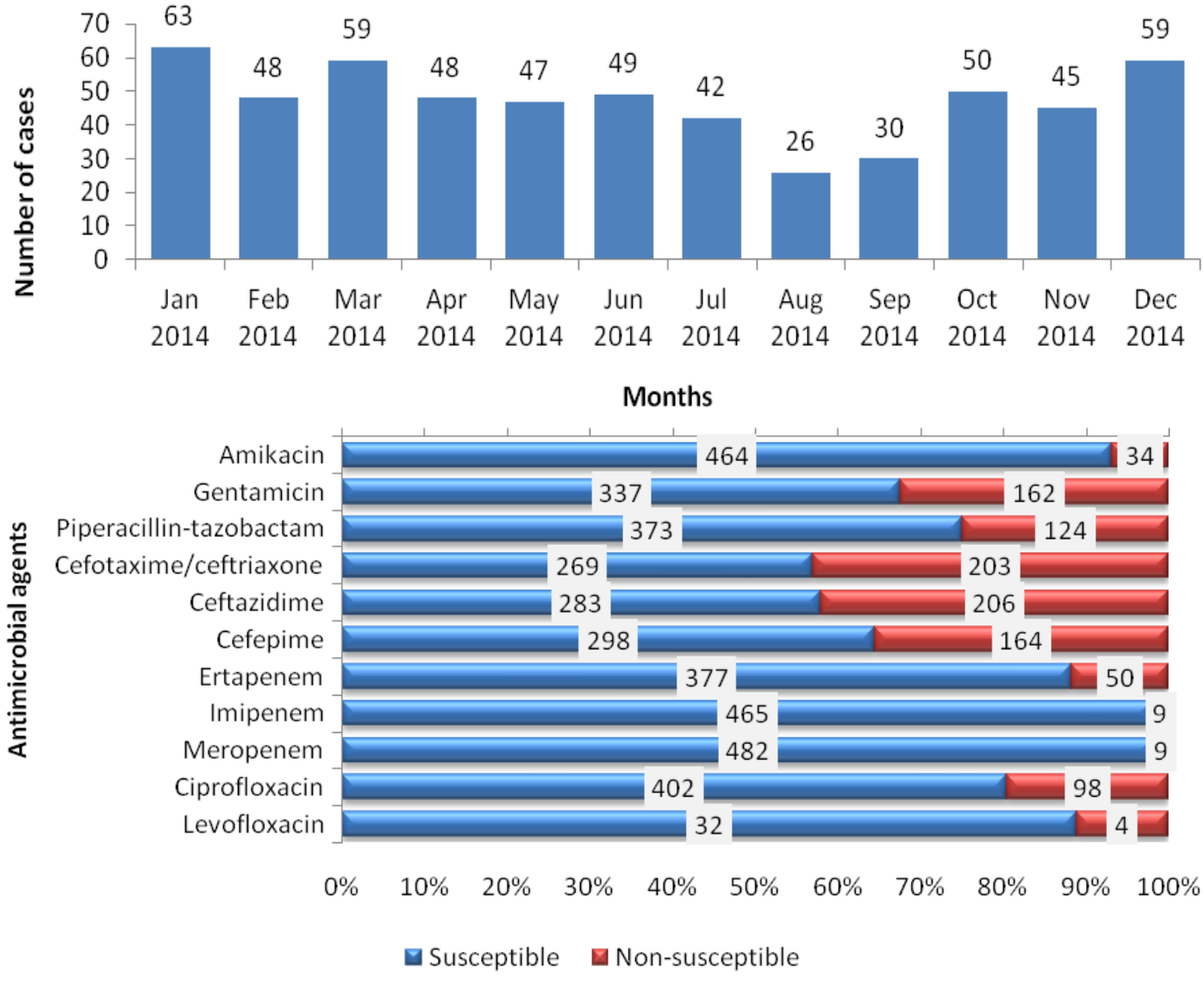


Figure 2: *Enterobacter cloacae* cases by month, and numbers and percentages of susceptible and resistant *E. cloacae* complex isolates from blood cultures at public-sector sentinel sites, 2014. Total number of isolates analyzed = 566.

Enterococcus faecalis

Enterococcus faecalis exhibited 17% resistance to penicillins and 2% (non-confirmed) resistance to vancomycin. There were no significant changes in comparison to the previous year. Results obtained from phenotypic methods for linezolid-intermediate or resistant *Enterococcus* spp. should be interpreted with caution since the gold standard for confirmation and quantification of linezolid resistance in enterocci is detection of the G2576T mutation.

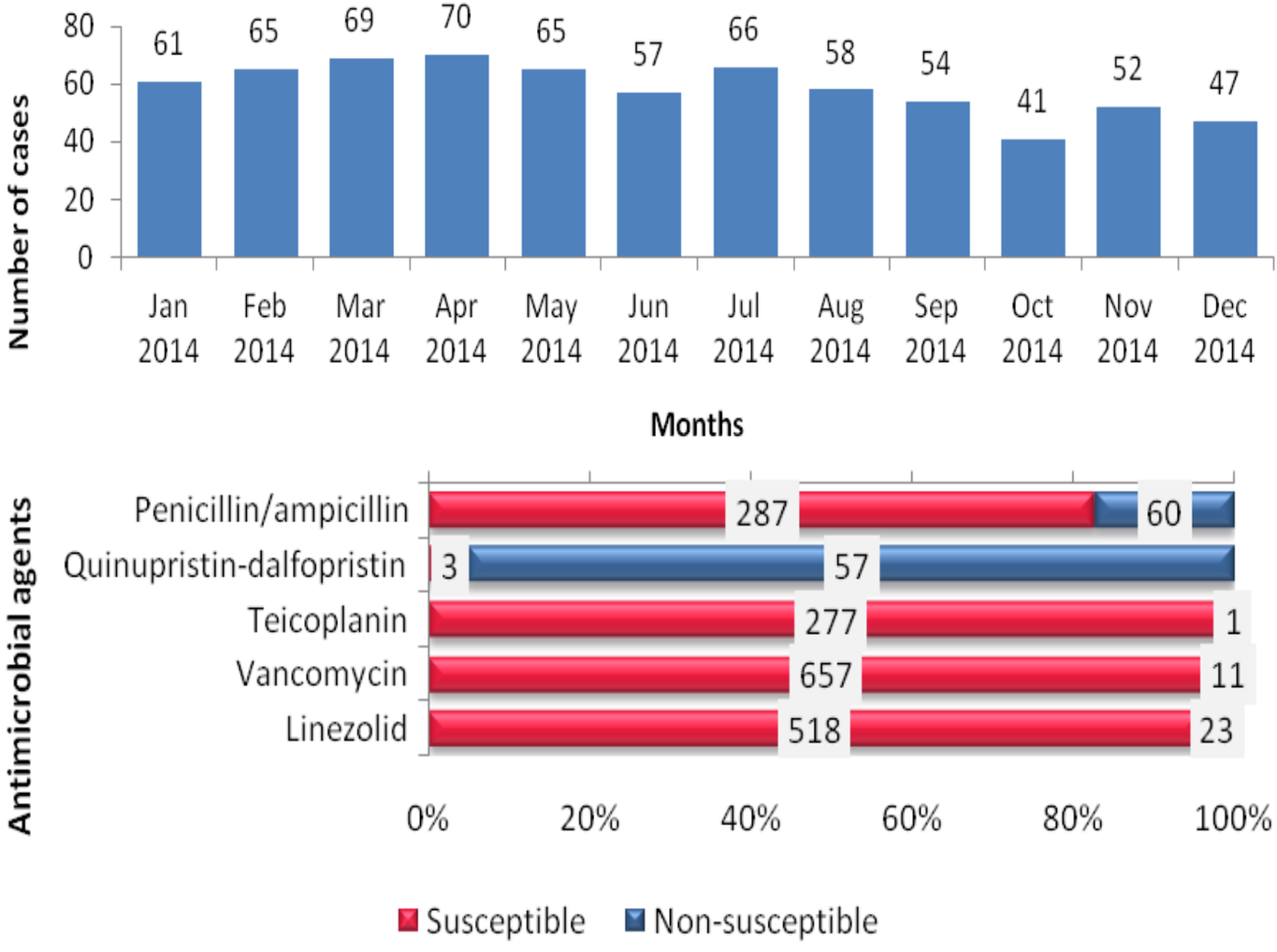


Figure 3: *Enterococcus faecalis* cases by month, and numbers and percentages of susceptible and resistant *E. faecalis* isolates from blood cultures at public-sector sentinel sites, 2014. Total number of isolates analyzed = 705.

Enterococcus faecium

Enterococcus faecium is inherently resistant to β-lactam agents. There was a decrease in resistance to vancomycin from 13% in 2013 to 5% in 2014, which may be explained by the containment of outbreaks in a few hospitals.

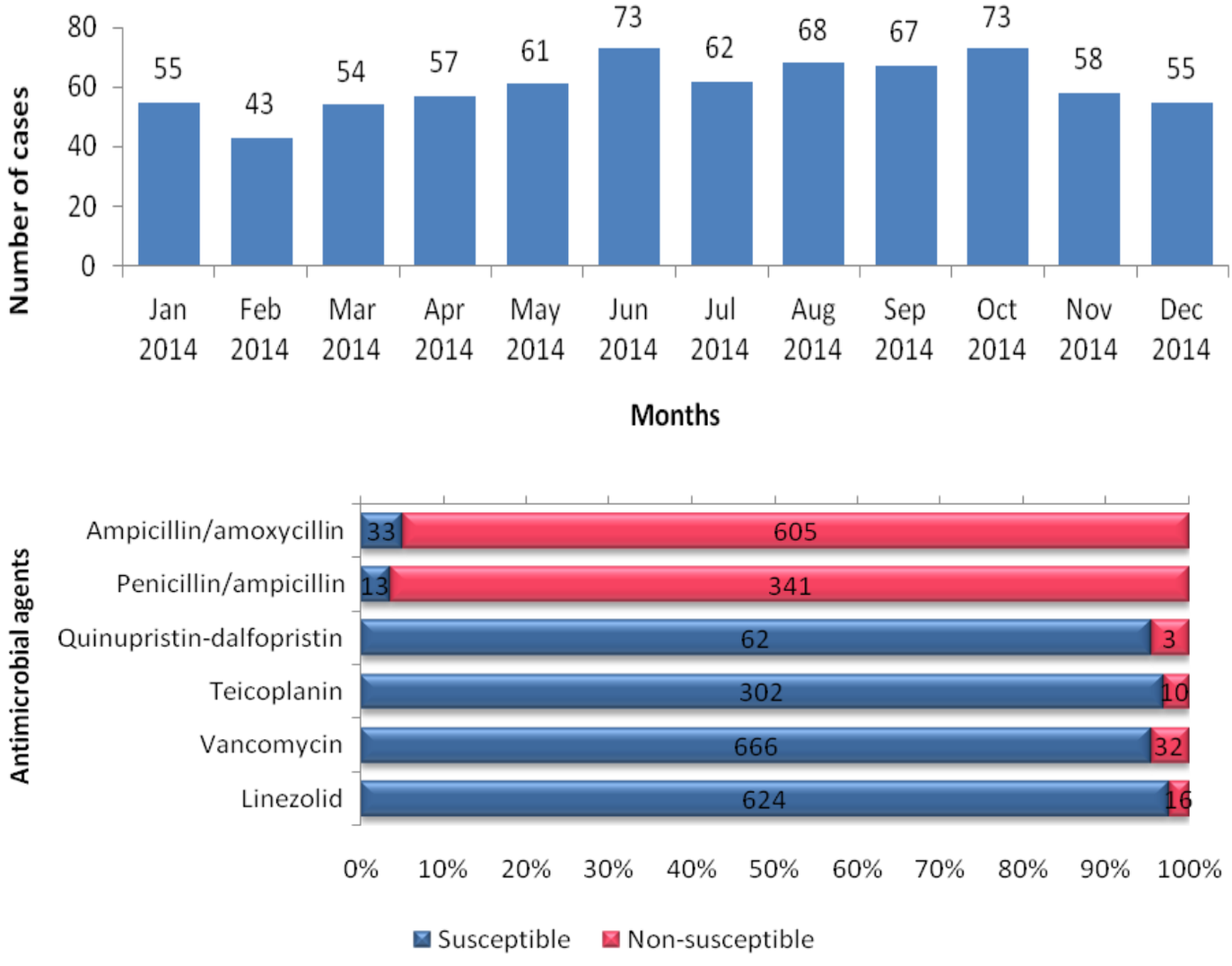


Figure 4: *Enterococcus faecium* cases by month, and numbers and percentages of susceptible and resistant *E. faecium* isolates from blood cultures at public-sector sentinel sites, 2014. Total number of isolates analyzed = 726.

Escherichia coli

Escherichia coli showed a minor increase in resistance to almost all β-lactams, whereas no change in resistance to ciprofloxacin over a two-year period was noted. Resistance to 3rd generation cephalosporins indicates the presence of extended spectrum β-lactamases (ESBLs) and was recorded in 25% of all isolates.

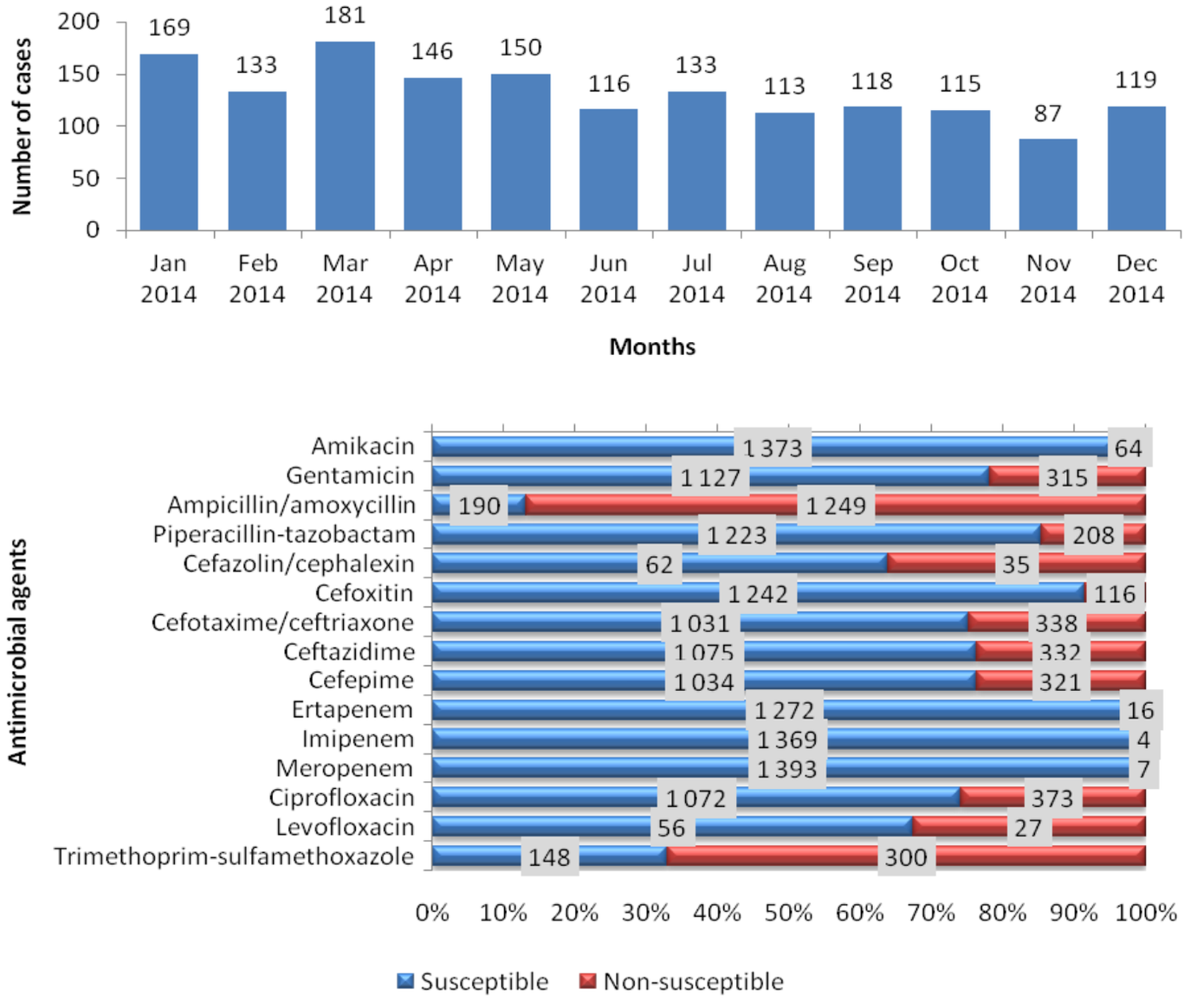


Figure 5: *Escherichia coli* cases by month, and numbers and percentages of susceptible and resistant *E. coli* isolates from blood cultures at public-sector sentinel sites, 2014. Total number of isolates analyzed = 1580.

Klebsiella pneumoniae

Klebsiella pneumoniae was resistant to multiple antimicrobials, including 3rd and 4th generation cephalosporinsthat indicate production of ESBLs (70%), ciprofloxacin (39%) and piperacillin-tazobactam (48%). The proportion of isolates resistant to ertapenem was low. Although resistance to other carbapenems was low, the rapid emergence of strains with carbapenemase production threatens the efficacy and use of this class of antimicrobials as a therapeutic option. Thus, continuous monitoring of resistance needs to be implemented. In hospitals where resistance is ≥10%, a nosocomial outbreak should be considered and investigated.

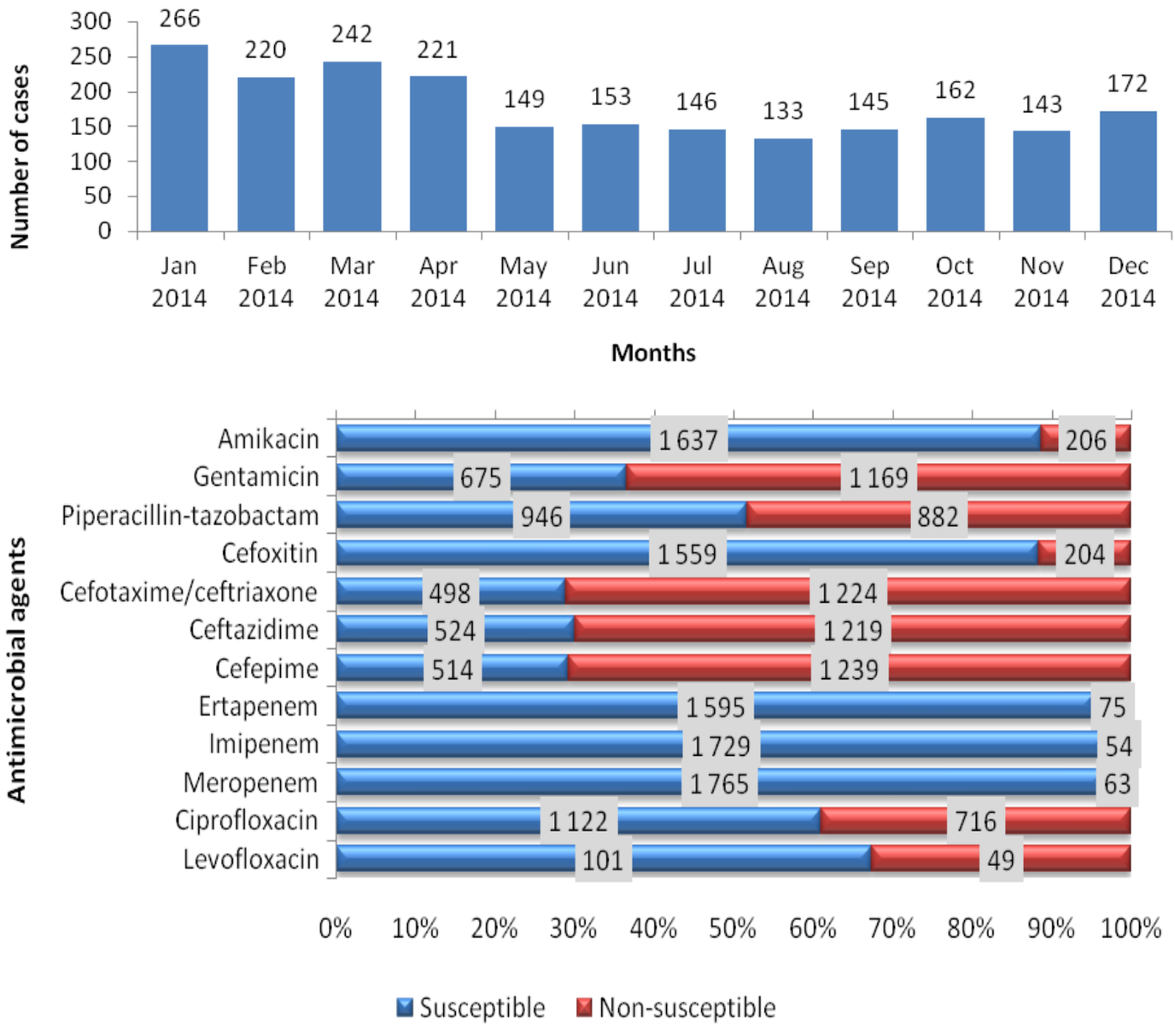


Figure 6: *Klebsiella pneumoniae* cases by month, and numbers and percentages of susceptible and resistant *K. pneumoniae* isolates from blood cultures at public-sector sentinel sites, 2014. Total number of isolates analyzed = 2152.

Pseudomonas aeruginosa

Compared to *A. baumannii, Pseudomonas aeruginosa* isolates displayed greater susceptibility to the antimicrobial agents tested. Resistance to piperacillin-tazobactam was high at 33%. There appeared to be modest decrease in resistance in 2014 compared to 2013 for the majority of antimicrobial agents, which may be explained by reasons listed in the limitations. Colistin resistance was the lowest.

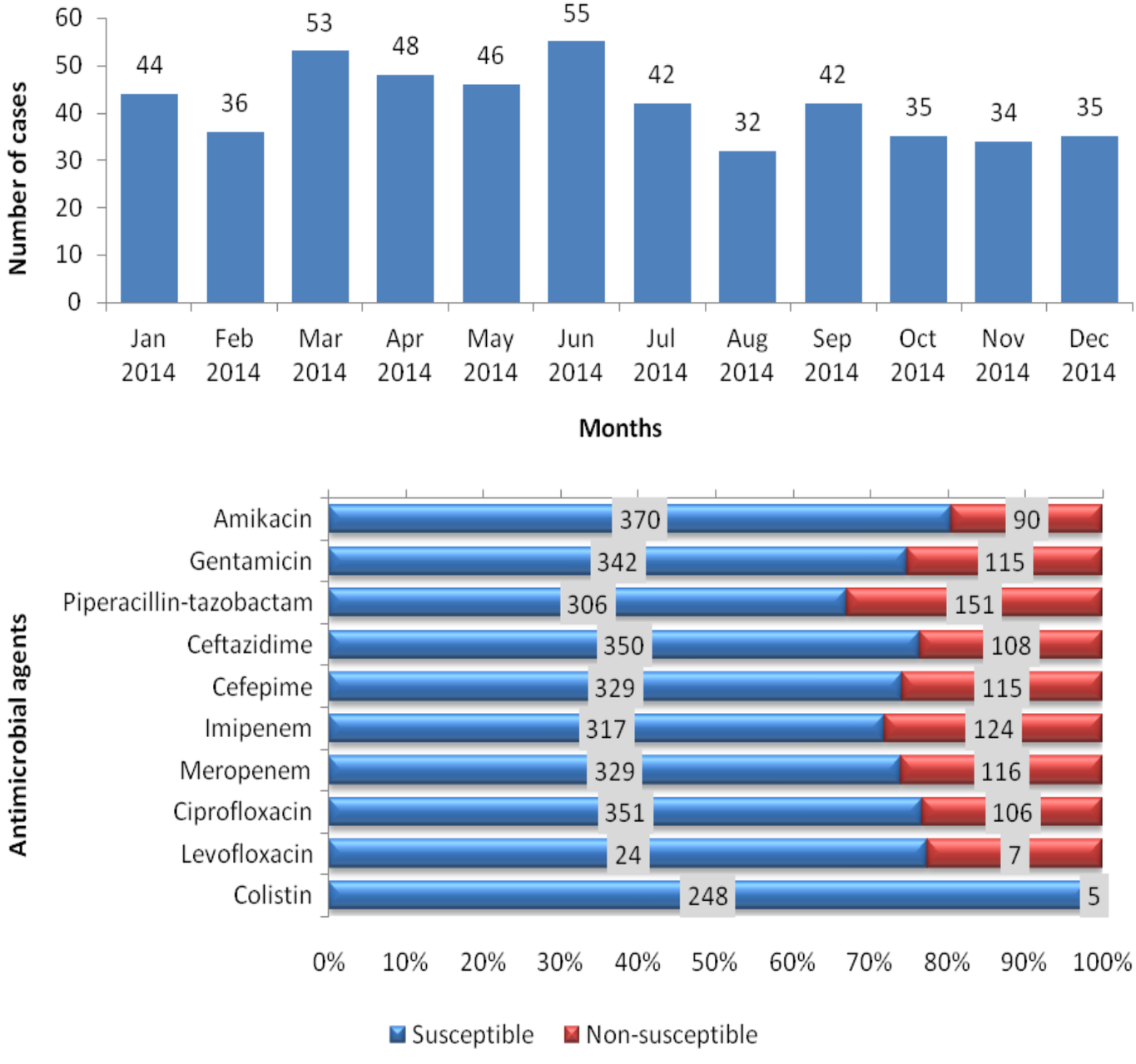
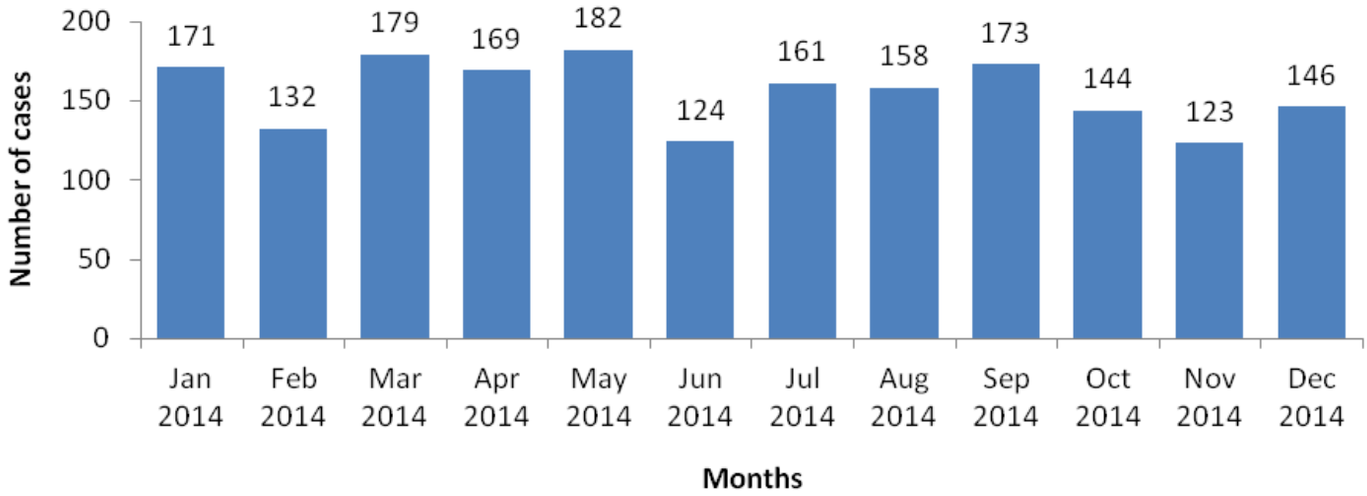


Figure 7: *Pseudomonas aeruginosa* cases by month, and numbers and percentages of susceptible and resistant *P. aeruginosa* isolates from blood cultures at public-sector sentinel sites, 2014. Total number of isolates analyzed = 502.

Staphylococcus aureus

Nine *S. aureus* isolates were reported to be vancomycin resistant. However, this was not confirmed and these data should be treated with caution as vancomycin resistance is exceptionally rare. Confirmatory phenotypic gold standard methods are available internationally and should be performed on each isolate flagged as resistant. Resistance to methicillin/oxacillin and all other β-lactams have decreased compared to the previous year. Cefoxitin resistance indicated methicillin-resistant *Staphylococcus aureus* (MRSA). Resistances to erythromycin and clindamycin have marginally decreased compared to 2013.



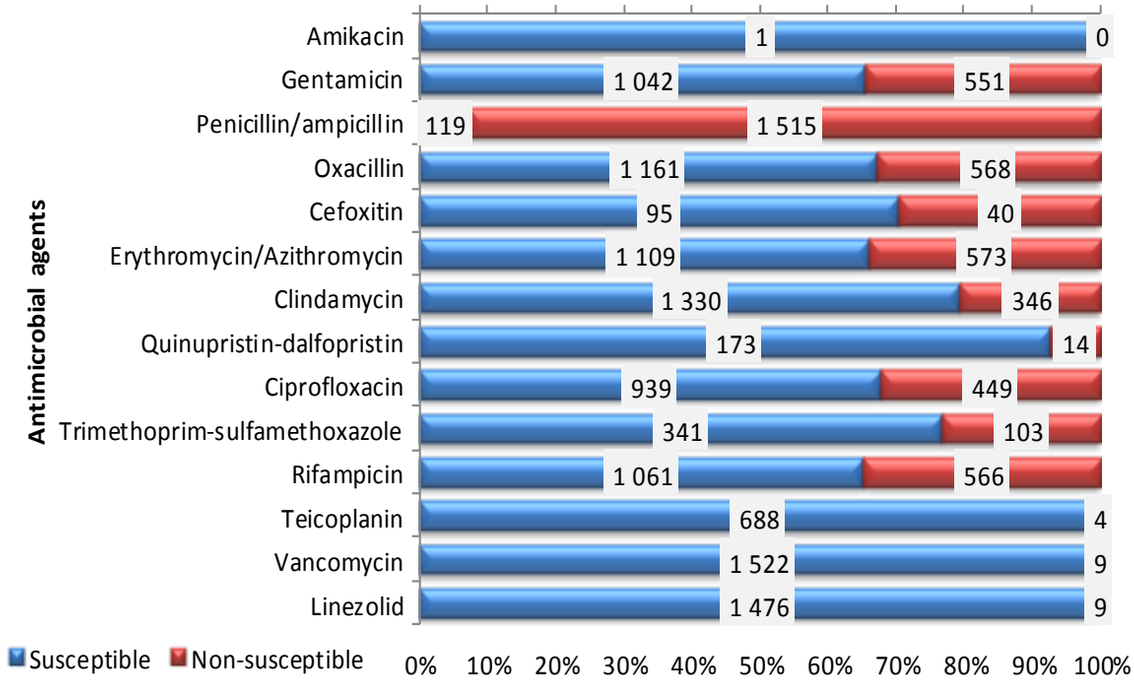


Figure 8: *Staphylococcus aureus* cases by month, and numbers and percentages of susceptible and resistant *S. aureus* isolates from blood cultures at public-sector sentinel sites, 2014. Total number of isolates analyzed = 1862.

Carbapenemase-producing Enterobacteriaceae (CPE)

The Antimicrobial Resistance Laboratory of the NICD (including the Cape Town satellite unit) analyzed the occurrence of CPE genes on all referred isolates from public laboratories based on phenotypic CLSI criteria for carbapenem resistance (table 2).[3] Isolates were sent to the reference labs on a voluntary basis. Few organisms presented with more than one carbapenemase gene.

Table 2: Numbers of confirmed carbapenemase-producing Enterobactericeae by species and genoptype. Percentages in parentheses represent proportions positive for the CPE genotype.

Carbapenemase-producing Enterobacteriaceae	No. of isolates
Species	
Klebsiella pneumoniae	186
Serratia marcescens	4
Enterobacter cloacae	87
Citrobacter freundii	5
Escherichia coli	9
Morganella morganii	3
Others	23
Total	**317**
Genotype	
OXA-48	43 (24%)
VIM	43 (24%)
NDM	85 (47%)
GES	3 (1,5%)
KPC	5 (3%)
IMP	1 (0.5%)
Total	**180**

Discussion and conclusion

Certain limitations are inherent in the data presented. Data may be incomplete due to missing cases not captured on the LIS or non-standardised coding of pathogens and antibiotics. Testing methods and microbiological practice vary between sites and this could account for variation in the results presented. Confirmatory antimicrobial susceptibility test (AST) methods were not performed for any of these organisms and results presented here are reported as captured on the LIS. Thus, while some results may suggest the occurrence of an outbreak, it is not possible to confirm this. For certain sites, not all organisms are represented. This may be due to organisms not being identified at a particular site for 2014. Nevertheless, the data presented in this report highlight the importance of surveillance for antimicrobial resistance patterns. Active surveillance needs to be ongoing in order to identify trends as well as possible outbreaks.

Disclaimer

Data are reported as received through the Central Data Warehouse. No clinical data or molecular data were available to distinguish between hospital-associated and community-acquired infections.

Acknowledgements

The NHLS CDW team is acknowledged for cleaning the data and preparing the tables and figures. Ashika Singh-Moodley and Diane Rip for CPE are thanked for gene identification.

References

1. Langmuir AD. The surveillance of communicable diseases of national importance. *N Engl J Med* 1963; 268: 182-92.
2. Garner JS, et al. CDC definitions for nosocomial infections. *Am J Infect Control* 1988; 16: 128-140.
3. Performance Standards for Antimicrobial Susceptibility Testing. Clinical and Laboratory Standards Institute (CLSI), 2014; M 100-S24, Vol. 34 No.3