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# The Prevalence of Multidrug-Resistant and Extensively Drug-Resistant Infections in Respiratory Intensive Care Unit, Causative Microorganisms and Mortality

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**Aim:** This study aims to analyze the incidence of multidrug-resistant (MDR) retrospectively and extensively drug-resistant (XDR) infections, characteristics of patients with these infections, causative microorganisms, and mortality rates in a tertiary respiratory intensive care unit (ICU).

**Material and Method:** Between 01.01.2022 and 31.12.2023, the data of patients treated in the third-level respiratory ICU were analyzed retrospectively. Adult patients over 18 years of age with MDR and XDR infections were included in the study. Demographic characteristics, age, gender, comorbid systemic diseases, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, mechanical ventilation support status, duration of ICU stay and prognosis of the patients were analyzed and recorded through the hospital information management system.

**Results:** The study included 261 patients. Of these patients, 184 (70.5%) were male, 77 (29.5%) were female, and their ages were 65.54 ± 14.43 years. The majority of the patients had chronic diseases such as chronic obstructive pulmonary disease, hypertension, coronary artery disease, malignancy, and diabetes mellitus. There was no statistically significant difference between the resistance status of *Klebsiella spp. Pseudomonas spp. and Acinetobacter spp*. and the prognosis of the patients ($p>0.05$). No statistically significant difference was found between MDR and XDR *Klebsiella spp. Pseudomonas spp. and Acinetobacter spp*. patients in terms of the need for invasive mechanical ventilation, non-invasive mechanical ventilation, respiratory support therapy with high flow, APACHE II score, SOFA score, length of stay in the ICU, and prognosis ($p>0.05$).

**Conclusion:** Early detection and close monitoring of MDR, XDR, and PDR bacterial strains are vital to combat antimicrobial resistance. This study shows that MDR and XDR infections are a major health problem in ICUs and that these infections have significant negative effects on patient prognosis.

**Keywords:** intensive care units, multi-drug resistance, extensively drug-resistant, antimicrobial resistance, mortality

## Introduction

Intensive care units (ICUs) are the units where invasive procedures such as mechanical ventilation, tracheostomy, and catheterization are frequently performed and, therefore, have the highest rates of nosocomial infections and mortality. In addition, the use of broad-spectrum antibiotics is more frequent, high-dose, and long-term in ICUs than in other departments. Therefore, resistant infections due to resistant microorganisms are more common in ICUs.[1,2]

Nosocomial infections caused by antibiotic-resistant bacteria, which are increasing worldwide, constitute a serious health problem. Such infections not only increase morbidity and mortality rates but also lead to prolonged hospitalization

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and serious complications.[3] Infectious agents and resistance profiles emerging in ICUs may differ between hospitals and ICUs over time. Gram-negative bacteria with clinical importance in nosocomial infections are mostly *Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa*, and *Acinetobacter baumannii*.[4] As a result, resistant microorganisms (*E.coli, K.pneumoniae, A.baumannii, P. aeruginosa*), which are an important cause of hospitalization, morbidity, mortality, and financial expenditures, have been included in the list of priority pathogens in the research and development of new antibiotics by the World Health Organization.[5]

As there are various definitions in the literature, the latest update from the European Center for Disease Prevention and Control and the United States Centers for Disease Control and Prevention defines multidrug-resistant (MDR) as microorganisms that show resistance to three or more classes of antimicrobial agents. Microorganisms that are resistant to almost all classes of antimicrobial agents but remain susceptible to only one or two classes are defined as extensively drug-resistant (XDR). Pandrug resistant (PDR) is defined as the insensitivity to all agents in all antimicrobial categories.[6]

The study aims to retrospectively investigate the incidence of MDR and XDR infections, characteristics of patients with infections, causative microorganisms, and mortality rate in the respiratory ICU.

# Materials and Method

## Study Design and Patients

Between 01.01.2022 and 31.12.2023, the data of patients followed up in the third level respiratory ICU were evaluated retrospectively. The study was conducted in accordance with the Declaration of Helsinki and ethics committee approval (approval no: 329) was obtained from Health Sciences University Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital. Due to the retrospective nature of the study, the requirement for informed consent was waived and the waiver was approved by the Ethics Committee of the University of Health Sciences Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital. All patient data were handled in strict adherence to ethical standards, ensuring confidentiality and anonymity. No personal identifiers were used in the analysis or reporting of study results. Adult patients over the age of 18 years who were hospitalized in the third level respiratory ICU with a prediagnosis of pneumonia, had respiratory tract specimens taken and had gram negative growth were included in the study. Patients under 18 years of age, patients who developed infection with gram-positive bacteria and patients with missing data were excluded.

## Data Collection and Definition

Demographic characteristics of the patients including age, gender, additional systemic diseases, acute physiology and chronic health evaluation II (APACHE II) score, sequential organ failure assessment (SOFA) score, presence of mechanical ventilation support, duration of ICU stay and prognosis were evaluated through their files in the hospital information management system, and data were recorded.

## Statistical Analysis

Descriptive statistics were used for demographic and clinical data, Chi-square analysis was used to show the relationship between categorical data, and Student's *t*-test analysis was used for continuous variables. A p-value <0.05 was considered significant in the study. SPSS program (Version 22, SPSS Inc., Chicago, IL, USA) was used for calculations.

# Results

## Characteristics of the Patients

During the study period, 1058 patients were admitted to the ICU. We evaluated 261 patients with gram-negative bacteria isolated from the third-level respiratory ICU with a mean age of 65.54 ± 14.43 years, 184 (70.5%) males and 77 (29.5%) females. One or more chronic diseases such as chronic obstructive pulmonary disease (COPD) was present in 130 (49.8%), hypertension in 129 (49.4%), coronary artery disease (CAD) in 86 (33%), malignancy in 79 (30%), and diabetes mellitus in 71 (27.2%). Demographic characteristics, clinical conditions, and the distribution of chronic diseases according to prognosis are given in the table (Table 1).

**Table 1** Clinical and Demographic Characteristics of Patients

| Variables | | Prognosis | | | | p-value |
|---|---|---|---|---|---|---|
| | | Exitus | | Discharge | | |
| | | n | % | n | % | |
| **Gender** | **Male** | 44 | 29.1 | 33 | 30 | 0.880 |
| | **Female** | 107 | 70.9 | 77 | 70 | |
| **Age (year)[a]** | | 67 | | 64 | | **<0.001** |
| **CCI Group** | **0–1** | 22 | 14.6 | 37 | 33.6 | **<0.001** |
| | **>2** | 129 | 85.4 | 73 | 66.4 | |
| **Bronchiectasis** | **No** | 132 | 87.4 | 92 | 83.6 | 0.387 |
| | **Yes** | 19 | 12.6 | 18 | 16.4 | |
| **Diabetes mellitus** | **No** | 103 | 68.2 | 87 | 79.1 | 0.051 |
| | **Yes** | 48 | 31.8 | 23 | 20.9 | |
| **Hypertension** | **No** | 69 | 45.7 | 63 | 57.3 | 0.065 |
| | **Yes** | 82 | 54.3 | 47 | 42.7 | |
| **Coronary artery disease** | **No** | 94 | 62.3 | 81 | 73.5 | 0.053 |
| | **Yes** | 57 | 37.7 | 29 | 26.4 | |
| **Cerebrovascular disease** | **No** | 145 | 96 | 101 | 91.8 | 0.149 |
| | **Yes** | 6 | 4 | 9 | 8.2 | |
| **Chronic obstructive pulmonary disease** | **No** | 75 | 49.7 | 56 | 50.9 | 0.843 |
| | **Yes** | 76 | 50.3 | 54 | 49.1 | |
| **Alzheimer's** | **No** | 140 | 92.7 | 107 | 97.3 | 0.107 |
| | **Yes** | 11 | 7.3 | 3 | 2.7 | |
| **Congestive heart failure** | **No** | 115 | 76.2 | 90 | 81.8 | 0.271 |
| | **Yes** | 36 | 23.8 | 20 | 18.2 | |
| **Chronic renal failure** | **No** | 139 | 92.1 | 104 | 94.5 | 0.433 |
| | **Yes** | 12 | 7.9 | 6 | 5.5 | |
| **Malignancy** | **No** | 95 | 62.9 | 86 | 78.2 | **0.008** |
| | **Yes** | 56 | 36.1 | 24 | 21.8 | |
| **Need for mechanical ventilation support** | **No** | 2 | 1.3 | 52 | 47.3 | **<0.001** |
| | **Yes** | 149 | 98.7 | 58 | 52.7 | |
| **APACHE II score[a]** | | 27 | | 18 | | **<0.001** |
| **SOFA score[a]** | | 9 | | 5 | | **<0.001** |

**Notes**: [a]Median. p< 0.05 in bold was considered statistically significant.
**Abbreviations**: CCI, Charlson Comorbidity Index; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; n, Number of patients; %, Percentage.

According to agent-independent resistance status, the number of susceptible patients was 111 and 57 of these patients died. Fifty of 81 XDR patients died, 71 patients were MDR and 44 of them died. No statistically significant result was obtained between these groups(p= 0.3).

*Klebsiella spp*. 61 (23.4%), *Pseudomonas spp*. 70 (26.8%), *Acinetobacter spp*. 60 (23.0%) strains were isolated from 191 patients, and the results of antibiotic susceptibility tests were evaluated. Thirteen patients with pan-drug-resistant *Klebsiella spp*. and 26 patients without resistance were identified. The distribution of 152 patients with MDR or XDR according to their resistance status is given in the table (Table 2).

When the resistance status of *Klebsiella spp., Pseudomonas spp*., and *Acinetobacter spp*. and the prognosis of the patients were evaluated, no statistically significant difference was found between them (Table 3).

No statistically significant difference was found between patients with MDR and XDR *Klebsiella spp*. and *Pseudomonas spp*. isolated in terms of the need for invasive mechanical ventilation, non-invasive mechanical ventilation, respiratory support therapy with high flow, APACHE II score, SOFA score, duration of ICU stay and prognosis (p>0.05) (Table 4).

Since the number of patients with MDR and susceptible *Acinetobacter spp*. isolated was not sufficient for statistical evaluation, they were not included in this evaluation.

**Table 2** Resistance Status of Klebsiella Spp., Pseudomonas Spp., and Acinetobacter Spp

| Resistance Status | *Klebsiella spp.* | *Pseudomonas spp.* | *Acinetobacter spp.* | |
|---|---|---|---|---|
| **MDR** n (%) | 24 (33.8%) | 46 (64.8%) | 1 (1.4%) | 71 (100.0%) |
| **XDR** n (%) | 14 (17.3%) | 9 (11.1%) | 58 (71.6%) | 81 (100.0%) |
| Total Number n (%) | 38 (25.0%) | 55 (36.2%) | 59 (38.8%) | 152 (100.0%) |

**Abbreviations**: n, Number of patients; %, Percentage.

**Table 3** Resistance Status of Klebsiella Spp., Pseudomonas Spp., and Acinetobacter Spp. and Prognosis of Patients

| | **Prognosis** | | |
|---|---|---|---|
| | **Exitus n (%)** | **Discharge n (%)** | **p-value** |
| ***Klebsiella spp.*** | | | 0.381 |
| MDR | 14 (40.0%) | 10 (38.5%) | |
| XDR | 10 (28.6%) | 4 (15.4%) | |
| Others[a] | 6 (17.1%) | 4 (15.4%) | |
| ***Pseudomonas spp.*** | | | 0.838 |
| MDR | 30 (66.7%) | 16 (64.0%) | |
| XDR | 5 (11.1%) | 4 (16.0%) | |
| Others[a] | 10 (22.2%) | 5 (20%) | |
| ***Acinetobacter spp.*** | | | |
| MDR | 0 | 1 (4.0%) | |
| XDR | 35 (100.0%) | 23 (92.0%) | |
| Others[a] | 0 | 1 (4.0%) | |

**Notes**: [a]Patients without resistance.
**Abbreviations**: n, Number of patients; %, Percentage; p< 0.05 was considered statistically significant.

**Table 4** Resistance Status of Klebsiella Spp., Pseudomonas Spp., and Acinetobacter Spp. and Patients' Clinical Variables

| Variables | Resistance Status of *Klebsiella spp., Pseudomonas spp.,* and *Acinetobacter spp.* Isolates | | |
|---|---|---|---|
| | MDR | XDR | p-value |
| High flow practice n (%) | 7 (% 35) | 13 (% 65) | 0.260 |
| Non-invasive mechanical ventilation n (%) | 26 (% 53.1) | 23 (% 46.9) | 0.279 |
| Invasive mechanical ventilation n (%) | 60 (% 45.8) | 71 (% 54.2) | 0.575 |
| APACHE II score[a] | 23.03 ± 8.9 | 25.22 ± 8.6 | 0.481 |
| SOFA score[a] | 7.89 ± 3.92 | 8.31 ± 3.89 | 0.937 |
| Length of stay in ICU(days) | 18 (min: 1 max:109) | 14 (min: 1 max: 95) | 0.435 |
| Prognosis ending in death n (%) | 43 (% 45.3) | 52 (% 54.7) | 0.644 |

**Notes**: [a]Mean±SD. p< 0.05 was considered statistically significant.
**Abbreviations**: APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; n, Number of patients; %, Percentage; min, Minimum; max, Maximum.

When 64 patients (45.7%) with comorbidity and MDR were compared with 76 patients (54.3%) with comorbidity and XDR, no statistically significant difference was found (p=0.400).

## Discussion

MDR is emerging as one of the serious threats, especially in ICUs of hospitals. In 2019, approximately 4.95 million deaths globally were associated with MDR infections, including 1.27 million deaths due to drug resistance.[7] Shi et al reported that nosocomial infections caused by MDR and XDR *A.baumannii* are associated with high mortality in the ICU.[8]

Basak et al analyzed the antibiotic susceptibility profile of 1060 bacterial strains; 393 (37.1%) of the bacterial strains were MDR, 146 (13.8%) were XDR, but no PDR was isolated. All Gram-negative bacteria (GNB) strains were susceptible to colistin, while all Gram-positive bacteria strains were susceptible to vancomycin. Among the 250 GNB-MDR strains isolated, the most common MDR strains were *E. coli* 79/250 (31.6%), followed by *K. pneumoniae* 75/250 (30%). Similarly, among the 90 GNB-XDR strains isolated, the most common XDR strains were *P. aeruginosa* 29/90 (32.2%) *and K. pneumoniae* 25/90 (27.8%).[9] In our study, MDR *Klebsiella spp*. were found in 33.8% and XDR *Klebsiella spp*. in 17.8%, but MDR *Pseudomonas spp*. were found in 64.8% and XDR *Pseudomonas spp*. in 11.1%.

Aly and Balkhy reported that the most common MDR was *E. coli*, followed by *K. pneumoniae*.[10] In another study conducted in a tertiary hospital in Riyadh, it was reported that the most common MDR pathogens were *P. aeruginosa*, followed by *E. coli*.[11] In our study, the most common MDR was found to be *Pseudomonas spp*., and XDR was found to be *Acinetobacter spp*. strains.

Longer length of hospital stay and/or ICU stay, longer duration of mechanical ventilation, exposure to antimicrobial agents, colonization status, invasive procedures, the severity of underlying disease, and reintubation are known factors that increase the risk of MDR *A. baumannii* infection.[12–14] In another study, patients with Ventilator-associated Pneumonia (VAP) caused by XDR *A. baumannii* had significantly increased length of stay in the ICU and hospital. In addition, it was found that patients with XDR *A. baumannii* were older and stayed on mechanical ventilation longer before the development of VIP and had a higher rate of re-intubation due to VIP compared to patients without XDR *A. baumannii*. However, the difference was not statistically significant.[15] In our study, no statistical significance was found between XDR or MDR *Acinetobacter spp*. and prognosis, length of hospitalization, or being under mechanical ventilator support.

Wang et al showed that *A. baumannii* (n = 62, 30%) was the most common gram-negative bacterium in the ICU.[16] Another study showed that the main pathogen was *K. pneumoniae*.[1] In the study by Durdu et al, 73% of *Klebsiella* isolates were MDR, and an additional 14% were XDR.[17] In our study, *Klebsiella spp*. was the most common pathogen, and of the *Klebsiella* strains that developed resistance, MDR was 33.8%, and XDR was 17.3%.

In the study conducted by Durdu et al in an ICU, the XDR rate of *A. baumannii* was 72% in 2015, and similarly (71.6%) was found to be XDR in our study.[17] Unlike the literature, XDR or MDR status of *Acinetobacter spp*. was not found to be a risk factor for mortality in our study. No risk factors were detected because almost all strains were XDR and MDR. In our study, unlike the literature, MDR or XDR of gram-negative bacteria that developed antibiotic resistance was not associated with the prognosis, length of hospital stay, APACHE II score, SOFA score, and invasive mechanical ventilator support. In the prediction model of MDR and non-MDR strains isolated in the ICU in the study by Wu et al, comorbidities and resistance status were not found to be related as in our study.[1] We think that the reason for this was the isolates obtained only from the respiratory tract, the small number of patients, and the fact that the patients received treatment in the respiratory ICU.

In a European multicentre study, *K. aerogenes* showed the highest rate of both third- generation cephalosporins (3GC) resistance phenotype (29.8%) and AmpC overproduction (32.1%).[18] We could not show the resistance patterns because they were not studied in our laboratories.

In-hospital inspections and training programs for infections such as MDR and XDR are extremely important in terms of slowing the spread of resistance and increasing the life span of antibiotics.[19] We are trying to prevent the development of resistance by conducting inspections and informing all employees in our intensive care unit and hospital.

Active surveillance and screening policies to prevent carbapenem-resistant *Enterobacterales* (CRE) transmission are critical to control the spread of these bacteria and protect public health.[20] When admitting patients to our intensive care unit, necessary precautions are taken to prevent transmission from other wards and trainings on transmission are provided at frequent intervals.

## Limitations

The most important limitations of this study are its retrospective nature and single-center design. In order to determine the trend of infections caused by MDR and XDR bacterial species in Turkey, multicenter studies, including all ICUs for a longer period of time and including heterogeneous groups, are needed.

## Conclusion

We believe that early detection and close follow-up of MDR, XDR, and even PDR bacterial strains should be monitored by both intensive care specialists and infectious diseases and clinical microbiology specialists to reduce the threat of antimicrobial resistance, which has become a serious global problem.

## Abbreviations

APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; min, Minimum; max, Maximum.

## Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki and ethics committee approval (approval no: 329) was obtained from Health Sciences University Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital. Due to the retrospective nature of the study, the requirement for informed consent was waived and the waiver was approved by the Ethics Committee of Health Sciences University Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital. All patient data were handled in strict adherence to ethical standards, ensuring confidentiality and anonymity. No personal identifiers were used in the analysis or reporting of study results.

## Author Contributions

All authors have made significant contributions to the design, execution, data collection, analysis, and interpretation of the article, or to all these areas; have participated in the preparation, review, or critical appraisal of the article; have given their approval at the time of submission to the journal; have agreed on the journal to which the article will be submitted; and have accepted responsibility for all aspects of the work.

## Disclosure

The authors declare that they have no competing interests in this work.

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