Prevalence Of Gram-Negative Bacteremia Among Hospitalized Patients In Taif: A 12-Month Retrospective Single Center Study

Khalid M. Alhusayni[1], Abdullah M. Althomali[2], Ahmed R. Abdulwahab[3], Atheer D. Alghamdi[4], Hayat Y. Alzahrani[5], Manal A. Alghamdi[6], Jawaher S. Alharthi[7], Mona M. Alotaibi[8], Yahya J. Hazazzi[9], Bashaer A. Hakami[10], Ali J. Hazzazi[11], Abdulrahman H. Faqehi[12], Mohammed T. Alsulaimani[13], Adnan A. Altalhi[14], Abdulmajeed A. Almalki[15]

1. Department of Pharmacy, King Abdul-Aziz Hospital, Taif City, Saudi Arabia
2. Department of Pharmacy, King Faisal Medical Complex, Taif City, Saudi Arabia
3. Department of Pharmacy, King Abdul-Aziz Hospital, Taif City, Saudi Arabia
4. College of Pharmacy, Taif University, Saudi Arabia
5. College of Pharmacy, Taif University, Saudi Arabia
6. College of Pharmacy, Taif University, Saudi Arabia
7. Department of Laboratory, King Abdul-Aziz Hospital, Taif City, Saudi Arabia
8. Department of Laboratory, King Abdul-Aziz Hospital, Taif City, Saudi Arabia
9. King Fahad Central Hospital, Jazan City, Saudi Arabia
10. King Fahad Central Hospital, Jazan City, Saudi Arabia
11. King Fahad Central Hospital, Jazan City, Saudi Arabia
12. King Fahad Central Hospital, Jazan City, Saudi Arabia
13. Department of Pharmacy, King Abdul-Aziz Hospital, Taif City, Saudi Arabia
14. Department of Pharmacy, King Faisal Medical Complex, Taif City, Saudi Arabia
15. Department of Pharmacy, King Abdul-Aziz Hospital, Taif City, Saudi Arabia

Abstract

Background: Antimicrobial resistance (AMR) in Gram-negative bacteremia (GNB) poses a major threat to patient outcomes and challenges healthcare systems. Local resistance data are essential to guide effective stewardship strategies.

Methods: This retrospective study included patients aged ≥18 years with positive blood cultures for GNB at a 500-bed tertiary hospital in Taif, Saudi Arabia, from January 2023 to January 2024. Data included demographics, infection sources, microbial resistance, treatment, and outcomes.

Results: Among 151 patients, 41% had resistant Gram-negative bloodstream infections. Urinary tract and skin/soft tissue infections were the most common sources (28.5% each). The surgical ward had the highest infection rate (41.7%). ESBL-producing and carbapenem resistant Enterobacterales were the leading resistant strains. Median times to Gram stain and final identification were 12 and 72 hours, respectively. Delayed de-escalation (>24 hours post-culture) occurred in 37% of cases. Median hospital stay was 240 hours. Intensive Care Units (ICU) patients had significantly higher mortality (53% vs. 11.8%, $p < 0.001$). Intensive Care Unit (ICU) admission (OR = 4.67) and delayed therapy (OR = 3.25) were independent mortality predictors.

Conclusions: Resistant GNB infections are common and linked to high ICU mortality. Prompt de-escalation and strong infection control are essential. Multi-center studies are needed to inform broader strategies.

Key words: antimicrobial resistance, Gram-negative bacteremia, ESBL, de-escalation, ICU.

INTRODUCTION

Gram-negative bacteria (GNB) bloodstream infections (BSI) remain to be a leading cause of morbidity and mortality within admitted hospital patients. This increase in both BSI cases and mortality might be attributed to the increase in bacterial resistance to antibiotics. For example, and according to WHO Global Antimicrobial Resistance (AMR) and Use Surveillance System (GLASS) report in 2022, resistance of *Escherichia coli* (*E. coli*) to third-gen cephalosporins have increased from 20% to about 80%, and to carbapenems from 20% to 82% from the years 2016 to 2020 [1]. Unfortunately, more cases of GNB bacteremia have rose over the las years, for example, BSI related to GNB increased from 63.23% to 66.54% from 2012 to 2017 in China [2]. *Escherichia coli* appears to be the most common contributor GNB in bacteremia cases by 6 to 27%, with *Klebsiella pneumoniae* (*K. pneumoniae*) coming second by 5 to 13%, both mainly originating from the urinary tract. Extended spectrum β-lactamases (ESBLs) bacteria such as *E. coli* achieve resistance through production of β-lactamase enzyme against β-lactams antibiotics [3]. Bacterial resistance to antibiotics is achieved through multiple mechanisms, such as efflux pumps, degrading enzymes, and gene mutations. But concerning GNB resistance in hospital settings, a few common mechanisms are seen in different types of bacteria, for Carbapenem Resistant Enterobacteriaceae (CRE), resistance to carbapenems can be achieved through enzymatic degradation by production of carbapenemase enzyme, or efflux pumps [4]. Multidrug resistant GNB (MDR-GNB) describes gram negative bacterial infection that have failed antibiotic treatment from different antibiotic classes, due to the organism harboring variable resistance mechanisms, against variable drugs [5]. According to Leal, H.F et al., previous use of antibiotic treatment, male patients aged > 60 years, are risk factors associated with contracting MDR-GNB bacteremia [6]. Typical gram-staining methods used for blood culture analysis usually take 24-48 hours in order to provide final results [7]. However, novel rapid tests for microbial identification such as fluorescent in situ hybridization (FISH) may shorten wait time significantly, which helps in choosing the more accurate antimicrobial treatment and reduce risk of mortality [8]. The aim of this study is to determine the prevalence of resistant gram-negative bacteremia among hospitalized patients, evaluate antibiotic use and determine the time taken for gram staining for final species identification results.

METHODOLOGY

This retrospective study includes all patients aged 18 and older with positive blood cultures Gram-negative bacteremia who were admitted to a 500-bed tertiary care hospital in Taif, Saudi Arabia, from January 2023 to January 2024. No exclusion criteria were defined. We collected patient data from the electronic medical record system (Oasis). Demographic information, source of infection, hospitalization duration, identified microorganisms, collection of samples timing, time for Gram stain results, time required for final culture sensitive and the susceptibility results, outcomes of final cultures indicating sensitivities and susceptibilities, initial antibiotics administered, timing of antibiotic administration, duration of broad-spectrum antibiotic therapy, and time taken to transition to narrow spectrum antibiotics. The source of infection was determined based on clinical documentation supported by relevant microbiological data (e.g., matching cultures from urine, sputum, or wound swabs) and radiological imaging. Only patients with confirmed Gram-negative bacteremia (positive blood culture) were included; the source of bacteremia was retrospectively inferred from the clinical diagnosis recorded at the time of infection. Only

the first episode of Gram-negative bacteremia per patient during the study period was included. Multiple episodes were defined as distinct bacteremia events separated by ≥14 days and with microbiologically different organisms. The primary infection site was determined based on clinical diagnosis and supporting culture/imaging findings, as documented by the treating physician.

Key definitions used in the study were:

• Time to Gram stain: The period from sample collection to the collection of Gram stain results.

• Time to final culture sensitivities and susceptibilities: The period from sample collection to the receipt of final culture sensitivity and susceptibility data.

• Time to de-escalation: The duration required to transition to narrower spectrum antibiotics following the receipt of final culture findings.

• Delayed de-escalation: >24 hours after final culture sensitivities and susceptibilities.

• Broad-spectrum antibiotics: antibiotics with pseudomonal coverage or two injectable antibiotics with different spectra of activity

• First antibiotic use: any antibiotic used after sample collection but before final culture sensitivities and susceptibilities

• Length of ICU stay was defined as the total number of days from ICU admission to discharge or death. However, since ICU stay duration may be influenced by survival status, we only used binary ICU admission as a variable in mortality comparisons.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize baseline demographic and clinical characteristics. Continuous variables were reported as means and standard deviations (SD) or medians with interquartile ranges (IQR) based on distribution normality, assessed via the Shapiro-Wilk test. Categorical variables were expressed as counts and percentages. Associations between categorical variables, including ICU admission status and mortality, were evaluated using the chi-square test. Univariate logistic regression was conducted to explore potential predictors of in-hospital mortality. Variables with a p-value < 0.10 in univariate analysis were included in a multivariate logistic regression model to identify independent predictors. Odds ratios (OR) with 95% confidence intervals (CI) and p-values were reported. A two-sided p-value < 0.05 was considered statistically significant.

RESULTS

Demographic characteristics of participants:

Table **1** displays the demographic characteristics of all participants. The patient population with Gram-negative infections nearly evenly splits between those under and over 60, with 48.3% younger than 60 and 51.7% older than 60. The gender distribution shows a higher proportion of females (57%) compared to males (43%). Regarding nationality, a significant majority of the patients are Saudi nationals, accounting for 72.2% of the cases, while 27.8% are non-Saudi. Table 1. Demographic characteristics of participants Baseline characteristics N (%) Age <60 73 (48.3) >60 78 (51.7) Gender Male 65 (43) Female 86 (57) Nationality Saudi 109 (72.2) non-Saudi 42 (27.8).

Table 1. Demographic characteristics of participants

Character		**N (%)**
Age	<60	73 (48.3)
	>60	78 (51.7)

Gender	Male	65 (43)
	Female	86 (57)
Nationality	Saudi	109 (72.2)
	Non- Saudi	42 (27.8)

Data are presented as n (%)

Sources of infection

The most common sources of infection in patients are urinary tract infections or skin and soft tissue infections, each accounting for 28.5% (43 cases) of the total infections. Pneumonia is also a significant source, contributing to 26.5% (40 cases) of infections. 5.9% (9 cases) of infections are vascular catheter related. Gastrointestinal sources are less common, accounting for 3.4% (5 cases), while other sources contribute to 7.2% (11 cases), **Table 2** shows the source of infection.

Table 2. Sources of infection.

Sources Of Infection.	**N (%)**
Urinary Tract Infection	43 (28.5)
Skin And Soft Tissue Infection	43 (28.5)
Pneumonia	40 (26.5)
Vascular Catheter Related Infection	9 (5.9)
Gastrointestinal	5 (3.4)
Others	11(7.2)

Data are presented as n (%)

Isolated microorganisms

Figure 1 illustrates the distribution of microorganisms isolated from patients with Gramnegative bacteremia. The majority of infections were caused by *Enterobacterales*, which accounted for 64.9% (n=98) of all cases. *Pseudomonas aeruginosa* 9.5% (n=14) of all cases,*Klebsiella pneumoniae* accounted for 8.6% (n=13) of all cases,*Acinetobacter baumannii*, and *Escherichia coli* each contributed 6.6% (n=10) of infections. The remaining isolates, grouped under "Others," represented 4.0% (n = 6) and included *Proteus mirabilis, Stenotrophomonas maltophilia, Providencia stuartii, Serratia marcescens*, and a mixed infection involving *Acinetobacter baumannii* and *Providencia alcalifaciens*.

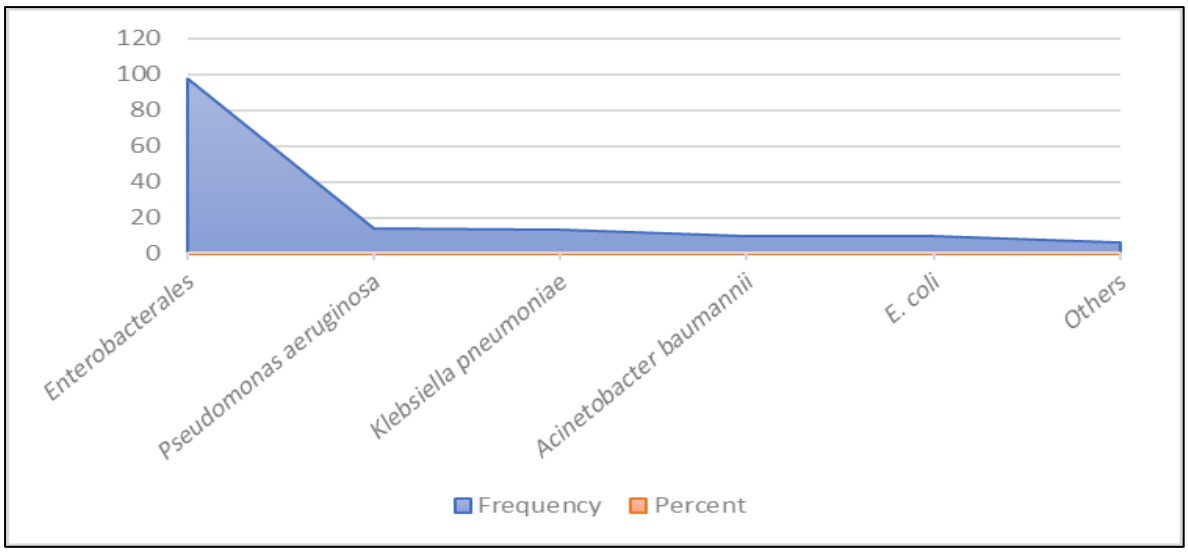

Figure 1. Isolated Microorganisms (n=151).

This figure presents the frequency of Gram-negative bacterial isolates identified in blood cultures.

Enterobacterales were the most dominant group (64.9%, n = 98), followed by *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Escherichia coli* (each 6.6%, n = 10). Other less common organisms (4.0%, n = 6) included *Proteus mirabilis*, *Stenotrophomonas maltophilia*, *Providencia stuartii*, *Serratia marcescens*, and a co-infection with *Acinetobacter baumannii* and *Providencia alcalifaciens*.

Frequencies of Infections by Ward

As shown in table 4. The analysis of infections across different wards reveals that the highest relative frequency of infections, accounting for 63 patients (41.7%), is observed in the Surgical ward. This is followed by the ICU, which alone accounts for 32 patients (21.2%) of infections. The Medical ward contributes to 29 patients (19.2%) of the total infections. Other significant contributions come from the HDU with 15 patients (9.9%), while Oncology and CCU report lower frequencies of 7 patients (4.6%) and 5 patients (3.3%) respectively. This distribution highlights the need for targeted infection control measures, particularly in the wards with the highest infection rates.

Table 4. Frequencies of Infections by Ward

Ward	**Relative Frequency**	**Percent**
Surgical	63	41.7%
ICU	32	21.2%
Medical	29	19.2%
HDU	15	9.9%
Oncology	7	4.6%
CCU	5	3.3%
Total	151	100%

Association between Length of ICU Stay vs. Patient Mortality

There is a relationship between ICU stay and patient mortality (**table 5**). Among patients who stayed in the ICU, 35(53%) died, while 31(47%) survived, totaling 66 patients. In contrast, among patients who did not stay in the ICU, only 10 (11.8%) died, whereas 75 (88.2%) survived, totaling 85 patients.

Table 5. Association between Length of ICU Stay

Length of ICU Stay	The Patient Died?		Total
Yes	Yes	No	
	35	31	66
No	10	75	85
Total	45	106	151

Association Between ICU Admission and Mortality

A total of 66 patients were admitted to the ICU. Of these, 35 (53%) died, compared to 10 of 85 (11.8%) among non-ICU patients. This association was statistically significant ($\chi^2 = 28.3$, $p < 0.0001$). The odds of death were 8.47 times higher for ICU patients compared to non-ICU patients (OR = 8.47).

Univariate Logistic Regression (Mortality Predictors)

As showed in table 5.1 univariate logistic regression analysis was performed to assess potential predictors of in-hospital mortality among patients with Gram-negative bacteremia. ICU admission was significantly associated with increased mortality (OR = 7.95; 95% CI: 3.45–18.32; $p = 0.0001$). Broad-spectrum antibiotic use was also a significant predictor (OR = 2.30; 95% CI: 1.12–4.72; $p = 0.02$), suggesting an association with poorer outcomes. Although age greater than 60 years showed a trend toward higher mortality (OR = 1.65; 95% CI: 0.85–3.21), this did not reach statistical significance ($p = 0.12$). Delayed de-escalation of antibiotics (>24 hours post-final culture) was also evaluated and showed a non-significant association (OR = 1.85; 95% CI: 0.90–3.78; $p = 0.09$). These findings highlight the need for careful clinical management and timely therapeutic adjustments in high-risk patient populations.

Table 5.1. Univariate Logistic Regression (Mortality Predictors)

Variable	**OR**	**95% CI**	**p-value**
ICU Admission	7.95	3.45–18.32	0.0001
Age > 60	1.65	0.85–3.21	0.12
Broad-spectrum use	2.30	1.12–4.72	0.02
Delayed De-escalation	1.85	0.90–3.78	0.09

Multivariate Logistic Regression (Adjusted for Confounders)

A multivariate logistic regression model was constructed to identify independent predictors of in-hospital mortality while adjusting for potential confounding variables. Variables included in the model were ICU admission, age >60 years, broad-spectrum antibiotic use, and delayed de-escalation, based on significance thresholds from the univariate analysis. After adjustment, ICU admission remained a strong independent predictor of mortality (adjusted OR = 6.22; 95% CI: 2.44–15.87; $p = 0.0003$). Broadspectrum antibiotic use was also independently associated with increased odds of death (adjusted OR = 1.95; 95% CI:

1.01–3.75; $p = 0.045$). Age and delayed de-escalation did not retain statistical significance in the final model. These findings suggest that clinical setting and antimicrobial therapy decisions have significant implications for patient outcomes in Gram-negative bacteremia.

Table 5.2 Multivariate Logistic Regression (Adjusted for Confounders)

Variable	Adjusted OR	95% CI	p-value
ICU Admission	6.22	2.44–15.87	0.0003
Broad-spectrum use	1.95	1.01–3.75	0.045

ICU admission and use of broad-spectrum antibiotics were independently associated with higher odds of mortality in patients with GNB.

Antibiotic-resistant bacterial strains are prevalent:

Figure 2 presents the distribution of antibiotic-resistant Gram-negative bacterial strains isolated from bloodstream infections. The most prevalent were extended-spectrum betalactamase (ESBL)-producing *Enterobacterales* (n = 37), followed by *carbapenem-resistant Enterobacterales* (CRE, n = 7). Other resistant organisms included *Acinetobacter baumannii* (CRE, n = 5), *Klebsiella pneumoniae* (CRE, n = 4; ESBL, n = 2), *and Escherichia coli* (ESBL, n = 3). Less frequently observed strains included Proteus spp. (CRE), *Pseudomonas aeruginosa* (CRE), and *Providencia stuartii* (ESBL). These findings highlight the burden of multidrug-resistant organisms, particularly ESBL- and carbapenemase-producing strains, and underscore the need for robust antimicrobial stewardship and resistance surveillance.

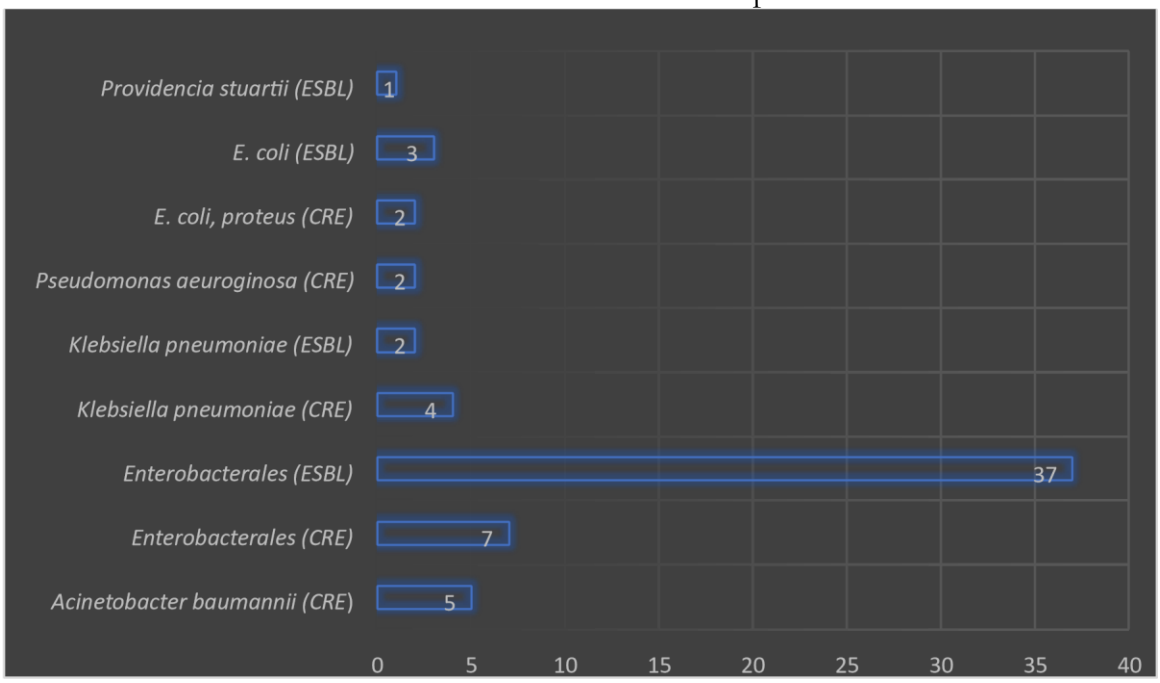

Figure 2. Prevalence of Antibiotic-Resistant Bacterial Strains (n=63). This figure illustrates the frequency of antibiotic-resistant Gram-negative organisms isolated from bloodstream infections. ESBL-producing *Enterobacterales* were the most common (n = 37), followed by carbapenem-resistant *Enterobacterales* (n = 7), *Acinetobacter baumannii* (CRE, n = 5), and *Klebsiella pneumoniae* (CRE, n = 4; ESBL, n = 2). Additional resistant isolates included *Escherichia coli* (ESBL, n = 3), *Proteus* spp. (CRE), *Pseudomonas aeruginosa* (CRE), and *Providencia stuartii* (ESBL).

Time to sample collection and final culture:

The median time to Gram stain result was 12 hours (IQR: 8–18). Broad-spectrum antibiotics were initiated in 62% of patients; however, only 25% were de-escalated within 24 hours of receiving final culture sensitivity. The median length of hospital stay for these patients was 240 hours (range: 72–672 hours).

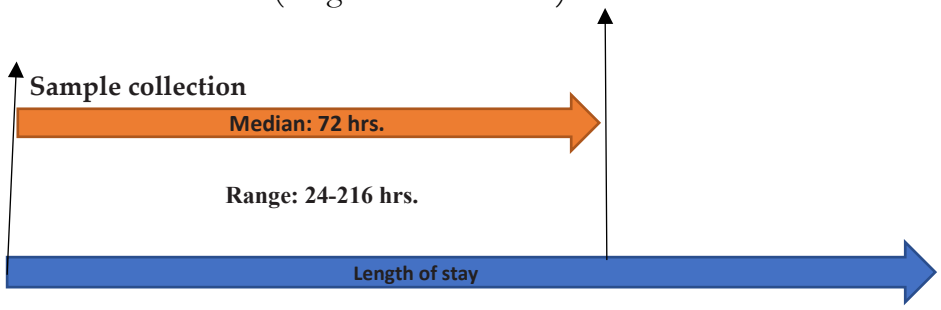

Figure 3. Time to sample collection and final culture.

The median time to final culture across the entire patient group was 72 hours, with a range between 24 and 216 hours.

DISCUSSION

This retrospective study offers a detailed evaluation of Gram-negative bacteremia (GNB) within a tertiary care hospital in Taif, Saudi Arabia, revealing a high burden of AMR and substantial mortality rates. Resistant Gram-negative organisms accounted for 41% of bloodstream infections—consistent with global trends indicating the rise of multidrug-resistant Gram-negative pathogens. A recent systematic review estimated that 21.2% of patients with ESBL-producing Enterobacteriaceae (ESBL-PE) bacteremia died, highlighting the severe outcomes associated with these infections [9].

The most common sources of infection in our cohort were urinary tract infections (UTIs) and skin and soft tissue infections (SSTIs), each comprising 28.5% of cases. This distribution aligns with previous studies identifying the urinary tract as a primary source of E. coli and

K. pneumoniae-associated bacteremia [3,4]. These pathogens, especially when producing ESBLs or carbapenemases, present a challenge due to limited therapeutic options and delayed effective treatment.

Our microbiological analysis revealed a predominance of ESBL-producing Enterobacterales (58.7% of resistant isolates) and an emerging burden of carbapenem-resistant Enterobacterales (CRE). These findings are consistent with WHO GLASS reports and other regional data indicating increasing resistance to third-generation cephalosporins and carbapenems [1,9]. In a Brazilian study, CRE accounted for 14.3% of Enterobacterales bloodstream infections, with a 37.7% mortality rate—comparable to the case fatality observed in ICU patients in our study [10].

Timely de-escalation of broad-spectrum antibiotics is a core principle of antimicrobial stewardship, as prolonged empirical therapy has been associated with increased risk of AMR, drug toxicity, and mortality. In our study, only 25% of patients were de-escalated within 24 hours after final culture results, while 37% experienced delayed de-escalation. These findings are consistent with a multicenter prospective cohort study that found delayed de-escalation (>48 hours) was independently associated with higher 30-day mortality in patients with bloodstream infections caused by Gram-negative organisms, especially in ICU settings (adjusted HR: 1.72; 95% CI: 1.12–2.63; $p = 0.01$) [11].

Additionally, early de-escalation has been shown to reduce the duration of antibiotic therapy, ICU length of stay, and overall antibiotic exposure without compromising patient safety. The overuse of broad-spectrum agents, such as carbapenems and anti-pseudomonal

β-lactams, often reflects diagnostic uncertainty but can lead to selection of multidrug-resistant organisms. These data reinforce the importance of integrating timely microbiologic data with structured antimicrobial review to enable safe and effective narrowing of therapy.

The significantly higher mortality among ICU patients (53%) compared to non-ICU patients (11.8%, $p < 0.001$) underscores the vulnerability of critically ill populations to GNB. ICU admission was independently associated with increased mortality (adjusted OR = 6.22), in line with Leal et al., who demonstrated that advanced age, critical illness, and prior antibiotic exposure contribute to poor outcomes in MDR-GNB infections [6].

Another independent predictor of mortality was the use of broad-spectrum antibiotics (adjusted OR = 1.95). Although empiric broad-spectrum coverage is often necessary, inappropriate or prolonged use may contribute to poor outcomes and promote resistance. Delayed de-escalation of antibiotics (>24 hours after final culture) occurred in 37% of patients in our study. Although not statistically significant in multivariate analysis ($p = 0.09$), this delay is clinically meaningful and consistent with literature advocating early narrowing of therapy to reduce toxicity, cost, and mortality [6,7].

The median time to final identification and susceptibility results was 72 hours, while Gram stain results were available at a median of 12 hours. These turnaround times are typical in many hospitals; however, newer diagnostic platforms such as MALDI-TOF MS, PCR-based panels, and FISH may reduce diagnostic delays and improve early management decisions [7,8]. A recent review emphasized that the use of rapid microbiological diagnostics can decrease mortality and time to appropriate therapy in multidrug-resistant GNB infections
[8].

Surgical wards had the highest infection burden (41.7% of cases), followed by the ICU (21.2%) and medical wards. This pattern likely reflects increased exposure to invasive procedures and broad-spectrum antibiotics in these settings. These findings emphasize the need for enhanced infection control measures, such as hand hygiene adherence, device care protocols, and targeted decolonization strategies in high-risk wards.

Strengths and limitations

This research is among the first comprehensive real-world evaluations of resistance patterns of Gram-negative bacteremia in a tertiary care facility in Taif, Saudi Arabia, offering valuable local epidemiological data, filling an essential gap in understanding the antimicrobial resistance situation connected with the region. The study employed an extensive database that combined clinical, microbiological, and treatment information, allowing for a more integrated examination of the various aspects of resistance, antibiotic prescribing, and the clinical outcomes of the patients. The use of logistic regression to assess the predictors of mortality independently enhances the clinical relevance and translatability of the outcomes. This study further highlights the significance of antimicrobial de-escalation in a timely manner and the risk stratification related to the ICU, which are basic elements of improving antimicrobial stewardship. This is particularly important in the study's context.

Specific limitations must be acknowledged. The investigation's retrospective design leaves our analysis open to documentation bias and restricts our ability to pinpoint causation between the studied variables and the clinical outcomes. It also limits our ability to generalize our findings. The generalization of our findings is limited given the clinic's single-center nature, and the antimicrobial resistance and clinical practices of other organizations. In the future, this will need to be validated with multicenter studies. The mortality models may be less robust due to the lack of standardized illness severity measures, i.e. APACHE II or SOFA scores. Our sample size may be adequate for basic regression analysis, but for advanced analyses, I.e. resistance organisms in particular, fragile resistance phenotype

analyses, or for the advanced analytics needed to analyze the epidemiology of resistance patterns, and sub-group analyses may be needed. The epidemiology in this case may reflect real clinical practice but it also may result in variable interpretations that lack congruence with the epidemiology of the resistance as a whole. This is the epidemiology of resistance patterns rather than the clinically observed patterns of infection. Lastly, one of the main limitations in this scenario is the reliance on clinical judgment in defining the infection source. This is reflective of practical clinical work, and is very commonly seen in other areas of epidemiology, and thus leaves a gap in the evidence.

CONCLUSION

This study's findings highlight the significant prevalence of resistant Gram-negative bacteremia in hospitalized patients, particularly in high-risk areas such as the surgical ward and ICU. The presence of resistant strains, including *ESBL* and *CRE*, emphasizes the need for stringent infection control practices and adherence to antimicrobial guidelines. ICU patients are especially vulnerable, as reflected by the high mortality rates. Further research is necessary to validate these findings across larger and more diverse populations, even though this study provides important insights. Enhanced surveillance, coupled with targeted interventions, will be crucial in combating antimicrobial resistance and improving patient outcomes in healthcare settings.

Author contribution

All listed authors meet ICMJE authorship criteria (substantial contributions; drafting/revising; final approval; and accountability) and agree to be accountable for all aspects of the work.

References

1- Global antimicrobial resistance and use surveillance system (GLASS) report 2022. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO

2- Yang S, Xu H, Sun J, Sun S. Shifting trends and age distribution of ESKAPEEc resistance in bloodstream infection, Southwest China, 2012-2017. Antimicrob Resist Infect Control. 2019 Mar 29;8:61. doi: 10.1186/s13756-019-0499-1. PMID: 30976388; PMCID: PMC6441235.

3- Holmes CL,Anderson MT, Mobley HLT, Bachman MA,2021.Pathogenesis of Gram-Negative Bacteremia. Clin Microbiol Rev
34:10.1128/cmr.00234-20.https://doi.org/10.1128/cmr.00234-20

4- Eichenberger EM, Thaden JT. Epidemiology and Mechanisms of Resistance of Extensively Drug Resistant Gram-Negative Bacteria. Antibiotics. 2019; 8(2):37.
https://doi.org/10.3390/antibiotics8020037

5- Nikaido H. Multidrug resistance in bacteria. Annu Rev Biochem. 2009;78:119-46. doi: 10.1146/annurev.biochem.78.082907.145923. PMID: 19231985; PMCID: PMC2839888.

6- Leal, H.F., Azevedo, J., Silva, G.E.O. et al. Bloodstream infections caused by multidrugresistant gram-negative bacteria: epidemiological, clinical and microbiological features. BMC Infect Dis 19, 609 (2019).
https://doi.org/10.1186/s12879-019-4265-z

Kothari A, Morgan M, Haake DA. Emerging technologies for rapid identification of bloodstream pathogens. Clin Infect Dis. 2014 Jul 15;59(2):272-8. doi: 10.1093/cid/ciu292. Epub 2014 Apr 24. PMID: 24771332; PMCID: PMC4368854.

7- D.R. Giacobbe, T. Giani, M. Bassetti, A. Marchese, C. Viscoli, G.M. Rossolini, Rapid microbiological tests for bloodstream infections due to multidrug resistant Gram-negative

bacteria: therapeutic implications, Clinical Microbiology and Infection, Volume 26, Issue 6, 2020, Pages 713-722,ISSN 1198-743X,
https://doi.org/10.1016/j.cmi.2019.09.023.
https://www.sciencedirect.com/science/article/pii/S1198743X19305245)
8- Almohsen K, et al. Predictors of mortality from extended-spectrum beta-lactamaseproducing Enterobacteriaceae bacteremia: A systematic review and meta-analysis. Antimicrobial Resistance & Infection Control. 2023; 12:59.
9- da Silva AC, et al. Outcomes of carbapenem-resistant Enterobacteriaceae bloodstream infections in a Brazilian tertiary hospital. Rev Soc Bras Med Trop. 2022; 55:e04492021.
10- Madaras-Kelly KJ, Remington RE, Oliphant CM, et al. Antimicrobial de-escalation of Gram-negative bloodstream infections in the critically ill: a multicenter prospective cohort study. Clinical Infectious Diseases. 2021;72(11):e859–e867.