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Article

Comparative Efficacy of Third and Fourth-Generation Cephalosporins against *Escherichia coli* and *Klebsiella pneumoniae* Isolates from Recurrent Urinary Tract Infections in Al-Najaf Province

Enas Jalil Baqer Al-Mayali*[1], Taghreed F. Almahbobi[2]

1,2. Faculty of Medicine, Jabir Ibn Hayyan University for Medical and Pharmaceutical Researches, Iraq
* Correspondence: enas.j.baqir@jmu.edu.iq

Abstract: Urinary Tract Infection (UTI) Urinary tract infections are among the most common infections worldwide. They are most often caused by bacteria entering the urethra from the skin or rectum. The most common bacterial causes of UTIs worldwide are *Escherichia coli* and *Klebsiella pneumoniae*, and women and the elderly are most affected. In recent years, these two bacteria have become more resistant to traditional antibiotics due to the production of enzymes ESBL that make them difficult to treat. This study included two main axes, the first was the isolation of *Escherichia coli* and *Klebsiella pneumoniae* from the urine of patients suffering from recurrent urinary tract infections, the second axis includes a study of the effect of the cephalosporin group commonly used in hospitals to treat urinary tract infections. Within the framework of this study, (31) isolates of *Escherichia coli* and (17) isolates of *Klebsiella pneumoniae* were isolated from a group of patients with recurrent urinary tract infections. After conducting a sensitivity test for the isolates in this study using a group of generations of Cephalosporin, which are widely used in hospitals, they showed high resistance to most generations. *E. coli* showed high resistance to ceftriaxone at a rate of 93.5%, followed by Cefepime 87.1%, Cefdinir 74.2%, Cefixime 64.5%. While *Klebsiella pneumoniae* gave higher resistance to cefixime 88%, followed by Cefdinir 87.5%, Ceftriaxone 87.5%, Cefepime 76.4%. Therefore, caution should be exercised when using these treatments excessively, especially in cases of recurrent infections and the use of alternative treatments to reduce resistance.

Keywords: rUTI, Cephalosporins, E. *coli*, *Klebsiella pneumonia*

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1. Introduction

Urinary tract infections are the most prevalent infections worldwide, placing a significant financial burden on patients and healthcare systems [1]. The most common bacterial cause responsible for most UTIs is *E. coli*, followed by *Klebsiella pneumoniae*, *Staphylococcus saprophyticus*, *Pseudomonas aeruginosa*, and *Proteus*. This infection is common among people, and almost everyone may experience it at least once in their lifetime. Therefore, it is one of the most common diseases for which patients visit hospitals and medical clinics, and it affects all age groups [2].

Recurrent Urinary Tract Infections (UTIs) are more common in women and are defined as occurring more than once every six months or three times a year. Urinary tract infection is defined as the presence of more than 100,000 colonized bacterial units (CFU) in

a urine sample, accompanied by health problems for the patient, including difficulty urinating, or an urgent need to urinate and pain during urination [3].

Complicated urinary tract infections are a type of infection that occurs as a result of treatment failure. These infections are not simple; they may be due to other factors that make treatment more difficult, such as the presence of kidney or ureter stones, chronic diseases such as diabetes, weak immunity, or high resistance to antibiotics by bacteria. Therefore, a longer period of treatment is required, or alternative antibiotics may be used due to high resistance, or additional tests may be performed to ensure that the infection has been completely eradicated [4].

E. coli a major cause of many intestinal and systemic infections in humans, and UPEC is a major pathogen in UTIs [5]. UPEC is one of the major causes of community-acquired (80–90%) and hospital-acquired (30–50%) urinary tract infections, pathogenic strains always contain multiple virulence factors that help them establish infection. These may include substances that aid adhesion, secrete toxins, or mechanisms that help them evade the body's immune system [6]. UTIs that are acquired in hospitals or in the community are often caused by the clinically significant bacteria *Klebsiella pneumoniae* [7]. *E. coli and Klebsiella pneumoniae* are among the most important Gram-negative bacteria that are normal commensals in the human gastrointestinal tract but they are the most common cause of hospital-acquired infections, including diarrhea and UTIs [8].

Cephalosporins are a group of antibiotics derived from the mold Cephalosporium. They are bactericidal, similar to penicillins, by damaging the cell wall by binding to the enzymes responsible for synthesizing peptidoglycan, it is responsible for building the cell wall of bacteria [9].

Third-generation cephalosporins (such as ceftriaxone and ceftazidime) are broad-spectrum antibiotics. They are more effective against gram-negative bacteria and more stable against beta-lactamases than previous generations. Although less effective against some gram-positive bacteria, they remain a popular choice for empiric treatment of many infections [10]. While maintaining their third-generation gram-negative action, fourth-generation cephalosporins (like cefepime) also exhibit enhanced gram-positive activity. Cefepime is used to treat serious infections such sepsis, meningitis, abdominal infections, and intensive care unit pneumonia because it is effective in contradiction of a many type of Gram-positive and Gram-negative germs [11].

Objective of the study

This study aims to assess the success of commonly used cephalosporin generations in hospitals against *Klebsiella pneumoniae* and *Escherichia coli* insulated from recurrent urinary tract infections.

2. Materials and Methods

Specimens collection

The collection of study samples has taken place at the period between December 2024 to June 2025, from several patients suffering from recurrent urinary tract infections from different hospitals and medical clinics in the governorate.

Diagnosis of isolates

Initially, traditional media used to diagnose Gram-negative bacteria, namely MacConkey agar, were used to study their morphological characteristics and isolate them, in addition to using the IMViC test to differentiate between species.

Antibiotic sensitivity

In this cross-sectional study, all identified isolates of *E. coli* and *Klebsiella pneumoniae* were subjected to susceptibility testing on Mueller-Hinton agar medium and using different types of 3- and 4-generation cephalosporins for comparison , cefdinir-3CG (30

μg), ceftriaxone-3CG (30 μg), Cefixime-3CG (30 μg), Cefepime- 4CG (30 μg) by the disc spread method and measurement method.

3. Results

Study samples description

More than 120 samples are collected from patients with recurrent urinary tract infections of both sexes and all age groups. These samples were distributed among 70 adult women, 30 adult men, and 20 children under the age of 12. These isolates were diagnosed using Gram staining, phenotypic culture, and biochemical tests, only 11 samples had no bacterial growth, While the isolates that contained bacterial growth were 109, the percentage of *E. coli* among them was 28.44%, and *Klebsiella pneumoniae* was 15.6%. The following Table shows the distribution of isolates diagnosed for *E. coli* and *Klebsiella pneumoniae* for the groups used in this study (sex, age).

Table 1. Distribution of patient isolates by sex and age.

Type (bacteria)	Adult women N=(70)	Adult men N=(30)	Children N=(20)	Total
E. coli	20	7	4	31
Klebsiella pneumoniae	13	2	2	17

Antibiotics susceptibility of *Escherichia coli* to Cephalosporin Generation.

In this cross-sectional study, a total of 31 isolates *E. coli* were collected and antimicrobial resistances to Cephalosporins (Cefdinir, ceftriaxone, Cefixime, Cefepime) were evaluated by disc diffusion method on Mueller–Hinton agar. Results were evaluated based on standards book CLSI (2024).

The highest resistance was recorded to ceftriaxone, at 93.5%, while the lowest resistance was to cefixime, at 64.5%. High resistance rates were also recorded to cefepime and cefdinir, at 87.1% and 74.2%, respectively, as shown in Table 2.

Table 2. Antibiotic susceptibility test to *Escherichia coli* isolated from clinical samples (n= 31).

Antibiotic	Generation	Antibiotic sensitive test result			Resistant (%)
		R	I	S	
Cefdinir	Third	23	4	4	74.2%
Ceftriaxone	Third	29	0	2	93.5%
Cefixime	Third	20	10	1	64.5%
Cefepime	Fourth	27	3	1	87.1%

Antibiotics susceptibility of *Klebsiella pneumoniae* to Cephalosporins Generation.

In this cross-sectional study, a total of 17 isolates *Klebsiella pneumoniae* were collected and antimicrobial resistances to Cephalosporins (Cefdinir, Ceftriaxone, Cefepime, Cefixime) were evaluated by disc diffusion method on Mueller–Hinton agar, results were evaluated based on standards book (CLSI 2024), and gave resistance to it (87.5%, 87.5%, 67.4%, 88.2%) respectively. As show in Table 3.

Table 3. Antibiotic susceptibility test to *Klebsiella pneumoniae* isolated from urinary tract samples (n= 17).

Antibiotic	Generation	Antibiotic sensitive test result			Resistant (%)
		R	I	S	
Cefdinir	**Third**	**14**	**0**	**3**	**87.5%**
Ceftriaxone	Third	14	2	1	87.5%
Cefixime	Third	15	1	1	88.2%
Cefepime	Fourth	13	0	4	76.4%

4. Discussion

In this study of ours, thirty-one *E. coli* isolates are isolated, twenty of which were from women suffering from recurrent urinary tract infections, while seventeen *Klebsiella pneumoniae* isolates were isolated, thirteen of which were also from women suffering from recurrent urinary tract infections. This shows that the largest number of isolates were from women. This is consistent with several other studies that have reported that *E. coli* and *Klebsiella pneumoniae* play a role in urinary tract infections including, *Escherichia coli* is certainly the most frequent bacterium that causes urinary tract infections in women. Approximately 74% of urine tests for illnesses show it [12,13]. *Proteus mirabilis* (5%), *Staphylococcus saprophyticus* (2%) and *Klebsiella pneumoniae* and *enterococci* (5% each) are other prevalent infections [12], [13].

Urinary tract infections are on the rise worldwide, particularly in women, particularly with recurrent infections occurring every three months in 80% of cases, often due to sexual activity or diabetes [14]. In order to pass on a disease in the urinary tract, UPEC strains of *Escherichia coli* deviate from their commensal position as intestinal flora, develop and continue there, and display a wide range of virulence characteristics. These *E. Coli* strains are known as UPEC and are frequently linked to uropathogenicity [15].

In another study conducted in India in 2025, it was stated that recurrent urinary tract infections (rUTIs) are strongly linked to an imbalance in the gut microbiome (the gut-bladder axis), particularly a lack of butyrate-producing bacteria. Antibiotics worsen this dysbiosis and fuel antimicrobial resistance (AMR). The gut-vagina and vagina-bladder axes also contribute by transferring pathogens and modulating immune responses. Factors like hormonal changes in pregnant women and adolescents further increase risk. Understanding these microbial pathways is key to developing future non-antibiotic treatments [16].

E. coli contains many virulence factors that make it pathogenic. These factors are separated into two types: cell surface structures and secreted virulence factors. Surface structures are usually pili that help adhere to the host cell surface. This is considered the first step in infection, followed by tissue invasion, which is very important in causing urinary tract infections caused by UPEC and the formation of mucous membranes. Other surface factors include flagella and other surface proteins. As for secreted factors, hemolysin and siderophores, they are important for bacterial colonization and survival despite the body's defenses [17], [18]. *K.pneumoniae* has many virulence factors, including those that help it adhere like a capsule, and other secreted factors such as toxins, in addition to ways of taking up iron, which enables it to remain alive and stabilize the infection during infection [19]. This is consistent with a study in Mosul, Iraq, where the highest rate of *E. coli* bacteria causing urinary tract infections was recorded at 51.94% [20].

In this study, sensitivity testing for third- and fourth-generation cephalosporins, which are widely used in hospitals, was investigated. The results showed high rates of resistance, which led to recurrent cases of infection. This is consistent with another study in Baghdad, Iraq, which recorded high resistance frequency to ceftriaxone and cefepime

treatment for *E. coli* and *Klebsiella pneumoniae* isolated from blood bacteria, at 84% and 90%, 80% and 90%, respectively [21].

Another study recorded high resistance frequency to 3-generation cephalosporin antibiotics in *E. coli* cultured from urinary tract infections. This is due to their production of multiple extended-spectrum beta-lactamases, which severely limits the effectiveness of treatment [22]. Beta-lactam resistance is associated with the making of diverse types of beta-lactamases. Amid the genes often found on plasmids are those encoding several types of beta-lactamases (bla genes) [23].

Another recent study in Algeria reported a rise in the number of *E. coli* affecting urinary tract infections that are resistant to 3-generation cephalosporins and other antibiotics as a result of their possession of many broad-spectrum beta-lactamase enzymes. Therefore, *E. coli* has become responsible for recurrent urinary tract infections [24]. In another study conducted in Sudan in 2020, it was recorded that *E. coli* and *Klebsiella pneumoniae* possessed a high percentage of ESBL genes, which made them resistant to enormous number of antibiotics [25].

The World Health Organization stated that the most common pathogens in the world are *E. coli* and *Klebsiella pneumoniae*, as they play a major role in infections including bloodstream infections, pneumonia, and urinary tract infections. Since most of these isolates contain broad-spectrum beta-lactamase enzymes, they are resistant to many antibiotics, including the cephalosporin family [26].

5. Conclusion

Based on the current findings, it can be said that foliar spraying with ascorbic acid and applying nitrogen fertiliser to the soil had a positive impact on improving the vegetative growth parameters of wheat (*Triticum aestivum L.*, var. Abu Ghraib) cultivated in sandy loam soil. Plant height, leaf count, and flag leaf area were all significantly and successfully increased by foliar spraying with ascorbic acid. In a same vein, nitrogen fertilisation improved vegetative development characteristics, especially heightening plants. More significantly, the study found that the two factors had an integrative and synergistic effect, with the combined impacts of foliar spraying and nitrogen fertilisation outperforming the effects of each element alone . This was clearly demonstrated by the treatment that combined the highest nitrogen level (100 kg $N \cdot ha^{-1}$) with the highest concentration of ascorbic acid (500 $mg \cdot L^{-1}$), which recorded the best performance and highest values for all studied traits without exception. Therefore, it is concluded that adopting an integrated approach that combines soil mineral nutrition with the application of foliar biostimulants represents an effective and recommended strategy for maximizing vegetative growth and improving the overall performance of wheat plants under the experimental conditions.

REFERENCES

[1] X. Yang, H. Chen, Y. Zheng, S. Qu, H. Wang, and F. Yi, "Disease burden and long-term trends of urinary tract infections: A worldwide report," *Front. Public Health*, vol. 10, p. 888205, 2022.

[2] S. Biswas, R. Rana, M. Bal, S. Pati, M. Suar, and M. Ranjit, "Escherichia coli associated urinary tract infection: Epidemiology and possible strategies for control," *One Health Bull.*, vol. 5, no. 2, pp. 51–57, 2025.

[3] N. Aggarwal and S. W. Leslie, "Recurrent Urinary Tract Infections," in *StatPearls* [Internet]. Treasure Island, FL: StatPearls Publishing, Jan. 2025. [PMID: 32491411].

[4] A. Sabih and S. W. Leslie, "Complicated Urinary Tract Infections," in *StatPearls* [Internet]. Treasure Island, FL: StatPearls Publishing, Dec. 2024–Jan. 2025. [PMID: 28613784].

[5] A. O. Hassan, B. O. Ojo, and A. O. Abdulrahman, "Escherichia coli as a global pathogen," *Funksec Here*, vol. 3, no. 1, pp. 239–260, 2021.

[6] R. Kucheria, P. Dasgupta, S. Sacks, M. Khan, and N. Sheerin, "Urinary tract infections: new insights into a common problem," *Postgrad. Med. J.*, vol. 81, no. 952, p. 83, 2005.

[7] C. Caneiras, L. Lito, J. Melo-Cristino, and A. Duarte, "Community- and hospital-acquired Klebsiella pneumoniae urinary tract infections in Portugal: virulence and antibiotic resistance," *Microorganisms*, vol. 7, no. 5, p. 138, 2019.

[8] Y. Mouanga-Ndzime, C. Bisseye, N. M. Longo-Pendy, M. Bignoumba, A. C. Dikoumba, and R. Onanga, "Trends in Escherichia coli and Klebsiella pneumoniae urinary tract infections and antibiotic resistance over a 5-year period in southeastern Gabon," *Antibiotics*, vol. 14, no. 1, p. 14, 2024.

[9] W. C. Hsieh and S. W. Ho, "Evaluation of antibacterial activities of cephalosporin antibiotics: cefazolin, cephaloridine, cephalothin, and cephalexin," *Chin. J. Microbiol.*, vol. 8, no. 1, pp. 1–11, 1975.

[10] D. B. Sunjaya, R. J. Lennon, V. H. Shah, P. S. Kamath, and D. A. Simonetto, "Prevalence and predictors of third-generation cephalosporin resistance in the empirical treatment of spontaneous bacterial peritonitis," *Mayo Clin. Proc.*, vol. 94, no. 8, pp. 1499–1508, Aug. 2019.

[11] A. E. Maraolo, M. Cascella, S. Corcione, A. Cuomo, S. Nappa, G. Borgia, … and I. Gentile, "Management of multidrug-resistant Pseudomonas aeruginosa in the intensive care unit: state of the art," *Expert Rev. Anti-Infect. Ther.*, vol. 15, no. 9, pp. 861–871, 2017.

[12] A. Klingeberg, N. Willrich, M. Schneider, G. Schmiemann, I. Gágyor, D. Richter, … and T. Eckmanns, "The Percentage of Antibiotic Resistance in Uncomplicated Community-Acquired Urinary Tract Infections: Findings of the RedAres Project," *Dtsch. Ärztebl. Int.*, vol. 121, no. 6, p. 175, 2024.

[13] G. Schmiemann, A. Greser, A. Maun, J. Bleidorn, A. Schuster, O. Miljukov, … and I. Gágyor, "Effects of a multimodal intervention in primary care to reduce second line antibiotic prescriptions for urinary tract infections in women: parallel, cluster randomised, controlled trial," *BMJ*, vol. 383, 2023.

[14] F. L. Turcu, I. A. Vacaroiu, A. E. Balcangiu-Stroescu, A. R. Mitrea, D. Miricescu, D. G. Balan, and A. M. Stanigut, "Recurrent Urinary Tract Infections in Female Patients—A Clinical Review," *J. Mind Med. Sci.*, vol. 12, no. 1, p. 5, 2025.

[15] B. Foxman, R. Barlow, H. D'Arcy, B. Gillespie, and J. D. Sobel, "Urinary tract infection: self-reported incidence and associated costs," *Ann. Epidemiol.*, vol. 10, no. 8, pp. 509–515, 2000.

[16] S. Bhuiya, S. Kaushik, J. Logheeswaran, P. Karthika, R. Prathiviraj, J. Selvin, and G. S. Kiran, "Emergence of recurrent urinary tract infection: Dissecting the mechanism of antimicrobial resistance, host-pathogen interaction, and hormonal imbalance," *Microb. Pathog.*, p. 107698, 2025.

[17] L. Emody, M. Kerenyi, and G. Nagy, "Virulence factors of uropathogenic Escherichia coli," *Int. J. Antimicrob. Agents*, vol. 22, pp. 29–33, 2003.

[18] M. A. Vagarali, S. G. Karadesai, C. S. Patil, S. C. Metgud, and M. B. Mutnal, "Haemagglutination and siderophore production as the urovirulence markers of uropathogenic Escherichia coli," *Indian J. Med. Microbiol.*, vol. 26, no. 1, pp. 68–70, 2008.

[19] C. Hennequin and F. Robin, "Correlation between antimicrobial resistance and virulence in Klebsiella pneumoniae," *Eur. J. Clin. Microbiol. Infect. Dis.*, vol. 35, no. 3, pp. 333–341, 2016.

[20] R. N. Al-Zidan, S. M. Mahmood, and Z. M. Younus, "The antibiotic susceptibility patterns of uropathogens among adults with recurrent urinary tract infection in Mosul, Iraq," *Pharmakeftiki*, vol. 36, no. 2, 2024.

[21] J. H. Al-Eqaby, A. H. Al-Charrakh, and A. A. Mustafa, "Resistance to third-generation cephalosporins among hospitalized patients with monomicrobial Enterobacteriaceae bacteremia (mEB) in Baghdad, Iraq," *J. Pharm. Negat. Results*, vol. 13, no. 8, pp. 1–9, 2022.

[22] A. Chander and C. D. Shrestha, "Prevalence of extended spectrum beta lactamase producing Escherichia coli and Klebsiella pneumoniae urinary isolates in a tertiary care hospital in Kathmandu, Nepal," *BMC Res. Notes*, vol. 6, no. 1, p. 487, 2013.

[23] W. Adamus-Białek, A. Baraniak, M. Wawszczak, S. Głuszek, B. Gad, K. Wróbel, … and P. Parniewski, "The genetic background of antibiotic resistance among clinical uropathogenic Escherichia coli strains," *Mol. Biol. Rep.*, vol. 45, no. 5, pp. 1055–1065, 2018.

[24] A. Bougouizi, A. D. Tagueha, D. Scribano, Z. Chekroud, Z. E. I. Lamraoui, L. Nencioni, … and H. Rahab, "Third-generation cephalosporin-resistant uropathogenic Escherichia coli from community- and hospital-acquired infections show high level of antibiotic resistance and specific virulence traits," *Can. J. Infect. Dis. Med. Microbiol.*, vol. 2025, no. 1, p. 9021465, 2025.

[25] M. H. Dirar, N. E. Bilal, M. E. Ibrahim, and M. E. Hamid, "Prevalence of extended-spectrum β-lactamase (ESBL) and molecular detection of blaTEM, blaSHV and blaCTX-M genotypes among Enterobacteriaceae isolates from patients in Khartoum, Sudan," *Pan Afr. Med. J.*, vol. 37, no. 1, 2020.

[26] S. M. Maveke, "Phenotypic and molecular characterization of extended spectrum beta-lactamase producing Escherichia coli and Klebsiella pneumoniae in clinical isolates at Embu Level Five Hospital and Kenyatta National Hospital, Kenya," Ph.D. dissertation, Univ. of Nairobi, 2023.