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Cumulative antimicrobial susceptibility data for a tertiary-level paediatric oncology unit in Johannesburg, South Africa

Authors:
Nina von Knorring[1,2]
Trusha Nana[1,2]
Vindana Chibabhai[1,2]

Affiliations:
[1]Division of Clinical Microbiology and Infectious Diseases, School of Pathology, University of the Witwatersrand, Johannesburg, South Africa

[2]Microbiology Laboratory, Charlotte Maxeke Johannesburg Academic Hospital, National Health Laboratory Service, Johannesburg, South Africa

Corresponding author:
Nina von Knorring,
ninavonknorring@gmail.com

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Background: There is global concern regarding the spread of antimicrobial resistance in bacteria and fungi. Oncology patients are at particular risk of infections with multidrug resistant organisms. These patients require urgent initiation of empiric antimicrobial therapy when presenting with neutropenic fever. Currently, piperacillin-tazobactam and amikacin with or without vancomycin is the treatment of choice in the unit.

Aim: The purpose of this study was to develop a cumulative antibiogram for the paediatric oncology unit at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) to guide empiric treatment recommendations for patients presenting with suspected bacterial or fungal infection.

Setting: Tertiary-level paediatric oncology unit.

Methods: A retrospective observational analysis was performed of bacterial and fungal antimicrobial susceptibility data extracted from the microbiology laboratory information system for clinical specimens submitted from the paediatric oncology unit at CMJAH. Data was analysed for the period January 2015 to May 2018. In addition, analysis and comparison of two 17-month time periods was performed in order to elicit any changes over time.

Results: *Klebsiella pneumoniae* and *Escherichia coli* were the most common gram-negative organisms isolated. Twenty-one percent of Enterobacteriaceae showed resistance to third generation cephalosporins and 9% to carbapenems. Rates of carbapenem-resistant isolates decreased significantly over time. Adding amikacin to piperacillin-tazobactam significantly increased bacterial coverage. Coagulase-negative staphylococci and *Candida parapsilosis* were the most common gram-positive and fungal isolates recovered during the study.

Conclusion: The results support the continued use of piperacillin-tazobactam and amikacin for paediatric oncology patients presenting with neutropenic fever in this unit. Antibiograms are an important component of antimicrobial stewardship in conjunction with efficient infection prevention and control measures.

Keywords: governance; big data; controls; control framework; antibiogram; paediatric oncology; antimicrobial resistance; antimicrobial stewardship; infection prevention and control.

Introduction

The World Economic Forum has declared antimicrobial resistance the next major global challenge.[1] It is a significant cause of morbidity and mortality, especially in hospitalised patients.[2,3] Oncology patients on chemotherapy are at particular risk of bacterial and fungal infections and require urgent initiation of empiric antibiotics when presenting with neutropenic fever. They are also likely to harbour drug resistant organisms, and delayed initiation of appropriate therapy is associated with poor outcomes.[4,5,6]

Numerous studies in paediatric oncology units have raised concerns about the increase in resistant pathogens.[7,8,9,10] The National Institute for Communicable Diseases (NICD) carries out surveillance in South Africa and collates resistance data from both public- and private-sector laboratories, which it publishes annually. The data shows that resistance in general is increasing in certain gram-negative bacteria and yeasts. Gram-negative organisms are increasingly producing extended spectrum β-lactamase (ESBL) and carbapenemase enzymes, which hydrolyse broad-spectrum antibiotics. The NICD surveillance of bloodstream infections Group of Enteric,

Respiratory and Meningeal Diseases Surveillance in South Africa (GERMS-SA) showed an increase in *Klebsiella pneumoniae* isolates with ESBL phenotype from 62% to 75% between 2010 and 2012. Reporting of carbapenem-resistant Enterobacteriaceae (CRE) isolates was added in 2015, and case numbers increased significantly over the subsequent years.[11] Resistance to commonly used antifungal drugs, such as azoles, is developing in yeasts, and there is a shift towards a higher prevalence of species that are inherently resistant to these agents, such as *Candida glabrata* and *C. auris*.[12,13] Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE), which are known to be particularly difficult to treat in neutropenic patients, are being detected in 24% and 5% of the respective species according to GERMS-SA reports.[11]

Antimicrobial stewardship is a crucial intervention to guide the appropriate use of antibiotics, and stewardship programmes are recommended for all health care facilities.[14,15] Ideally these programmes should be in place where patients with cancer are treated to guide and monitor antimicrobial treatment practices.[16,17,18] A recent meta-analysis by Baur et al. demonstrated that antimicrobial stewardship can indeed significantly reduce infection and colonisation with multidrug resistant organisms especially in the haemato-oncology setting.[19] It has also been associated with lower mortality in adult oncology patients with neutropenia.[20] In addition, stewardship can have a positive impact on the rate of adverse drug reactions and overall health care expenditure.[21]

Cumulative antibiograms are an integral aspect of antimicrobial stewardship programmes.[14] They depict the spectrum of microorganisms and susceptibility profiles in a specific location or hospital unit over time and are used to direct the choice of empiric treatment of suspected bacterial or fungal infection prior to the availability of results from cultured specimens.[21,22] In addition to optimising patient management, antibiograms inform infection prevention and control practices and assist with monitoring strategies of these interventions. The Clinical and Laboratory Standards Institute (CLSI) has published guidelines in order to standardise the methodology used for antibiogram development and reporting.[23,24]

The 24-bed paediatric oncology ward and outpatient department at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) manages medical and surgical patients with haemato-lymphatic malignancies, solid tumours as well as benign haematological disorders. Prior to this analysis, patients with suspected neutropenic fever were treated empirically with piperacillin-tazobactam and amikacin with the addition of vancomycin for those with intravenous catheters.

The aim of the study was to compile an antibiogram for the paediatric oncology unit at CMJAH with the intention of guiding empiric treatment recommendations for patients presenting with suspected bacterial or fungal infection. Results may further be used to direct infection prevention and control measures in this unit.

Methods

A retrospective observational analysis was performed of bacterial and fungal identification and susceptibility data generated for paediatric oncology patients at the National Health Laboratory Service (NHLS) Microbiology Laboratory at CMJAH between January 2015 and May 2018. Isolates cultured from blood, cerebrospinal fluid, urine, the respiratory tract, tissue, pus, catheter tips and swabs were included in the analysis. As per the laboratory's standard operating procedures, the majority of isolates were processed using the automated identification and susceptibility testing system Vitek®2 (bioMérieux, Marcy l'Étoile, France). A smaller proportion of isolates were identified using manual biochemical and conventional Kirby-Bauer disk diffusion susceptibility testing methods (mainly urinary isolates). Enterobacteriaceae with reduced susceptibility to carbapenems were tested using a gradient diffusion susceptibility test (ETEST® bioMérieux) for accurate determination of the minimum inhibitory concentration (MIC). From 2017 organism identification was also performed using matrix-assisted laser desorption ionisation time-of-flight mass spectrometry (MALDI-TOF MS, Vitek® MS bioMérieux). Susceptibility results were only reported for antimicrobials routinely tested by the laboratory and used for clinical management and were interpreted according to CLSI guidelines for the relevant year.[25,26]

Data for paediatric oncology outpatients and ward patients at CMJAH was extracted from the laboratory interface system database TrakCare® (InterSystems, Cambridge, MA, USA) and sorted per organism to species level (for gram-positive bacteria, gram-negative bacteria and yeasts). In order to reduce selection bias, repeat patient isolates of the same species were removed according to the patient-based algorithm described in the CLSI guidelines.[24] Therefore, only the first isolate of a specific organism per patient was included regardless of specimen type or site. In addition to the susceptibility to individual antimicrobials, analysis of the empiric combination of agents used in the unit was also performed to assess the effect on antimicrobial coverage. In order to obtain the highest possible number of isolates per species, data was collated and analysed for the period January 2015 to May 2018. To determine if a change in susceptibility rates occurred amongst the most prevalent pathogens, a second analysis was performed for two separate periods representing the start and end of the analysis period, January 2015 to May 2016 and January 2017 to May 2018. Analysis of the gram-negative organisms was performed both at species level and combined as Enterobacteriaceae and non-fermenters because of the relatively lower isolate numbers available for analysis in the chosen periods. Data were presented as proportions and percentages with confidence intervals for individual

antimicrobials. Fisher's exact test (GraphPad Software, San Diego, USA) was used to establish any statistically significant differences in susceptibility rates between the two 17-month periods. The *p*-values were reported as two-tailed, with values < 0.05 considered to be statistically significant.

Isolates with any carbapenem MIC above the susceptible range were referred for molecular confirmation of carbapenemase genes. For the purpose of this analysis a CRE describes isolates that had non-susceptible carbapenem MICs on gradient diffusion test with or without molecular confirmation. *Pseudomonas* and *Acinetobacter* species were reported as extensively drug resistant if only susceptible to two or fewer classes of antibiotics. Colistin susceptibility was not analysed, as the majority of isolates were not tested by broth microdilution according to current CLSI recommendations. Data on tobramycin was also excluded as it was only available for urinary isolates processed by the Kirby-Bauer disk diffusion method.

Ethical consideration

The study was approved by the Human Research Ethics Committee, University of the Witwatersrand (protocol no. M180991).

Results

A total of 263 paediatric patients seen in the oncology department at CMJAH between January 2015 and May 2018 were included in the analysis, generating 438 initial episodes of cultured isolates after removal of duplicate specimens (n = 215) and miscellaneous species (n = 17).

Gram-negative bacteria

The majority of organisms were gram-negative bacilli (n = 214, 49%; Figure 1), mainly cultured from blood and urine specimens (Table 1). *Klebsiella pneumoniae* and *Escherichia coli* in equal numbers were the main species in this group (Table 2). Of the Enterobacteriaceae, 35 (21%, 95% confidence interval [CI] 15–28) showed resistance to one or both third generation cephalosporins (ceftriaxone/ceftazidime). All gram-negative organisms combined appear highly susceptible to the carbapenems, imipenem and meropenem (93% and 92%, respectively). Fifteen Enterobacteriaceae isolates displayed resistance to the carbapenems (9%, 95% CI 5–14; ertapenem, meropenem or imipenem).

Extensive drug resistance was found in 15% (n = 7, 95% CI 7–28) of non-fermenters analysed. *Pseudomonas* species were the most common non-fermenter organisms and showed susceptibilities between 79% and 89% to antimicrobial agents tested. Susceptibility to the anti-pseudomonal carbapenems, meropenem and imipenem, was particularly high (89%; n = 28 and 27, respectively). *Acinetobacter* species represented the second largest group of non-fermenters; these demonstrated lower susceptibility rates to the standard antibiotics tested compared to *Pseudomonas* species (range 47% – 79%).

A comparison of the two analysis periods shows a significant increase in *E. coli* isolates mainly from urine specimens (20% to 36%, p = 0.02). The proportion of Enterobacteriaceae resistant to third generation cephalosporins remained unchanged (21% and 17%, p = 0.53). However, of note, the proportion with carbapenem resistance decreased significantly (18% and 4%, p = 0.008).

At species level there was a considerable increase in susceptibility of *K. pneumoniae* isolates to piperacillin-tazobactam and ciprofloxacin, though these were not statistically significant (42% vs. 70%, p = 0.08, and 54% vs. 91%, p = 0.06, respectively). Overall there was a non-significant increase in susceptibility of gram-negative organisms with regard to meropenem and imipenem between the two time periods (89% vs. 97%, p = 0.07). Ciprofloxacin susceptibility also increased from 79% to 87% across all gram-negative bacteria, but this was not statistically significant (p = 0.21).

Comparing piperacillin-tazobactam susceptibility alone versus piperacillin-tazobactam and amikacin in combination reveals a statistically significant increase in the proportion of susceptible isolates in favour of combination therapy (76% monotherapy vs. 89% for combination therapy, p = 0.0005; Table 3).

Gram-positive bacteria

Staphylococcus species represent the largest proportion of gram-positive organisms cultured (n = 134, 72%; Figure 2). The vast majority of these were identified as coagulase-negative staphylococci (CONS) from blood culture specimens; approximately one-third was susceptible to cloxacillin (n = 35, 35%). The proportion of CONS isolates considered clinically significant was not retrospectively established. Methicillin resistance was found in five (15%) *S. aureus* isolates. Enterococcus species accounted for the second largest group of gram-positive organisms (n = 29, 16%) and showed a non-significant trend towards increased vancomycin resistance between the two time periods, although overall numbers remained low (n = 1 and n = 7, p = 0.09). Seven of the nine vancomycin-resistant isolates cultured over the entire time period originated from sterile sites. In total 22 (12%) isolates belonging to the viridans streptococci were isolated from sterile sites.

Yeasts

Only 39 yeast isolates (comprising 9% of all isolates; Figure 3) were identified during the study period. *Candida parapsilosis* accounted for the majority of specimens (n = 17, 44%); all but one of these isolates were susceptible to fluconazole. There were 11 (28%) *Candida albicans* isolates. The first and only isolate of multidrug resistant *C. auris* in the unit at the time of writing this manuscript was detected in January 2018.

January 2015 to May 2018 | January 2015 to May 2016 | January 2017 to May 2018

Organisms	Number of isolates	Percentage susceptibility (%)												Percentage resistance (%)		
		Ampicillin	Amoxicillin-clavulanate	Piperacillin-tazobactam	Ceftiaxone	Ceftazidime	Cefepime	Ertapenem	Meropenem	Imipenem	Ciprofloxacin	Gentamicin	Amikacin	Cotrimoxazole	Percentage ESBL (%)	Percentage CRE (%)	Percentage XDR (%)
Klebsiella spp.	61	-	41	57	47	46	51	82	90	93	68	51	85	41	36	20	-
	26	-	27	42	38	31	38	64	77	81	54	35	81	27	31	39	-
	23	-	52	70	56	61	61	96	100	100	91	65	87	56	39	4	-
Escherichia coli	61	26	70	93	85	85	87	98	98	98	86	83	95	32	16	2	-
	17	29	65	88	75	82	81	94	94	94	82	88	87	18	18	6	-
	36	22	69	94	92	89	92	100	100	100	89	79	97	29	11	**0**	-
Enterobacter spp.	24	-	-	86	79	83	83	96	100	100	89	87	87	-	13	4	-
	13	-	-	85	85	92	92	100	100	100	92	92	92	-	15	0	-
	9	-	-	86	67	67	67	87	100	100	80	67	78	-	11	11	-
Other Enterobacteriaceae	21	-	-	85	95	94	94	95	95	92	93	82	88	-	-	-	-
	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	14	-	-	-	-	-	-	-	-	-	-	-	-	-	-	7	-
Acinetobacter spp.	19	-	-	47	-	53	58	-	72	72	79	58	54	-	-	-	26
	8	-	-	62	-	62	62	-	86	75	87	75	80	-	-	-	25
	9	-	-	43	-	55	67	-	78	87	78	44	43	-	-	-	22
Pseudomonas spp.	28	-	-	85	-	82	79	-	89	89	86	79	86	-	-	-	7
	15	-	-	79	-	93	80	-	93	93	93	73	80	-	-	-	-
	8	-	-	87	-	62	87	-	100	87	87	75	100	-	-	-	-

ESBL, extended spectrum β-lactamase; CRE, carbapenem-resistant Enterobacteriaceae; XDR, extensively drug-resistant.

FIGURE 1: Gram-negative antibiogram.

TABLE 1: Organism distribution and site.

Organism type	Total number of isolates *n* (%)	Blood cultures (% organism type)	Other sterile sites† (% organism type)	Non-sterile sites‡ (% organism type)
Gram-negative organisms	214 (49)	106 (49)	10 (5)	98 (46)
Gram-positive organisms	185 (42)	138 (75)	16 (9)	31 (17)
Yeast	39 (9)	36 (92)	0 (0)	3 (8)
Total	**438**	**280**	**26**	**132**

†, Cerebrospinal fluid (CSF), pus, fluid, tissue, catheter tips.

‡, Urine, respiratory samples, swabs.

TABLE 2: Bacterial and fungal identification and frequency.

Organism type	Total number of isolates 2015–2018 (*n*)	2015–2016†	2017–2018†	*p*
Gram-negative organisms	214	85	99	0.61
Enterobacteriaceae	167	62	82	0.17
Klebsiella spp.	61	26	23	0.32
E. coli	61	17	36	0.02
Enterobacter spp.	24	13	9	0.25
Other Enterobacteriaceae	21	6	14	0.16
Non-fermenters	47	23	17	0.24
Acinetobacter spp.	19	8	9	1.00
Pseudomonas spp.	28	15	8	0.07
Gram-positive organisms	185	83	79	0.25
Coagulase-negative Staphyloccoci	100	42	44	0.53
Staphylococcus aureus	34	19	11	0.16
Enterococcus spp.	29	11	16	0.29
Viridans streptococci	22	11	8	0.63
Yeasts	39	13	21	0.28
Candida parapsilosis	17	4	11	0.29
Candida albicans	11	3	7	1.00
Other yeast spp.	11	6	1	0.06

†, Isolates between June and December 2016 were excluded from this period of analysis.

TABLE 3: Comparison of overall antibacterial coverage achieved by piperacillin-tazobactam alone versus piperacillin-tazobactam and amikacin. combined. Gram-negative organisms 2015–2018.

Number of strains†	Percentage susceptible (%)			*p*
	Piperacillin-tazobactam	Amikacin	Piperacillin-tazobactam and/or Amikacin‡	
200	76	87	89.5	0.0005

†, Excludes 15 isolates with missing susceptibility to either agent.

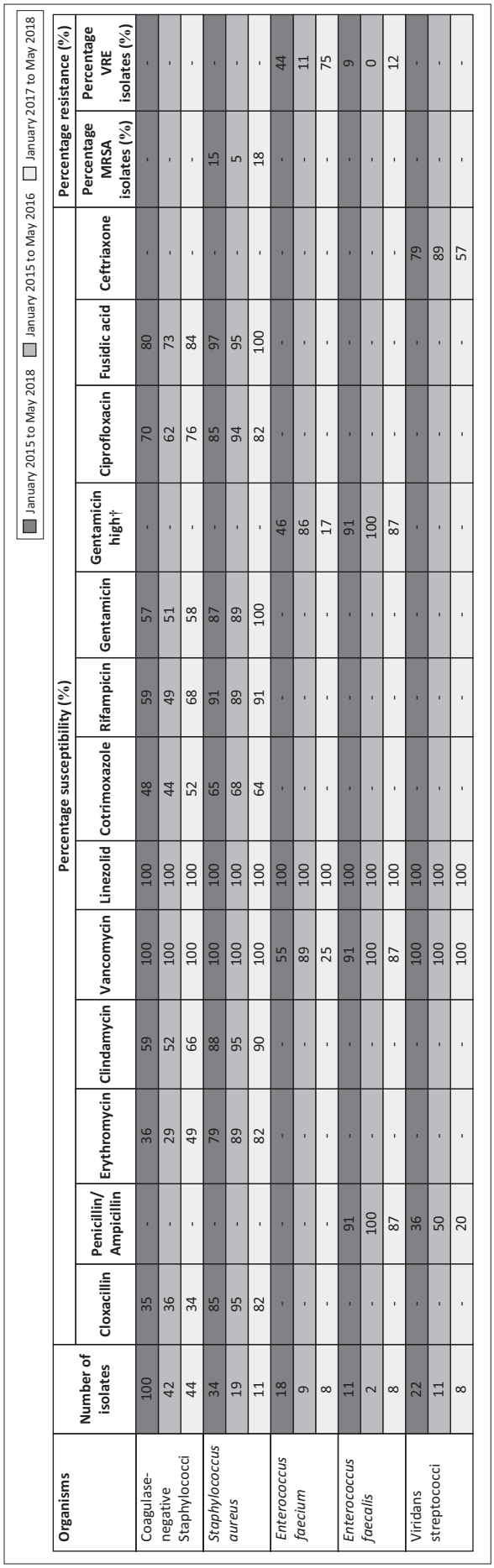
‡, Includes isolates susceptible to piperacillin-tazobactam and resistant to amikacin, susceptible to amikacin and resistant to piperacillin-tazobactam, or susceptible to both.[24]

Discussion

The results of this cumulative antibiogram provide a basis for the rational selection of empiric antimicrobial therapy in the paediatric oncology ward at CMJAH. They confirm the broad coverage provided bypiperacillin-tazobactam and amikacin against the main initial bacterial pathogens cultured from these patients.

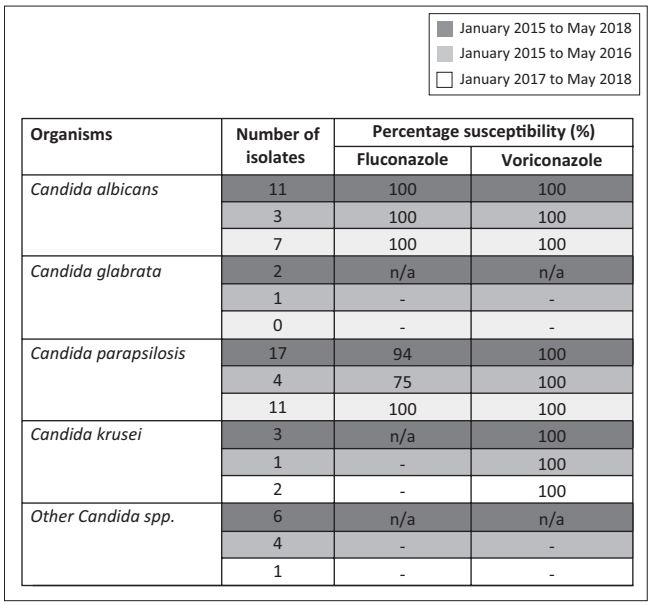
Compliance with CLSI guidance on antibiogram development as well as analysis of individual episodes according to the CLSI patient-based algorithm was undertaken to minimise selection bias and provide a basis for selection of empiric therapy for initial presentation with suspected bacterial or fungal infection. However, this method is likely to miss changes in resistance profiles within individual patients presenting with repeated episodes of infection caused by the same organism and the emergence of new patterns of resistance within the unit. To address this issue a comparison of isolates taken at the beginning and end of the observation period was performed. This allowed a cautious assessment of possible changes over time to be made. It remains critically important to take any previous culture results into consideration when making individual antimicrobial choices.[24] Differentiating between community-acquired and nosocomial infections is often less clear in these high-risk patients because of their frequent exposure to health care facilities and antimicrobial therapy.

Differences in methodology limit comparison of our findings to previous research on infections and microbial susceptibility in paediatric oncology patients in South Africa.[27,28,29] A study at the Chris Hani Baragwanath Hospital oncology unit situated in the same province reported on a large cohort of patients enrolled and followed up between 2009 and 2014.[27] Their analysis of blood cultures taken during septic episodes showed overall lower susceptibility to commonly used antibiotics with larger proportions of ESBL producers in gram-negative isolates and MRSA and VRE in gram-positives. However, all patient samples were included rather than initial episodes, thus reflecting possible treatment-induced resistance. The large variation in susceptibility profiles between centres and sites is evident in an extensive literature review by Mikulska et al.[30] and underlines the importance of acquiring local and current data. The results presented here should therefore not be extrapolated to other centres and require periodic updates.



Organisms	Number of isolates	Percentage susceptibility (%)											Percentage resistance (%)	
		Cloxacillin	Penicillin/ Ampicillin	Erythromycin	Clindamycin	Vancomycin	Linezolid	Cotrimoxazole	Rifampicin	Gentamicin	Gentamicin high†	Ciprofloxacin	Fusidic acid	Ceftriaxone	Percentage MRSA isolates (%)	Percentage VRE isolates (%)
Coagulase-negative Staphylococci	100	35	-	36	59	100	100	48	59	57	-	70	80	-	-	-
	42	36	-	29	52	100	100	44	49	51	-	62	73	-	-	-
	44	34	-	49	66	100	100	52	68	58	-	76	84	-	-	-
Staphylococcus aureus	34	85	-	79	88	100	100	65	91	87	-	85	97	-	15	-
	19	95	-	89	95	100	100	68	89	89	-	94	95	-	5	-
	11	82	-	82	90	100	100	64	91	100	-	82	100	-	18	-
Enterococcus faecium	18	-	-	-	-	55	100	-	-	-	46	-	-	-	-	44
	9	-	-	-	-	89	100	-	-	-	86	-	-	-	-	11
	8	-	-	-	-	25	100	-	-	-	17	-	-	-	-	75
Enterococcus faecalis	11	-	91	-	-	91	100	-	-	-	91	-	-	-	-	9
	2	-	100	-	-	100	100	-	-	-	100	-	-	-	-	0
	8	-	87	-	-	87	100	-	-	-	87	-	-	-	-	12
Viridans streptococci	22	-	36	-	-	100	100	-	-	-	-	-	-	79	-	-
	11	-	50	-	-	100	100	-	-	-	-	-	-	89	-	-
	8	-	20	-	-	100	100	-	-	-	-	-	-	57	-	-

MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci.
†, 120µg.
FIGURE 2: Gram-positive antibiogram.



Organisms	Number of isolates	Percentage susceptibility (%)	
		Fluconazole	Voriconazole
Candida albicans	11	100	100
	3	100	100
	7	100	100
Candida glabrata	2	n/a	n/a
	1	-	-
	0	-	-
Candida parapsilosis	17	94	100
	4	75	100
	11	100	100
Candida krusei	3	n/a	100
	1	-	100
	2	-	100
Other Candida spp.	6	n/a	n/a
	4	-	-
	1	-	-

n/a, not applicable.
FIGURE 3: Yeasts.

The relatively high levels of susceptibility to antimicrobials observed in gram-negative organisms and the positive trend of decreasing resistance seen over time is encouraging. The carbapenem-free empiric treatment regimen employed by the oncology unit and effective infection control measures may have contributed to this outcome. Increasing numbers of CRE isolates detected between September 2015 and March 2016 led to the implementation of more rigorous hand hygiene measures and environmental cleaning, which may have had a positive influence on resistance rates. However, the antimicrobial resistance rates of *Acinetobacter* spp. seen in this antibiogram are of concern. These are in keeping with national results, which have now led to enhanced surveillance of *Acinetobacter baumannii* in South Africa.

Other aspects of antimicrobial stewardship with regard to the combination piperacillin-tazobactam and amikacin such as drug side-effects and cost have not been assessed here. The search for the optimal carbapenem-sparing regimen with sufficient activity against ESBL-producers and acceptable safety profile is ongoing.[31] To date there is no consensus on the ideal empiric choice of antimicrobial treatment for this patient group.[17] Local and patient-specific factors such as age, microbial profiles, drug side-effects, likely effect on selection of resistance and cost need to be considered. In these vulnerable patients it is important to balance the need for initial broad antimicrobial coverage against the possible increase in selection pressure and development of resistance. A study by Castagnola et al. on empiric therapy for patients with neutropenic fever suggests adding a second drug if resistance to the single agent is ≥ 10%, hence the addition of amikacin to piperacillin-tazobactam for patients in this unit is indicated.[32] Unfortunately antibiotics with activity against multidrug resistant gram-negative organisms are scarce and are often associated with considerable collateral damage.[33] This dilemma highlights the importance of using

antibiograms in addition to patient treatment history to tailor empiric therapy. The antibiogram can also be employed in conjunction with rapid identification methods such as MALDI-TOF when choosing empiric antimicrobials based on organism identification while susceptibility results are still pending.

The decision to add vancomycin to the empiric regimen should be taken judiciously in order to avoid overuse and further selection of resistance in enterococcal isolates. Broad-spectrum antibiotics such as vancomycin alter the resident gut flora and favour overgrowth of bacteria with acquired or natural resistance. There is some evidence to support the use of chlorhexidine baths for patients colonised or infected with VRE.[34] Gastrointestinal decolonisation strategies have unfortunately not been successful, and infection control measures are largely based on standard precautions, contact precautions, rectal screening and patient isolation.[35,36] In cases where vancomycin is given, care should be taken to review the need to continue this once Gram stain and culture results are available. The decision to add vancomycin to the empiric treatment regimen in this unit will be based on the large number of CONS isolates and the perceived risk for an invasive CONS infection in the individual patient. These are often of uncertain clinical significance in these complex patients. The microbiology laboratory should assist in assessing the relevance of these and encourage appropriate culture techniques where possible. The relatively large proportion of viridians species seen in our study is also in keeping with the literature.[30] Despite being commensals of the respiratory and gastrointestinal tract they are recognised opportunistic pathogens in this group of patients.

The shift in yeast isolates from *C. albicans* to non-albicans *Candida* species as seen in comparison to previous studies in the region is in keeping with countrywide epidemiology.[11,27] Surprisingly the *C. parapsilosis* isolates found in our patients were almost exclusively susceptible to fluconazole in contrast to other hospital units where azole-resistant *C. parapsilosis* isolates predominate.[37] However, this is unlikely to affect empiric antifungal treatment recommendations for the unit as fungicidal agents like the echinocandins or amphotericin B are indicated for initial therapy in neutropenic patients.[38] Antifungal stewardship should remain a critical component of antimicrobial stewardship in these patients.

There are several limitations to this study. Despite collating and analysing a large data set, several organisms did not achieve the CLSI recommended target of 30 isolates per species. This was especially problematic for the analysis of the two separate data sets comparing 2015–2016 and 2017–2018. Therefore, these results should be interpreted with caution. These types of challenges are well recognised and discussed in the CLSI guidelines themselves, as well as in other publications.[15,22,24] A further limiting factor was the retrospective nature of this analysis, which did not allow for confirmation of species identification or susceptibility results. Advances in microbial identification methods during the study period and subsequent changes to processing may have affected results. Moreover, inadvertent changes to collection practices of clinical samples over the years may have had an impact on the number and types of organisms isolated. This may explain the increase in urinary *E.coli* isolates observed here. The study population represents a heterogeneous group of patients in terms of diagnoses, and this study did not include analysis of demographic and clinical data. Neither the clinical significance of known skin and mucous membrane commensals nor the significance of samples taken from non-sterile sites could be established.

Going forward, it would be beneficial to include and interpret repeat patient isolates in a separate analysis, enabling more accurate assessment of the development of antimicrobial resistance and guidance on the management of health care associated infections. Further data analysis should also look at possible treatment recommendations for infectious syndromes and the development of a local protocol for the unit. Because antimicrobial *in vitro* susceptibility does not necessarily equate to *in vivo* activity, clinical outcome data would be of value to assess the efficacy of the empiric regimen.[16] While continuous antimicrobial resistance monitoring takes place at CMJAH, this analysis of the bacterial spectrum and susceptibility is the first to be conducted specifically for the paediatric oncology unit, with further assessment planned at 12–18 month intervals.

In conclusion, the findings of this cumulative antibiogram support the continued use of piperacillin-tazobactam and amikacin as empiric regimen for paediatric oncology patients presenting with suspected bacterial infection at CMJAH. This is encouraging, since this combination is in keeping with recommendations made by various international guidelines.[4,39] Cumulative antibiograms are a fundamental component of antimicrobial stewardship programmes guiding the appropriate selection of empiric therapeutic agents. This is of paramount importance for optimal patient outcomes and preservation of the activity of the limited antimicrobials currently available in an era of multidrug and extensive drug resistance.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

V.C. and T.N. conceptualised the study. N.v.K. collated and analysed the data. All authors read and approved the manuscript.

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