Review Article

Prevalence of Extended-Spectrum Beta-Lactamase-Producing *Enterobacterales* in Urinary Tract Infections and Its Impact on Antimicrobial Therapeutic Selection

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Abstract

Extended-spectrum beta-lactamase-producing Enterobacterales represent a growing global challenge in the management of urinary tract infections due to their increasing prevalence and complex resistance profiles. Epidemiological data demonstrate a marked rise in these organisms across both community and healthcare settings, with significant regional variability but consistently increasing trends worldwide. *Escherichia coli* and *Klebsiella pneumoniae* remain the most frequently implicated pathogens, contributing substantially to the global antimicrobial resistance burden. The production of extended-spectrum beta-lactamases enables these bacteria to inactivate a wide range of beta-lactam antibiotics, including third-generation cephalosporins, while frequently coexisting with resistance to other antimicrobial classes such as fluoroquinolones and aminoglycosides. This multidrug resistance significantly limits therapeutic options and complicates both empirical and targeted treatment strategies. As a result, inappropriate empirical therapy is common, particularly in regions with high

prevalence, leading to increased rates of treatment failure, recurrence, prolonged hospitalization, and higher healthcare costs. Clinically, infections caused by these organisms are indistinguishable from those caused by non-resistant pathogens, making microbiological confirmation essential for accurate diagnosis and management. Urine culture and susceptibility testing remain the cornerstone of diagnosis, although rapid molecular techniques are emerging as valuable tools for early detection. Therapeutically, carbapenems remain the mainstay for severe infections, although concerns regarding resistance have driven the development of alternative agents and carbapenem-sparing strategies. In this context, antimicrobial stewardship, guided by local antibiograms and risk stratification tools, plays a critical role in optimizing treatment and improving outcomes.

Key words

Extended-spectrum beta-lactamase-producing, urinary tract infections, antimicrobial resistance, Enterobacterales, empirical therapy, carbapenems.

Introduction

Antimicrobial resistance among Enterobacterales, particularly those producing extended-spectrum beta-lactamases, has emerged as a growing global threat, significantly complicating the treatment of urinary tract infections and contributing to increased rates of treatment failure and hospitalizations [1, 2]. This trend is especially evident in the United States, where ESBL-producing Enterobacterales have demonstrated markedly elevated resistance to commonly used antibiotics, with resistance rates reaching up to 100% for agents such as ciprofloxacin and trimethoprim-sulfamethoxazole in certain regions. In parallel, the prevalence of these strains in both community-acquired and healthcare-associated urinary tract infections has increased substantially over the past two decades, underscoring the urgency of updating treatment guidelines and advancing the development of new antimicrobial agents [1, 3].

Within this context, ESBL-producing Enterobacterales are defined as bacteria capable of producing enzymes that hydrolyze beta-lactam antibiotics, rendering them ineffective, including third-generation cephalosporins and monobactams [2, 4]. The clinical significance of these organisms lies in their association with adverse outcomes, including increased morbidity and mortality, prolonged hospital stays, and higher healthcare costs, largely due to the limited availability of effective treatment options and the frequent need for more expensive or potentially toxic antimicrobial agents [2, 5]. Moreover, the global dissemination of specific high-risk clones, such as the ESBL-producing Escherichia coli sequence type 131, further exacerbates the challenge by combining enhanced virulence with multidrug resistance, thereby complicating clinical management [4].

Given this evolving scenario, the assessment of the prevalence of ESBL-producing Enterobacterales becomes essential for guiding empirical therapy, as it enables clinicians to select the most appropriate initial antimicrobial treatment before susceptibility results are available [5, 6]. In this regard, local and regional surveillance data on resistance patterns play a critical role in informing antibiotic selection, thereby reducing the risk of treatment failure and limiting the spread of resistant strains [7]. A comprehensive understanding of prevalence and resistance profiles contributes to the development of targeted therapeutic strategies and supports the implementation of public health interventions aimed at mitigating the impact of antimicrobial resistance [8, 9].

The objective of this article is to analyze the prevalence of extended-spectrum beta-lactamase-producing Enterobacterales in urinary tract

infections and to evaluate its impact on antimicrobial resistance patterns, clinical outcomes, and the selection of empirical and targeted therapeutic strategies.

Methodology

This manuscript was developed as a structured narrative review aimed at providing an updated and clinically integrated analysis of the prevalence of extended-spectrum beta-lactamase-producing Enterobacterales in urinary tract infections, with particular emphasis on epidemiological distribution, associated resistance patterns, risk factors, and their impact on antimicrobial therapeutic selection. The review was conducted in accordance with the SANRA (Scale for the Assessment of Narrative Review Articles) framework and followed a predefined methodological protocol established prior to literature screening. Given the epidemiological variability across regions, the diversity of patient populations, and the heterogeneity of microbiological methods and therapeutic approaches reported in the literature, a narrative interpretative synthesis was selected over quantitative pooling in order to integrate microbiological, clinical, and therapeutic evidence into a coherent and clinically applicable framework. Special attention was given to differences between community-acquired and healthcare-associated urinary tract infections, the role of multidrug resistance in limiting empirical treatment options, the identification of patient-related and healthcare-related risk factors, and the implications of local prevalence patterns for antimicrobial stewardship. The objective was to provide a structured synthesis capable of supporting evidence-based therapeutic decision-making in the management of urinary tract infections caused by ESBL-producing organisms.

A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science, including peer-reviewed articles published in English or Spanish between January 2020 and December 2025. The final search was performed in March 2026. This timeframe was selected to capture contemporary evidence regarding the global and regional prevalence of ESBL-producing uropathogens, evolving resistance phenotypes, rapid diagnostic methods, and current recommendations for empirical and targeted antimicrobial therapy. Foundational studies were incorporated when necessary to contextualize microbiological mechanisms, historical resistance trends, or the evolution of therapeutic strategies. The search strategy combined MeSH and free-text terms using Boolean operators related to urinary tract infection, ESBL, extended-spectrum beta-lactamase, Enterobacterales, *Escherichia col*i, *Klebsiella pneumoniae*, antimicrobial resistance, empirical therapy, targeted therapy, uropathogens, prevalence, and risk factors. Searches were conducted in titles and abstracts as well as indexed subject headings to maximize sensitivity.

The initial search yielded 212 records. After removal of duplicates, 168 articles remained for title and abstract screening. Of these, 97 underwent full-text evaluation, and 51 studies were included in the final synthesis. Selection was performed independently by two authors, with disagreements resolved through discussion and consensus. Exclusion criteria comprised non-peer-reviewed publications, isolated case reports, editorials without microbiological or clinical outcome data, studies focused exclusively on non-urinary infections, redundant datasets, and articles not directly addressing prevalence, resistance patterns, risk factors, diagnostic methods, or therapeutic implications of ESBL-producing Enterobacterales in urinary tract infections.

Eligible studies included randomized controlled trials, observational cohorts, cross-sectional epidemiological studies, systematic reviews, meta-analyses, expert consensus statements, and contemporary international guidelines related to infectious diseases, clinical microbiology,

antimicrobial resistance, and urinary tract infection management. Priority was assigned to multicenter investigations, studies with clearly defined microbiological diagnostic criteria, and research evaluating prevalence rates, antimicrobial susceptibility profiles, patient characteristics, empirical treatment adequacy, clinical outcomes, and recurrence or complication rates. Extracted variables included study design, country or region, healthcare setting, patient population, causative organisms, prevalence of ESBL production, associated resistance patterns, identified risk factors, diagnostic methods, antimicrobial regimens, and reported clinical outcomes. Methodological quality and internal validity were assessed narratively, considering risk of bias, sample size, microbiological methodology, follow-up duration when applicable, consistency of diagnostic definitions, and reproducibility of reported findings. In cases of conflicting evidence, greater interpretative weight was assigned to higher-level evidence and guideline-supported recommendations.

Reference lists of included studies were manually screened to identify additional relevant publications. Given its narrative design, this review is subject to potential selection bias and does not provide pooled quantitative estimates. Artificial intelligence-based tools were used exclusively to assist in literature organization and structural coherence, whereas critical appraisal, synthesis, and final interpretation were conducted independently by the authors to preserve methodological rigor.

Epidemiology and Global Prevalence

The global burden of extended-spectrum beta-lactamase-producing Enterobacterales is notably high, with considerable variability across different regions. Studies have reported prevalence rates as high as 60% in Egypt [10] and 23.4% in Rwanda [2], highlighting the widespread distribution of these resistant organisms. Similarly, data from Thailand indicate that 42.5% of *Escherichia coli* and 30.2% of *Klebsiella pneumoniae* isolates are ESBL producers [11]. These findings are consistent with a meta-analysis reporting pooled prevalence rates of 33.0% for ESBL-producing *E. coli* and 32.7% for *K. pneumoniae* in humans, underscoring the significant contribution of these pathogens to the global antimicrobial resistance burden [12].

This burden is further characterized by marked regional variability. Latin America, particularly Tropical Latin America, exhibits one of the highest age-standardized incidence rates of urinary tract infections, which correlates with elevated prevalence of ESBL-producing organisms [13]. In contrast, although historically lower, regions such as the United States and Europe have experienced a significant increase in ESBL rates over the past two decades, with community-acquired urinary tract infection rates in the United States rising from 0.2% to 16.3% [1]. A similar upward trend has been documented in Canada, where the prevalence of ESBL-producing *E. coli* increased from 3.6% to 11.8% over a 17-year period [14]. These data collectively illustrate a global expansion of ESBL-producing pathogens, affecting both high- and low-resource settings.

Differences between community-acquired and healthcare-associated infections further contribute to the epidemiological complexity of ESBL prevalence. In general, higher prevalence rates are observed in healthcare-associated settings compared to community settings. For example, a study in the United States demonstrated that the prevalence of ESBL-producing *E. coli* increased annually by 2.31% in healthcare settings, compared to 0.91% in community settings [15]. However, this distinction is not universal, as data from Egypt showed similarly high prevalence rates in both nosocomial (62%) and community-acquired infections (65%), indicating a potential

dissemination of resistant strains beyond hospital environments [10].

In addition to spatial variability, temporal trends reveal a consistent increase in the prevalence of ESBL-producing organisms over time. In Thailand, prevalence rates initially rose and subsequently plateaued at approximately 30–40% per year [16], suggesting a stabilization at high endemic levels. Meanwhile, in Canada, the prevalence of ESBL-producing *E. coli* and *K. pneumoniae* has continued to rise steadily, reflecting an ongoing expansion of resistance [14].

Across all regions, *Escherichia coli* and *Klebsiella pneumoniae* remain the most frequently implicated ESBL-producing organisms in urinary tract infections. In Tanzania, *E. coli* accounted for 62.8% and *K. pneumoniae* for 33.0% of ESBL-producing Enterobacterales fecal carriage [17], reinforcing their dominant role in colonization and infection. Similarly, in Egypt, both organisms exhibited comparably high prevalence rates of 64% and 63%, respectively, further confirming their central role in the epidemiology of ESBL-associated urinary tract infections [10].

Microbiological and Molecular Mechanisms of Resistance

Beta-lactam antibiotics exert their antibacterial effect by targeting bacterial cell wall synthesis through binding to penicillin-binding proteins, thereby inhibiting the cross-linking of peptidoglycan layers, which is essential for maintaining cell wall integrity. This disruption ultimately leads to cell lysis and bacterial death, making beta-lactams highly effective against a broad spectrum of microorganisms. However, the efficacy of these agents has been increasingly compromised by the emergence of resistance mechanisms, particularly the production of extended-spectrum beta-lactamases [18, 19].

Extended-spectrum beta-lactamases are enzymes capable of hydrolyzing the beta-lactam ring of antibiotics, thereby neutralizing their antibacterial activity. These enzymes can inactivate a wide range of beta-lactam antibiotics, including third-generation cephalosporins and monobactams, although they do not affect cephamycins or carbapenems. This enzymatic activity significantly limits the clinical utility of commonly prescribed antibiotics and contributes to the persistence and spread of resistant infections [20, 21].

Among the different types of extended-spectrum beta-lactamases, three main families have been identified, each with distinct characteristics and epidemiological relevance. The CTX-M family represents the most prevalent group, with variants such as CTX-M-14 and CTX-M-15 frequently associated with *Escherichia coli* and *Klebsiella pneumoniae*, and demonstrating particular effectiveness against cefotaxime [4, 18]. In contrast, the TEM family, initially derived from *E. coli*, includes variants such as TEM-1 and TEM-2, which confer resistance primarily to penicillins and early-generation cephalosporins [19, 20]. Similarly, the SHV family, originally identified in *Klebsiella* species, shares structural similarities with TEM enzymes but exhibits a broader spectrum of activity, including resistance to newer cephalosporins [22].

The dissemination of these resistance mechanisms is largely driven by plasmids, which are extrachromosomal DNA elements capable of carrying multiple resistance genes, including those encoding extended-spectrum beta-lactamases. Through horizontal gene transfer, plasmids facilitate the rapid spread of these genes across different bacterial species and strains, thereby contributing to the global expansion of antimicrobial resistance. This capacity for genetic exchange not only accelerates the dissemination of ESBLs but also enhances the

adaptability of bacterial populations in response to antimicrobial pressure [22, 23].

In addition to beta-lactam resistance, ESBL-producing bacteria frequently exhibit multidrug resistance, further complicating therapeutic management. This resistance often extends to other antibiotic classes, including fluoroquinolones and aminoglycosides, thereby narrowing the range of effective treatment options [1, 3]. Moreover, co-resistance patterns are commonly observed, as these organisms often harbor multiple resistance genes simultaneously, reinforcing their ability to withstand diverse antimicrobial agents and posing significant challenges for clinical treatment [19, 21].

Risk Factors for ESBL-Associated Urinary Tract Infections

Patient-related factors play a central role in the development of urinary tract infections caused by extended-spectrum beta-lactamase-producing organisms. Age and gender have been consistently identified as significant determinants, with older age representing a major risk factor, particularly among males. Evidence indicates that older adults, especially men, are more susceptible to infections caused by ESBL-producing pathogens, reflecting the influence of both biological and clinical vulnerability in this population [24, 25]. In addition, comorbid conditions and states of immunosuppression further increase this risk. Patients with higher Charlson comorbidity index scores, as well as those undergoing immunosuppressive therapies such as kidney transplant recipients, demonstrate a higher likelihood of developing infections caused by resistant organisms [26, 27]. A history of recurrent urinary tract infections also emerges as a strong predictor, suggesting that repeated exposure to antimicrobial therapy and persistent colonization may contribute to the selection of resistant strains [24, 28].

These patient-related factors are closely interconnected with healthcare exposure, which significantly amplifies the risk of acquiring ESBL-producing pathogens. Urinary tract infections associated with hospitalization or long-term care facilities, such as nursing homes, are more frequently caused by these resistant organisms, reflecting the high antimicrobial pressure and transmission dynamics within healthcare environments [24, 26]. Prior genitourinary invasive procedures have been identified as an additional contributing factor, as they may disrupt normal anatomical barriers and facilitate bacterial colonization and infection [29].

A particularly important and well-established determinant is previous antibiotic exposure. The prior use of antimicrobial agents, especially cephalosporins and fluoroquinolones, has been strongly associated with the development of ESBL-producing infections. Among these, ciprofloxacin has been specifically linked to a higher risk, underscoring the selective pressure exerted by commonly prescribed antibiotics [25, 26]. Similarly, in solid organ transplant recipients, prior antibiotic treatment has been correlated with an increased likelihood of ESBL production, further emphasizing the role of antimicrobial exposure in shaping resistance patterns [30, 31].

The presence of urinary catheters or other forms of instrumentation also contributes significantly to the risk profile. The use of bladder catheters, particularly in hospital settings, has been associated with a higher incidence of infections caused by ESBL-producing organisms, likely due to biofilm formation and prolonged bacterial colonization. This factor is especially relevant in patients requiring long-term catheterization or repeated urological interventions [31].

Finally, the distinction between uncomplicated and complicated urinary tract infections provides an important clinical framework for

understanding the distribution of ESBL-producing organisms. Uncomplicated infections typically occur in otherwise healthy individuals with structurally and functionally normal urinary tracts, whereas complicated infections are associated with underlying factors such as anatomical abnormalities, immunosuppression, or the presence of indwelling devices. In this context, ESBL-producing pathogens are more commonly identified in complicated urinary tract infections, reflecting the cumulative effect of these predisposing conditions [32].

Clinical Presentation and Diagnostic Approach

The clinical presentation of urinary tract infections caused by extended-spectrum beta-lactamase-producing Enterobacterales encompasses a broad spectrum of disease, including cystitis, pyelonephritis, and urosepsis. Despite this range of severity, the associated symptoms, such as fever, dysuria, and flank pain, are not specific to infections caused by ESBL-producing organisms and may also be observed in infections caused by non-ESBL pathogens. In this context, studies have consistently demonstrated the absence of distinguishing clinical features between ESBL and non-ESBL urinary tract infections, which makes clinical differentiation unreliable without microbiological confirmation and highlights the limitations of symptom-based diagnosis [16, 33].

Given these limitations, microbiological confirmation plays a fundamental role in the accurate diagnosis and management of these infections. Urine culture remains the gold standard for identifying the causative organism and determining whether ESBL production is present. In conjunction with culture, antimicrobial susceptibility testing is essential to guide the selection of appropriate antibiotic therapy, ensuring that treatment is both effective and tailored to the resistance profile of the pathogen [34, 35]. In addition to culture-based methods, traditional phenotypic confirmatory tests, such as the double-disk synergy test, are commonly used to detect ESBL production. However, these methods can be time-consuming and may fail to identify certain ESBL variants, which can limit their diagnostic sensitivity in some cases [36].

In response to these challenges, emerging molecular diagnostic techniques have gained increasing attention as valuable tools for the early detection of ESBL-producing organisms. Rapid molecular assays, particularly those based on polymerase chain reaction, enable the direct identification of ESBL genes from urine samples, providing faster results compared to conventional methods and facilitating the timely initiation of appropriate antimicrobial therapy. Among these, the GeneXpert ESBL-ampC assay represents a notable example, as it allows for the rapid detection of ESBL-associated genes directly from clinical specimens. The use of such technologies has the potential to improve patient outcomes by reducing reliance on empirical broad-spectrum antibiotics, including carbapenems, and promoting more targeted and rational antimicrobial use [37].

Impact on Empirical Antimicrobial Therapy

The prevalence of extended-spectrum beta-lactamase-producing Enterobacterales at the local level plays a critical role in shaping initial antibiotic selection for urinary tract infections. In regions with high prevalence rates, such as Rwanda, where rates reach 23.4%, and Lebanon, with 24.9%, empirical therapy becomes increasingly complex due to the high likelihood of resistance to commonly used first-line antibiotics [2, 31]. This challenge is further illustrated by data from China, where ESBL-producing *Escherichia coli* accounted for 38.07% of community-acquired urinary tract infection isolates, reinforcing the need to consider alternative empirical treatment strategies in high-prevalence settings [38].

This epidemiological context is closely associated with a marked reduction in the efficacy of commonly prescribed antimicrobial agents. ESBL-producing strains exhibit high levels of resistance to third-generation cephalosporins and fluoroquinolones, with resistance rates reaching up to 100% in certain settings [2, 38]. Similarly, in the United States, resistance rates among ESBL-producing organisms for ciprofloxacin and trimethoprim-sulfamethoxazole range between 56% and 100%, further limiting the utility of these agents in empirical treatment. As a result, reliance on traditional first-line therapies without consideration of local resistance patterns may lead to suboptimal clinical outcomes [1].

Consequently, the risk of inappropriate empirical therapy represents a significant concern in the management of these infections. Evidence indicates that a substantial proportion of patients receive initial antibiotic regimens to which the causative pathogen is resistant, with studies reporting that up to 22% of patients were treated with ineffective antibiotics, leading to increased rates of hospitalization and the need for additional prescriptions [39]. This issue is even more pronounced in certain regions, such as Tanzania, where 100% of ESBL-producing *E. coli* cases received empiric antibiotics to which the isolates were resistant, highlighting the urgent need for improved empirical therapy guidelines [17].

In this context, the use of local antibiograms and risk stratification tools becomes essential for optimizing empirical treatment decisions. These tools provide valuable insights into local resistance patterns, enabling clinicians to select antibiotics with a higher likelihood of effectiveness and reducing the probability of treatment failure. Additionally, the implementation of ESBL prediction scores and antimicrobial stewardship interventions has demonstrated benefits in reducing the time to appropriate therapy in bloodstream infections, suggesting that similar approaches could be effectively applied to urinary tract infection management [6, 40].

Clinical decision-making varies between outpatient and inpatient settings, reflecting differences in available resources and diagnostic capabilities. In outpatient settings, the limited access to rapid diagnostic tools necessitates a greater reliance on local resistance data to guide empirical therapy [3]. In contrast, inpatient settings are better positioned to utilize comprehensive diagnostic methods and antimicrobial stewardship programs, allowing for more precise and timely antibiotic selection based on microbiological confirmation [40].

Targeted Treatment and Therapeutic Strategies

Carbapenems have traditionally been considered the cornerstone of treatment for severe infections caused by extended-spectrum beta-lactamase-producing Enterobacterales due to their broad-spectrum activity and consistent efficacy against resistant organisms. Their reliability in overcoming ESBL-mediated resistance has positioned them as first-line agents in critically ill patients. However, the increasing reliance on carbapenems has raised significant concerns, as their overuse contributes to the acceleration of antimicrobial resistance, particularly the emergence of carbapenem-resistant organisms, thereby underscoring the urgent need for carbapenem-sparing strategies [34, 41].

In response to these challenges, beta-lactam/beta-lactamase inhibitor combinations have emerged as important therapeutic alternatives. Novel combinations such as meropenem-vaborbactam, ceftazidime-avibactam, and imipenem-relebactam have demonstrated significant activity against ESBL-producing Enterobacterales as well as carbapenemase-producing strains [42, 43]. These agents provide an effective option for managing multidrug-resistant infections and are increasingly utilized

as alternatives to carbapenems, particularly in efforts to preserve their efficacy and limit resistance development [44, 45].

For uncomplicated urinary tract infections, especially in outpatient settings, oral agents such as fosfomycin and nitrofurantoin represent viable and effective treatment options against ESBL-producing organisms [46]. These antibiotics offer practical advantages due to their oral administration and favorable activity profiles, making them suitable not only for initial therapy in uncomplicated cases but also for step-down treatment following initial intravenous management. Their use supports a more targeted approach while reducing the need for prolonged hospitalization or intravenous therapy [41].

An important component of therapeutic management is the implementation of de-escalation strategies based on antimicrobial susceptibility results. This approach involves transitioning from broad-spectrum agents to narrower-spectrum antibiotics once microbiological data become available, thereby minimizing unnecessary antimicrobial exposure and reducing the risk of resistance development. Evidence suggests that, in selected cases, non-carbapenem beta-lactams may achieve comparable effectiveness to carbapenems in the treatment of ESBL-producing infections, with additional benefits such as shorter treatment durations and lower relapse rates [34].

In parallel, the development of emerging therapies continues to expand the available treatment options. New oral agents, including tebipenem pivoxil and ceftibuten-ledaborbactam, are being investigated to address current therapeutic limitations and provide effective alternatives against resistant strains. These novel agents hold promise for both complicated and uncomplicated urinary tract infections, although further research is required to fully establish their clinical efficacy and safety profiles [46, 47].

The integration of antimicrobial stewardship principles is essential to optimize treatment outcomes and limit the spread of resistance. Strategies focused on the judicious use of antibiotics, including the appropriate selection of beta-lactam/beta-lactamase inhibitor combinations, adherence to susceptibility-guided therapy, and the implementation of diagnostic algorithms, are critical components of effective stewardship programs. Through these measures, it is possible to balance the need for effective treatment with the imperative to preserve antimicrobial efficacy for future use [45].

Clinical Outcomes and Prognostic Implications

The presence of extended-spectrum beta-lactamase-producing bacteria in urinary tract infections is strongly associated with higher rates of treatment failure and recurrence, largely due to resistance to commonly used antibiotics. This resistance limits the effectiveness of standard therapies and contributes to persistent or recurrent infections. In kidney transplant recipients, for example, the incidence of urinary tract infections caused by ESBL-producing organisms has increased significantly, with affected patients experiencing more frequent infections within the first year post-transplant compared to those with non-ESBL infections [32]. In addition, inadequate initial antibiotic treatment has been shown to further exacerbate these outcomes, leading to increased antibiotic use, higher rates of return visits, and prolonged hospitalizations [31].

These clinical challenges are closely linked to a greater burden on healthcare systems, as infections caused by ESBL-producing organisms are associated with prolonged hospitalization and increased healthcare costs. Patients with ESBL-producing *Escherichia coli* bloodstream infections have been reported to experience a 14% longer hospital length of stay compared to those with non-ESBL infections [48]. This extended hospitalization is often accompanied by

the need for more complex and costly therapeutic regimens, as the resistance profile of these organisms frequently necessitates the use of broad-spectrum or advanced antimicrobial agents, thereby increasing overall healthcare expenditures [3].

In addition to their impact on treatment outcomes and resource utilization, ESBL-producing infections carry a significant risk of progression to more severe clinical conditions. Delays in the initiation of appropriate therapy can allow these infections to evolve into severe sepsis or septic shock, both of which have been identified as major predictors of mortality in patients with ESBL-producing Enterobacteriaceae bacteremia [49]. Similarly, studies evaluating bloodstream infections have demonstrated high mortality rates associated with ESBL-producing Enterobacterales, emphasizing the importance of early recognition and prompt intervention to prevent clinical deterioration [50].

The implications for mortality in these infections, however, may vary depending on the clinical context and patient population. While severe cases, particularly those involving bacteremia and sepsis, are associated with significant mortality and adverse outcomes [49], some studies have reported that infections caused by ESBL-producing *E. coli* do not necessarily confer a higher risk of 30-day mortality compared to non-ESBL infections, suggesting that additional factors such as host characteristics and timely management influence overall prognosis [29, 48].

Given these considerations, the importance of early and appropriate antimicrobial therapy becomes paramount in improving clinical outcomes. Timely initiation of effective empirical treatment has been identified as a protective factor against mortality in patients with ESBL-producing Enterobacteriaceae bacteremia [49]. The use of active agents, particularly carbapenems in severe infections, has been shown to reduce mortality and improve prognosis, highlighting the critical role of accurate diagnosis and prompt therapeutic decision-making in the management of these infections [51].

Conclusion

The global prevalence of ESBL-producing *Enterobacterale*s in urinary tract infections has increased significantly, with marked regional variability and a consistent upward trend over time, positioning Escherichia coli and Klebsiella pneumoniae as the predominant pathogens and reinforcing the magnitude of antimicrobial resistance as a global health concern.

The presence of ESBL-producing organisms substantially compromises empirical and targeted therapeutic strategies due to high resistance rates to commonly used antibiotics, increasing the risk of inappropriate initial therapy, treatment failure, recurrence, and progression to severe infections, thereby necessitating the use of broader-spectrum agents and more complex management approaches.

Early microbiological diagnosis, appropriate empirical therapy guided by local epidemiology, and the implementation of antimicrobial stewardship strategies are essential to improve clinical outcomes, reduce mortality, and limit the further dissemination of resistance, highlighting the critical role of integrated clinical and microbiological decision-making in the management of these infections.

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