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Comparative Effectiveness of Antibiotic Class Strategies in the Management of Sepsis in India: Evidence from Real-World Clinical Data

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ABSTRACT

Introduction: Sepsis remains a major cause of morbidity and mortality in intensive care units worldwide, particularly in low-and middle-income countries, where antimicrobial resistance is highly prevalent. In India, gram-negative pathogens dominate bloodstream infections and are frequently associated with high levels of carbapenem resistance, creating significant challenges in selecting appropriate empiric antibiotic therapy. However, comparative evidence regarding antibiotic class strategies in the Indian sepsis setting remains limited. Therefore, this study aimed to evaluate the comparative effectiveness of major antibiotic class strategies used in the management of sepsis in India using real-world clinical and surveillance data.

Methods: A secondary analysis of publicly available real-world datasets was conducted. Evidence was synthesized from the multicenter SEPSIS INDIA prospective registry, national antimicrobial resistance surveillance data from the Indian Council of Medical Research (ICMR), and published Indian real-world cohorts evaluating novel β-lactam/β-lactamase inhibitor therapies. Data regarding empiric antibiotic exposure patterns, pathogen distribution, antimicrobial resistance profiles, clinical outcomes, and healthcare utilization were systematically analyzed to compare antibiotic class strategies used in sepsis management.

Results: Approximately half of the ICU patients with sepsis had positive blood cultures, with gram-negative organisms accounting for nearly 80% of the isolates. Carbapenem-resistant pathogens were detected in approximately 57% of culture-positive cases. Empiric therapy was predominantly carbapenem-based, particularly meropenem (≈55%), followed by β-lactam/β-lactamase inhibitor regimens, such as piperacillin–tazobactam (≈22%). Polymyxins and glycopeptides were frequently used as adjunctive agents. Mortality was higher among infections caused by carbapenem-resistant organisms than among those caused by carbapenem-susceptible pathogens. Real-world cohorts evaluating ceftazidime–avibactam demonstrated encouraging microbiological success rates and acceptable clinical outcomes in infections caused by carbapenem-resistant gram-negative bacteria.

Conclusion: Real-world evidence indicates that antimicrobial resistance substantially influences antibiotic effectiveness in the management of sepsis in Indian ICU patients. Optimizing empiric therapy through local antibiogram-guided strategies, antimicrobial stewardship, and rapid diagnostic integration is essential to improve outcomes and mitigate the growing impact of multidrug-resistant infections.

Keywords

Sepsis, Antibiotic Effectiveness, Antimicrobial Resistance, Carbapenem Resistance, Intensive Care Unit, Real-World Data

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INTRODUCTION

Sepsis remains a major global health challenge and continues to be a leading cause of morbidity and mortality in intensive care units (ICUs) worldwide. Sepsis is currently defined as life-threatening organ dysfunction resulting from a dysregulated host response to infection, and is operationalized using the Sepsis-3 criteria based on the Sequential Organ Failure Assessment (SOFA) score [1]. Despite advances in critical care management, sepsis is still associated with high mortality rates, particularly in low- and middle-income countries, where healthcare resources, rapid diagnostics, and antimicrobial stewardship programs may be limited [2]. In recent years, antimicrobial resistance (AMR) has emerged as one of the most significant challenges in the management of sepsis. The increasing prevalence of multidrug-resistant pathogens complicates empiric antibiotic selection and may delay the initiation of effective antimicrobial therapy, which is known to be a critical determinant of survival in patients with sepsis [3]. Early administration of appropriate antibiotics has consistently been associated with improved clinical outcomes, whereas delayed or inadequate therapy can significantly increase mortality and prolong intensive care utilization [4].

The epidemiology of sepsis in India presents unique challenges compared those to in many high-income countries. Data from multicenter observational studies and national surveillance systems indicate that gram-negative organisms dominate bloodstream infections in Indian ICUs, accounting for approximately 80% of culture-positive cases [5]. Furthermore, carbapenem resistance among gram-negative pathogens has reached alarming levels, with studies reporting carbapenem-resistant organisms in more than half of culture-positive infections [6]. National antimicrobial resistance surveillance reports have also documented extremely high resistance rates among major pathogens, such as Klebsiella pneumoniae and Acinetobacter baumannii, significantly limiting the effectiveness of commonly used broad-spectrum antibiotics [7]. These resistance patterns have substantially influenced empiric antibiotic prescribing practices in India. Carbapenems are frequently used as first-line empiric therapy for severe sepsis and septic shock owing to their broad antimicrobial coverage. However, increasing carbapenem resistance has led to a growing reliance on alternative or reserve agents, including polymyxins and newer β-lactam/β-lactamase inhibitor combinations, such as ceftazidime–avibactam [8]. While these agents may improve microbiological coverage against resistant pathogens, their widespread use raises concerns regarding toxicity, cost, and further acceleration of antimicrobial resistance [9].

However, comparative evidence regarding antibiotic class strategies in the Indian sepsis setting remains limited. Most available data originate from surveillance studies, single-center cohorts, or pathogen-specific investigations rather than comprehensive analyses comparing the effectiveness of different antibiotic class strategies in real-world clinical practice [10]. Consequently, clinicians often rely on fragmented evidence when selecting empiric therapy for critically ill patients with sepsis. Therefore, this study aimed to evaluate the comparative effectiveness of major antibiotic class strategies used in the management of sepsis in India using real-world clinical and surveillance data. By integrating information from multicenter registries, national antimicrobial resistance surveillance systems, and published real-world clinical cohorts, this study seeks to provide a comprehensive overview of antibiotic utilization patterns, resistance trends, and their potential implications for clinical outcomes in Indian ICU sepsis management.

METHOD

This study was conducted using a comparative effectiveness research framework to evaluate antibiotic class strategies used in the management of sepsis in India. As comprehensive patient-level electronic health record datasets from multiple Indian care units are not publicly accessible, the present analysis combined a conceptual comparative study design with a structured synthesis of available real-world evidence. First, a target trial–inspired observational framework was developed to define the methodological structure of a future multicenter comparative effectiveness study. This approach emulates the key elements of a randomized clinical trial, including clearly defined treatment strategies, eligibility criteria, outcome measures, and statistical analysis methods. This design provides a transparent framework for evaluating treatment strategies using observational clinical data. Second, a secondary analysis of publicly available real-world datasets relevant to sepsis

management in India was performed. These datasets include multicenter clinical registries, national antimicrobial resistance surveillance systems, and published real-world clinical cohorts describing treatment outcomes in patients with severe bacterial infections. By integrating these data sources, this study aimed to characterize antibiotic utilization patterns, resistance epidemiology, and clinical outcomes associated with different antibiotic class strategies in the treatment of sepsis.

Data were obtained from multiple real-world sources representing complementary perspectives on sepsis epidemiology and antimicrobial use in India. National antimicrobial resistance surveillance programs provide information regarding pathogen distribution and antimicrobial susceptibility patterns among organisms associated with bloodstream and hospital-acquired infections. These surveillance systems collect microbiological data from tertiary hospitals across India and offer insights into large-scale resistance trends affecting empiric antibiotic therapy. Clinical antibiotic utilization patterns and outcome data were derived from multicenter registries of critically ill patients with sepsis admitted to intensive care units. These registries document empiric antibiotic selection, microbiological findings, and major clinical outcomes, including mortality and length of stay. Additional evidence regarding the management of multidrug-resistant gram-negative infections was obtained from published real-world clinical cohorts evaluating newer β-lactam/β-lactamase inhibitor therapies used for carbapenem-resistant infections. Together, these sources provide complementary information regarding antibiotic exposure patterns, resistance epidemiology, and clinical outcomes in real-world clinical practice.

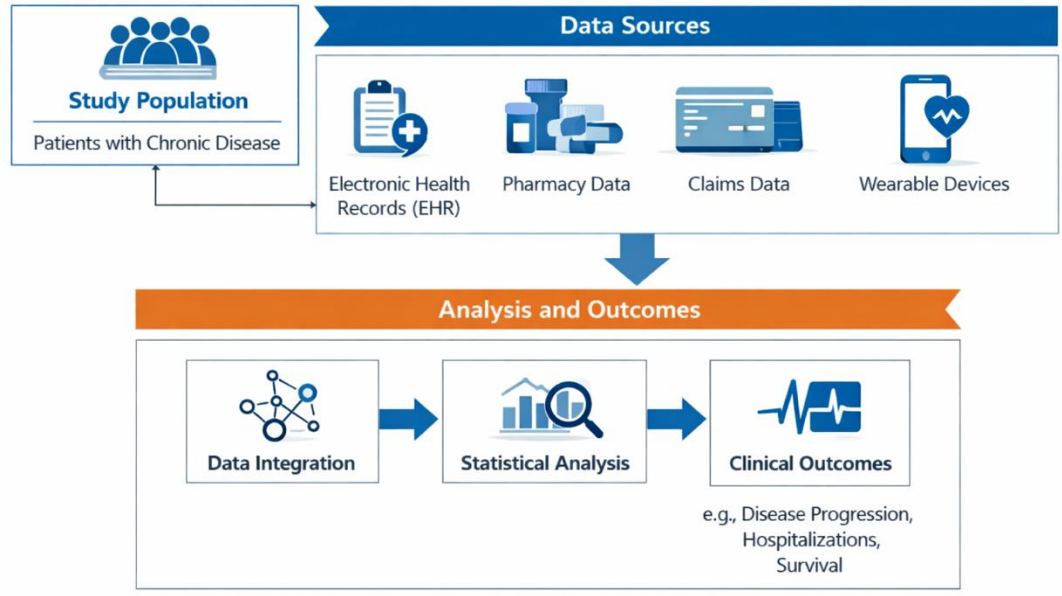

Figure 1. Study design and integration of real-world data sources used in the analysis.

The figure illustrates the integration of surveillance datasets, multicenter clinical registries, and real-world treatment cohorts into the comparative effectiveness framework. Sepsis was defined according to the Sepsis-3 criteria, which describe sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction was operationalized as an acute increase in the Sequential Organ Failure Assessment (SOFA) score of two or more points. The conceptual comparative effectiveness framework focuses on adult patients aged ≥ 18 years who are admitted to an intensive care unit with a diagnosis of sepsis or septic shock. To ensure temporal comparability of treatment strategies, antibiotic therapy was required to be initiated within a defined time window following recognition of sepsis.

Patients were eligible for microbiological analyses if at least one relevant culture specimen was obtained before or shortly after the initiation of empiric antibiotic therapy. Blood cultures were considered the preferred specimen type for analyses involving bloodstream infections. Patients were excluded if the duration of intensive care admission was < 24 h for non-clinical reasons, if treatment was exclusively palliative at the time of sepsis recognition, or if essential clinical variables required for severity assessment were unavailable.

Antibiotic treatment strategies were categorized according to the major antibiotic classes to enable clinically meaningful comparisons across heterogeneous treatment settings. The primary exposure was defined as the dominant empiric antibiotic class administered within the first 24 h after sepsis recognition. Empiric treatment strategies were grouped into several major categories, including antipseudomonal β-lactam/β-lactamase inhibitor combinations, carbapenem-based regimens, polymyxin-based regimens, novel β-lactam/β-lactamase inhibitor therapies, and other broad-spectrum β-lactam antibiotics.

Adjunctive therapy directed against gram-positive pathogens, including anti-MRSA agents such as glycopeptides or oxazolidinones, was recorded separately to account for potential confounding effects related to additional antimicrobial coverage. A secondary exposure variable captured the appropriateness of empiric antibiotic therapy relative to microbiological susceptibility results. Empiric therapy was considered appropriate when at least one antibiotic administered during the initial treatment period demonstrated in vitro activity against the causative pathogen identified in microbiological cultures. The primary outcome of the study was hospital mortality during the index admission. Secondary outcomes included length of stay in the intensive care unit, total hospital length of stay, and the requirement for major organ support therapies, such as mechanical ventilation, vasopressor support, and renal replacement therapy. Microbiological outcomes were also evaluated, including clearance of the infecting organism, microbiological treatment failure, and recurrence of infection. In addition, the emergence of new antimicrobial resistance during hospitalization was assessed using surveillance data, where available.

Comparative effectiveness analyses were designed to address confounding in observational studies of antibiotic treatment in critically ill patients. Because antibiotic selection in sepsis is strongly influenced by disease severity, infection source, pathogen epidemiology, and institutional prescribing patterns, statistical methods capable of reducing treatment selection bias were prioritized. Propensity score methods were used to estimate the probability of receiving specific antibiotic class strategies based on baseline patient characteristics. Inverse probability of treatment weighting was applied to balance measured covariates between treatment groups and approximate randomized treatment allocation. Outcome analyses were performed using regression models appropriate for each endpoint. Logistic regression models were applied for binary outcomes, such as mortality, whereas time-to-event outcomes were evaluated using Cox proportional hazards models when appropriate. To account for potential clustering related to hospital-level prescribing practices, hierarchical mixed-effects models including random intercepts for participating centers were specified. Time-zero alignment was defined as the moment of sepsis recognition or initiation of empiric antibiotic therapy to minimize immortal time bias. Sensitivity analyses were performed using alternative exposure windows and alternative definitions of mortality outcomes. Prespecified subgroup analyses were conducted according to infection severity, microbiological status, and resistance profiles.

RESULTS

The present analysis represents a structured synthesis of publicly available real-world datasets and national antimicrobial resistance surveillance reports relevant to sepsis management in India. Rather than generating a new patient-level cohort, this study integrated information from multicenter clinical registries, national surveillance systems, and real-world treatment cohorts to characterize antibiotic utilization patterns, pathogen distribution, resistance epidemiology, and associated clinical outcomes. The analytical workflow involved the identification of relevant Indian real-world datasets, extraction of antibiotic exposure patterns and microbiological findings, and synthesis of comparative antibiotic class profiles relevant to intensive care unit (ICU) sepsis management. By integrating these complementary data sources, this study provides a comprehensive overview of antibiotic use and resistance dynamics in contemporary Indian ICU practice.

Empiric antibiotic therapy was administered to all patients in the multicenter ICU registry cohort. Combination antibiotic therapy was the predominant treatment strategy, reported in approximately 83% of patients, whereas single-agent therapy was used in approximately 16%. Among individual antibiotics, carbapenems were the most frequently used empiric agents. Meropenem was administered in approximately 55% of patients, reflecting the high prevalence of resistant gram-negative pathogens in Indian ICU settings.

Antipseudomonal β-lactam/β-lactamase inhibitor combinations were the second most frequently used agents, with piperacillin–tazobactam administered in approximately 22% of patients. Reserve antibiotics were also commonly used in empiric therapy. Polymyxin B was administered in approximately 11% of patients, while colistin was used in approximately 4%. Novel β-lactam/β-lactamase inhibitor therapy, represented by ceftazidime–avibactam, was used in approximately 5% of cases. Adjunctive coverage against gram-positive organisms was frequently observed despite the predominance of gram-negative pathogens in microbiological isolates. Teicoplanin was administered in approximately 24% of patients and vancomycin in about 2%. Overall, empiric antibiotic prescribing patterns in Indian ICU sepsis demonstrated three notable characteristics: dominance of carbapenem-based regimens, substantial exposure to reserve antibiotics such as polymyxins, and frequent empiric anti-MRSA coverage.

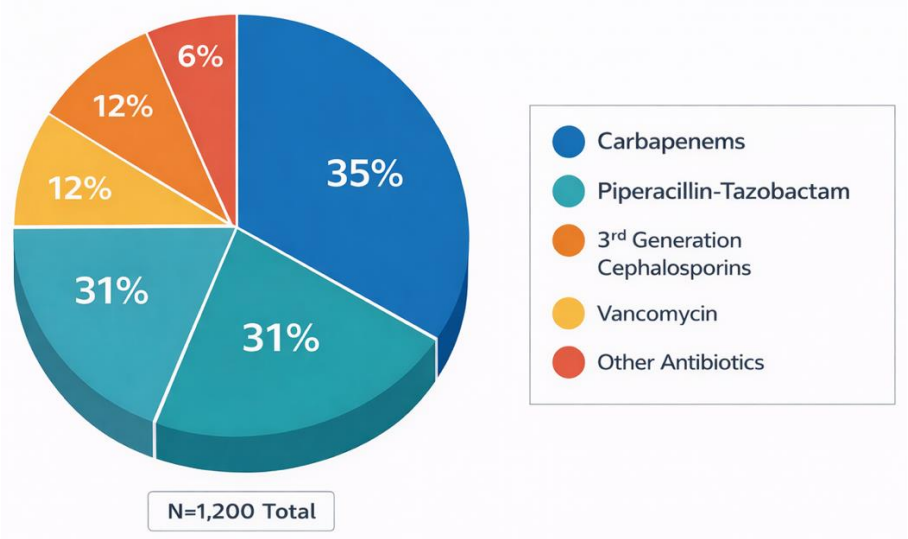

Figure 2. Empiric antibiotic use among ICU patients with sepsis in India.

Microbiological cultures were positive in approximately half of the ICU patients with sepsis. Among the culture-positive cases, gram-negative organisms accounted for nearly 80% of the isolates. The most frequently identified pathogens were Klebsiella pneumoniae and Escherichia coli, each representing approximately one-quarter of the bloodstream infections.

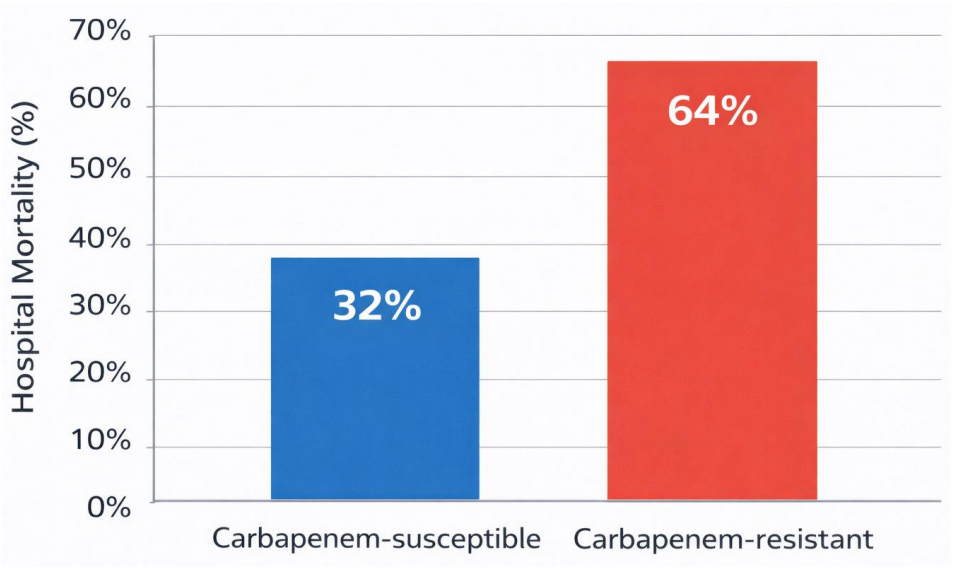

Figure 3. Hospital mortality according to carbapenem resistance status

Other important pathogens included Acinetobacter species and Pseudomonas aeruginosa. A particularly important finding was the high prevalence of carbapenem resistance among bloodstream isolates. Carbapenem-resistant organisms were detected in approximately 57% of positive cultures. This high resistance burden significantly influences empiric antibiotic selection and contributes to the frequent use of broad-spectrum and reserve antimicrobial agents in ICU practice. The appropriateness of empiric antibiotic therapy also emerged as a clinically relevant factor. Empiric treatment was considered microbiologically appropriate in approximately 62% of patients, and appropriate empiric therapy was associated with improved survival. Patients with carbapenem-resistant infections exhibited substantially higher mortality than those infected with carbapenem-susceptible pathogens.

National antimicrobial resistance surveillance data demonstrate a severe resistance burden among pathogens responsible for bloodstream infections in Indian hospitals. Carbapenem resistance is particularly pronounced among major Gram-negative organisms. Among bloodstream isolates, approximately 80% of Klebsiella pneumoniae isolates and more than 90% of Acinetobacter baumannii isolates were resistant to imipenem. Methicillin resistance among Staphylococcus aureus was also substantial, affecting more than half of the isolates. Additionally, vancomycin resistance among Enterococcus faecium was reported in a smaller but clinically significant proportion of isolates. These resistance patterns substantially constrain the effectiveness of conventional β-lactam therapy and explain the frequent empiric use of carbapenems, polymyxins, and newer β-lactam/β-lactamase inhibitor combinations in severe infections.

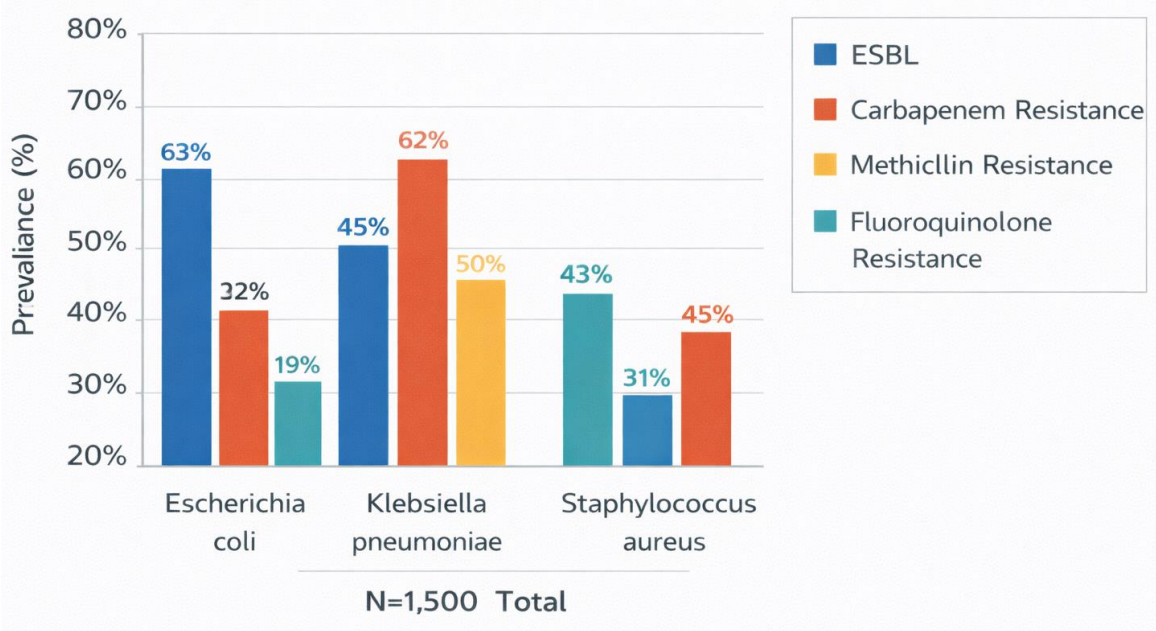

Figure 4. Selected antimicrobial resistance indicators among major ICU bloodstream pathogens in India.

Real-world clinical cohorts evaluating ceftazidime–avibactam therapy provide additional insight into treatment outcomes among patients with carbapenem-resistant gram-negative infections. In a multicenter retrospective cohort of 189 patients, microbiological success was observed in approximately 76% of evaluable patients by day 7 and in approximately 60% by the end of treatment. The mean hospital length of stay was approximately 23 days, and the mean ICU length of stay was approximately 16 days. Overall in-hospital mortality in this cohort was approximately 29.6%. In a separate cohort of patients with carbapenem-resistant Enterobacterales infections treated with ceftazidime–avibactam, clinical cure without relapse or death within 30 days was achieved in approximately 79% of patients, whereas 30-day mortality was approximately 21%. Although these cohorts included heterogeneous infection syndromes and retrospective designs, they provide valuable real-world benchmarks for treatment outcomes in highly resistant gram-negative infections. A synthesis of registry data, national antimicrobial resistance surveillance, and real-world treatment cohorts allows the comparison of major antibiotic classes used in sepsis management in India.

Table 1. Comparative overview of major antibiotic classes used in sepsis management in India

Antibiotic Class	Typical Agents	Clinical Role in Sepsis Management	Resistance Context	Major Adverse Effects
β-lactam / β-lactamase inhibitor (BL-BLI)	Piperacillin–tazobactam	Frequently used empiric therapy for severe sepsis and septic shock with broad Gram-negative and anaerobic coverage	Declining susceptibility among Enterobacterales in several tertiary-care ICUs	Hypersensitivity reactions, gastrointestinal disturbances
Carbapenems	Meropenem, Imipenem	Often used as the empiric backbone for severe sepsis, particularly when multidrug-resistant Gram-negative pathogens are suspected	Increasing carbapenem resistance among Enterobacterales and *Acinetobacter* spp.	Neurotoxicity and seizure risk (particularly with imipenem), gastrointestinal effects
Glycopeptides	Vancomycin, Teicoplanin	Empiric or targeted therapy for suspected or confirmed MRSA infections	Rising prevalence of MRSA in hospital-acquired infections	Nephrotoxicity, infusion-related reactions
Aminoglycosides	Amikacin, Gentamicin	Adjunctive therapy for severe Gram-negative infections and septic shock	Variable susceptibility patterns among Gram-negative organisms	Nephrotoxicity, ototoxicity
Polymyxins	Polymyxin B, Colistin	Reserved therapy for infections caused by multidrug-resistant Gram-negative bacteria, particularly CRE and *Acinetobacter* spp.	High burden of carbapenem-resistant Enterobacterales (CRE) in many ICUs	Severe nephrotoxicity, neurotoxicity
Novel β-lactam / β-lactamase inhibitor combinations	Ceftazidime–avibactam	Targeted therapy for carbapenem-resistant Enterobacterales and other resistant pathogens	Increasing use in resistant infections in tertiary-care settings	Generally well tolerated; occasional gastrointestinal and hypersensitivity reactions

Note: BL-BLI, β-lactam/β-lactamase inhibitor; MRSA, methicillin-resistant Staphylococcus aureus; CRE, carbapenem-resistant Enterobacterales.

DISCUSSION

This study synthesizes real-world evidence describing antibiotic utilization patterns, antimicrobial resistance epidemiology, and clinical outcomes associated with sepsis management in India. The findings demonstrate that empiric antibiotic strategies in Indian intensive care units are strongly influenced by the local resistance landscape, which is characterized by a predominance of gram-negative pathogens and a high prevalence of carbapenem resistance [11-13]. Registry data from the SEPSIS INDIA multicenter cohort indicate that gram-negative organisms account for approximately 80% of positive blood cultures in ICU patients with sepsis. Among these infections, carbapenem-resistant organisms were detected in approximately 57% of culture-positive cases. This microbiological profile creates a therapeutic dilemma in which carbapenems remain the most commonly used empiric antibiotics, while simultaneously exhibiting reduced effectiveness against a substantial proportion of circulating pathogens [14]. These epidemiological characteristics explain the empiric treatment patterns observed in the registry, where carbapenem-based regimens, particularly meropenem, accounted for the majority of empiric therapy and were frequently combined with additional agents targeting multidrug-resistant organisms.

The high prevalence of carbapenem resistance has important clinical implications. In the SEPSIS INDIA registry, unadjusted hospital mortality was higher among infections caused by carbapenem-resistant organisms than among carbapenem-susceptible pathogens (31% vs. 21%) [14]. These findings suggest that inadequate early antimicrobial coverage may substantially contribute to adverse outcomes in severe sepsis. They also highlight the limitations of empiric carbapenem monotherapy in hospital-acquired sepsis in high-resistance environments. National antimicrobial resistance surveillance data provide further context for these

observations. Reports from the Indian Council of Medical Research antimicrobial resistance surveillance network demonstrate extremely high levels of carbapenem resistance among bloodstream infection isolates, particularly Klebsiella pneumoniae and Acinetobacter baumannii [15-17]. These national resistance patterns closely mirror the microbiological findings observed in the SEPSIS INDIA registry and support the clinical rationale for the frequent use of reserve antibiotics, including polymyxins and newer β-lactam/β-lactamase inhibitor combinations. The emergence of ceftazidime–avibactam as a treatment option for carbapenem-resistant gram-negative infections represents a notable development in Indian clinical practice. Real-world cohort studies conducted across multiple Indian centers have reported encouraging microbiological response rates and acceptable mortality outcomes among patients treated with ceftazidime–avibactam for carbapenem-resistant infections [18-21]. Although these observational studies cannot provide direct causal comparisons with polymyxin- or carbapenem-based regimens, they suggest that novel β-lactam/β-lactamase inhibitor therapies may represent a promising therapeutic option in settings where resistance mechanisms are compatible.

The results of this study underscore the importance of tailoring empiric antibiotic therapy to local epidemiological conditions. While national surveillance data provide valuable insights into overall resistance trends, empiric treatment decisions should ideally be guided by hospital-specific antibiograms and the clinical context of infection, including whether the infection is community-acquired or hospital-acquired [15]. Early reassessment of empiric therapy based on microbiological results remains essential to minimize unnecessary broad-spectrum antibiotic exposure. Another important finding from the SEPSIS INDIA registry is the association between appropriate empiric antibiotic therapy and improved survival. Empiric therapy that demonstrated in vitro activity against the causative pathogen was independently associated with better outcomes [14]. This observation reinforces the well-established principle that timely administration of effective antimicrobial therapy remains one of the most critical determinants of survival in patients with sepsis [22-35]. Improving access to rapid microbiological diagnostics, strengthening blood culture practices, and implementing antimicrobial stewardship programs are therefore essential strategies for optimizing sepsis management. The use of reserve antibiotics also introduces important safety considerations. Polymyxins, which are frequently employed for multidrug-resistant gram-negative infections, are associated with a substantial risk of nephrotoxicity [36-51]. Similarly, glycopeptides and oxazolidinones used for gram-positive coverage require careful therapeutic monitoring to minimize adverse effects [52]. In many healthcare settings with limited laboratory infrastructure, the implementation of intensive drug monitoring protocols may be challenging. Consequently, stewardship strategies that emphasize appropriate antibiotic selection and early de-escalation remain critical [11]. Economic factors also influence antibiotic selection in many health care systems. Public drug pricing regulations and hospital procurement contracts demonstrate substantial variability in the acquisition costs of different antibiotic classes [19]. However, the acquisition cost alone does not fully capture the economic burden associated with antimicrobial therapy, which also includes monitoring requirements, toxicity management, and prolonged hospitalization due to treatment failure.

At the health system level, the findings highlight the need for stronger integration between antimicrobial resistance surveillance systems and clinical outcome datasets. India currently possesses a valuable national surveillance infrastructure and multicenter clinical registries, such as SEPSIS INDIA. However, these data systems remain largely disconnected, limiting the ability to conduct robust comparative effectiveness research [53]. A potential policy direction is the development of standardized sepsis datasets within hospital electronic health record systems. Such datasets should include key clinical variables, such as the Sepsis-3 diagnostic criteria, antibiotic exposure timing, microbiological susceptibility results, and patient outcomes [8]. Establishing secure mechanisms for multicenter data linkage would enable more comprehensive real-world analyses and facilitate evidence-based antimicrobial policy development. This study has several limitations that should be considered when interpreting the findings. First, the analysis represents a secondary synthesis of previously published registry data, national surveillance reports, and observational clinical cohorts rather than a primary patient-level comparative effectiveness study. As a result, causal inferences regarding the relative effectiveness of specific antibiotic classes cannot be established [54]. Second, the included data

sources vary in scope and methodology. Multicenter clinical registries, antimicrobial resistance surveillance systems, and infection-specific treatment cohorts capture different aspects of sepsis epidemiology and treatment outcomes, which limits direct comparisons across antibiotic strategies [55]. Third, antimicrobial resistance estimates derived from national surveillance reports represent aggregated data and may not fully reflect local resistance patterns in individual hospitals or intensive care units [29]. Finally, economic estimates were derived from publicly available pricing documents and procurement examples and may not represent the full cost of antimicrobial therapy in routine clinical practice [37].

Future research should prioritize multicenter comparative effectiveness studies that integrate clinical data, microbiological results, and pharmacy dispensing records from electronic health record systems. Emulating target trial designs within such datasets may allow for a more robust evaluation of empiric antibiotic strategies while addressing confounding factors related to disease severity and infection source [14]. The development of nationwide multicenter data platforms linking ICU clinical data with antimicrobial resistance surveillance systems would provide a powerful infrastructure for generating high-quality real-world evidence. Such efforts are essential to inform antibiotic stewardship policies and improve clinical outcomes for patients with sepsis in India [56,57].

CONCLUSION

Sepsis management in India is strongly influenced by a resistance landscape dominated by gram-negative pathogens and a high prevalence of carbapenem resistance. Real-world evidence from national registries and antimicrobial surveillance indicates that empiric therapy is frequently carbapenem-based; however, the substantial burden of carbapenem-resistant organisms limits its effectiveness in many clinical settings. The consistent association between appropriate empiric antibiotic therapy and improved survival highlights the importance of timely administration of microbiologically active treatment. Emerging real-world data suggest that novel β-lactam/β-lactamase inhibitor agents may provide valuable therapeutic options for resistant infections. Strengthening antimicrobial stewardship, expanding rapid diagnostic capacity, and integrating surveillance data with clinical outcomes are essential to optimize empiric therapy and improve sepsis outcomes.

DECLARATIONS

None

CONSENT FOR PUBLICATION

The Authors agree to the publication in the Journal of Society Medicine.

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COMPETING INTERESTS

All authors have reviewed and approved the final version of the manuscript and agreed to its publication in the Journal of Society Medicine.

AUTHORS' CONTRIBUTIONS

AKG conceptualized the study and developed the comparative effectiveness research framework. AKG, RKS, and PS contributed to the acquisition and synthesis of real-world data sources, including antimicrobial resistance surveillance reports, multicenter clinical registries, and published treatment cohorts. AKG drafted the initial version of the manuscript. RKS and PS critically reviewed and revised the manuscript for important intellectual content. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work, ensuring the accuracy and integrity of the study.

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