Seven-year surveillance of antimicrobial resistance in respiratory pathogens at a Ugandan referral hospital: Emerging trends and stewardship priorities

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Background. Respiratory tract infections remain a leading cause of global morbidity and mortality. Their management is increasingly complicated by the emergence and spread of antimicrobial resistance (AMR), particularly in resource-limited settings such as Uganda.
Objectives. To describe the prevalence, distribution and AMR patterns of bacterial pathogens isolated from respiratory tract specimens collected at Mbarara Regional Referral Hospital (MRRH), Uganda, between 2018 and 2024.
Methods. We conducted a retrospective analysis of 583 bacterial isolates from respiratory specimens collected at MRRH between 2018 and 2024. Data extracted from the WHONET system were analysed using Python to assess pathogen distribution, resistance patterns and multidrug resistance (MDR).
Results. *Streptococcus pneumoniae* (48.9%) and *Klebsiella pneumoniae* (32.9%) were the most frequently isolated organisms. Over time, *S. pneumoniae* prevalence declined, while *K. pneumoniae* and *Pseudomonas aeruginosa* became more prominent. High resistance was observed to tetracyclines, macrolides, sulphonamides and beta-lactams. MDR was detected in 74.7% of *S. pneumoniae* and 77.1% of *Klebsiella* species.
Conclusion. The rising prevalence of MDR among respiratory pathogens, particularly *K. pneumoniae* and *P. aeruginosa*, signals an urgent need to revise treatment guidelines and strengthen local stewardship, diagnostic capacity and AMR surveillance systems.

Keywords. Respiratory tract infections, antimicrobial resistance, Uganda.

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Study synopsis
What the study adds. This study investigated the clinical and microbial characteristics of respiratory tract infections (RTIs) in patients at a tertiary hospital in Uganda between 2018 and 2024. Key findings were a high prevalence of multidrug-resistant organisms, particularly *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*.
Implications of the findings. The results underscore the need for routine microbial surveillance and antibiotic stewardship to guide empirical therapy and curb antimicrobial resistance, especially in RTIs.

Respiratory tract infections (RTIs) are among the commonest human infections globally.[1] According to World Health Organization (WHO) and Global Burden of Disease data, over 450 million cases of RTI occur each year, contributing to more than 2.5 million deaths. These infections, which include pharyngitis, sinusitis, laryngitis, tonsillitis, bronchitis and pneumonia, are usually viral in origin.[2] However, they are frequently mismanaged with antibiotics, contributing to antimicrobial resistance (AMR). The misuse of antibiotics in the treatment of RTIs has been widely reported and has led to increased resistance among common bacterial pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*.[3] According to Uganda's 2018/2019 Annual Health Sector Report, RTI was the second leading cause of hospital admissions after malaria, accounting for 10.6% of cases.[2] Furthermore, although the Uganda National Clinical Guidelines advocate supportive management of RTIs given their predominantly viral aetiology, various studies have documented a persistently high prevalence of inappropriate antibiotic use in clinical practice.[4-7]

AMR in respiratory pathogens is primarily driven by the misuse of antibiotics, and limited diagnostic skills.[8] It is estimated that

AMR infections cause >541 000 deaths a year in Europe and the USA alone.[9] Owing to the severity of these infections, there is often an urgent need to begin empirical antimicrobial treatment before receiving results on bacterial aetiology and antimicrobial susceptibility patterns. The proliferation of extended-spectrum beta-lactamases (ESBLs) and carbapenems has reduced the therapeutic efficacy of beta-lactam medicines. The advent of multidrug-resistant (MDR) bacteria, such as *Klebsiella pneumoniae* carbapenemase and *H. influenzae* beta-lactamase, has further exacerbated the situation.[1]

Given the substantial morbidity, mortality and economic burden associated with AMR, the WHO has emphasised the importance of antibiotic surveillance and rational drug use in its global action plan against AMR. However, minimal research has been conducted to determine the trend of AMR in respiratory infections in south-western Uganda.

Mbarara Regional Referral Hospital (MRRH) has reported a high prevalence of bacterial respiratory infections in recent years. The increasing resistance of these bacteria to commonly prescribed antibiotics complicates treatment and highlights the need for a comprehensive assessment of their epidemiology and resistance patterns. The aim of this study was to describe the prevalence and patterns of AMR of respiratory bacterial pathogens isolated from patients attending MRRH, to improve treatment outcomes.

Methods

Study design and setting

This study employed a retrospective observational design to analyse the epidemiology and AMR patterns of isolated bacterial respiratory pathogens in the Microbiology Department of MRRH, south-western Uganda, from 1 January 2018 to 31 December 2024.

Data were obtained from the WHONET microbiology laboratory database, which contains records of bacterial isolates from respiratory specimens submitted for routine diagnostic testing. The study population included both inpatient and outpatient cases, enabling a comparison between community-acquired and hospital-acquired infections.

Sample collection and bacterial identification

Respiratory specimens were collected from patients presenting with symptoms of respiratory tract infection (RTI), including both upper (e.g. pharyngitis, tonsillitis) and lower (e.g. pneumonia, bronchitis) respiratory conditions. The specimen types analysed were sputum, tracheal aspirates, throat swabs, pleural fluid, nasopharyngeal swabs, chest fluid and endotracheal tube specimens, with sputum being the most frequently collected sample. The samples were inoculated with a 0.01 mL loop on blood, chocolate and MacConkey agar (Hi-Media, India) and incubated at 37°C for 24 hours (the chocolate plates were placed in a carbon dioxide jar before incubation).[10] Bacteria that exhibited significant growth were identified based on visual characteristics on culture media and standard biochemical tests, including Gram staining, catalase and oxidase tests, the Triple Sugar Iron (TSI) test, and Sulphur Indole Motility (SIM) medium.[10,11]

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing (AST) was performed by the disc diffusion method on Mueller-Hinton agar plates (Hi-Media, India).

The beta-lactam class consisted of ampicillin (10 µg), piperacillin (100 µg), penicillin (10 U), cefixime (5 µg), cefuroxime (30 µg), cefepime (30 µg), cefazolin (30 µg), ceftriaxone (30 µg), amoxicillin/clavulanic acid (20/10 µg) and cefoxitin (30 µg). The monobactam class was represented by aztreonam (30 µg). The fluoroquinolone class consisted of levofloxacin (5 µg) and ciprofloxacin (5 µg), while the aminoglycosides tested were amikacin (30 µg) and gentamicin (10 µg). The macrolides tested were azithromycin (15 µg) and erythromycin (15 µg), while the lincosamides were represented by clindamycin (2 µg). The tetracycline class consisted of tetracycline (30 µg) and doxycycline (30 µg), while the sulphonamides were represented by sulphamethoxazole/trimethoprim (1.25/23.75 µg). The carbapenems were represented by imipenem (10 µg), the phenicols by chloramphenicol (30 µg), and the nitroimidazoles by metronidazole (5 µg). The results were interpreted according to Clinical and Laboratory Standards Institute guidelines and were used to assess patterns of MDR, which was defined as resistance to at least three distinct antibiotic classes.

Data collection and processing

To ensure data quality and minimise bias, only one isolate per patient per year was included in the analysis. Duplicate records and specimens with mixed bacterial growth, suggestive of contamination, were excluded from the dataset. Only bacterial isolates that had undergone AST were included in the final analysis.

A computational approach was used to process the data, ensuring systematic classification of antibiotic resistance profiles and Gram stain characteristics. Antibiotic resistance data were mapped to their respective pharmacological classes to determine resistance trends across bacterial isolates.

Bacterial isolates were classified as either Gram positive or Gram negative, with *S. pneumoniae* and *Streptococcus pyogenes* categorised as Gram positive, while *Klebsiella* species and *Pseudomonas aeruginosa* were categorised as Gram negative. The final data set included each isolate's identification number, specimen type, bacterial classification, complete antibiotic resistance profile, MDR status and Gram stain classification. This structured data set was used for statistical analysis.

Statistical analysis

All statistical analyses were performed using Python in Google Colab, utilising the Pandas, NumPy, SciPy, Seaborn and Matplotlib libraries for data processing and visualisation. Descriptive statistics, including means, medians and frequency distributions, were used to summarise bacterial prevalence and the demographic characteristics of the study population. Temporal trends in bacterial isolates over the study period were analysed using line plots, while a χ^2 test was employed to determine associations between bacterial distribution and gender. Antibiotic resistance patterns were analysed across different drug classes. Bar plots and radar charts were used to visualise the prevalence of AMR in Gram-positive and Gram-negative bacteria, as well as to illustrate MDR trends.

Ethical considerations

Ethical approval for this study was waived by the Mbarara University Research Ethics Committee because the study was a retrospective analysis of laboratory records and therefore involved no direct patient contact or risk to participants. Despite the waiver, all ethical guidelines regarding participant confidentiality, informed consent and data protection were strictly followed.

Results

A total of 583 bacterial isolates were analysed. *S. pneumoniae* was the most frequently isolated organism, accounting for 285 (48.9%) of the total isolates. *K. pneumoniae* followed as the second most common pathogen, with 192 isolates (32.9%), while other Klebsiella species constituted 83 isolates (14.2%). P. aeruginosa was the least isolated organism, with 23 isolates (3.9%).

Organism distribution by specimen type

The distribution of bacterial isolates varied by specimen type. Sputum was the most common specimen (450 isolates; 77.2%), and predominantly held *S. pneumoniae* (*n*=242 isolates; 53.8%). Tracheal aspirates (*n*=61 isolates; 10.5%) held predominantly *Klebsiella* species and *K. pneumoniae*, while throat swabs (*n*=52 isolates; 8.9%) held a majority of *S. pneumoniae* (76.9%). Pleural fluid (*n*=14 isolates; 2.4%) held a high percentage of *P. aeruginosa* (42.9%). The other categories of specimens, nasopharyngeal swabs, chest fluid and endotracheal tube specimens, had extremely low numbers of isolates (Fig. 1).

Temporal trends of bacterial isolates

Between 2018 and 2024, the distribution of bacterial isolates at MRRH exhibited significant shifts, as shown in Fig. 2. *S. pneumoniae* was the predominant pathogen from 2018 to 2022, consistently accounting for the largest proportion of isolates, but it was completely absent in 2024. (Data for 2023 were not available owing to incomplete records in the WHONET system for that year.)

K. pneumoniae showed an increase in 2020 and 2021, becoming the dominant organism in 2024. *Klebsiella* species exhibited fluctuations, peaking in 2022 before stabilising. *P. aeruginosa* was rarely detected in earlier years but showed a notable increase in 2024.

Gender-based prevalence of bacterial isolates

The interaction between gender and bacterial species had a statistically significant association (χ^2=8.05; p=0.04499; df=3), as shown in Table 1. A total of 583 bacterial isolates were retrieved, of which 327 (56.1%) were from males and 256 (43.9%) from females.

Age-based distribution of respiratory pathogens

Among the 583 analysed cases, patient ages ranged from 1 to 98 years, with a median (interquartile range) age of 46 (29 - 63) years.

S. pneumoniae was the most frequently isolated organism in children and younger adults, consistent with its dominant role in community-acquired respiratory infections. In contrast, *K. pneumoniae* and *P. aeruginosa* showed increasing prevalence with age, particularly among patients aged ≥46 years (Fig. 3).

Organism distribution per department

The distribution of bacterial pathogens varied between inpatient and outpatient departments (Table 2). *K. pneumoniae* and *S. pneumoniae* were the most prevalent pathogens in both inpatient and outpatient departments, while *P. aeruginosa* was less prevalent.

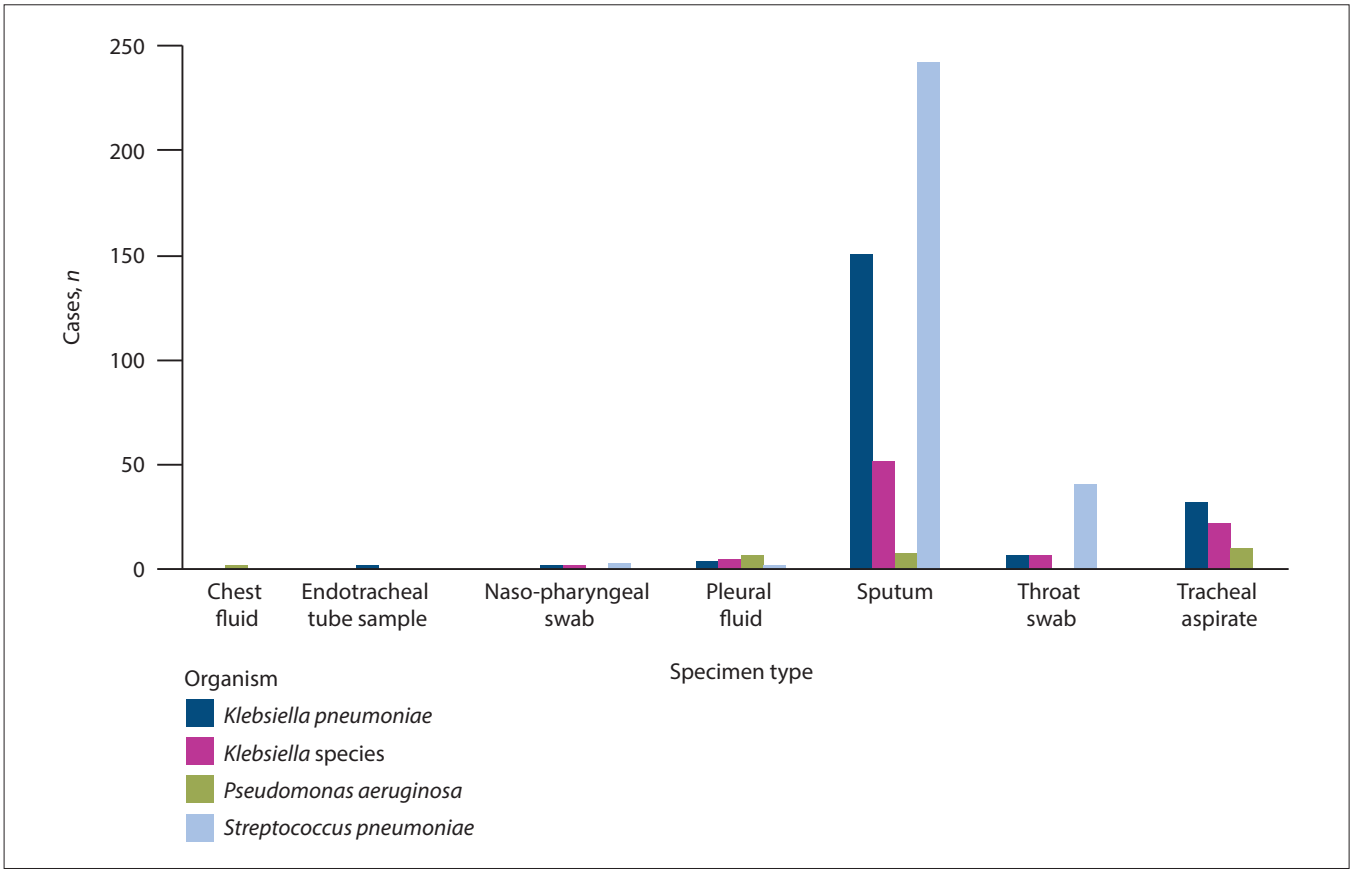

Fig. 1. Distribution of bacterial isolates by specimen type at Mbarara Regional Referral Hospital, Uganda, 2018 - 2024. Sputum was the most common specimen type, predominantly yielding Streptococcus pneumoniae.

Antibiotic resistance patterns in Gram-positive and Gram-negative bacteria

S. pneumoniae demonstrated high levels of resistance to tetracycline (83.2%), sulphamethoxazole (94.4%) and erythromycin (70.6%). Penicillin susceptibility was assessed in 250 (87.7%) of the isolates, of which 55 (22.0%) were resistant (95% confidence interval 17.3 - 27.5). *K. pneumoniae* in Gram-negative bacteria showed resistance against cefixime (54.5%), cefepime (50.0%) and piperacillin (50.0%), whereas *P. aeruginosa* was 100% resistant against cefixime and showed strong resistance to aztreonam (50.0%) and levofloxacin (50.0%), indicating problems of MDR. Other *Klebsiella* species were intermediate resistant, but gentamicin (20.5%) and imipenem (4.8%) remained highly effective (Fig. 4).

Prevalence of MDR bacteria isolated from the respiratory tract

Analysis of MDR bacteria among the identified respiratory pathogens (Fig. 5) showed a high prevalence of resistance. *Klebsiella* species had the highest proportion of MDR isolates at 77.1%, followed by *S. pneumoniae* at 74.7%. *K. pneumoniae* had an MDR rate of 66.1%, while *P. aeruginosa* had the lowest MDR rate at 47.8%.

Beta-lactam drug resistance was the most commonly involved class in the pathogens as a whole, with the highest rates of resistance in *K. pneumoniae* and *P. aeruginosa*. Sulphonamides, tetracyclines and macrolides were also significantly involved in MDR in these organisms, with *Klebsiella* species and *S. pneumoniae* having high resistance to these classes. In *P. aeruginosa*, resistance was widely distributed among aminoglycosides, tetracyclines and carbapenems, in line with its large-spectrum mechanisms of resistance (Fig. 6).

Discussion

This 7-year surveillance study provides the first longitudinal view of respiratory pathogen resistance trends in south-western Uganda. The sharp decline of *S. pneumoniae* and the rise of MDR *K. pneumoniae* and *P. aeruginosa* reflect evolving microbiological dynamics potentially driven by selective pressure from empirical treatment and the community immunity profiles. These trends have profound implications for both clinical practice and public health in Uganda and similar contexts.

The dominance of *S. pneumoniae* and *K. pneumoniae* aligns with findings from previous studies conducted in Asia,[12,13] America,[14] East Africa[15] and other parts of Africa,[16,17] where these organisms remain the principal causes of community- and hospital-acquired respiratory infections. Notably, in the present study *S. pneumoniae* accounted for over half of the isolates during the earlier years of surveillance, but was completely absent by 2024. This sharp decline may be attributed to the widespread adoption of pneumococcal conjugate vaccines (PCVs), particularly PCV10/PCV13, as well as non-pharmaceutical interventions during the COVID-19 pandemic that reduced bacterial transmission.[18]

In contrast, the sharp rise in *K. pneumoniae* and *P. aeruginosa*, particularly in inpatient and tracheal aspirate samples, is likely to reflect nosocomial transmission, prolonged hospital stays, mechanical ventilation and excessive empirical antibiotic use.[19,20] These organisms are known for their ability to acquire resistance genes, and their increasing prevalence suggests a shift towards more resistant, healthcare-associated pathogens.

Differentiating between community-acquired and nosocomial respiratory infections is essential to guiding appropriate treatment. While our dataset did not include explicit information on prior hospitalisation, we used inpatient v. outpatient classification as a proxy. In this context, *K. pneumoniae* and *P. aeruginosa* were notably more common among inpatients, particularly in tracheal aspirates and pleural fluid specimens, sample types often associated with critically ill or ventilated patients. This distribution pattern strongly suggests a nosocomial origin.

Of particular note, *P. aeruginosa* accounted for a disproportionately high percentage of isolates from pleural fluid, a typically sterile site. Although we lacked detailed clinical data such as intensive care unit (ICU) admission, comorbidities or prior antibiotic exposure, this finding is consistent with the known role of *P. aeruginosa* in ventilator-associated pneumonia and empyema, especially in patients with structural lung disease, diabetes mellitus, immunosuppression, or recent

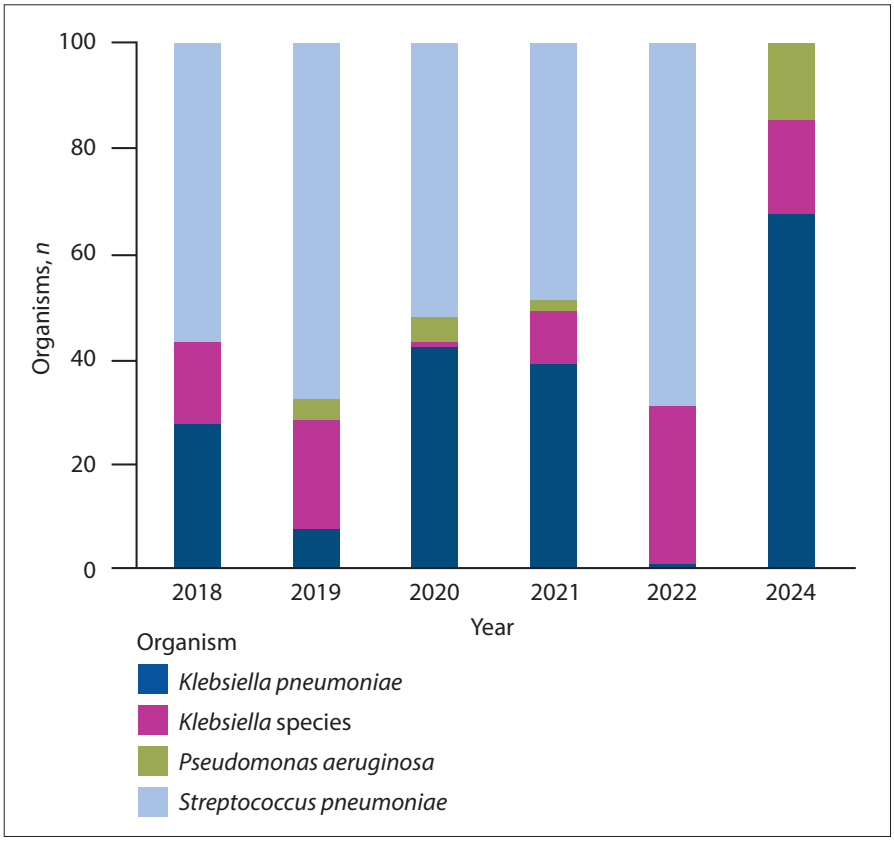

Fig. 2. Annual distribution of bacterial isolates at Mbarara Regional Referral Hospital, Uganda, 2018 - 2024 (data for 2023 not available). Streptococcus pneumoniae was not recorded in 2024, while Klebsiella pneumoniae and Pseudomonas aeruginosa increased significantly in that year.

antimicrobial treatment.[21-23]

In contrast, *S. pneumoniae*, a classic community-acquired pathogen, was most frequently isolated from outpatient specimens, particularly sputum and throat swabs.[24] These findings reinforce the clinical utility of specimen-specific surveillance in distinguishing between community- and hospital-acquired infections.

This study demonstrated clear age-related patterns in respiratory infections. *S. pneumoniae* was predominant among children and young adults, probably reflecting community-acquired infections and gaps in vaccine coverage.[12,25,26] In contrast, *K. pneumoniae* and *P. aeruginosa* were more common in older adults, who also exhibited higher rates of MDR. These findings may be attributed to age-related comorbidities, frequent healthcare exposure, prior antibiotic use and declining immune function,[27,28] and underscore the need for age-specific treatment protocols and targeted antimicrobial stewardship interventions, particularly in older populations at greater risk for resistant infections.

The distribution of bacterial isolates by specimen type offers important clinical insights. *S. pneumoniae* was most commonly isolated from sputum and throat swabs,

Table 1. Distribution of bacterial isolates by gender at Mbarara Regional Referral Hospital, Uganda, 2018 - 2024, showing the number of cases in males and females for each organism

Organism	Female, *n*	Male, *n*	Total
Klebsiella pneumoniae	98	94	192
Klebsiella species	33	50	83
Pseudomonas aeruginosa	6	17	23
Streptococcus pneumoniae	119	166	285
Total	256	327	583

χ^2=8.05; *p*=0.04499; df=3.

Table 2. Distribution of bacterial pathogens by department at Mbarara Regional Referral Hospital, Uganda, 2018 - 2024

	Organism			
Department	*Klebsiella pneumoniae*	*Klebsiella species*	*Pseudomonas aeruginosa*	*Streptococcus pneumoniae*
Inpatient	129	45	17	126
Outpatient	63	38	6	159

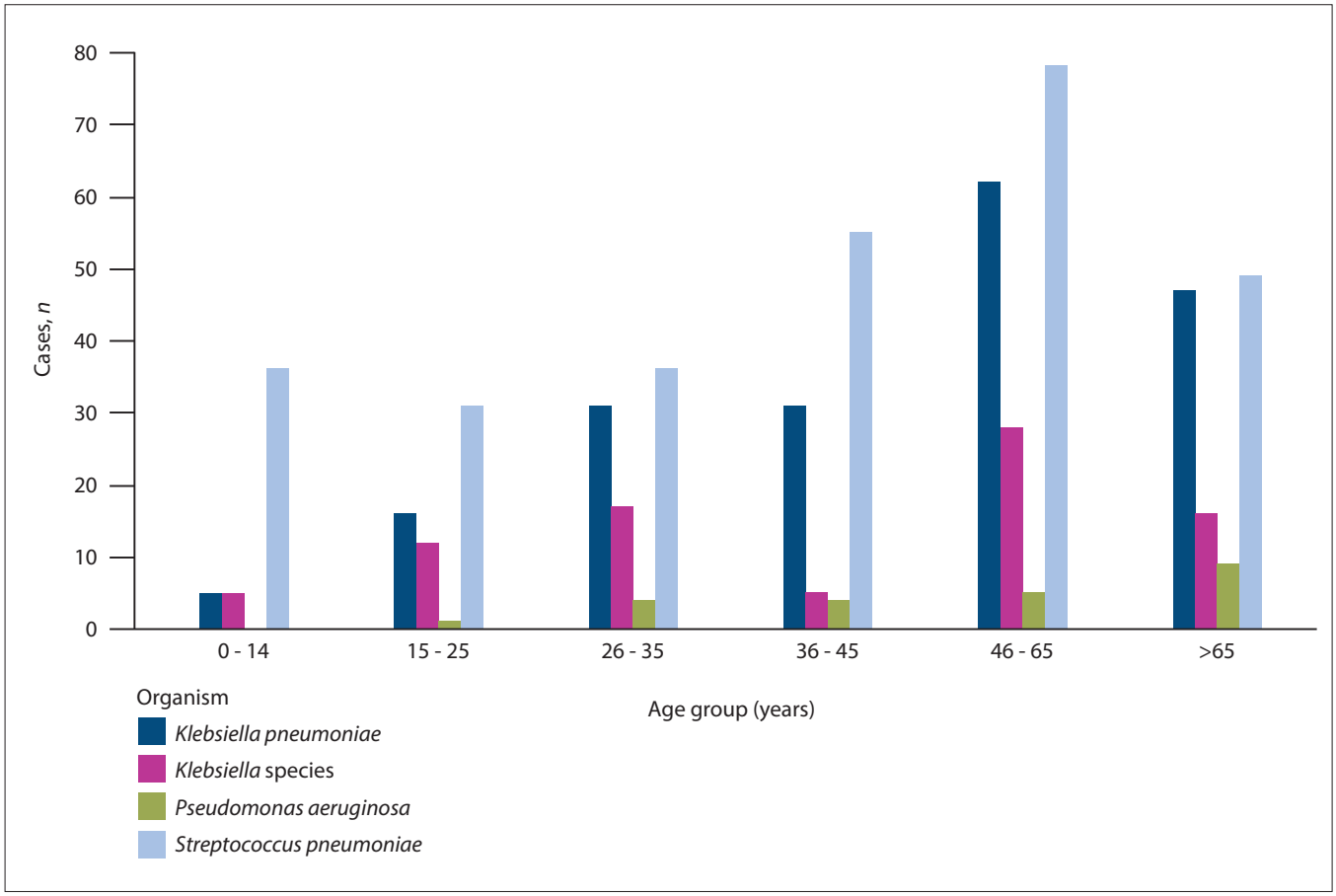

Fig. 3. Age-based distribution of respiratory pathogens at Mbarara Regional Referral Hospital, Uganda, 2018 - 2024. Middle-aged and elderly patients (≥46 years) had the highest rates of bacterial isolates. Streptococcus pneumoniae and Klebsiella pneumoniae were the most prevalent across age groups.

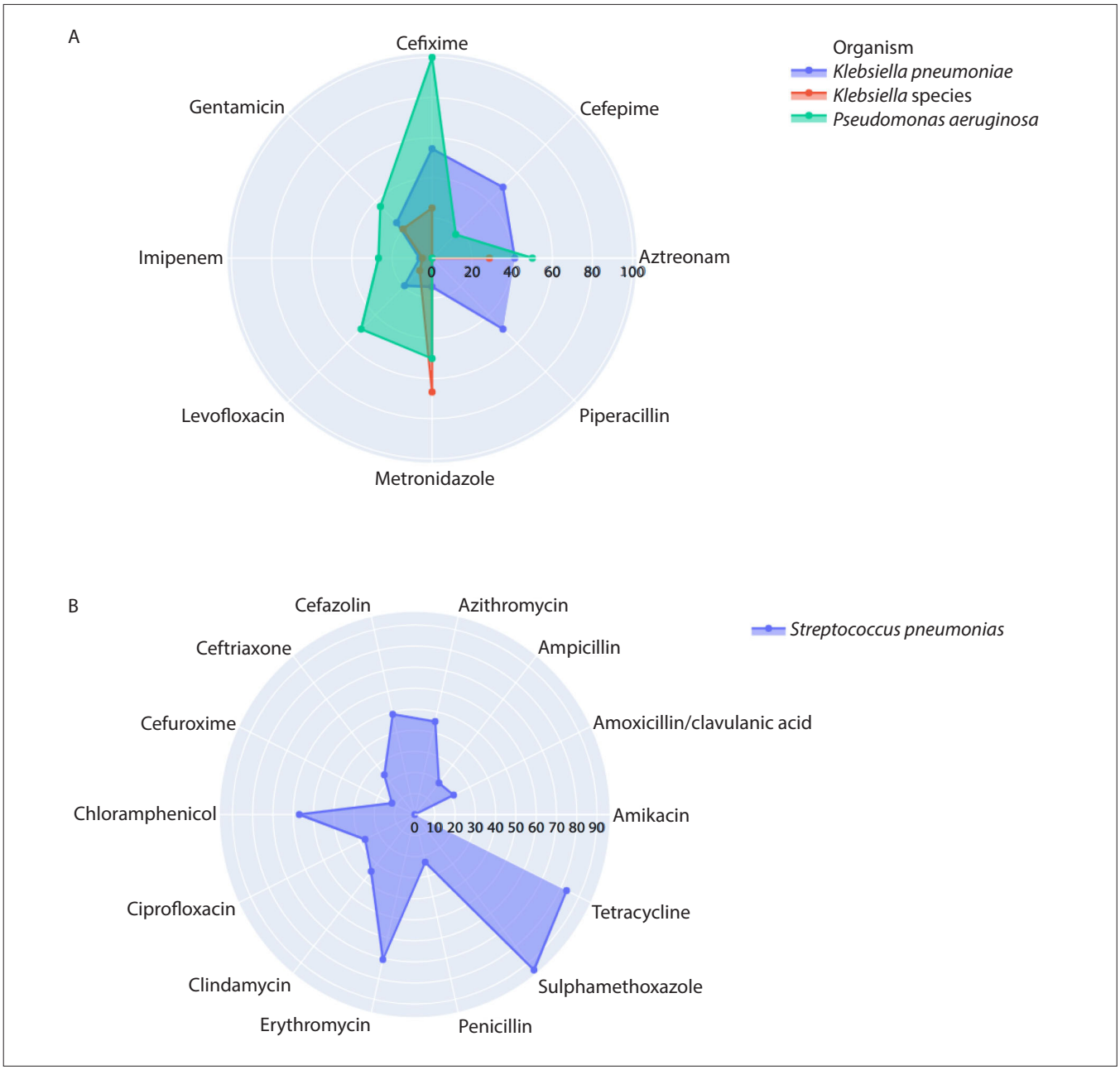

Fig. 4. Antibiotic resistance at Mbarara Regional Referral Hospital, Uganda, 2018 - 2024. Radar chart A shows resistance among Gram-positive isolates, mainly Streptococcus pneumoniae, while radar chart B shows Gram-negative resistance patterns, with high resistance rates in Klebsiella pneumoniae and Pseudomonas aeruginosa to cephalosporins, fluoroquinolones and carbapenems.

specimens typically associated with community-acquired RTIs, supporting its well-established role in pharyngitis, bronchitis and pneumococcal pneumonia.[29,30] In contrast, *K. pneumoniae* was the organism most frequently recovered from tracheal aspirates, often obtained from intubated or critically ill patients, suggesting a strong association with hospital-acquired pneumonia and ventilator-associated infections.[31]

Our findings are consistent with regional and global trends. The high prevalence of MDR *K. pneumoniae* aligns with surveillance data globally,[6,32,33] with ESBL-producing strains increasingly reported. The rise in *P. aeruginosa*, particularly in ICU settings, has been documented in several studies.[34,35] This organism is commonly associated with resistance to cephalosporins, carbapenems and fluoroquinolones, patterns also observed in our study and highlighting the difficulty of treating such infections in resource-limited settings.

The dominant resistance patterns among *S. pneumoniae*, notably to tetracycline, sulphamethoxazole and erythromycin, reflect decades of widespread, often unregulated antibiotic use. Similar resistance trends have been reported in both community and hospital settings across Africa, Europe and Asia.[9,36-38] Alarmingly, the MDR rates of 74.7% in *S. pneumoniae* and 77.1% in *Klebsiella* species far exceed those reported in earlier Ugandan studies,[7,39] suggesting a rapid and ongoing evolution of resistance.

The growing prevalence of MDR organisms poses a significant threat to effective clinical management. Our data show that many

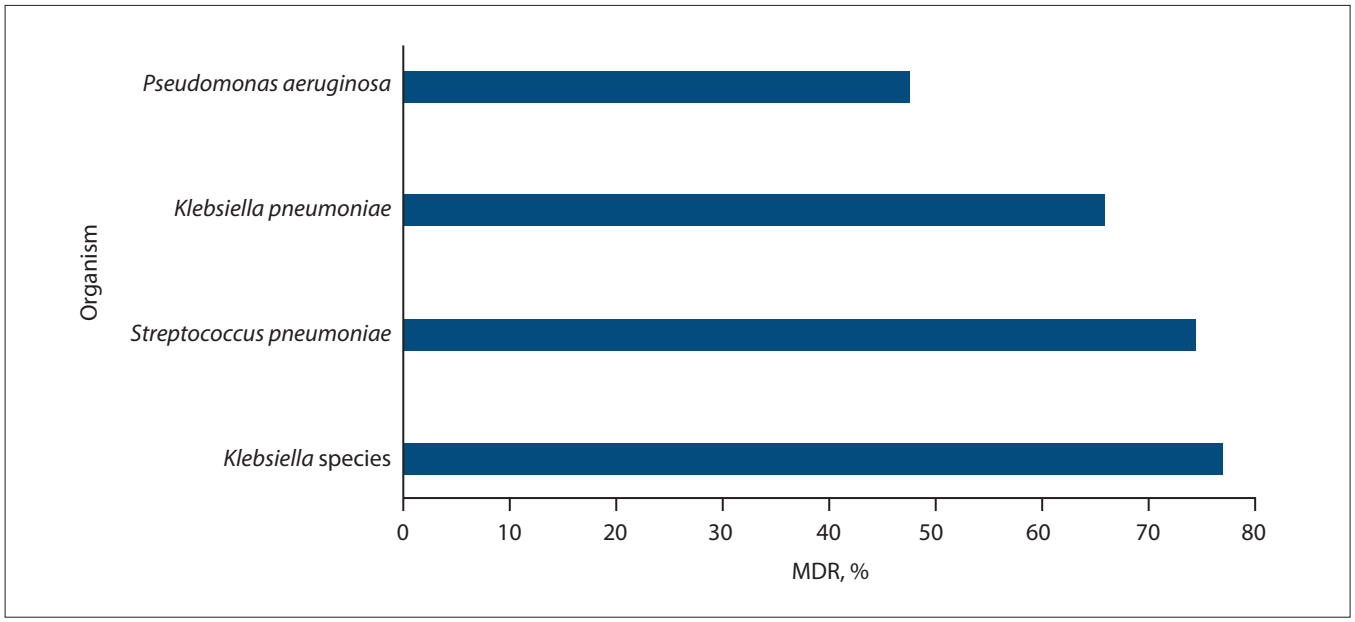

Fig. 5. Prevalence of MDR bacterial pathogens at Mbarara Regional Referral Hospital, Uganda, 2018 - 2024. Klebsiella species had the highest MDR prevalence, followed by Streptococcus pneumoniae and Klebsiella pneumoniae, while Pseudomonas aeruginosa showed the lowest MDR rate. (MDR = multidrug resistant/resistance.)

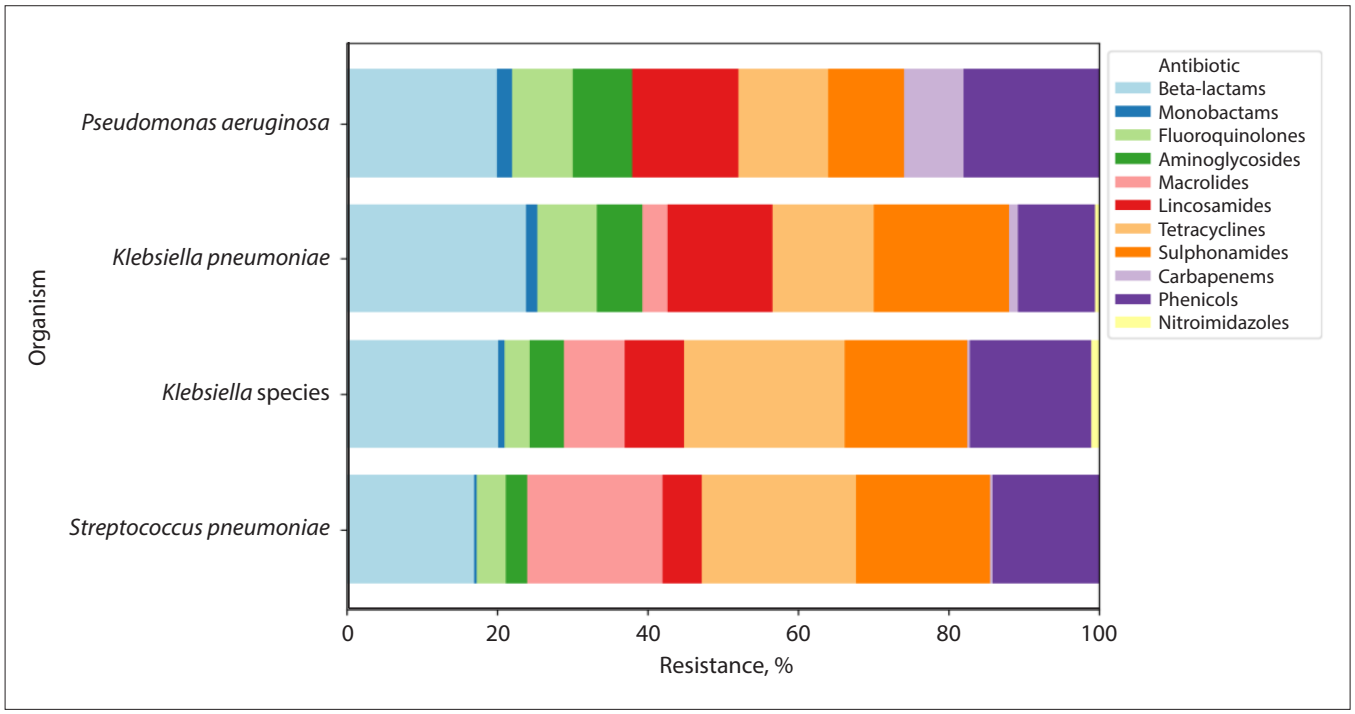

Fig. 6. Contribution of antibiotic classes to multidrug resistance among pathogens at Mbarara Regional Referral Hospital, Uganda, 2018 - 2024. Beta-lactams, sulphonamides, macrolides and tetracyclines were the most implicated classes, with resistance patterns differing among different pathogens.

commonly prescribed antibiotics, including first-line agents such as amoxicillin-clavulanic acid, cefixime and erythromycin, are now largely ineffective against prevalent pathogens. The resistance of *P. aeruginosa* to carbapenems and monobactams is particularly concerning, as these are often considered drugs of last resort.

These findings underscore the urgent need for revised national treatment guidelines that reflect up-to-date resistance profiles. Hospital-specific antibiograms should be developed and disseminated regularly to inform empirical therapy. Moreover, the reliance on empirical treatment without microbiological confirmation, driven by limited diagnostic capacity, must be addressed through investment in point-of-care diagnostic tools and microbiology infrastructure.

Beyond clinical practice, these results have broader implications for public health policy. Antibiotic stewardship programmes must be strengthened, with focused training for healthcare workers on rational prescription practices. Public awareness campaigns are also

needed to discourage the inappropriate use of antibiotics, particularly for viral infections.

A major strength of this study is the large, longitudinal dataset derived from WHONET, offering a rare temporal perspective on resistance trends in a Ugandan tertiary setting. The integration of computational tools to analyse and visualise AMR adds further value to the robustness of the findings.

The study has several limitations. As a retrospective analysis, it lacked clinical metadata on patient outcomes, comorbidities and prior antibiotic exposure, which may influence resistance patterns. Molecular characterisation of resistance genes was not performed, limiting insight into underlying mechanisms of MDR. Bartlett scoring was not conducted to assess sputum specimen quality, potentially affecting the accuracy of culture-based diagnoses. The exclusion of viral, fungal and *Mycobacterium tuberculosis* pathogens narrowed the aetiological spectrum. Tuberculosis was not included owing to its very specific diagnostic requirements, including GeneXpert testing and biosafety level 3 culture protocols, which were beyond the scope of routine bacteriological methods used in this study.

Conclusion

This study highlights the growing burden of RTIs and the alarming rise in AMR at a Ugandan referral hospital. The shift towards MDR pathogens, particularly *K. pneumoniae* and *P. aeruginosa*, underscores the need for updated treatment guidelines, strengthened stewardship, and improved diagnostic surveillance to guide effective therapy.

Data availability. The data sets generated and analysed during the present study are available from the corresponding author (JB) on reasonable request.

Declaration. None.

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Author contributions. All authors contributed equally to the conceptualisation of the study, data collection, analysis, and drafting and revision of the manuscript. All authors approved the final version for submission.

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Conflicts of interest. None.

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