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Age-Related Antimicrobial Resistance in Adults with Lower Respiratory Tract Infections in Nepal

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ABSTRACT

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Introduction: Lower respiratory tract infections remain a major health burden in Nepal, and the rising prevalence of antimicrobial resistance poses a significant challenge, particularly in older adults.

Objectives: To evaluate antimicrobial resistance patterns among adults with lower respiratory tract infections in Nepal, with a focus on age-related differences.

Methods: This retrospective analysis looked at 1,636 culture-positive respiratory specimens collected at Dhulikhel Hospital between January and December 2024. The Clinical and Laboratory Standards Institute guidelines were followed. Extended-spectrum beta-lactamase production was confirmed phenotypically, and multidrug resistance was defined as non-susceptibility to at least one drug in three or more antimicrobial classes. The relationship between age (≥60 years) and resistance outcomes was determined using multivariable logistic regression.

Results: Klebsiella pneumoniae (24.90%), Streptococcus pneumoniae (17.50%), and Pseudomonas aeruginosa (11.80%) were the most common isolates. Compared to younger adults, elderly patients (≥60 years) showed a significantly higher prevalence of Multidrug Resistance (56.10% vs 47.20%, p = 0.004) and a higher prevalence of Extended-spectrum beta-lactamase production (31.60% vs 24.50%, p = 0.01). Elderly age was validated by multivariable analysis as an independent predictor of both Extended-spectrum beta-lactamase production (aOR 1.42, 95% CI 1.03–1.97) and Multidrug Resistance (aOR 1.36, 95% CI 1.07–1.74). There were no appreciable age-related differences in the 11.4% of isolates with carbapenem resistance.

Conclusion: Adult lower respiratory tract infection patients in Nepal show high antimicrobial resistance rates, with multidrug resistance and Extended-spectrum beta-lactamase pathogens mainly affecting older adults, emphasizing the need for better infection control, age-specific treatments, and antimicrobial stewardship.

Keywords: Aged; anti-bacterial agents; drug resistance, multiple, bacterial; respiratory tract infections.

INTRODUCTION

Lower respiratory tract infections (LRTIs) remain a leading global health problem, contributing significantly to morbidity and mortality, particularly among older adults and individuals with comorbidities.[1]

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The Global Burden of Disease study ranks LRTIs as the fourth leading cause of death worldwide, with disproportionate impact in low- and middle-income countries such as Nepal.[2] In South Asia, factors like antibiotic misuse, delayed diagnosis, and limited healthcare access further exacerbate this burden.[3,4] Rising antimicrobial resistance (AMR) has complicated treatment, leading to worse clinical outcomes.[5,6]

LRTIs are caused by diverse pathogens, including *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Klebsiella pneumoniae*.[7] However, the effectiveness of first-line antibiotics is declining due to multidrug resistance (MDR), extended-spectrum beta-lactamase (ESBL) production, and carbapenem resistance, which increase hospital stays, healthcare costs, and mortality.[8,9] The World Health Organization has recognized AMR as one of the top ten global public health threats.[10]

Older adults are particularly susceptible to resistant LRTIs due to immunosenescence, comorbidities, hospital exposures, and cumulative antibiotic use.[11–14] Although international studies highlight higher AMR rates in aging populations,[15] data from Nepal remain scarce.[16] This study assess the impact of age on antimicrobial resistance patterns among adults with LRTIs, with emphasis on MDR and ESBL production.

METHODS

The study employed a retrospective comparative design utilizing routine microbiology data collected from Dhulikhel Hospital, which serves as a major tertiary care referral center for both urban and rural populations in central Nepal. The investigation focused on respiratory specimens processed between January 1 and December 31, 2024, ensuring a contemporary analysis of bacterial profiles and resistance patterns. All adult patients aged 18 years or older with culture-positive respiratory specimens, such as sputum, tracheal aspirates, and bronchoalveolar lavage samples, were eligible for inclusion. For analysis, patients were categorized into two groups based on age, i.e, Young adults (18-49 years) and Elderly adults (≥60 years). Young adults were further categorized in age groups 18- 39 years (youngest) and 40- 59 years (middle aged). Ethical approval for the study was obtained from the Institutional Review Board of Kathmandu University School of Medical Sciences.

In situations where the same bacterial species was isolated from a single patient more than once, only the first isolate per patient species combination was examined to preserve data integrity and prevent duplication. In cases of polymicrobial growth, all organisms were recorded; however, for statistical analysis only the first isolate per patient species combination was included. This approach prevented overrepresentation of repeated isolates while still acknowledging polymicrobial infections at the descriptive level. Exclusion criteria were applied to maintain the accuracy and reliability of findings. Patients with missed or incomplete data were excluded, as were those transferred to another facility before the initiation of antibiotics. Additionally, patients discharged within 24 hours of admission were not considered for analysis.

Standardized laboratory procedures for handling specimens, cultivating them, and identifying the organisms were followed during microbiological processing. Antimicrobial susceptibility testing (AST) was performed according to the Clinical and Laboratory Standards Institute (CLSI) M100, 34th edition (2024) guidelines. Extended-spectrum β-lactamase (ESBL) production among Enterobacterales was confirmed phenotypically, multidrug resistance (MDR) was defined as non-susceptibility to at least one drug in three or more antimicrobial classes, and carbapenem resistance was defined as resistance to imipenem and/or meropenem. Internal quality control was maintained using appropriate American Type Culture Collection (ATCC) reference strains, in line with CLSI.[17]

This study was designed as a retrospective comparative study utilizing routine microbiology data from culture-positive respiratory specimens. Statistical analyses were performed using SPSS version 26**.** Continuous variables were summarized as medians with interquartile ranges (IQRs), and categorical variables were expressed as counts and percentages. Depending on data distribution and sample size, either the Fisher's exact test or the chi-square test was applied for group comparisons. To evaluate the independent association between elderly age (≥60 years) and antimicrobial resistance outcomes (MDR, ESBL production, and carbapenem resistance), multivariable logistic regression models were constructed. These models produced adjusted odds ratios (aORs) with 95% confidence intervals (CIs), controlling for confounders such as sex, specimen type, bacterial group, and inpatient or ICU status. A two-sided p-value of <0.05 was considered statistically significant.

The research utilized de-identified laboratory data, ensuring patient confidentiality and compliance with ethical standards for retrospective studies. This methodological approach facilitated a robust examination of age-related differences in antimicrobial resistance while maintaining scientific rigor and adherence to ethical guidelines.

RESULTS

A total of 1,636 adult patients with culture-confirmed bacterial lower respiratory tract infections (LRTIs) were included in the analysis. The study population was predominantly composed of older adults, consistent with their increased vulnerability to respiratory infections. The age distribution is summarized in **(**Table 1**)**. The majority of patients were aged ≥60 years (64.70%), followed by those aged 40–59 years (24.60%), while the youngest group (18–39 years) accounted for 11% of cases. This distribution highlights the disproportionate burden of LRTIs among the elderly population.

Table 1: Distribution of patients with LRTIs by age group.

Age group	n (%)
18–39	174 (11)
40–59	403 (24.60)
≥60	1,059 (64.70)

The ten most frequently isolated bacterial species from all adult samples. Among all culture-positive isolates, Klebsiella pneumoniae emerged as the most common pathogen, accounting for 24.90% of cases, followed by Streptococcus pneumoniae (17.50%) and Pseudomonas aeruginosa (11.80%). These findings underscore the dominance of Gram-negative bacilli in adult LRTIs, with Klebsiella species and Pseudomonas posing a particularly significant threat in terms of both frequency and resistance potential. (Table 2)

Table 2: Top ten bacterial isolates from culture-positive lower respiratory tract specimens.

Organism	n (=1636)	% of total
Klebsiella pneumonia	408	24.90
Streptococcus pneumonia	287	17.50
Pseudomonas aeruginosa	193	11.80
Escherichia coli	148	9
Klebsiella oxytoca	82	5
Acinetobacter baumannii	64	3.90
Haemophilus influenza	57	3.50
Staphylococcus aureus	54	3.30
Enterobacter cloacae	47	2.90
Serratia marcescens	41	2.50

High resistance to β-lactams, with Amoxyclav resistant in 53.2% of isolates was seen. Resistance to Ceftazidime (33.2%) and Cotrimoxazole (36%) was also notable. Carbapenems (Meropenem 14.4%, Imipenem 13.7%), aminoglycosides (Gentamicin 12.3%), and fluoroquinolones (Levofloxacin 12.5%) remained more effective, underscoring the need for cautious antibiotic stewardship. (Table 3)

Table 3: Overall antibiotic susceptibility (% Resistant).

Antibiotic	% Resistant
Amoxyclav	53.20
Ceftazidime	33.20
Cotrimoxazole	36.0
Meropenem	14.40
Imipenem	13.70
Levofloxacin	12.50
Gentamicin	12.30
Cefepime	28.40
Ampicillin	–
Piperacillin–Tazobactam	–
Amikacin	–
Ciprofloxacin	–

(Note: "–" indicates data not among top 12 by test frequency in the dataset)

Age-stratified analysis demonstrated significantly higher resistance among elderly patients (≥65 years) compared with younger adults (<65 years) (Table 4).The prevalence of multidrug resistance (MDR) was 56.10% in elderly patients versus 47.20% in younger adults, a statistically significant difference ($p = 0.004$). Similarly, extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae were more common in the elderly cohort (31.60% vs. 24.50%; $p = 0.01$). Although carbapenem resistance was slightly higher among elderly patients (12.10% vs. 10.10%), this difference did not reach statistical significance ($p = 0.28$). These findings indicate that older adults not only represent the majority of LRTI cases but also carry a disproportionate burden of drug-resistant pathogens, complicating treatment decisions and clinical management.

Table 4: Prevalence of Antimicrobial Resistance Patterns by Age Group.

Resistance Pattern	Elderly (≥60 years)	Younger adults (<60 years)	p value
Multidrug resistance (MDR)	56.10%	47.20%	0.004
ESBL-producing Enterobacterales	31.60%	24.50%	0.01
Carbapenem resistance	12.10%	10.10%	0.28

Multivariable logistic regression analysis, adjusted for potential confounders such as sex, specimen type, bacterial group, and inpatient/ICU status, confirmed that elderly age (≥65 years) was an independent predictor of antimicrobial resistance outcomes. Elderly patients had a 36% higher likelihood of harboring multidrug-resistant (MDR) organisms (adjusted OR 1.36; 95% CI, 1.07–1.74; $p = 0.004$). Similarly, the odds of isolating extended-spectrum β-lactamase (ESBL)-producing Enterobacterales were 42% higher in the elderly cohort (adjusted OR 1.42; 95% CI, 1.03–1.97; $p = 0.01$). These findings reinforce advanced age as a significant and independent risk factor for antimicrobial resistance, beyond other clinical and microbiological variables. (Table 5)

Table 5: Association between Elderly Age and Antimicrobial Resistance Patterns (Multivariable Analysis).

Outcome	Adjusted OR	95% CI	p-value*
MDR	1.36	1.07 - 1.74	0.004
ESBL Production	1.42	1.03 - 1.97	0.01

DISCUSSION

The study's conclusions demonstrate the concerningly high rate of antimicrobial resistance (AMR) among LRTI patients in Nepal, especially among the elderly. The vulnerability of older adults to resistant infections is highlighted by their higher rates of multidrug resistance (MDR) and ESBL production, which are consistent with global trends[15,18] According to earlier research from Nepal and other low-resource settings, Klebsiella pneumoniae and Streptococcus pneumoniae are the most common pathogens,[7,16] but the growing resistance to β-lactams and fluoroquinolones indicates the urgent need for updated empirical treatment guidelines.

The observed association between advanced age and MDR (aOR 1.36) corroborates international evidence linking immunosenescence, comorbidities, and cumulative antibiotic exposure to heightened AMR risks.[11,13] The higher ESBL prevalence among elderly patients (aOR 1.42) further reflects the widespread misuse of cephalosporins in clinical practice, as documented in South Asian studies.[3,19] Although carbapenem resistance did not reach statistical significance, its numerical elevation in the elderly (12.1% vs. 10.1%) warrants vigilance, given the dire therapeutic implications of carbapenem-resistant Enterobacterales (CRE).[8,20]

The study's resistance patterns are consistent with regional AMR issues, where resistance is sustained by uncontrolled antibiotic use and a lack of diagnostic resources.[4,21] The high fluoroquinolone resistance, for example, is consistent with findings by Shrestha et al. (2020),[11] highlighting the necessity of antimicrobial stewardship programs (ASPs) to prevent inappropriate prescribing.[22] The decreased resistance to carbapenems and aminoglycosides indicates that these agents may still be useful, but to stop new resistance from emerging, their selective use needs to be governed by strict surveillance.[23]

The skewed age distribution (64.7% ≥60 years) reflects Nepal's aging population and their heightened susceptibility to LRTIs due to comorbid conditions like chronic obstructive pulmonary disease (COPD) and diabetes.[24] This demographic shift necessitates targeted interventions, including vaccination (e.g., pneumococcal and influenza vaccines) and infection control measures in healthcare settings.[25]

The retrospective reliance on laboratory data without clinical outcomes and the single-center design, which may restrict generalizability, are among the limitations. Prospective designs should be used in future research to link treatment failures and mortality to resistance patterns.

CONCLUSIONS

This study highlights the substantial burden of antimicrobial resistance among adults with lower respiratory tract infections in Nepal, with elderly patients disproportionately affected by multidrug-resistant and ESBL-producing pathogens. This vulnerable group's high prevalence of resistant organisms highlights the difficulty of clinical management and the urgent need for specialized interventions. Healthcare systems should prioritize routine surveillance of resistance patterns, especially in high-risk groups like the elderly, institute age-specific treatment protocols, and improve infection control procedures in order to meet this challenge. To maximize treatment and stop the spread of resistant organisms, improved diagnostic capabilities, focused antimicrobial stewardship programs, and immunization tactics will be essential. To further improve patient outcomes and preserve antibiotic efficacy for future generations, policymakers and clinicians must work together to create evidence-based, context-specific guidelines that take demographics and resistance trends into account.

Conflict of Interest: None

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