Original Article

DOI: 10.7860/JCDR/2026/84913.23145

Internal Medicine Section

Prevalence, Risk Factors and Clinical Outcomes of Multidrug-resistant Gram-negative Sepsis: A Cross-sectional Study from a Railway Hospital in Western India

A MEENU[1], AJAY KHOBRAGADE[2], ASHWINI P JADHAV[3]

ABSTRACT

Introduction: Multidrug-resistant (MDR) Gram-negative Bacteria (GNB) represent a growing global health threat, particularly in Intensive Care Units (ICUs), where they contribute significantly to morbidity and mortality. There is a paucity of data regarding MDR sepsis, specifically among railway beneficiaries at tertiary care settings in India.

Aim: to determine the prevalence, risk factors and clinical outcomes of MDR-GNB sepsis among patients admitted to the ICU of Jagjivan Ram Hospital, Mumbai, Maharashtra, India.

Materials and Methods: A cross-sectional study was conducted at the Department of General Medicine, Jagjivan Ram Hospital, Mumbai, Maharashtra, India, from December 2022 to December 2024, on 100 adult patients with sepsis admitted to the ICU. Patients with culture-proven Gram-negative sepsis were included. Identification and sensitivity testing were performed using the Bacterial Detection System (BACTEC) and Vitek Identification and Susceptibility Testing System (VITEK-2) system in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines. Clinical outcomes (length of stay, mortality) and risk factors were compared between the MDR and non-MDR groups using Chi-square and t-tests, with statistical significance set at p-value<0.05.

Results: The prevalence of MDR-GNB was 67%. The study population was predominantly elderly (55% aged >60 years) with a male preponderance (55%). Common co-morbidities included Diabetes Mellitus (DM) (86%) and Ischaemic Heart Disease (IHD) (39%). Significant risk factors for MDR infection included prior antibiotic use (p-value<0.05) and invasive instrumentation. *Klebsiella pneumoniae* and *Escherichia coli* were the predominant pathogens. Mortality was 55.2% in the MDR group and 57.6% in the non-MDR group; this difference was not statistically significant (p=0.82).

Conclusion: A high burden of MDR-GNB sepsis was observed in this tertiary ICU, driven by advanced age, comorbidities, and prior antibiotic exposure. The association with high mortality underscores the urgent need for strict antimicrobial stewardship and infection control protocols.

Keywords: Antibacterial agents, Cross infection, Drug resistance

INTRODUCTION

Sepsis represents a worldwide health emergency, leading to approximately 49 million fatalities annually based on the Global Burden of Disease Study [1] and MDR-GNB is an increasing existential danger in ICUs, which are the primary setting for sepsis care [2]. These patients are critically ill and possess an extremely defective iatrogenic immunosuppression, undergo repeated invasive procedures, maintain long-lasting mechanical ventilation and are exposed to indiscriminate broad-spectrum antibiotics, which collectively create a selective environment that amplifies antimicrobial resistance [3,4].

According to the international consensus, MDR-GNB could be categorically defined as microorganisms that are non-susceptible to to ≥1 agent in ≥3 antimicrobial classes [5]. Major pathogens include Extended-spectrum B-lactamase (ESBL)-producing *Enterobacteriaceae*, Carbapenem-resistant *Enterobacteriaceae* (CRE) and MDR *Pseudomonas aeruginosa* and Carbapenem-resistant *Acinetobacter Baumannii* [6,7]. All these pathogens orchestrate multi-layered resistance via carbapenemase enzymes such as *Klebsiella pneumoniae* carbapenemase (KPC), New Delhi metallo-β-lactamase-1 (NDM-1) and Oxacillinase-48 (OXA-48), efflux-hydrolysis, porin-downregulation, and target-site hypermutation-molecular virtuosity which inevitably oblige resistant evolution in the ICU microenvironment via Darwinian antibiotic saturation and unrestrained horizontal gene transfer mechanisms [8].

Epidemiological surveillance unmasks profound geoclimatic disparities demanding contextualised interventions. High-income Western ICUs document MDR-GNB prevalence of 20-40%, [9], whereas Asian cohorts consistently exceed 60%, mirroring divergent antibiotic consumption trajectories and healthcare ecosystem dynamics [10]. The Indian Council of Medical Research – Antimicrobial Resistance Surveillance Network (ICMR-AMRSN) (2021-2023) indicates *Klebsiella pneumoniae* (45-60% carbapenem resistance) and *Escherichia coli* (30-50% ESBL) as hegemonic ICU pathogens [9]. Clinically, these manifestations cluster as bloodstream infections (25-35%), ventilator-associated pneumonia (20-30%) and catheter-associated Urinary Tract Infections (UTI) (15-25%)—the lethal triad propelling attributable mortality [11].

The meta-analytically synthesised recurrent determinants of risk architecture include antecedent antibiotic exposure, central venous catheterisation, mechanical ventilation, ICU stay >7 days, DM and Chronic Kidney Disease (CKD) [9,10]. MDR infections exact disproportionate toll: 28-day mortality escalates from 20-40% (non-MDR) to 40-70%, ICU length-of-stay doubles (median 12 vs 7 days) and economic burden amplifies 2-3-fold through protracted resource consumption [12-14].

The heterogeneous healthcare ecosystem of India, particularly the government, in which the railway hospital systems are served with the socio-economically differentiated populations, has significant gaps in the literature. The 13 million Indians on the railway healthcare benefit gain lifetime free healthcare, which may influence patterns of antibiotic utilisation and stewardship practices. This creates a great ecology of resistance with diabetes hyperendemicity (25-30% vs national 11.4%), a type of evidence gap that underscores the urgent need for implementation of the National Action Plan on Antimicrobial Resistance (NAP-AMR) [1,11]. Remarkably, there are no prospective studies that identified the epidemiology of MDR-GNB sepsis in the ICU, an evidence gap that is paramount to the implementation of the National AMR Action Plan. There is a paucity of evidence of MDR sepsis in tertiary care ICUs, specifically among the railway hospital beneficiaries [7]. Hence, the present study systematically dealt with these limitations and aimed to determine the prevalence of MDR-GNB, to characterise the risk factors associated with MDR versus susceptible phenotypes, and to assess the impact on 28-day mortality, ICU/hospital length of stay, and duration of antimicrobial use.

This study characterised local antimicrobial susceptibility patterns using Clinical and Laboratory Standards Institute (CLSI)-compliant automated systems (VITEK-2), supplemented by the Kirby–Bauer disc diffusion method and quality control strains obtained from the American Type Culture Collection (ATCC), to generate a reliable institutional antibiogram [13,14]. The research bridges a gap in substantive evidence, which can offer practical intelligence to resource-constrained ICUs across the rest of the country. The present study aimed to determine the prevalence, risk factors and clinical outcomes of MDR-GNB sepsis among patients admitted to the ICU.

MATERIALS AND METHODS

This cross-sectional study was conducted at the Department of General Medicine, in the Intensive Care Unit (ICU) of Jagjivan Ram Hospital, a tertiary care railway hospital in Mumbai, Maharashtra, India, over a period of 24 months from December 2022 to December 2024. The study protocol was approved by the Institutional Ethics Committee [IEC No: EC/19/00153]. Written informed consent was obtained from all participants or their legal guardians.

Sample size calculation: Sample size was calculated using the incidence and outcomes of MDR-GNB infections in the ICU reported in a study by Siwakoti S et al., a total of 64 patients were found to have MDR-GNB infections per 137 ICU admissions (47%) [15]. Using the formula

n= Z2p(1-p)/d2,

with a 95% Confidence Interval (CI) (Z=1.96) and an allowable error of 10% (d=0.10), the required sample size was determined as 96. During the study period, 100 patients with culture-confirmed Gram-negative sepsis were included.

Inclusion criteria: Patients aged >18 years admitted to the ICU with a diagnosis of sepsis and culture-confirmed GNB infection were included.

Exclusion criteria: Patients aged <18 years, patients with incomplete medical records, those Discharged Against Medical Advice (LAMA) within 24 hours of admission and sterile culture reports or Gram-positive infections.

The present study recorded the patient demographic characteristics, underlying conditions and reason for hospital admission, history, and previous antibiotics received were recorded in the participant record form at the time of admission. Patient was routinely followed-up again each morning and data on clinical or laboratory parameters were collected, including previous antibiotic therapy and clinical manifestations. Clinical samples (blood, urine, respiratory secretions, pus) were collected using aseptic techniques. Bacterial identification was performed using the BACTEC system and antimicrobial susceptibility was determined using the VITEK-2 automated system and Kirby-Bauer disc diffusion method on Mueller-Hinton agar, in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines (2022) [10]. MDR was defined as non susceptibility to at least one agent in three or more antimicrobial categories [11].

STATISTICAL ANALYSIS

Data were entered into MS Excel and analysed using Statistical Package for Social Sciences (SPSS) version 23.0. Quantitative variables were expressed as Mean±SD and compared using the Independent t-test. Qualitative variables were expressed as frequencies and percentages and compared using the Chi-square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant.

RESULTS

The study included 100 patients with Gram-negative sepsis. The prevalence of MDR infections was found to be in 67 patients (67%), while 33 (33%) were non-MDR.

Demographic and Clinical Characteristics

The majority of the study population was elderly, with more than half of the patients aged over 60 years. There was a slight male preponderance in the study cohort. Co-morbidities were highly prevalent, with DM being the most common condition, followed by Hypertension (HTN) and IHD. Notably, all patients included in the study had invasive devices such as Foley catheters and central lines [Table/Fig-1].

Parameters	Category	n (%)
Age group (in years)	<35	2 (2%)
	36-60	43 (43%)
	>60	55 (55%)
Gender	Male	55 (55%)
	Female	45 (45%)
Co-morbidities	Diabetes Mellitus (DM)	86 (86%)
	Hypertension (HTN)	45 (45%)
	Ischaemic Heart Disease (IHD)	39 (39%)
	Chronic Kidney Disease (CKD)	21 (21%)
Risk factors	Previous hospital admission	42 (42%)
	Prior antibiotics	44 (44%)
Invasive devices	Foley catheter	100 (100%)
	Central line	100 (100%)
	Mechanical ventilation	10 (10%)

[Table/Fig-1]: Baseline characteristics of study population (N=100).

Comparison of MDR vs non-MDR Groups

Patients in the MDR group had a significantly lower mean age compared to the non-MDR group (59.33±10.2 vs 65.79±11.3 years; p=0.001). While gender distribution was similar between groups, specific infections like UTI and Surgical Site Infections (SSI) were frequently observed in both cohorts [Table/Fig-2].

Variables	Category	MDR (n=67) n (%)	Non-MDR (n=33) n (%)	p-value
Age (in years)	Mean±SD	59.33±10.2	65.79±11.3	0.001*
Gender	Male	38 (56.7%)	17 (51.5%)	0.623
	Female	29 (43.3%)	16 (48.5%)	
Diagnosis^	UTI	22 (32.8%)	17 (51.5%)	>0.05
	BSI	14 (20.9%)	4 (12.1%)	
	Pneumonia	14 (20.9%)	9 (27.3%)	
	SSI	26 (38.8%)	9 (27.3%)	

[Table/Fig-2]: Comparison of clinical parameters between MDR and Non-MDR groups.
^Diagnosis counts may exceed total n due to polymicrobial/multi-site infections; UTI: Urinary tract infection; BSI: Bloodstream infection; SSI: Surgical site infection

Risk Factor Analysis

Prior antibiotic use was a statistically significant factor associated with MDR status. While invasive procedures were universally present, mechanical ventilation and previous hospital admissions did not show a statistically significant difference between the two groups in this sample size [Table/Fig-3].

Variables	MDR (n=67) n (%)	Non-MDR (n=33) n (%)	p-value
Previous hospital admissions	27 (40.3%)	15 (45.5%)	0.62
Prior antibiotics	32 (47.8%)	12 (36.4%)	0.04*
Previous surgery	27 (40.3%)	15 (45.5%)	0.62
Mechanical ventilation	6 (9.0%)	4 (12.1%)	0.62

[Table/Fig-3]: Association of risk factors with MDR status.

Microbiological Profile

The distribution of organisms varied between samples. *Klebsiella pneumoniae* was the most frequently isolated pathogen in the MDR group (41.8%), followed by *Escherichia coli* (28.4%). *Pseudomonas aeruginosa* and *Acinetobacter baumannii* were also identified, but in smaller proportions [Table/Fig-4].

Organism	MDR Isolates n (%)	Non-MDR Isolates n (%)	p-value
Klebsiella pneumoniae	28 (41.8%)	10 (30.3%)	0.26
Escherichia coli	19 (28.4%)	11 (33.3%)	0.61
Pseudomonas aeruginosa	12 (17.9%)	7 (21.2%)	0.69
Acinetobacter baumannii	8 (11.9%)	5 (15.2%)	0.75

[Table/Fig-4]: Distribution of pathogens in MDR vs non-MDR Samples.

Mortality and Survival

Mortality was 55.2% in the MDR group and 57.6% in the non-MDR group; the difference was not statistically significant (p=0.82). However, this difference was not statistically significant (p-value = 0.82) [Table/Fig-5].

Mortality	MDR (n=67) n (%)	Non-MDR (n=33) n (%)	p-value
Survivors	30 (44.8%)	14 (42.4%)	0.82
Non survivors	37 (55.2%)	19 (57.6%)	

[Table/Fig-5]: Comparison of mortality.

DISCUSSION

The present study identified that the prevalence of MDR-GNB was 67% of sepsis cases in the current study ICU in Jagjivan Ram Hospital. This is a very high rate compared to the Western ICU rate of 20-40% [16] but very much lower than the range of 55-75% characteristic of the Indian ICU [17,18]. Microbiologically, the MDR group was led by *Klebsiella pneumoniae* (41.8%) and *E. coli* (28.4%). ICMR Surveillance data (2024) also aligns with findings, which identify these *Enterobacteriaceae* as the primary drivers of healthcare-associated bloodstream infections in India, with Klebsiella showing a higher decline in imipenem susceptibility to around 31.2% [19]. However, the current study findings differ from the study by Gautam G et al., in the North Indian ICU, where Acinetobacter spp. (33.02%) was the most common isolate, highlighting how the local hospital ecology can influence pathogen distribution [17].

Socio-demographic profile of the present study showed a predominant geriatric population, with 55% of patients aged above 60 years and an average age of 59.33±10.2 years in the MDR group. This type of distribution is similar to the global data, where advancing age is a known predictor of MDR acquisition due to immunosenescence and frequent healthcare-associated contacts [20]. There was a high prevalence of co-morbidity distribution among the study participants, especially DM (86%). While studies show that the prevalence data of 8.49% DM among the general employee population of the Northern Railway implies that diabetic beneficiaries were at a very high risk of contracting severe, culture-positive Gram-negative infections [21]. This relationship is further corroborated by findings in Mumbai that indicate that 66% of infected diabetic foot ulcers harbour MDR organisms, probably because neutrophil chemotaxis is impaired and biofilm formation is enhanced [22].

Prior antibiotic exposure in the last 30 days was found by risk factor analysis to be a significant predictor of MDR status (p-value=0.04). The present study finding is fully consistent with the meta-analyses of the rest of the world, which report pooled odds ratios of 2.8 for the risk of MDR infection following antecedent antibiotic use. Although the current study did not find statistical differentiation since the use of Foley's catheters and central venous lines is 100% utilised, it highlights the overall role of invasive instrumentation in generating selection. These findings align with Nagvekar et al. [8], who reported that 37% of patients in a Mumbai multispeciality hospital already harboured MDR-GNB at admission. This suggests that colonisation or infection with resistant strains may occur prior to ICU entry, possibly reflecting antibiotic use within the railway healthcare system [8]. Furthermore, the IMPRES study noted that 56% of ICU patients in India obtain incorrect empirical treatment, a fundamental challenge that mirrors the pharmacological pressure seen in the current study cohort [23].

In the current study, MDR patients had a mortality proportion of 55.2% compared to 57.6% in the non-MDR group. This difference was not statistically significant (p=0.82). This is in agreement with Siwakoti S et al., who found that MDR status approximately doubled the risk of death [15]. In addition to mortality, the MDR patients had a mean ICU stay of 20.44 days, longer than that of patients with susceptible infections. This is astounding when compared to the Indian Sepsis Registry and the analysis of the financial impact of MDR sepsis treatment by Flawrance M et al., which described MDR sepsis care as being incredibly resource-consuming in terms of its long hospitalisation and the requirement of expensive last-line treatment options such as colistin [20].

Limitation(s)

There are a number of shortcomings that are worth discussing. The 13 million cases of the railway beneficiaries served in the same facilities across the country are represented by a single-centre design, which is inherently limited in generalisability, although the demographic and healthcare access patterns of the beneficiaries are similar. The granular data on the precise dosage of antibiotics, serum levels, or precise control of the source at the time of clinical outcomes, which are known confounders of clinical outcomes, were not measured. An observational type of study does not allow the attribution of causality, but the time-related order of previous antibiotic exposure before MDR infection is a good indicator of biological plausibility.

CONCLUSION(S)

The present study highlights a critical public health issue within the railway beneficiary population, revealing a high burden of MDR Gram-negative sepsis. Advanced age, diabetes, and prior antibiotic use were key drivers of this epidemic. Although the association between MDR status and mortality did not reach statistical significance in this study, the high absolute mortality rates warrant an urgent review of empirical antibiotic policies. The implementation of strict antibiotic stewardship programmes and rigorous infection control bundles for invasive devices to curb the spread of these resistant pathogens was recommended.

REFERENCES

[1] Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: Analysis for the Global Burden of Disease Study. Lancet. 2020;395(10219):200-11.

[2] Ranjbar R, Alam M. Antimicrobial Resistance Collaborators (2022). Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. Evid Based Nurs. 2023:ebnurs-2022-103540. Doi: 10.1136/ebnurs-2022-103540. Epub ahead of print. PMID: 37500506.

[3] Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA. 2009;302(21):2323-29.

[4] Timsit JF, Bassetti M, Cremer O, Daikos G, de Waele J, Kallil A, et al. Rationalizing antimicrobial therapy in the ICU: A narrative review. Intensive Care Med. 2019;45(2):172-89.

[5] Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: An international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012;18(3):268-81.

[6] Ruppé É, Woerther PL, Barbier F. Mechanisms of antimicrobial resistance in Gram-negative bacilli. Ann Intensive Care. 2015;5(1):61.

[7] Kumar NR, Balraj TA, Kempegowda SN, Prashant A. Multidrug-Resistant Sepsis: A Critical Healthcare Challenge. Antibiotics (Basel). 2024;13(1):46.

[8] Nagvekar V, Sawant S, Amey S. Prevalence of multidrug-resistant Gram-negative bacteria cases at admission in a multispeciality hospital. J Glob Antimicrob Resist. 2020;22:457-61.

[9] India's Antimicrobial Resistance Surveillance & Research Initiative [Internet]. ICMR; [cited 2025 Dec 24]. Available from: https://iamrsn.icmr.org.in/.

[10] M100. Performance Standards for Antimicrobial Susceptibility Testing [Internet]. [cited 2025 Dec 24]. Available from: https://clsi.org/shop/standards/m100/.

[11] National action plan on AMR (NAP-AMR) - National Centre for Disease Control (NCDC) [Internet]. [cited 2025 Dec 24]. Available from: https://ncdc.mohfw.gov.in/national-action-plan-on-amr-nap-amr/.

[12] Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: A global multifaceted phenomenon. Pathog Glob Health. 2015;109(7):309-18.

[13] Llor C, Bjerrum L. Antimicrobial resistance: Risk associated with antibiotic overuse and initiatives to reduce the problem. Ther Adv Drug Saf. 2014;5(6):229-41.

[14] Chelazzi C, Pettini E, Villa G, De Gaudio AR. Epidemiology, associated factors and outcomes of ICU-acquired infections caused by Gram-negative bacteria in critically ill patients: An observational, retrospective study. BMC Anesthesiol. 2015;15:125.

[15] Siwakoti S, Subedi A, Sharma A, Baral R, Bhattarai NR, Khanal B. Incidence and outcomes of multidrug-resistant gram-negative bacteria infections in intensive care unit from Nepal- a prospective cohort study. Antimicrob Resist Infect Control. 2018;7(1):114.

[16] Al-Sunaidar KA, Aziz NA, Hassan Y, Jamshed S, Sekar M. Association of Multidrug Resistance Bacteria and Clinical Outcomes of Adult Patients with Sepsis in the Intensive Care Unit. Trop Med Infect Dis. 2022;7(11):365. Doi: 10.3390/tropicalmed7110365. PMID: 36355907; PMCID: PMC9692934.

[17] Gautam G, Satija S, Kaur R, Kumar A, Sharma D, Dhakad MS. Insight into the Burden of Antimicrobial Resistance among Bacterial Pathogens Isolated from Patients Admitted in ICUs of a Tertiary Care Hospital in India. Can J Infect Dis Med Microbiol. 2024;2024:7403044.

[18] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis. 1987;40(5):373-83.

[19] ICMR Antimicrobial Resistance Surveillance Network Report [Internet]. [cited 2025 Dec 24]. Available from: https://www.icmr.gov.in/icmrobject/uploads/Documents/1744706555_icmr_annualreport_2023-24_78804328_1.pdf.

[20] Flawrance M, Krishna B, Thekkekara JV. To Assess the Financial Impact of Multidrug Resistant Organisms in Adult Critically Ill Patients at A Tertiary Care Hospital. Indian J Crit Care Med. 2025;29(Suppl 1):S252.

[21] Pareek MS. Prevalence of Pre-diabetes and Diabetes mellitus among the Northern Railway Employees: A retrospective study. International Journal of Advances in Nursing Management. 2017;5(4):347-50.

[22] Chatterjee D, Shivashamugam K. Insights on MDR Mechanism of Pseudomonas aeruginosa with Emphasis on Diabetic Foot Ulcer in the Indian Subcontinent. J Pure Appl Microbiol. 2024;18(2):837-852. Doi: 10.22207/JPAM.18.2.08.

[23] Das SK, Joshi Z, Govil D, Shah MS, Jakaraddi GN, Sinha S, et al. Epidemiology and Clinical Outcome of Common Multi-drug Resistant Gram-negative Bacterial Infections in a Network of Hospitals in India (IMPRES): A Multicenter Intensive Care Unit-based Prospective Clinical Study. Indian J Crit Care Med. 2025;29(6):504-09.

PARTICULARS OF CONTRIBUTORS:

1. Resident Physician, Department of General Medicine, Jagjivan Ram Hospital, Mumbai, Maharashtra, India.
2. Senior Consultant, Department of General Medicine, Jagjivan Ram Hospital, Mumbai, Maharashtra, India.
3. Consultant, Department of Obstetrics and Gynaecology, Yashoda Hospital, New Panvel, Mumbai, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. A Meenu,
Resident Physician, Department of General Medicine, Jagjivan Ram Hospital,
Mumbai-400027, Maharashtra, India.
E-mail: meenugokul512@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Oct 24, 2025
- Manual Googling: Jan 31, 2026
- iThenticate Software: Feb 03, 2026 (10%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Oct 14, 2025**
Date of Peer Review: **Dec 04, 2025**
Date of Acceptance: **Feb 05, 2026**
Date of Publishing: **Apr 01, 2026**