THE PATHCARE NEWS

Western Cape Province Antimicrobial Surveillance Data for organisms causing bacteraemia that are frequently associated with Hospital-Acquired Infections: 2021 and 2022.

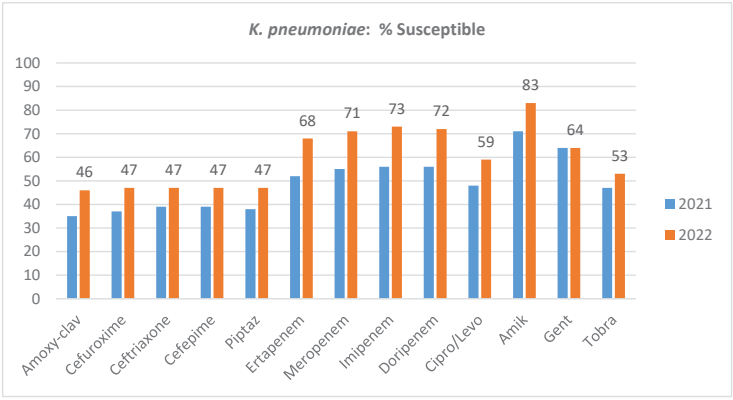
We are presenting here the PathCare susceptibility data for common hospital-acquired organisms isolated from blood cultures from patients in the Western Cape Province over the last 2 years. The focus is on the ESKAPE organisms, an acronym coined by die Infectious Diseases Society of America to emphasize the group of pathogens that cause hospital infections that may 'escape' the effects of antimicrobial agents.[1] These organisms include Gram-negative organisms *Pseudomonas aeruginosa, Acinetobacter spp.*, and extended spectrum beta-lactamase producing (ESBL) and carbapenem-resistant Enterobacterales (CRE); and the Gram-positive organisms methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VRE).

The rate of infection with multi-resistant organisms is generally higher in critical-care settings due to long hospital stays, broad-spectrum antibiotic therapy and multiple invasive procedures, but resistant infections may also occur in at-risk patients in other settings, especially those who have been recently exposed to multiple or broad-spectrum antimicrobial treatment. ESBL and CRE is most frequently associated with *Klebsiella pneumoniae,* but also occur sporadically in other *Enterobacterales* bacteria e.g. *Enterobacter* spp. CRE infection is usually preceded by colonisation, mainly of the gastro-intestinal tract, where it may persist for extended periods after the patient has been discharged from hospital. CRE carriage also poses a risk to other patients in the health-care setting and infection prevention measures are crucial to prevent further spread.

The trend in rising resistance in Gram negative organisms in healthcare facilities is a concern, which emphasize the need for careful stewardship and the importance of taking appropriate samples for culture prior to the administration of broad-spectrum antimicrobial agents to enable subsequent targeted therapy and de-escalation to narrow spectrum agents where appropriate. This strategy is important to reduce the volume of carbapenem use, which drives the increase in CREs.

Klebsiella pneumoniae

2021 (n=497); 2022 (n=305)

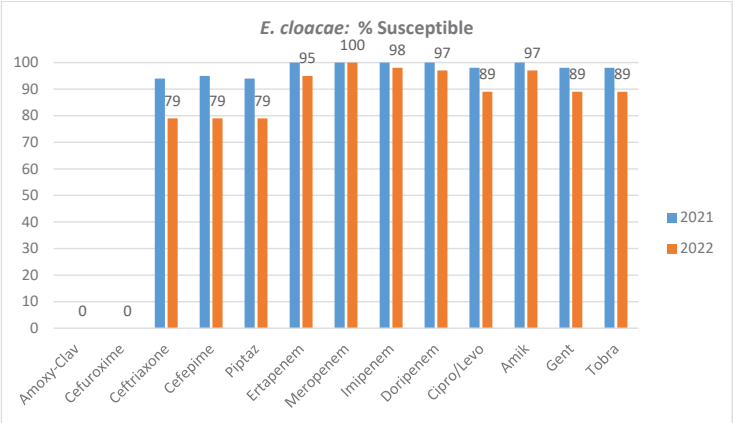


Klebsiella pneumoniae is one of the most common pathogens isolated from blood and is a frequent cause of hospital-acquired pneumonia, hospital-acquired urinary tract infection and central-line associated bloodstream infections. The prevalence of ESBL-producing *K. pneumoniae* (represented here by resistance to cefepime) was 53% during 2022. These ESBL isolates frequently harbour resistance determinants to other antibiotic classes as well e.g. quinolone resistance (41% in 2022) and therefore therapeutic options are often limited to the carbapenems. The emergence of carbapenem resistance is therefore a great concern, with 32% of *K. pneumoniae* showing ertapenem resistance during the 2022 surveillance period. This shows an increase from 15% reported for ertapenem in a 2016 survey of private sector laboratory data.[2] In the 2022 survey, the carbapenemases that were detected comprised OXA-48-like enzymes in 75% of CRE isolates, NDM in 24% and VIM was detected in one CRE isolate. The subset of isolates exhibiting resistance to the carbapenems were also tested for susceptibility to the following agents, with the 2022 data showed in brackets: tigecycline (54% susceptible); colistin (99% susceptible) and ceftazidime-avibactam (73% susceptible). Ceftazidime-avibactam is a novel beta-lactam beta-lactamase inhibitor with excellent activity against OXA-48 type carbapenemase producers. It does not have any activity against NDM producers.

Although a high proportion of isolates are ESBL-producers, the 2022 versus 2021 data shows a decrease in ESBLs (from 61% to 53%) and CREs (from 48% to 32%). During 2021, an increase in *K. pneumoniae* blood isolates were observed during COVID-19 peaks. This may have been due to a combination of factors such as long hospital stays in high care settings and poor adherence to infection prevention measures which increase the risk of hospital-acquired infections.

Enterobacter cloacae

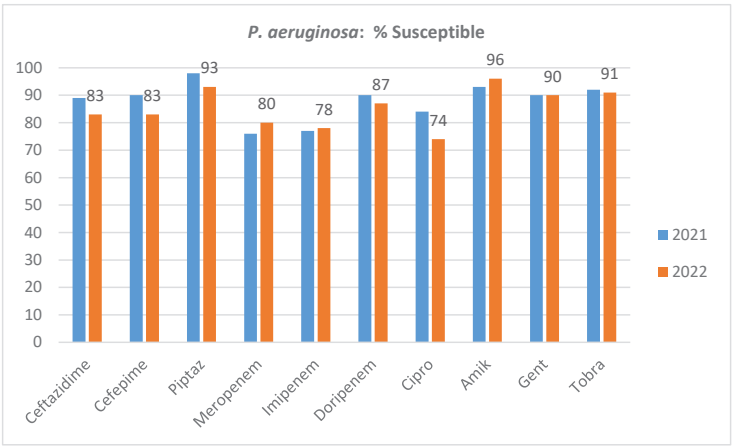
2021 (n=63); 2022 (n=62)



Enterobacter cloacae causes similar infections to *Klebsiella* spp. It carries the Amp C chromosomal gene which renders it intrinsically resistant to amoxycillin-clavulanate and cefuroxime. Exposure to third generation cephalosporins can select for de-repressed mutants that are also resistant to ceftriaxone, cefotaxime and ceftazidime, but remain susceptible to cefepime. However, the acquisition of ESBL genes may also render cefepime resistant. The prevalence of ESBL-producing *E. cloacae*, represented here by resistance to cefepime, was 21% in 2022, compared to 5% in 2021. Ertapenem resistance was detected in 5% of isolates in 2022, compared to no carbapenem resistance in 2021.

Pseudomonas aeruginosa

2021 (n=82); 2022 (n=69)



Pseudomonas aeruginosa is a cause of ventilator-associated pneumonia, catheter-associated urinary tract infection, wound and soft tissue infections, and central-line associated bloodstream infections. Antimicrobial resistance in *P. aeruginosa* may emerge from chromosomal mutations such as overproduction of intrinsic beta-lactamases, hyper-expression of efflux pumps and loss of outer membrane porins. Porin loss affect carbapenem susceptibility, particularly imipenem susceptibility. This organism may also acquire mobile genetic elements encoding for carbapenemases such as VIM.

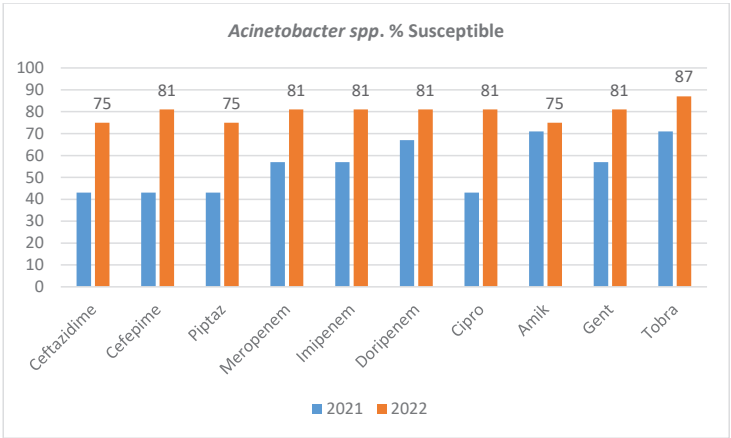
In 2022, the susceptibility to the carbapenems ranged from 78 to 87% with doripenem being the most active carbapenem. Susceptibility rates were similar to 2021. The novel beta-lactam beta-lactamase inhibitor, ceftolozane-tazobactam showed a similar susceptibility rate to piperacillin-tazobactam in 2022 (94% versus 93% respectively). Ceftolozane-tazobactam was not included in the bar chart for the 2021/2022 comparison, because only a subset of isolates was tested in 2021.

In a critically ill patient where a multidrug-resistant strain is suspected (e.g. previous broad-spectrum antibiotic therapy), it may be reasonable to consider combination therapy and higher dosing strategies to ensure that at least one agent is active against the organism. Amikacin showed excellent activity against *P. aeruginosa* (96% susceptible in 2022) and may be considered in combination therapy.

Colistin/Polymyxin B is regarded as a last-resort agent for pan-resistant strains. A minority subset of pan-resistant isolates that were tested, were all susceptible to this agent. With the exception of therapy for UTI, colistin should not be used as monotherapy. For indications other than UTI, polymyxin B is preferred over colistin due to faster attainment of serum concentrations, less inter-patient variability in pharmacokinetics and no renal dose adjustments are required for polymyxin B. However, the polymyxins are regarded as sub-optimal agents if the site of infection is the respiratory tract. Adjunctive inhalation therapy with colistin may be required for pneumonia.

Acinetobacter spp.

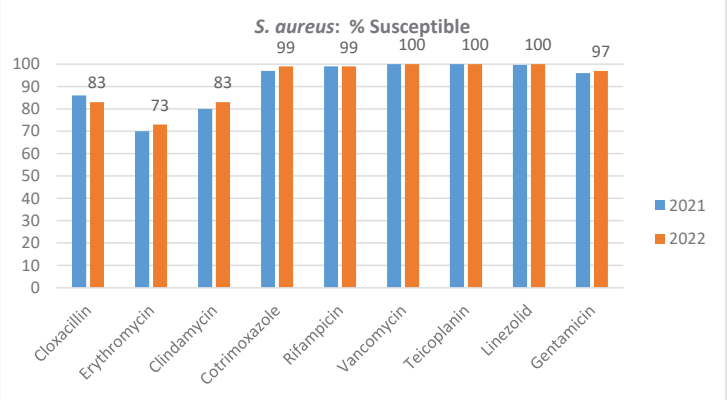
2021 (n=7); 2022 (n=16)



Acinetobacter may cause hospital-acquired infections such as ventilator-associated pneumonia and is known to acquire resistance to multiple antibiotics, including the carbapenems. Resistant phenotypes may be selected due to carbapenem exposure. Over the last 2 years there were few *Acinetobacter* spp. isolated from blood culture specimens. In 2022, 81% of isolates were susceptible to the carbapenems, compared to 57% in 2021. However due to the low numbers, these percentages may not necessarily be reflective of the overall susceptibilities of this organism. In units where the prevalence of carbapenem-resistance is high, combination therapy is advised to broaden the spectrum of empiric therapy. Colistin/ Polymyxin B or tigecycline are alternative agents that may be required to treat these multi-resistant infections. In 2022, 87% of isolates were susceptible to tigecycline, and a subset of isolates tested against colistin were all susceptible.

Staphylococcus aureus

2021 (n=286); 2022 (n=275)



Staphylococcus aureus is a frequent cause of community and hospital-acquired infections. In the hospital setting *S. aureus* may be associated with post-operative wound infections, line-related bloodstream infections, prosthetic joint or other prosthetic/implant-related infections and hospital-acquired pneumonia. Persistent bacteraemia despite appropriate therapy suggests endovascular infection or poor source control and should prompt further investigations and interventions e.g. assessment for endocarditis, central-line removal or surgical drainage and debridement.

In 2022, 17% of *S. aureus* blood culture isolates were resistant to cloxacillin and classified as MRSA. These isolates are also resistant to other beta-lactam agents with the exclusion of the novel cephalosporin, ceftaroline. MRSA isolates were also tested against daptomycin and no resistance to this agent was detected. Treatment options for MRSA infections include vancomycin, teicoplanin, daptomycin (excluding pneumonia), linezolid and ceftaroline. For localised MRSA infections such as prosthetic joint infections, cotrimoxazole in combination with rifampicin may be considered as a therapeutic oral option. These agents show excellent susceptibility and good oral bioavailability and tissue penetration. Rifampicin must be combined with another active agent to prevent emergence of resistance during therapy.

MRSA was detected in a lower percentage of *S. aureus* isolates than the 26% reported in the 2016 survey of antimicrobial resistance in the private sector.[2] Similar trends have been reported nationally (combined public and private sector data) with resistance levels for *S. aureus* declining over the survey period 2012-2017 from 36% to 23%.[3] More recent data from the private sector (SASCM surveillance data, 2019-September 2022) show a similar decrease in MRSA bloodstream isolates in the Western Cape.[4] This follows trends occasionally reported in the international literature, where a decrease in the prevalence of MRSA is linked to antimicrobial stewardship and improved infection control.[5]

Enterococci

2021 (n= 109); 2022 (n=128)

The *Enterococci* include predominantly *Enterococcus faecalis* (84% of Enterococci isolated from blood culture specimens in 2022) and less frequently *Enterococcus faecium* (16%). Similarly, 87% of *Enterococci* were *E. faecalis* and 13% *E. faecium* in 2021. The enterococci cause urinary tract infections, polymicrobial abdominal and soft tissue infections and endocarditis. All patients with Enterococcal bacteraemia should be assessed for endocarditis. *E. faecalis* is usually susceptible to ampicillin (98-100% susceptible in this survey) and penicillin (98% susceptible) whereas *E. faecium* is resistant (86-95% resistant in this survey). *E. faecium* is mostly associated with hospital-acquired infections and display resistance to multiple antibiotic agents with few therapeutic options which include vancomycin, teicoplanin, linezolid (no resistance detected against these agents) and high-dose daptomycin (all tested susceptible dose dependent). VRE has emerged globally and has also been reported from South Africa.[3] No VRE has been detected in this survey.

References:

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2. Olga Perovic, Husna Ismail, Erika Van Schalkwyk, Warren Lowman, Elizabeth Prentice, Marthinus Senekal & Chetna N Govind (2018) Antimicrobial resistance surveillance in the South African private sector report for 2016, Southern African Journal of Infectious Diseases, 33:4,114-117, DOI: 10.1080/23120053.2018.1482646
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