Clinical Phenotypes and Risk Predictors of Multidrug-Resistant Klebsiella Infection in a Level 3 ICU in Nepal: A Retrospective Analysis

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ABSTRACT

BACKGROUND

Multidrug-resistant (MDR) Klebsiella infections in ICU patients are associated with increased morbidity, mortality, and prolonged ICU stay. Identifying predictors can guide empiric therapy and infection control.

METHODS

We conducted a retrospective review of 88 ICU patients with culture-confirmed Klebsiella over two years at Nepal Mediciti Hospital. Data collected included demographics, comorbidities, severity (APACHE II), ICU procedures, antibiotic exposure, and outcomes. Univariate and multivariable logistic regression analyses were performed to identify predictors of MDR infection.

RESULTS

MDR Klebsiella was identified in 65 patients (73.9%). Independent predictors included higher APACHE II score (OR 1.15; 95% CI 1.02–1.30; p = 0.022), prior antibiotic exposure (OR 4.31; 95% CI 1.34–13.9; p = 0.015), and central venous catheter (OR 3.48; 95% CI 1.05–11.5; p = 0.041). MDR patients had longer ICU stays (14.3 ± 5.8 days vs 9.7 ± 4.1 days).

CONCLUSIONS

Severity of illness, prior antibiotic exposure, and invasive devices are predictors of MDR Klebsiella in ICU patients. Implementation of targeted infection control measures and antimicrobial stewardship programs can effectively reduce the MDR infection burden.

KEY WORDS

Antimicrobial resistance, Intensive care unit, Klebsiella, Multidrug resistance

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BACKGROUND

Multidrug-resistant (MDR) Klebsiella pneumoniae has emerged as a major cause of healthcare-associated infections worldwide, particularly in intensive care units (ICUs), where patients are highly vulnerable due to critical illness, invasive devices, and frequent antibiotic exposure.[1] MDR Klebsiella infections, including bloodstream infections, ventilator-associated pneumonia, urinary tract infections, and surgical site infections, are associated with increased morbidity, mortality, prolonged ICU and hospital stay, and substantial healthcare costs.[2, 3, 4]

The prevalence of MDR Klebsiella varies geographically and is notably high in South Asia due to widespread use of broad-spectrum antibiotics, limited antimicrobial stewardship, and variable infection control practices. [5, 6] Mechanisms of resistance include production of extended-spectrum β-lactamases (ESBLs), carbapenemases (e.g., KPC, NDM), and acquisition of resistance genes via plasmids, making treatment options increasingly limited and complex. [6, 7]

ICU-specific risk factors for MDR Klebsiella include high severity of illness, prior antibiotic exposure, mechanical ventilation, central venous catheters, urinary catheters, and recent surgery. [8, 9] Comorbidities such as diabetes mellitus, chronic kidney disease, and immunosuppression further increase susceptibility. Understanding the local epidemiology and risk factors is essential to guide empiric therapy, implement targeted infection prevention strategies, and optimize antimicrobial stewardship.

Despite the growing burden, data on MDR Klebsiella infections in Nepalese ICUs are limited, and existing studies often focus on general antimicrobial resistance without detailed analysis of ICU-specific predictors. [10, 11] As ICUs serve as referral centers, patients often present with complex comorbidities and prior healthcare exposure, which may increase the risk of MDR infection.

This study aimed to identify clinical, demographic, and procedural predictors of MDR Klebsiella infection in a tertiary ICU in Nepal to support empiric therapy decisions and infection prevention strategies.

METHODS

We conducted a retrospective observational study in the 33-bed multidisciplinary ICU of Nepal Mediciti Hospital, a tertiary referral center in Kathmandu, Nepal, including all adult patients (≥18 years) admitted between January 1, 2023, and December 31, 2024, with culture-confirmed Klebsiella infection. Patients with incomplete records and pediatric patients were excluded. Demographic data, admission category, comorbidities (diabetes, chronic kidney disease or lung disease, malignancy), severity of illness (APACHE II score), ICU procedures and devices (endotracheal intubation, central venous catheter, urinary catheter), recent antibiotic exposure, and ICU length of stay were extracted from medical records using a standardized form.

The primary outcome was multidrug-resistant (MDR) Klebsiella, defined as resistance to at least one agent in three or more antimicrobial categories according to international consensus definitions. Microbiological identification and susceptibility testing followed standard laboratory protocols in accordance with the CLSI (Clinical & Laboratory Standards Institute) guidelines.

Continuous variables were expressed as mean ± SD or median (IQR), and categorical variables as frequencies and percentages. Univariate analysis was performed using t-tests or Mann–Whitney U tests for continuous variables and Chi-square or Fisher's exact tests for categorical variables. Variables with $p < 0.20$ in univariate analysis were included in a multivariable logistic regression model to identify independent predictors of MDR Klebsiella, with results expressed as adjusted odds ratios (OR) and 95% confidence intervals (CI). Statistical significance was set at $p < 0.05$. The study was approved by the Institutional Review Committee at Nepal Mediciti Hospital (ID: IRC-RP-2081/82-34).

RESULTS

A total of 88 ICU patients with culture-confirmed Klebsiella infection were included in the analysis. Of these, 65 (73.9%) were multidrug-resistant (MDR). The mean age of the cohort was 59.8 ± 15.1 years, and 51.1% were male. Respiratory specimens represented the most common source of Klebsiella isolates among ICU patients (n=36, 40.9%). (Figure 1)

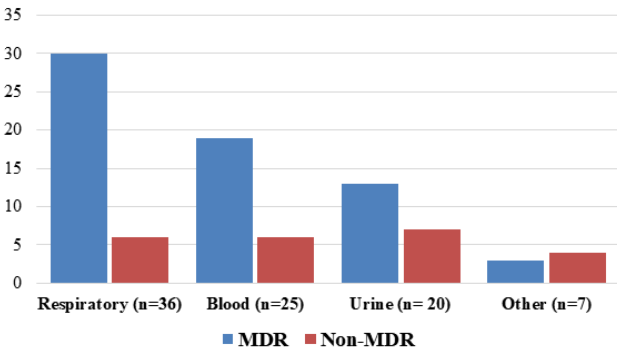

Figure 1: Bar Diagram Showing the Distribution of MDR vs. Non-MDR by Specimen Type.

The baseline characteristics of patients with MDR and non-MDR Klebsiella infections are summarized in Table 1. Although age and sex distribution were comparable between the two groups, MDR infection was significantly more frequent among patients transferred from other hospitals. The mean APACHE II score was notably higher among patients with MDR Klebsiella, indicating greater illness

severity at admission.

Regarding procedures and exposures, MDR cases were significantly higher in patients with endotracheal intubation, central venous catheterization, and prior antibiotic exposure within 90 days. ICU length of stay was also significantly longer among MDR patients.

Table 1: Comparison of Baseline & Clinical Characteristics Between MDR & Non-MDR Klebsiella Infections (N = 88).

Variable	MDR (n = 65)	Non-MDR (n = 23)	p-value
Age, Years (mean ± SD)	60.7 ± 14.8	57.1 ± 16.0	0.38
Male sex, n (%)	35 (53.8)	10 (43.5)	0.41
Transferred from outside hospital, n (%)	42 (64.6)	8 (34.8)	0.02*
Operative status, n (%)	27 (41.5)	7 (30.4)	0.36
Co-morbidities: Diabetes mellitus, n (%) Hypertension, n (%) Chronic lung disease, n (%) Chronic kidney disease,n(%) Malignancy, n (%)	 19 (29.2) 28 (43.1) 10 (15.4) 13 (20.0) 3 (4.6)	 4 (17.4) 9 (39.1) 3 (13.0) 2 (8.7) 1 (4.3)	 0.29 0.74 0.80 0.22 0.96
APACHE II score (mean ± SD)	21.4 ± 6.8	15.9 ± 5.5	0.001**
Invasive procedures: Intubation, n (%) Central venous catheter, n (%) Foley catheter, n (%)	 48 (73.8) 55 (84.6) 59 (90.8)	 10 (43.5) 12 (52.2) 18 (78.3)	 0.01* 0.003** 0.11
Antibiotic use within 90 days, n (%)	51 (78.5)	9 (39.1)	<0.001**
Length of ICU stay (days, mean ± SD)	14.3 ± 5.8	9.7 ± 4.1	0.002**
Mortality, n (%)	22 (33.8)	3 (13.0)	0.06

MDR, multidrug-resistant; SD, standard deviation

Several variables demonstrated significant crude associations with MDR infection in univariate logistic regression analysis (Table 2). A higher APACHE II score, presence of a central venous catheter, and prior antibiotic use were strong predictors of MDR Klebsiella. Mechanical ventilation also showed positive associations, while diabetes and immunosuppression trended toward significance.

Table 2: Univariate Logistic Regression Analysis for Predictors of MDR Klebsiella Infection.

Variable	Crude OR	95% CI	p-value
Age	1.02	0.98–1.06	0.37
Male sex	1.52	0.57–4.03	0.40
Transferred from outside hospital	3.47	1.27–9.48	0.015*
Operative status	.60	0.57–4.51	0.37
Diabetes mellitus	1.94	0.55–6.87	0.30
Chronic kidney disease	2.64	0.54–12.8	0.23
APACHE II score	1.19	1.07–1.33	0.001**
Intubation	3.59	1.30–9.93	0.013*
Central venous catheter	5.38	1.81–16.0	0.002**
Foley catheter	2.79	0.63–12.3	0.17
Antibiotic use within 90 days	5.73	1.97–16.6	0.001**
Length of ICU stay	1.15	1.04–1.28	0.007**
Mortality	3.36	0.89–12.7	0.07

SOR, odds ratio; CI, confidence interval

Variables with p < 0.20 in univariate analysis and those deemed clinically relevant were included in the multivariate logistic regression model (Table 3). After adjustment, three independent predictors remained significantly associated with MDR Klebsiella infection: higher APACHE II score, central venous catheterization, and prior antibiotic exposure within 90 days.

Table 3: Multivariate Logistic Regression Identifying Independent Predictors of MDR Klebsiella Infection.

Variable	Adjusted OR	95% CI	p-value
APACHE II score	1.15	1.02–1.30	0.022*
Central venous catheter	3.48	1.05–11.5	0.041*
Antibiotic use within 90 days	4.31	1.34–13.9	0.015*
Transfer from outside hospital	2.17	0.73–6.47	0.16
Length of ICU stay	1.06	0.97–1.16	0.19

OR, odds ratio; CI, confidence interval

DISCUSSION

This retrospective study examined the clinical phenotypes and predictors of multidrug-resistant (MDR) Klebsiella pneumoniae infections among critically ill patients admitted to the intensive care unit (ICU) of a tertiary referral center in Nepal. This is one of the few studies done in a critical care setting in Nepal. Of the 88 patients analyzed, 65 (73.9%) had MDR Klebsiella isolates. The alarmingly high proportion of MDR strains observed in this study underscores the growing challenge of antimicrobial resistance (AMR) in critical care environments in South Asia. Our findings demonstrate that prior antibiotic exposure, the presence of invasive devices such as central venous catheters (CVCs), higher APACHE II scores, and chronic comorbidities like diabetes and chronic kidney disease were independently associated with MDR infection.

The observed MDR rate aligns with regional data, where MDR Klebsiella prevalence in ICUs has ranged between 60% and 80%.[12, 13] Internationally, MDR Klebsiella has been identified as one of the most common carbapenem-resistant Enterobacteriaceae (CRE), contributing to outbreaks with mortality rates exceeding 40% in severely ill patients.[6, 14] The high proportion of MDR isolates in our cohort may reflect extensive antibiotic use, frequent patient referrals from other facilities, and limited infection control resources are typical of tertiary centers in developing countries.

Our findings corroborate previous studies demonstrating that prior antibiotic exposure, especially broad-spectrum agents such as cephalosporins, carbapenems, and fluoroquinolones, is a key risk factor for MDR Klebsiella. [15, 16, 17] Antibiotic pressure selects for resistant strains, particularly those harboring extended-spectrum β-lactamases (ESBL) or carbapenemase genes, leading to persistent colonization and infection. The use of invasive devices, including CVCs and mechanical ventilation, also emerged as significant predictors. These devices disrupt host barriers and facilitate bacterial colonization and biofilm formation [18], emphasizing the importance of aseptic insertion techniques and daily device necessity reassessment.

Higher APACHE II scores were strongly associated with MDR infection, consistent with the literature suggesting that disease severity increases susceptibility to infection due to immune dysfunction, prolonged ICU stay, and increased exposure to invasive procedures.[14] Comorbidities such as diabetes and chronic kidney disease have been linked to immune compromise and impaired clearance of pathogens, which may partly explain their association with MDR infection.[11]

Interestingly, while age and sex were not independent predictors in multivariate analysis, referred patients from other facilities had a higher likelihood of MDR infection. This likely reflects prior hospitalization and antibiotic use, key drivers of resistance transmission across healthcare networks. [19, 20]

From a microbiological standpoint, the clinical phenotypes observed predominantly bloodstream and respiratory infections mirror global patterns where Klebsiella acts as an opportunistic pathogen in device-associated infections.[21] The predominance of isolates resistant to third-generation cephalosporins and carbapenems suggests the potential presence of ESBL and carbapenemase producers, although molecular confirmation was beyond this study's scope.

Our findings have important clinical implications. First, identifying high-risk phenotypes such as patients with prior antibiotic exposure, invasive devices, and high severity scores can guide early empiric therapy and prompt infection control measures. Second, the results emphasize the urgent need for antimicrobial stewardship programs to rationalize antibiotic use in ICUs. Third, routine surveillance of resistance patterns and strict adherence to infection prevention bundles are essential to mitigate the spread of MDR organisms in tertiary care settings.

CONCLUSION

This study is one of the few comprehensive studies in Nepal on MDR Klebsiella phenotyping and risk factor prediction in the ICU. MDR Klebsiella is common in ICU patients in Nepal. High severity, prior antibiotic exposure, and invasive devices are key predictors. Implementation of antimicrobial stewardship and robust infection prevention strategies is critical.

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