IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, June 2026
Impact Factor: 8.2

Extended-Spectrum Beta-Lactamase (ESBL)-Producing Klebsiella pneumoniae in Urinary Tract Infections: Current Challenges and Future Perspectives

Shiva Yadav
M.Sc. Microbiology
Amity University Lucknow Campus, Uttar Pradesh, India

Abstract: *Escherichia coli and Klebsiella pneumoniae are responsible for the majority of urinary tract infections (UTIs). UTIs are among the most prevalent infections in humans globally and therefore pose a significant public health problem (1,2). As a result of its nocturnal position as one of the most important Uropathogen responsible for either community-acquired or hospital-acquired UTIs, Klebsiella pneumoniae is now regarded as a significant medical threat (1). The increasing number of ESBL-producing Klebsiella pneumoniae, especially within the last two decades, has made it increasingly difficult to treat these infections; the number of effective treatment options has diminished due to the emergence of this pathogen, which is resistant to multiple antibiotic classes (2,3). As a result of the resistance exhibited by ESBL-producing Klebsiella pneumoniae to many β-lactam antibiotics in particular, the option of using extended-spectrum cephalosporins and monobactams as treatment options for these infections is significantly reduced (2). Therefore, the increased incidence of morbidity, mortality, and healthcare costs associated with the use of antibiotics to treat UTIs caused by ESBL-producing Klebsiella pneumoniae is due to the fact that ESBLs hydrolyze extended-spectrum cephalosporins and monobactams (3,4). This review will examine the epidemiology, pathogenesis, virulence factors, and mechanisms of ESBL production in Klebsiella pneumoniae UTI infections, discuss patterns of antimicrobial resistance, and summarize the diagnostic and treatment methods and emerging therapeutic alternatives associated with this pathogen(5). The review will also highlight some of the challenges associated with multidrug-resistant strains of Klebsiella pneumoniae causing UTIs and will provide a future perspective on infection control, antibiotic stewardship, and novel therapeutic interventions. An understanding of the evolving resistance of Klebsiella pneumoniae to antibiotics, especially ESBL-producing strains, will be important for the development of appropriate therapeutic strategies to reduce the global impact of antimicrobial resistance and the occurrence of UTIs (4,5).*

Keywords: ESBL, Klebsiella pneumoniae, Urinary Tract Infection, Antimicrobial Resistance, Multidrug Resistance, Antibiotic Stewardship.

I. INTRODUCTION

The prevalence of urinary tract infections (UTIs) globally is high with millions experiencing UTIs yearly. UTIs may affect all areas of the urinary tract such as urethra, bladder, ureters, and kidneys (6,7). Women have a higher propensity to develop UTIs due to their anatomy and physiology (7). Escherichia coli continues to be the most common cause of UTIs; however, Klebsiella pneumoniae has emerged as another important cause of community-acquired and nosocomial infections (1). The emergence of antimicrobial resistance has established K. pneumoniae as a major clinical threat (4,5). Extended-Spectrum Beta-Lactamase (ESBL) production is one mechanism for resistance that has raised

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 4, June 2026 Impact Factor: 8.2

significant concern. K. pneumoniae strains that produce ESBL can hydrolyzed Penicillins, cephalosporins, and aztreonam therefore greatly reducing the therapeutic options available (2,3). The increasing prevalence of ESBL-producing K. pneumoniae strains is also associated with longer hospital stays, increased treatment failure, increased healthcare costs, and increased mortality (3,4). Therefore, it is important to understand the biology, epidemiology, and resistance mechanisms of ESBL-producing K. pneumoniae for the Nitrofurantoin development of effective treatment protocols and organization of infection control programs (5).

II. EPIDEMIOLOGIC DATA RELATED TO ESBL-ASSOCIATED KLEBSIELLA PNEUMONIAE IN THE URINARY TRACT

Urinary tract infections represent an enormous burden on healthcare systems across the globe every year, resulting in millions of visits to doctors and hospitals (6,7). Klebsiella pneumoniae is one of the leading Gram-negative organisms causing both community-acquired and healthcare-associated urinary tract infections (1). The growing number of isolates capable of producing Extended-Spectrum Beta-lactamase (ESBL)-enzymes has complicated the management of patients suffering from these infections because of antibiotic resistance related to multiple drug classes (2,3). Reports of the prevalence of K. pneumoniae capable of producing ESBL vary considerably by location, with low prevalence (generally being reported) in developed countries; however, developing nations generally report much higher prevalence rates due to the overuse of antibiotics, poor infection control practices and limited efforts to engage in antimicrobial stewardship programs (5,12). Tertiary care hospitals often report that a significant percentage of their nosocomial urinary tract infections are due to (or isolated from) patients that have contracted K. pneumoniae isolates capable of producing ESBL (3). There are numerous documented risk factors which contribute to the acquisition of K. pneumonia producing ESBL include: presence of urinary catheters, urinary tract infections (particularly recurrent), prolonged hospitalization, treatment in an intensive care unit, prior antibiotic therapy, presence of diabetic, chronic kidney disease, immunosuppression (e.g. ongoing prednisone therapy and/or chronic corticosteroids), and advanced age (4,5). The spread of these resistant organisms is facilitated through the transfer of plasmids containing resistance genes between populations (4). Additionally, the number of community-acquired infections attributable to K. pneumoniae producing ESBL is growing, indicating that antimicrobial resistance is no longer limited to just healthcare-related infections (3,5).

III. VIRULENCE FACTORS OF KLEBSIELLA PNEUMONIAE

Pathogenicity of Klebsiella pneumoniae is due to various virulent factors that promote bacterial survival, colonization, evasion of host immunity, and invasion of tissues (4,5).

3.1 Capsule Polysaccharide (Capsule):

Capsule is the principal virulent factor of K. pneumoniae; it protects bacterial from phagocytosis and from being killed by the complement system. Hypervirulent strains of K. pneumoniae have thick capsules that increase the organisms pathogenicity (4).

3.2 Lipopolysaccharide (LPS):

LPS protects the bacteria from host immune defence and promotes bacterial growth under conditions of low iron availability (5).

3.3 Fimbriae and Adhesins:

Type I and Type III fimbriae facilitate adherence to uroepithelial cells, through which bacteria can establish infection and develop a biofilm (7).

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, June 2026
Impact Factor: 8.2

3.4 Siderophores:
Siderophores allow the bacteria to acquire iron as an essential nutrient, which enhances bacterial survival and virulence (4).

3.5 Biofilm:
Biofilms are highly organized communities of bacteria embedded in an extracellular matrix, providing persistence of bacteria, providing protection from antibiotics, and contributing to the establishment of recurrent UTIs (4,7).

IV. EXTENDED-SPECTRUM BETA-LACTAMASES (ESBLS)

ESBLs are enzymes that can hydrolyze many different types of β-lactam antibiotics including third generation cephalosporins and monobactams. The first discovery of an ESBL occurred in the 1980's when mutations of traditional TEM and SHV type beta-lactamases occurred (2). Since this time many different subtypes of ESBLs have emerged all over the world (3).

4.1TEM type ESBLs
TEM is one of the first identified ESBLs. TEM-1 and TEM-2 through mutation could hydrolyze larger numbers of β-lactam antibiotics allowing K. pneumoniae and other bacterial pathogens to become resistant to extended spectrum cephalosporins (2,13).

4.2SHV type ESBLs
SHV type ESBLs have been found to be most often associated with K. pneumoniae. Different subtypes of SHV ESBLs have been developed and have hydrolytic activities that are much higher than the older generation types of cephalosporins (i.e., third generation cephalosporins) (2,14).

4.3CTX-M type ESBLs
CTX-M type ESBLs have become the most prevalent family of ESBLs worldwide and have spread rapidly through plasmid-mediated gene transfer and successful clones of bacteria(3,13). The numbers of strains producing CTX-M ESBLs are increasing rapidly and changing the epidemiology of antimicrobial resistance and drastically reducing treatment options for urinary tract infections (UTIs) (3,14).

V. MECHANISMS OF ANTIMICROBIAL RESISTANCE

Antimicrobial resistance in Extended Spectrum Beta-Lactamases (ESBL)-producing Klebsiella pneumoniae results from various molecular mechanisms working synergistically to decrease the effectiveness of antibiotics (2,13).

5.1 Enzymatic Inactivation
ESBL-producing bacteria can inactivate β-lactam antibiotics by hydrolysis (removing the β-lactam ring) prior to reaching the target of action, thus rendering antibiotic therapy ineffective (2,13).

5.2 Mediated Efflux of Antibiotics:
Efflux pumps transport antibiotics out of the bacterial cell, thereby lowering intracellular levels of antibiotics (13).

5.3 Loss of Porins:
Changes to or loss of the outer membrane porins on the bacteria lead to decreased penetration of antibiotics into the bacterial cell (13).

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, June 2026
Impact Factor: 8.2

5.4 Biofilm-Mediated Resistance:

Biofims limit the diffusion of antibiotics into the surrounding area and create microenvironments conducive to the survival of the bacteria (4,7).

5.5 Horizontal Gene Transfer:

Resistance genes are most commonly located on plasmids, transposons, and integrons, which allow for the rapid transmission of resistance genes between bacterial strains (4,5).

VI. LAB TESTS TO DIAGNOSE ESBL-CREATING KLEBSIELLA PNEUMONIAE

Rapid and accurate lab tests are needed to confirm the presence of ESBL-producing Klebsiella pneumoniae so proper treatment (antimicrobial therapy) and infection control can happen. The use of traditional microbiological methods for diagnosis continues as the main form of identification for detection of the resistance genes but newer molecular methods can be used for very rapid identification as well (6,7).

6.1 Urine Culture

Urine Culture is considered to be the “gold standard” of detecting K. pneumoniae infection in the urinary tract. In clean-catch urine specimens, significant bacteriuria is defined as $\geqslant 10^5$ colony forming units (CFU)/mL (8).

6.2 Phenotypic Identification

K. pneumoniae forms large mucoid colonies that ferment lactose on MacConkey Agar. To biochemically identify K. pneumoniae the organism must be positive for citrate utilization, produce urease, and have a positive Voges-Proskauer Reaction. Indole testing is negative (9).

6.3 Antimicrobial Susceptibility Testing

The Kirby-Bauer disk diffusion method and automated methods are routinely used to determine the susceptibility patterns of bacteria to various antibiotics. These tests are reported according to the Clinical and Laboratory Standards Institute (CLSI) criteria (10).

6.4 ESBL Detection Methods

Phenotypic confirmation of ESBL production is usually performed through the use of the combination disk test and the double-disk synergy test. Molecular methods such as polymerase chain reaction (PCR) can be used to identify the ESBL genes, including blaTEM, blaSHV, and blaCTX-M (11).

VII. PATTERNS OF ANTIMICROBIAL RESISTANCE

ESBL-producing K. pneumoniae displays resistance against a number of antibiotic classes, thereby severely limiting the number of possibilities for treating these infections. Resistance rates are determined by location and are influenced by local practices regarding the prescription of antibiotics (12,13). Third-generation cephalosporins, such as cefotaxime, ceftriaxone, and ceftazidime, have especially high rates of resistance because of the hydrolytic enzyme activity of ESBL (14). Resistance to fluoroquinolones is common as well; this is because ESBL genes are often found together with plasmid-mediated quinolone resistance determinants (15). Resistance to aminoglycosides is also increasing due to the acquisition of aminoglycoside-modifying enzymes and 16S rRNA methylases (16). Another major threat is the rise of carbapenem-resistant K. pneumoniae (CRKP), as carbapenems are frequently used as the last option to treat ESBL infections (17).

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, June 2026
Impact Factor: 8.2

Table 1 Common Resistance Profile of ESBL- Producing K. pneumoniae

Antibiotic class	Common Drugs	Resistance Trend
Penicillin	Ampicillin	Very High
Cephalosporins	Cefotaxime, Ceftriaxone	Very High
Fluroquinolones	Ciprofloxacin	High
Aminoglycosides	Gentamicin	Moderate to High
Carbapenems	Imipenem, Meropenem	Increasing
Nitrofurantoin	Nitrofurantoin	Variable
Fosfomycin	Fosfomycin	Relatively low

VIII. MANAGEMENT OF URINARY TRACT INFECTIONS (UTIS):

UTIs caused by ESBL-producing K. pneumoniae continue to be difficult to treat due to the limited number of options and the increased level of multidrug resistance (18).

8.1 Carbapenem antibiotics

Meropenem, imipenem, and ertapenem are examples of carbapenem antibiotics that are recommended for the treatment of severe infections associated with ESBL as they have broad-spectrum killing ability and are stable to the action of the ESBL enzymes (19).

8.2 ß-Lactam/ß-Lactamase inhibitor combinations

Piperacillin-tazobactam is an example of an agent that can be used in some cases as a treatment option for ESBL infections where susceptibility testing has been performed and the organism is susceptible to the drug (20).

8.3Fosfomycin

Fosfomycin has been shown to have good activity against multidrug-resistant urinary pathogens, and is commonly utilized in the treatment of uncomplicated UTIs (21).

8.4 Nitrofurantoin

Nitrofurantoin remains an appropriate treatment for uncomplicated lower UTIs as it achieves high urinary concentrations, and resistance rates are relatively low (22).

8.5Combination therapy

Combination therapies are being investigated to improve antibiotic efficacy and decrease the potential for the development of resistance from multidrug-resistant organisms (23).

IX. THERAPEUTIC APPROACHES ON THE RISE – THE FUTURE OF TREATMENT FOR K. PNEUMONIAE (ESBLS)

Antimicrobial resistance (AMR) is rampant and has sparked a wave of new research development into alternative and novel treatment options for ESBL-producing K. pneumoniae (24).

9.1 Phage Therapy

Bacteriophages specifically attack bacterial pathogens and have shown strong efficacy against multidrug-resistant K. pneumoniae (25).

9.2 Antimicrobial Peptides

Antimicrobial peptides disrupt the bacteria's membrane and could potentially replace traditional antibiotics (26).

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, June 2026
Impact Factor: 8.2

9.3 CRISPR/Cas Technology

CRISPR systems enable selection and destruction of resistance genes from bacterial strains (27).

9.4 Nanotechnology

Nanoparticles can improve antimicrobial delivery and increase antibacterial efficacy against resistant biofilm (28).

9.5 Vaccines

There are more than several vaccine candidates that target capsular polysaccharides and virulence factors currently in development (29).

X. CONCLUSION

Klebsiella pneumoniae that produce extended-spectrum beta-lactamase (ESBL) have become increasingly prevalent among the most important pathogens causing urinary tract infections (UTIs). The emergence of these strains poses a serious threat to healthcare systems worldwide. The growing number of ESBL-producing strains has made many of the antibiotics (especially β-lactam antibiotics) that are commonly used to treat UTIs less effective. This has resulted in a higher incidence and duration of treatment failures, longer hospital stays, higher healthcare costs and increased rates of morbidity and mortality. K. pneumoniae can acquire and transmit resistance genes via mobile genetic elements and can persist and cause infections with the contributions of multiple virulence factors (capsule, biofilm, adhesin and siderophore production) (3,4,17). The further emergence of multidrug-resistant (MDR) and carbapenem-resistant K. pneumoniae has created additional challenges in treating UTIs and reduced the number of effective medications available for use in these infections. To provide appropriate clinical care and prevent the spread of these organisms, accurate laboratory diagnosis, ongoing tracking of patterns of antimicrobial resistance, and adherence to evidence-based susceptibility testing principles are necessary (10,18). The most commonly used drug to treat severe ESBL-associated infections continues to be carbapenems. However, the increasing frequency of carbapenem-resistant strains of K. pneumoniae underscores the need for the development of alternative therapies and more judicious use of antibiotics (19). Newer approaches to treating

K. pneumoniae infections include the use of bacteriophages, antimicrobial peptides, CRISPR-Cas-based technologies and nanotechnology-based antimicrobials.

REFERENCES

1. Podschun R, Ullmann U. Klebsiella spp. as nosocomial pathogens. Clin Microbiol Rev. 1998;11(4):589–603.
2. Paterson DL, Bonomo RA. Extended-spectrum beta-lactamases: a clinical update. Clin Microbiol Rev. 2005;18(4):657–686.
3. Pitout JD, Laupland KB. Extended-spectrum beta-lactamase-producing Enterobacteriaceae. Lancet Infect Dis. 2008;8(3):159–166.
4. Wyres KL, Holt KE. Klebsiella pneumoniae population genomics and antimicrobial-resistant clones. Nat Rev Microbiol. 2018;16(6):344–357.
5. Navon-Venezia S, Kondratyeva K, Carattoli A. Klebsiella pneumoniae: a major worldwide source and shuttle for antibiotic resistance. FEMS Microbiol Rev. 2017;41(3):252–275.
6. Gupta K, Hooton TM, Naber KG, et al. Clin Infect Dis. 2011;52(5):e103-e120.
7. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Nat Rev Microbiol. 2015;13(5):269-284.
8. Stamm WE. Ann Intern Med. 1982;97(5):709-714.
9. Winn W, Allen S, Janda W, et al. Koneman's Color Atlas and Textbook of Diagnostic Microbiology. 7th ed. 2017.
10. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing. CLSI; 2024.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, June 2026
Impact Factor: 8.2

11. Paterson DL. Clin Microbiol Rev. 2005;18(4):657-686.
12. WHO. Global Antimicrobial Resistance Surveillance System Report. 2024.
13. Bush K, Bradford PA. Cold Spring Harb Perspect Med. 2020;10:a025247.
14. Rawat D, Nair D. J Glob Infect Dis. 2010;2(3):263-274.
15. Jacoby GA. Clin Infect Dis. 2005;41(Suppl 2):S120-S126.
16. Ramirez MS, Tolmasky ME. Drug Resist Updat. 2010;13(6):151-171.
17. Logan LK, Weinstein RA. J Infect Dis. 2017;215(Suppl 1):S28-S36.
18. Tamma PD, Rodriguez-Bano J. Clin Microbiol Rev. 2017;30(2):440-458.
19. Harris PNA, Tambyah PA, Paterson DL. Int J Antimicrob Agents. 2015;45(5):457-463.
20. Rodriguez-Bano J, Navarro MD, Retamar P, et al. Clin Infect Dis. 2012;54(2):167-174.
21. Falagas ME, Vouloumanou EK, Samonis G, Vardakas KZ. Lancet Infect Dis. 2016;16(1):43-54.
22. Huttner A, Kowalczyk A, Turjeman A, et al. Clin Microbiol Infect. 2018;24(4):355 362.
23. Paul M, Daikos GL, Durante-Mangoni E, et al. Clin Microbiol Infect. 2018;24(9):937-944.
24. Aslam B, Wang W, Arshad MI, et al. Front Microbiol. 2018;9:2066.
25. Kortright KE, Chan BK, Koff JL, Turner PE. Cell Host Microbe. 2019;25(2):219-232.
26. Mookherjee N, Anderson MA, Haagsman HP, Davidson DJ. Nat Rev Drug Discovery 2020;19(5):311-332.
27. Bikard D, Barrangou R. Nat Biotechnol. 2017;35(12):1140-1148.
28. Baptista PV, McCusker MP, Carvalho A, et al. Front Microbiol. 2018;9:1441.
29. Feldman MF, Mayer Bridwell AE, Scott NE, et al. Proc Natl Acad Sci USA. 2019;116(37):18655-18663.