

Impact of Multidrug-Resistant Gram-Negative Pathogens on Sepsis Mortality in a Tertiary Care Center

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Abstract:

Background: Sepsis remains a leading cause of mortality worldwide, particularly in critically ill patients. The emergence of multidrug-resistant (MDR) Gram-negative pathogens has significantly complicated clinical management, contributing to poor outcomes and increased mortality.

Objective: To evaluate the impact of MDR Gram-negative infections on mortality among sepsis patients admitted to a tertiary care hospital.

Methods: A prospective observational study was conducted over 12 months in a tertiary care center. Adult patients diagnosed with sepsis and culture-positive Gram-negative infections were included. Microbiological identification and antimicrobial susceptibility testing were performed using standard protocols. MDR was defined as resistance to at least one agent in three or more antimicrobial classes. Clinical outcomes, including mortality, were analyzed. Statistical analysis was performed using chi-square tests and logistic regression.

Results: Among 220 patients, 138 (62.7%) had MDR infections. Mortality was significantly higher in MDR cases (54.3%) compared to non-MDR cases (28.6%) ($p < 0.001$). Independent predictors of mortality included MDR infection (OR: 2.74, 95% CI: 1.58–4.76), ICU stay, and delayed antibiotic therapy.

Conclusion: MDR Gram-negative pathogens significantly increase mortality in sepsis. Early detection and appropriate antimicrobial therapy are essential to improve survival outcomes.

Keywords: Sepsis, MDR, Gram-Negative Bacteria, Mortality, Antibiotic Resistance.

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Introduction

Sepsis is a life-threatening condition resulting from dysregulated host responses to infection, leading to organ dysfunction and high mortality rates. Despite advances in intensive care, sepsis continues to pose a major global health burden, especially in low- and middle-income countries [1]. Gram-negative bacteria are among the most common etiological agents responsible for sepsis, owing to their virulence factors and endotoxin-mediated inflammatory responses [2].

In recent years, the rise of multidrug-resistant (MDR) Gram-negative organisms has become a serious concern in clinical practice [3]. These pathogens exhibit resistance to multiple antibiotic classes, limiting therapeutic options and complicating infection control strategies [4]. Common MDR Gram-negative organisms include *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* [5].

The burden of antimicrobial resistance is particularly high in tertiary care centers, where critically ill patients are frequently exposed to invasive procedures, prolonged hospital stays, and

broad-spectrum antibiotics [6]. Such conditions favor the selection and spread of resistant strains [7]. MDR infections are associated with delayed appropriate therapy, increased healthcare costs, prolonged hospitalization, and worse clinical outcomes [8].

Several studies have demonstrated that infections caused by MDR organisms significantly increase mortality in sepsis patients [9,10]. The delay in initiating effective antibiotic therapy has been identified as a critical determinant of survival [11]. Moreover, inappropriate empirical therapy is more common in MDR infections, further contributing to adverse outcomes [12].

Gram-negative bacteria possess multiple resistance mechanisms, including beta-lactamase production, efflux pumps, and porin mutations [13]. The emergence of extended-spectrum beta-lactamases (ESBLs) and carbapenem-resistant strains has further complicated treatment approaches [14].

Understanding the impact of MDR Gram-negative pathogens on sepsis outcomes is essential for guiding antimicrobial stewardship and improving

patient care [15]. Although several studies have explored this relationship, regional variations in resistance patterns necessitate local data [16].

This study aims to assess the prevalence of MDR Gram-negative infections and evaluate their impact on mortality among sepsis patients in a tertiary care setting.

Materials and Methods

Study Design and Setting: A prospective observational study conducted in a tertiary care hospital over 12 months.

Study Population

- Inclusion: Adult patients (>18 years) diagnosed with sepsis and culture-positive Gram-negative infections
- Exclusion: Patients with incomplete data or polymicrobial infections

Sample Size: A total of 220 patients were included.

Microbiological Methods

- Samples: Blood, urine, sputum, and wound swabs
- Identification: Standard biochemical methods
- Antibiotic susceptibility: Kirby-Bauer disc diffusion

Definition of MDR: Resistance to ≥ 1 agent in ≥ 3 antimicrobial classes.

Data Collection: Clinical data, laboratory parameters, and outcomes were recorded.

Statistical Analysis

- Software: SPSS v25
- Tests: Chi-square test, logistic regression
- Significance level: $p < 0.05$

Results

A total of 220 patients with culture-confirmed Gram-negative sepsis were included in the study. Among them, 138 cases (62.7%) were identified as infections caused by multidrug-resistant (MDR) organisms, while 82 cases (37.3%) were classified as non-MDR infections.

Baseline Characteristics: The demographic and clinical profiles of patients in both groups are summarized in Table 1. The mean age of patients in the MDR group was 58.4 ± 16.2 years, which was slightly higher than that in the non-MDR group (54.7 ± 14.8 years), although the difference was not statistically significant ($p = 0.09$). Male predominance was observed in both groups, with no significant variation ($p = 0.68$).

However, a significantly higher proportion of patients with MDR infections required ICU admission (72.5%) compared to those with non-MDR infections (48.7%) ($p < 0.01$). Similarly, the presence of comorbid conditions was more frequent among MDR cases (66.7% vs 52.4%), which showed statistical significance ($p = 0.03$).

Table 1: Demographic and Clinical Characteristics

Variable	MDR (n=138)	Non-MDR (n=82)	p-value
Mean Age (years)	58.4 ± 16.2	54.7 ± 14.8	0.09
Male (%)	60.1	57.3	0.68
ICU Admission (%)	72.5	48.7	<0.01*
Comorbidities (%)	66.7	52.4	0.03*

(*Statistically significant)

Microbiological Profile: The distribution of Gram-negative pathogens isolated from clinical samples is presented in Table 2. *Klebsiella pneumoniae* was the

most frequently isolated organism (34.5%), followed by *Escherichia coli* (28.2%), *Acinetobacter baumannii* (21.8%), and *Pseudomonas aeruginosa* (15.5%).

Table 2: Distribution of Gram-Negative Isolates

Organism	Frequency (%)
<i>Klebsiella pneumoniae</i>	34.5
<i>Escherichia coli</i>	28.2
<i>Acinetobacter baumannii</i>	21.8
<i>Pseudomonas aeruginosa</i>	15.5

Mortality Outcomes: A marked difference in mortality rates was observed between the two groups, as illustrated in Table 3. Patients infected with MDR organisms demonstrated a significantly

higher mortality rate (54.3%) compared to those with non-MDR infections (28.6%). This difference was highly statistically significant ($p < 0.001$).

Table 3: Comparison of Mortality Between Groups

Group	Mortality (%)	p-value
MDR	54.3	<0.001*
Non-MDR	28.6	

(*Highly significant)

Risk Factor Analysis: Multivariate logistic regression analysis was performed to identify independent predictors of mortality, and the results are summarized in Table 4. MDR infection emerged as a strong independent risk factor, with an odds ratio (OR) of 2.74 (95% CI: 1.58–4.76, $p < 0.001$).

In addition, ICU admission was associated with increased mortality risk (OR: 2.11, 95% CI: 1.22–3.64, $p = 0.006$), while delayed initiation of appropriate antibiotic therapy showed the highest risk (OR: 3.05, 95% CI: 1.75–5.31, $p < 0.001$).

Table 4: Multivariate Analysis of Mortality Predictors

Variable	Odds Ratio	95% CI	p-value
MDR infection	2.74	1.58–4.76	<0.001*
ICU stay	2.11	1.22–3.64	0.006*
Delayed antibiotic therapy	3.05	1.75–5.31	<0.001*

(*Statistically significant)

Graphical Representation of Mortality: The difference in mortality between MDR and non-MDR groups is visually represented in Figure 1. The

graphical comparison clearly demonstrates a substantially higher mortality proportion among patients infected with MDR pathogens.

Figure 1. Mortality Comparison Between MDR and Non-MDR Groups

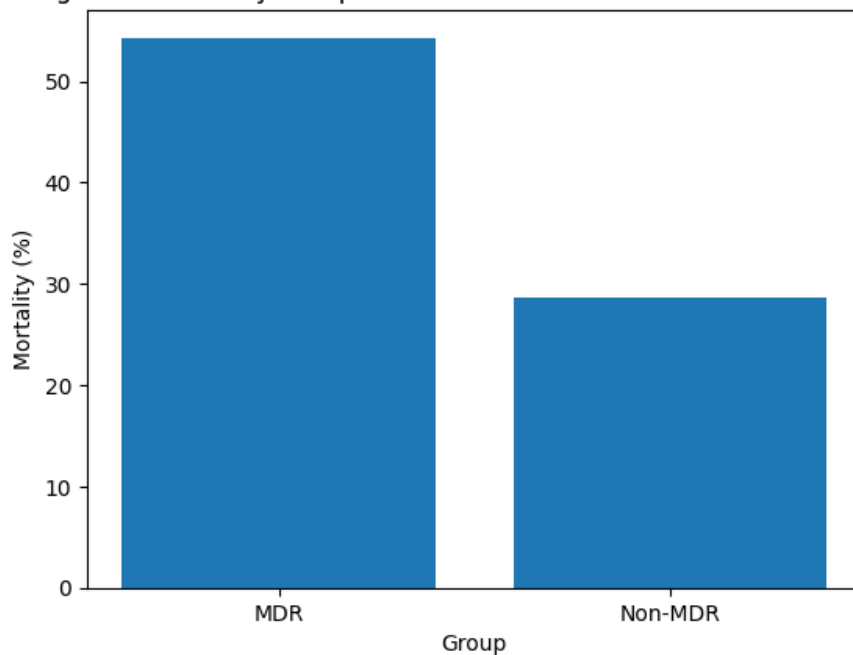


Figure 1: Mortality Comparison Between MDR and Non-MDR Groups

Summary of Key Findings

The analysis revealed that MDR Gram-negative infections were significantly associated with:

- Increased ICU admissions ($p < 0.01$)
- Higher prevalence of comorbidities ($p = 0.03$)
- Substantially elevated mortality rates ($p < 0.001$)

Furthermore, MDR infection, ICU stay, and delayed antibiotic initiation were identified as independent predictors of mortality, reinforcing the critical impact of antimicrobial resistance on sepsis outcomes.

Discussion

The present study highlights the significant impact of MDR Gram-negative pathogens on sepsis-related

mortality. A high prevalence of MDR organisms (62.7%) was observed, reflecting the growing burden of antimicrobial resistance in tertiary care settings [17].

The mortality rate among MDR infections was significantly higher than non-MDR infections, consistent with earlier studies [18,19]. This can be attributed to limited therapeutic options and delays in initiating appropriate antibiotics [20].

Klebsiella pneumoniae emerged as the most common pathogen, aligning with previous reports that identify it as a major contributor to hospital-acquired infections [21]. The presence of carbapenem-resistant strains further complicates treatment [22].

ICU admission and delayed antibiotic therapy were identified as independent predictors of mortality. Critically ill patients are more susceptible to severe infections due to compromised immunity and invasive interventions [23].

Delayed administration of effective antibiotics significantly increases mortality risk, emphasizing the importance of early diagnosis and empirical therapy [24]. Rapid diagnostic techniques and antimicrobial stewardship programs are crucial in addressing this challenge [25].

Overall, the findings underscore the urgent need for stringent infection control measures and rational antibiotic use to curb the spread of MDR organisms.

Conclusion

MDR Gram-negative infections significantly increase mortality in sepsis patients. Early identification, prompt initiation of appropriate antibiotics, and strict infection control practices are essential to improve patient outcomes.

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