

# *Klebsiella pneumoniae* Isolates from the Intensive Care Unit at South Qunfudah Hospital in Saudi Arabia: An Emerging Antimicrobial Resistance Profile

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**Introduction:** *Klebsiella pneumoniae* is a significant pathogen in healthcare settings, particularly in the Intensive Care Unit (ICU). Its antimicrobial resistance poses a serious threat to infection control and patient outcomes. This study aims to analyze the developing antimicrobial resistance profile of *Klebsiella pneumoniae* isolates in the ICU.

**Methods:** A big hospital in Qunfudah provided 137 cases of infected individuals for this retrospective analysis. It was conducted on the available data on ICU patients' records. Various types of specimens were used. The data collected includes patients' demographic data, laboratory investigation, and tests for antimicrobial susceptibility. The isolates were identified and subjected to antimicrobial susceptibility tests using the compact system identification method. Data input and analysis were done using SPSS, version 26.

**Results:** The outcomes of this study reflected that more than half of *K. pneumoniae* were isolated from males (62.4%), many of them are Patients aged 76–95 years (n;43) were the most infected, followed by individuals aged 56–75 years (n; 27), 36–55 years (n;14), 96–105 years (n;7), and 16–35 years (n;2). The high frequency of specimens, sputum, urine, blood, and endotracheal tube (37.2%, 19%,18.2%,16.1%), respectively. Sputum had the highest culture positivity (n 51; 37.2%) for pathogens, followed by urine (n 26;19%), blood (n 25;18.2%), endotracheal tube (n 22; 16.1%), wound swabs (n 8; 5.8%), central line tip (n 3; 2.2%) stool and urethral swab (n 1; 0.7% for each). *K. pneumoniae* demonstrated high resistance rates (100%) for Cefalotin, Cefoxitin, Ceftriaxone, Cefepime, and Ampicillin, followed by Ciprofloxacin and Trimethoprim/Sulfamethoxazole (97.8%), Nitrofurantion (94.6%), Meropenem (91.4%), Amikacin (90.3%) and Gentamicin (87.1%). The lowest resistance rate was Imipenem (30.10%).

**Conclusion:** In conclusion, this study examines the antimicrobial resistance of *Klebsiella pneumoniae* in the ICU of South Qunfudah Hospital, focusing on specific location data rather than general resistance trends.

**Keywords:** antibiotics, antimicrobial resistance, ICU patients, *Klebsiella pneumoniae*

## Introduction

The development of resistance mechanisms, such as extended-spectrum  $\beta$ -lactamases (ESBLs) and carbapenemases, is a characteristic of *Klebsiella pneumoniae*'s resistance profile to antibiotics in the intensive care unit. These enzymes provide resistance to a variety of antibiotics, such as aminoglycosides, fluoroquinolones, and  $\beta$ -lactams. There are fewer treatment choices and higher rates of morbidity and mortality due to the growing incidence of multidrug-resistant *Klebsiella pneumoniae* strains, especially carbapenem-resistant *Klebsiella pneumoniae* (CRKP).

Gram-negative and non-motile, *Klebsiella pneumoniae* (*K. pneumoniae*) belongs to the Enterobacteriaceae family of bacteria. Carl Friedlander discovered it for the first time in 1882, when he isolated a bacterium from the lungs of people

who had died of pneumonia. *K. pneumoniae* can colonize settings related to healthcare and is frequently found in soil, water, humans, and animals.<sup>1,2</sup>

In addition to bacteremia, *Klebsiella pneumoniae* causes respiratory, intra-abdominal, and urinary tract infections.<sup>3–5</sup> In the past decades, *K. pneumoniae* was of greater and greater concern worldwide, mainly due to its enhanced resistance and recently focused hypervirulence.<sup>6,7</sup>

The most widely used antibiotics for bacterial infections are  $\beta$ -lactams, and carbapenems are among the most significant members of this class. Bacteria have evolved a number of resistance strategies to these medications in recent years, such as changes in outer membrane permeability brought on by porin loss, efflux pumps, an excess of cAMP-type  $\beta$ -lactamases, and the synthesis of inactivating enzymes. The most prominent enzymes that can hydrolyze carbapenem antibiotics and make them ineffective against Enterobacteriaceae microorganisms are *Klebsiella pneumoniae* carbapenemases (KPC), New Delhi metallo- $\beta$ -lactamase (NDM), active-on-imipenem (IMP), Verona integron-mediated metallo- $\beta$ -lactamase (VIM), and oxacillin-hydrolyzing (OXA-type) carbapenemases.<sup>8–10</sup>

Furthermore, the genus *Klebsiella* Numerous nosocomial infections, such as bacteremia, pneumonia, wound infections, and infections of the intra-abdominal and urinary tracts, are caused by this important opportunistic pathogen.<sup>1</sup> Direct person-to-person contact in healthcare settings, such as contaminated medical equipment use, contaminated staff hands, or polluted environments, might result in KP transmission. The main treatment for KP infections is beta-lactam antibiotics. However, in recent years, KP has become resistant to various antibiotics, particularly carbapenems, which are only used as a last resort. Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) has increased as a result of the overuse and/or abuse of these drugs.<sup>11</sup> High rates of morbidity and mortality are associated with CRKP infections.<sup>11–13</sup> The mortality rate for patients infected with susceptible KP strains is three times lower than that of patients infected with CRKP, which ranges from 30 to 44% and can reach 70% in cases of bacteremia.<sup>14–17</sup> Concerningly, more than 30·0% of *K. pneumoniae* strains are now carbapenem-resistant (CRKP), which presents serious difficulties for clinical practice.<sup>18</sup>

The World Health Organization (WHO) released a list of the most “critical” bacteria in the world in 2016, emphasizing those that urgently require novel therapies. Among these, Enterobacteriaceae that are resistant to carbapenem (CRE) were designated as a critical priority organism. CRKP can arise by a number of processes, one of which is (i) carbapenemase synthesis. (ii) decreased expression or loss of outer membrane proteins along with increased expression of AmpC cephalosporinases and extended-spectrum  $\beta$ -lactamases, and (iii) efflux pump activation.<sup>19</sup> *K. pneumoniae* carbapenemases, imipenemase, oxacillinase, Verona integron encoded metallo  $\beta$ -lactamase, and New Delhi metallo  $\beta$ lactamase are examples of carbapenemases.<sup>20</sup> CRKP may result from *OmpK35* and *OmpK36* disruption or deficit.<sup>21</sup> Carbapenem resistance is also influenced by efflux pump overexpression.<sup>22</sup> Although the causes of CRKP differ greatly across the globe, it is mainly caused by mobile genetic elements that carry a variety of antibiotic resistance genes, including the oxacillinase-48 gene, New Delhi metallo- $\beta$ -lactamase gene, and the beta-lactamase *Klebsiella pneumoniae* carbapenemases gene (*bla* KPC).<sup>11,23</sup>

The study investigates the rising prevalence of antimicrobial resistance (AMR) in *Klebsiella pneumoniae* isolates from ICU patients at South Qunfudah Hospital, particularly to carbapenems. Factors such as long hospital stays, patient demographics, and specimen types contribute to this resistance, posing challenges for infection control and treatment.

The unique healthcare characteristics of the South Qunfudah region, including its geographical location and patient population, make it an ideal setting to assess local resistance patterns and guide targeted antimicrobial stewardship programs. By profiling *Klebsiella pneumoniae* resistance in South Qunfudah, the study aims to improve treatment approaches and patient outcomes in the region.

## Objectives

1. To analyze the prevalence, antimicrobial resistance patterns, and demographic factors associated with *Klebsiella pneumoniae* infections in ICU patients at South Qunfudah Hospital.
2. To offer suggestions for antimicrobial stewardship initiatives and infection control plans to lessen the effects of antibiotic resistance in the intensive care unit.

## Significant Research Findings

One of the main pathogens connected to infections in healthcare settings, especially in intensive care units (ICUs), is *Klebsiella pneumoniae*. This work advances our knowledge of the changing profile of antibiotic resistance in *K. pneumoniae* isolates in the intensive care unit, emphasizing the necessity of careful monitoring, prudent antibiotic usage, and infection control strategies to fight this important healthcare-associated pathogen.

## Materials and Methods

### Study Design

Analysis design: 137 instances of infected patients from a prominent Qunfudah hospital were included in this retrospective data-based analysis. The study analyzed medical records of ICU patients with infections. Patient contact was not made, and only data on isolated bacteria, without personal information, was collected. The study was sanctioned by South Qunfudah General Hospital's Research and Ethics Committee. This study was a retrospective used pre-existing clinical data and routine procedures. Patient information and medical records were anonymized and exclusively used for research purposes. The Ethics Committee determined that the study posed no additional risks or interventions, waiving the informed consent requirement. Furthermore, the data collection process did not alter patient treatment or affect their health status, which made informed consent unnecessary.

### Study Area

The South Qunfudah General Hospital in Southwest Saudi Arabia served as the study's site. The hospital, located in the Makkah region, has 100 beds and offers specialized services. It contains two intensive care units (ICUs) with a combined capacity of 27 beds: an 11-bed general ICU and a 16-bed neonatal ICU. For these units, a multidisciplinary care team provides support.

### Study Period

In order to gather information from the prior medical records of every patient admitted to the intensive care unit during the study period, a fourth-year retrospective analysis was carried out from January 2019 to December 2022. Selecting this specific timeframe based on the availability and completeness of data. Data prior to 2019 were excluded due to inconsistencies, and data for 2023–2024 were not included as the study was conducted before these years.

### Sampling and Sample Size

The study utilized data from laboratory records, specifically patient samples previously analyzed in the laboratory. 137 non-duplicate clinical specimens from intensive care unit patients were gathered and examined, comprising 51 sputum samples, 51 urine samples, 26 blood (n: 25), endotracheal aspirate (n: 22), wound swab (n: 8), central line tip (n:3), urethral swab (n: 1), and stool (n: 1). All specimens showed bacterial growth. The data collected included patients' demographic information, laboratory investigations, and antimicrobial susceptibility tests.

### Data Collection Techniques and Tools

Data on patients' demographic characteristics, such as age, gender, and residence, were extracted from medical records and data regarding laboratory findings of these *K. pneumoniae* infected patients. All data were treated as *K. Pneumoniae* cases and the response for this treatment was reported in medical records. The data were recorded in a standardized format by the study team. The clinical features (catheter, ventilation, and general level of activity) for each person were reported. In addition, any tests used for diagnosis and treatment, if available, were recorded.

### Inclusion and Exclusion Criteria

A standard data-collection form (Qu Chenier) was employed to manually, include criteria for all patients admitted to the ICU, both male and female, of all ages, and exclude out-patients and patients who attended other departments.

## Isolation and Identification of Pathogen

Isolation and identification of pathogens, which had already been performed in the laboratory, were cataloged. As previously stated, retrospective data was gathered for the laboratory study in the following manner: depending on the sample's origin, each clinical specimen was cultured on either blood agar, MacConkey agar, chocolate agar, or Cystine Lactose Electrolyte-Deficient (CLED) agar. The inoculation sample was then incubated aerobically at 37°C for 24 to 48 hours, except for the blood culture, which was cultivated for five to seven days. Colony morphology, Gram stain, and rapid biochemical tests like oxidase, catalase, and indole were used to identify some isolates at first. The isolates were then identified using the Vitek 2 compact system identification method. The Vitek 2 compact cards were infected in accordance with the guidelines provided by the manufacturer. Depending on the infection site and specimen type, each pathogen's notable growth was recognized and prepared for antibiotic susceptibility testing. The Clinical and Laboratory Standards Institute's (CLSI) guidelines were followed when conducting the antibiotic susceptibility test.<sup>24</sup> The discovered bacteria were examined in vitro using the Vitek 2 small, automated microbiology system against many kinds of antibacterial medications. The antimicrobial agents listed below were looked at: 500mg of Ampicillin, 1g of Cefalotin, 1g of Ceftriaxone, 1g of Cefepime, 500mg of Imipenem, 1g of Meropenem, 5mg of Amikacin, 1mg of Gentamicin, 500mg of Ciprofloxacin, 1g of Nitrofurantoin, and 23.75µg/1.25µg of Trimethoprim/Sulfamethoxazole. Maintenance and quality control were carried out in accordance with the manufacturer's guidelines. As previously mentioned, isolates that were resistant to at least three distinct classes of antimicrobial drugs were classified as multidrug-resistant.<sup>25</sup>

We recognize the use of phenotypic testing in this study as a practical and reliable method for identifying *Klebsiella pneumoniae* resistance patterns in clinical settings. This approach was chosen for its accessibility, ease of implementation in hospital labs, and timely results for treatment decisions.

## Statistical Analysis

Data input and analysis were conducted using SPSS version 26, often known as the Statistical Package for Social Sciences.

## Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Research and Ethics Committee of South Qunfudah General Hospital. This retrospective study was exempt from obtaining informed consent as per standard ethical guidelines. The data was collected from existing medical records without direct patient interaction or intervention. Patient confidentiality was maintained through anonymization and data abstraction. The study utilized routine clinical documentation for research purposes, and no new data was collected specifically for this study. The exemption from informed consent was granted by the ethics committee based on these considerations, aligning with ethical standards for retrospective research.

## Results

A fourth-year retrospective study was conducted at South Qunfudah General Hospital in Southwest Saudi Arabia, from January 2019 to December 2022.

The finding of this study reflected that more than half of *K. pneumoniae* were isolated from males (62.4%), many of them are Patients aged 76–95 years (n; 43) were the most infected, followed by those aged 56–75 years (n; 27), 36–55 years (n; 14), 96–105 years (n; 7), and 16–35 years (n; 2), see [Table 1](#).

[Table 2](#) and [Figure 1](#) shows the high frequency of specimens, sputum, urine, blood, and endotracheal tube (37.2%, 19%, 18.2%, 16.1%), respectively.

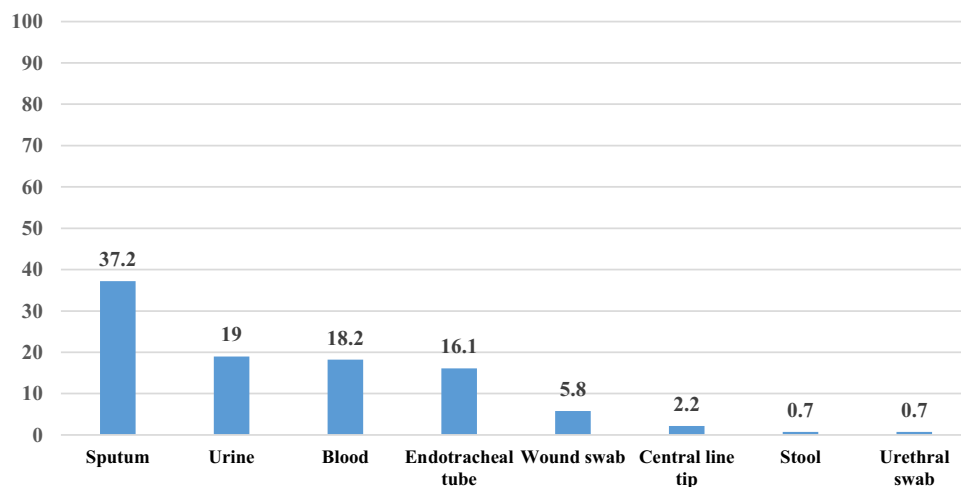
**Table 1** Frequency of *Klebsiella Pneumoniae* According to Demographic Data

Gender	<i>Klebsiella Pneumoniae</i> Frequency, n (%)
Male	58 (62.4%)
Female	35 (37.6%)
Age (years old)	
16–35yrs	2 (40%)
36–55yrs	14 (87.5%)
56–75yrs	27 (60%)
76–95yrs	43 (69.4%)
96–105yrs	7 (77.8%)

**Table 2** Frequency of Used Specimens

Specimen	Frequency	Percent
Sputum	51	37.2
Urine	26	19
Blood	25	18.2
Endotracheal tube	22	16.1
Wound swab	8	5.8
Central line tip	3	2.2
Stool	1	0.7
Urethral swab	1	0.7
<b>Total</b>	<b>137</b>	<b>100%</b>

Sputum had the highest culture positivity (n 51; 37.2%) of the 137 specimens cultured for pathogens, followed by urine (n 26; 19%), blood (n 25; 18.2%), endotracheal tube (n 22; 16.1%), wound swabs (n 8; 5.8%), central line tip (n 3; 2.2%) stool and urethral swab (n 1; 0.7% for each).

**Figure 1** Frequency of used specimens.

**Table 3** Patients' Stay Duration in Hospital

Duration (Days)	Frequency	Percent
01-5	45	32.8
06-10	28	20.4
11-15	15	10.9
16-30	28	20.2
31-45	11	8
46-60	6	4.4
61-100	4	2.9
<b>Total</b>	<b>137</b>	<b>100%</b>

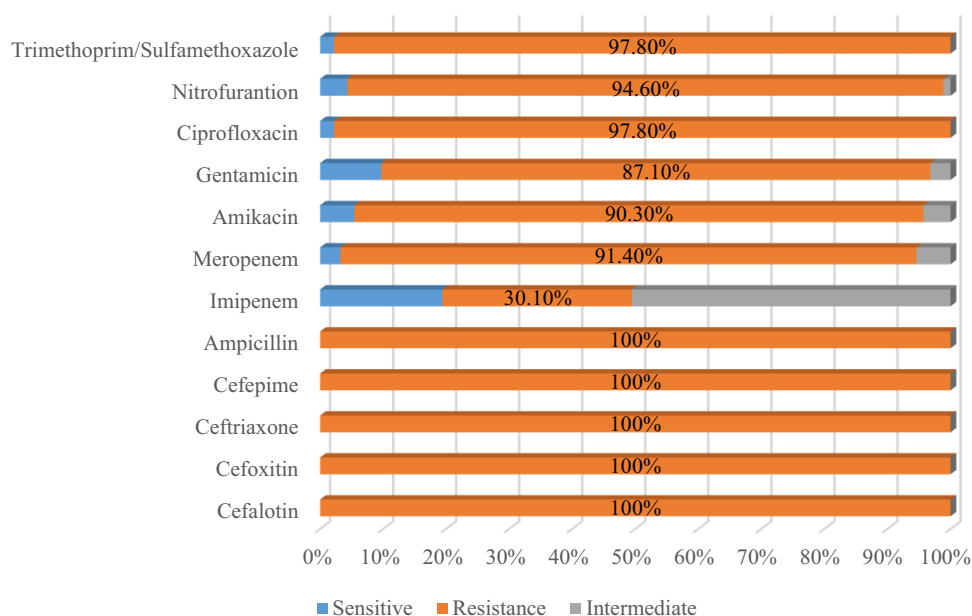
The study revealed that patients staying in the hospital for one to five days were at higher risk of contracting antibiotic-resistant bacteria in an intensive care unit. See [Table 3](#).

## Antimicrobial Susceptibility of Isolates

Out of 137 collected specimens, 93 (67.9%) *Klebsiella pneumoniae* were isolated. [Table 4](#) and [Figure 2](#) showed that *K. pneumoniae* demonstrated high resistance rates (100%) to Cefalotin, Cefoxitin, Ceftriaxone, Cefepime, and Ampicillin, followed by Ciprofloxacin and Trimethoprim/Sulfamethoxazole (97.8%), Nitrofurantoin (94.6%), Meropenem (91.4%), Amikacin (90.3%) and Gentamicin (87.1%). The lowest resistance rate was Imipenem: (30.10%).

**Table 4** Antimicrobial Susceptibility of *K. Pneumoniae*

Antibiotics	<i>K. Pneumoniae</i> Antibiotic Susceptibility		
	Sensitive, n (%)	Resistance, n (%)	Intermediate, n (%)
Cefalotin	00	93 (100%)	00
Cefoxitin	00	93 (100%)	00
Ceftriaxone	00	93 (100%)	00
Cefepime	00	93 (100%)	00
Ampicillin	00	93 (100%)	00
Imipenem	18 (19.4%)	28 (30.10%)	47 (50.50%)
Meropenem	3 (3.2%)	85 (91.4%)	5 (5.4%)
Amikacin	5 (5.4%)	84 (90.3%)	4 (4.3%)
Gentamicin	9 (9.7%)	81 (87.1%)	3 (3.2%)
Ciprofloxacin	2 (2.2%)	91 (97.8%)	00
Nitrofurantion	4 (4.3%)	88 (94.6%)	1 (1.1)
Trimethoprim/Sulfamethoxazole	2 (2.2%)	91 (97.8%)	00



**Figure 2** Antimicrobial susceptibility of *K. Pneumoniae*.

## Discussion

Antimicrobial resistance in *Klebsiella pneumoniae* is a growing global health concern. This discussion will focus on the latest trends in antibiotic resistance in *Klebsiella pneumoniae*, including emerging resistance mechanisms and their impact on treatment strategies, infection control practices, and healthcare outcomes.

In terms of the patient's demographic and social characteristics, the distribution of *Klebsiella Pneumoniae* by age group in this study was in line with earlier research,<sup>26</sup> but it differed from that of the same study by gender. This suggests that the sample population in this study is representative of patients in terms of these demographic factors. However, it is important to recognize that the generalizability of the study may be confined to the specific region of Makkah.

Furthermore, the distribution of *Klebsiella Pneumoniae* across several specimen sources was comparable to the results of a study conducted in China, which revealed that the most common source of *K. pneumoniae* isolates was sputum and broncho-alveolar lavage (73.9% in 2018, 66.9% in 2019, and 63.2% in 2020), followed by urine (9.9% in 2018, 6.1% in 2019, and 10.5% in 2020), blood (7.0% in 2018, 6.6% in 2019, and 7.8% in 2020), and pus (5.2% in 2018, 6.1% in 2019, and 6.7% in 2020).<sup>27</sup>

The distribution of *K. pneumoniae* and the duration of hospital stays for patients did not significantly correlate, according to the current study. Antimicrobial resistance in *Klebsiella pneumoniae* also has implications for infection control and Healthcare-Associated Infections (HAIs). Multidrug-resistant strains can spread within healthcare facilities, leading to outbreaks and increased transmission rates. *Klebsiella pneumoniae's* ability to acquire and transfer resistance genes worsens the issue, as it can lead to the development of multidrug-resistant pathogens in other bacterial species. This highlights the importance of robust infection control measures and surveillance systems to stop the spread of antimicrobial-resistant *Klebsiella pneumoniae*.<sup>28</sup>

In this study, our results showed that *K. pneumoniae* demonstrated high resistance rates (100%) to Cefalotin, Cefoxitin, Ceftriaxone, Cefepime, and Ampicillin, followed by Ciprofloxacin and Trimethoprim/Sulfamethoxazole (97.8%), Nitrofurantion (94.6%), Meropenem (91.4%), Amikacin (90.3%) and Gentamicin (87.1%). The lowest resistance rate was Imipenem: (30.10%). *K. pneumoniae* showed the greatest ceftriaxone resistance rates (86.6%) in another Iranian investigation. At a Korean tertiary care hospital, the usage of broad-spectrum antibiotics raises the prevalence of resistant bacteria.<sup>29</sup>

Additionally, our results show excessive use of aminoglycoside, cephalosporins, and meropenem, over time, these bacteria will become resistant to imipenem, as it is an almost used option for patients in this region. Also, excessive use

of Imipenem will lead to resistance to it and thus will become resistant to carbapenems, which poses the greatest risk in ICU, as proven by recent studies, the carbapenem-resistant Enterobacteriaceae showed an increase from 1% to 5% and were more common in eastern Switzerland (5% vs 3%).<sup>30</sup> Compared to isolates of KP that are susceptible to carbapenem (CSKP) (21.16%), Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) (42.14%) exhibits greater resistance to several antimicrobial medications. In critically ill patients, especially those admitted to the intensive care unit (ICU), where the mortality rate is higher than that of infections brought on by CSKP, these resistant strains have resulted in hospital-acquired infections.<sup>31,32</sup>

The impact of prolonged hospital stays associated with *Klebsiella pneumoniae* infections extends beyond the individual patient. It puts pressure on healthcare systems, which can result in higher medical expenses, strained resources, and possible alterations to patient flow and bed availability. Managing multidrug-resistant *Klebsiella pneumoniae* infections requires specialized expertise, dedicated infection control measures, and effective antimicrobial stewardship practices to enhance patient outcomes and decrease the length of hospitalization.<sup>33</sup>

The study revealed that 32.8% of patients had hospital stays ranging from one to five days, consistent with findings from a survey by.<sup>34</sup> This was followed by stays of 6–10 and 16–30 days (20.3%), 11–15 days (10.9%), 31–45 days (8%), 46–60 days (4.4%), and 61–100 days (2.9%). Extended hospital stays could potentially contribute to the spread of MDR infections.<sup>34</sup> Prolonged hospitalization can increase the risk of spreading multidrug-resistant infections. Older patients and those on prolonged artificial ventilation are at a higher risk of infections.<sup>35</sup>

In conclusion, the increasing antimicrobial resistance of *Klebsiella pneumoniae* in the ICU poses a significant threat to patients and infection control practices. Effective strategies, including infection control measures and antimicrobial stewardship, are crucial to combat the spread of resistant strains. Continued surveillance and research efforts are needed to identify new treatment options and address this public health concern.

A study at South Qunfudah Hospital, Saudi Arabia, highlights the high resistance rates of *Klebsiella pneumoniae* to common antibiotics, impacting patient outcomes. Urgent intervention is required to prevent further spread and ensure effective treatment options.

To tackle this challenge, enhanced infection control measures and antimicrobial stewardship programs should be implemented. Surveillance of resistance patterns and exploration of alternative treatment strategies are essential. Educating healthcare professionals and the public on responsible antibiotic use is key to improving patient outcomes in ICU settings.

## Study Limitations

The study relied on historical patient data, findings are specific to South Qunfudah Hospital and the study did not include genetic analysis of resistance mechanisms, which could provide further insights into resistance development due to the nature of the study as it is a retrospective study.

These limitations highlight the need for broader, multi-center research incorporating molecular diagnostics and real-time surveillance to gain a more comprehensive understanding of antimicrobial resistance in *K. pneumoniae*.

## Data Sharing Statement

All data from this study are included in the article. For further information, don't hesitate to get in touch with the corresponding author.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors attest that none of the work reported in this paper may have been influenced by any conflicting financial or non-financial interests or personal ties.

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