Ukrainian Journal of Nephrology and Dialysis
Scientific and Practical, Medical Journal

Founder:
- National Kidney Foundation of Ukraine

ISSN 2304-0238;
eISSN 2616-7352

Journal homepage: https://ukrjnd.com.ua

Research article

doi: 10.31450/ukrjnd.3(91).2026.06

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Phenotypic ESBL and AmpC in community-acquired urinary tract infections in Babylon, Iraq: Empirical therapy mismatch and clinical outcomes

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Citation: Al-Azzawi YRS, Mokif TA, Alajeel F, Saleh TH. Phenotypic ESBL and AmpC in community-acquired urinary tract infections in Babylon, Iraq: Empirical therapy mismatch and clinical outcomes. Ukr J Nephrol Dialys. 2026;3(91):44-53. doi: 10.31450/ukrjnd.3(91).2026.06.

Abstract. *Community-acquired urinary tract infections (UTI) are commonly treated empirically before culture and susceptibility results are available. The rising prevalence of extended-spectrum beta-lactamase (ESBL) and AmpC beta-lactamase phenotypes in uropathogens could lead to decreased effectiveness of empiric treatment and higher incidence of treatment failure and recurrence. The present study was carried out to investigate the prevalence of phenotypic ESBL and AmpC-producing community-acquired UTIs caused by E. Coli and K. Pneumoniae in Babylon, Iraq, and to determine their association with empirical therapy mismatch and clinical outcomes.*

Methods. This multicenter observational cohort study included 150 episodes of symptomatic community-acquired UTIs caused by E. coli or K. pneumoniae. ESBL and AmpC production were detected phenotypically. Empirical therapy mismatch was defined as initial antibiotic therapy that was inactive against the isolated organism according to susceptibility testing. Outcomes included treatment failure within 14 days and recurrence within 30 and 90 days. Logistic regression was used to assess predictors of empirical therapy mismatch and treatment failure.

Results. ESBL production was detected in 44 isolates (29.3%), AmpC production in 16 isolates (10.7%), and ESBL and/or AmpC positivity in 54 isolates (36.0%). Six isolates were positive for both ESBL and AmpC phenotypes. Multidrug resistance was detected in 48 isolates (32.0%). Empirical therapy mismatch occurred in 42 episodes (28.0%). In multivariable logistic regression, ESBL phenotype was independently associated with empirical therapy mismatch (aOR 4.10, 95% CI 1.90–8.90; $p < 0.001$), as was prior antibiotic exposure within 90 days (aOR 2.05, 95% CI 1.00–4.20; $p = 0.049$). Empirical therapy mismatch was independently associated with treatment failure within 14 days (aOR 3.02, 95% CI 1.20–7.60; $p = 0.019$). ESBL/AmpC-positive infections also showed higher rates of treatment failure, antibiotic escalation, and recurrence.

Conclusions. Phenotypic ESBL and AmpC production were common among community-acquired E. coli and K. pneumoniae urinary isolates in Babylon, Iraq. Empirical therapy mismatch occurred in more than one-quarter of cases and was associated with poorer short-term outcomes. Our findings support local antibiogram-guided, risk-stratified empirical therapy with early culture-directed adjustment.

Key words: *urinary tract infections, community-acquired infections, beta-lactamases, drug resistance, Escherichia coli, Klebsiella pneumoniae, treatment failure, recurrence.*

Article history:
Received May 05, 2026
Received in revised form July 29, 2026
Accepted August 01, 2026

Conflict of interest. The author declares no conflict of interest.

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УДК: 616.61/63-022.76:615.33]-085:616-036.8/.87(567)

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Фенотипова продукція β-лактамаз розширеного спектра дії та β-лактамаз типу AmpC серед збудників позалікарняних інфекцій сечової системи у Вавилоні, Ірак: невідповідність емпіричної антибактеріальної терапії та клінічні наслідки

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Резюме. *Позалікарняні інфекції сечової системи (ІСС) часто потребують емпіричної антибактеріальної терапії до отримання результатів бактеріологічного дослідження та визначення чутливості збудника до антимікробних препаратів. Поширення уропатогенів, які продукують β-лактамази розширеного спектра дії та β-лактамази типу AmpC, може знижувати ефективність емпіричної терапії та підвищувати ризик неефективності лікування і рецидивів. Метою дослідження було визначити поширеність фенотипової продукції β-лактамаз розширеного спектра дії та β-лактамаз типу AmpC серед Escherichia coli та Klebsiella pneumoniae, виділених у пацієнтів із позалікарняними ІСС у Вавилоні, Ірак, а також оцінити їх зв'язок з невідповідністю емпіричної антибактеріальної терапії та клінічними наслідками.*

Методи. До багатоцентрового обсерваційного когортного дослідження включено 150 епізодів симптомних позалікарняних інфекцій сечовивідних шляхів, спричинених E. coli або K. pneumoniae. Продукцію β-лактамаз розширеного спектра дії та β-лактамаз типу AmpC визначали фенотиповими методами. Невідповідність емпіричної антибактеріальної терапії оцінювали за ініціальним призначення антибактеріального засобу, до якого виділений збудник був нечутливим за результатами визначення антимікробної чутливості. Клінічними наслідками були неефективність лікування протягом 14 днів та рецидив інфекції протягом 30 і 90 днів. Для визначення чинників, пов'язаних з невідповідністю емпіричної терапії та неефективністю лікування, застосовували логістичний регресійний аналіз.

Результати. Продукцію β-лактамаз розширеного спектра дії виявлено в 44 ізолятах (29,3%), β-лактамаз типу AmpC – у 16 (10,7%), а щонайменше одного з цих типів β-лактамаз – в 54 ізолятах (36,0%). Шість ізолятів одночасно продукували β-лактамази обох типів. Мультирезистентність виявлено в 48 ізолятах (32,0%). Невідповідність емпіричної антибактеріальної терапії результатам визначення чутливості збудника встановлено у 42 випадках (28,0%). За результатами багатофакторного логістичного регресійного аналізу продукція β-лактамаз розширеного спектра дії була незалежно пов'язана з невідповідністю емпіричної антибактеріальної терапії (скориговане відношення шансів 4,10; 95% довірчий інтервал 1,90–8,90; p < 0,001). Незалежний зв'язок також встановлено для застосування антибактеріальних препаратів протягом попередніх 90 днів (скориговане відношення шансів 2,05; 95% довірчий інтервал 1,00–4,20; p = 0,049). Невідповідність емпіричної антибактеріальної терапії була незалежно пов'язана з неефективністю лікування протягом 14 днів (скориговане відношення шансів 3,02; 95% довірчий інтервал 1,20–7,60; p = 0,019). Інфекції, спричинені ізолятами, що продукували β-лактамази розширеного спектра дії та/або β-лактамази типу AmpC, також характеризувались вищою частотою неефективності лікування, ескалації антибактеріальної терапії та рецидивів.

Висновки. Фенотипова продукція β-лактамаз розширеного спектра дії та β-лактамаз типу AmpC була поширеною серед ізолятів E. coli та K. pneumoniae, виділених у пацієнтів з позалікарняними ІСС у Вавилоні, Ірак. Невідповідність емпіричної антибактеріальної терапії результатам визначення чутливості збудника спостерігали більш ніж у чверті випадків та асоціювалась з негативними короткостроковими клінічними наслідками. Отримані результати обґрунтовують вибір емпіричної антибактеріальної терапії з урахуванням локальних даних щодо антимікробної чутливості та індивідуальних чинників ризику резистентності з подальшою ранньою корекцією лікування після отримання результатів бактеріологічного дослідження.

Ключові слова: *інфекції сечової системи, позалікарняні інфекції, β-лактамази розширеного спектра дії, β-лактамази типу AmpC, антимікробна резистентність, Escherichia coli; Klebsiella pneumoniae, неефективність лікування, рецидив.*

Introduction. Community-acquired urinary tract infections (UTIs) are among the most common bacterial infections managed in outpatient clinics and in emergency departments [1]. *E. coli* and *K. pneumoniae* are identified as the most common causes of community-acquired UTIs [1, 2]. Initial therapy in an outpatient setting often begins empirically before obtaining culture and susceptibility results. Thus, the effectiveness of empiric therapy often relies heavily on the local prevalence of antimicrobial resistance [2, 3]. Extended-spectrum beta-lactamase (ESBL) and AmpC-producing strains of uropathogens are significant resistance mechanisms that can lead to the failure of many of the commonly used beta-lactam antibiotics [4, 5]. They can also lead to resistance against some oral antibiotics, thus decreasing the available options for the clinician and potentially leading to inadequate empiric therapy [4, 6].

Empiric therapy mismatch is defined as the situation where the prescribed empiric agent is not active against the bacteria isolated from a UTI according to the susceptibility data [2, 4]. In the setting of community-acquired UTIs, empiric therapy mismatch could potentially result in prolonged symptoms, escalation of antibiotics, hospital admission, treatment failure, and recurrent infections [7]. It is therefore imperative to identify high-risk populations in which to suspect empiric therapy mismatch in order to improve empiric prescribing practices and support antimicrobial stewardship. Limited data regarding phenotypic ESBL and AmpC prevalence among community-acquired uropathogens have been published in Iraq [8], particularly data that links resistance phenotypes with empiric therapy mismatch and clinical outcomes. Specific local information is required as resistance patterns and prescribing practices could differ between hospitals, outpatient clinics and the communities themselves.

This study **aimed** to assess the frequency of phenotypic ESBL and AmpC production in community-acquired *E. coli* and *K. pneumoniae* UTI isolates at Babylon, Iraq. We also aimed to estimate the empiric therapy mismatch rate, as well as to identify clinical variables associated with treatment failure and recurrence of UTIs.

Patients and methods. *Study design and setting*. This multicenter observational cohort study was conducted in Babylon, Iraq. Patients were recruited from Al-Hilla Surgical Hospital, Al-Imam Al-Sadiq Hospital, and affiliated community outpatient clinics between January to June 2025. The study protocol was reviewed and approved by the Ethics Committees of the College of Health and Medical Technologies, University of Hilla. (Reference No. 48 B, dated 25/12/2024). Written informed consent was obtained from all participants before being included in the study.

Study population. The study included patients presenting with community-acquired symptomatic UTIs and a positive urine culture for either *E. coli* or *K. pneumoniae*. Eligible patients were those with symptoms consistent with UTIs, including dysuria, urinary frequency, urgency, suprapubic pain, fever, flank pain, or other clinical features suggestive of UTIs. Cases were considered community-acquired when symptoms were present before admission or at the time of presentation to the outpatient clinic or emergency department. Patients were excluded if they had asymptomatic bacteriuria, polymicrobial urine culture not allowing reliable interpretation, urine culture growth of organisms other than *E. coli* or *K. pneumoniae*, or evidence that infection was acquired during hospitalization.

Clinical classification. UTI episodes were classified according to clinical presentation into uncomplicated cystitis, complicated UTI, or pyelonephritis. Uncomplicated cystitis was defined as lower urinary tract symptoms without systemic features or known structural or functional urinary tract abnormalities. Complicated UTI was defined as UTI occurring in the presence of relevant host or urological risk factors, such as diabetes mellitus, chronic kidney disease (CKD), urinary obstruction, stones, benign prostatic hyperplasia, recent catheterization, or immunosuppression. Pyelonephritis was defined by the presence of fever, flank pain, systemic symptoms, or clinical suspicion of upper urinary tract involvement.

Data collection. Clinical and demographic data were collected using a standardized case report form. The collected variables included age, sex, site of care, clinical syndrome, comorbidities, urological risk factors, recent antibiotic exposure within the previous 90 days, prior UTIs within the previous 12 months, recent healthcare contact, empirical antibiotic therapy, antibiotic route, treatment modification, and follow-up outcomes.

Microbiological values included the isolated microorganism, antimicrobial susceptibility, ESBL, AmpC phenotypes, and multidrug resistant status where relevant.

Urine sample collection and bacterial identification. Urine was collected before starting antibiotic treatment based on an empirical approach. A midstream clean-catch urine sample was collected by ambulatory patients with aseptic precautions and immediate transport of samples to the microbiology laboratory was conducted. Urine sample was cultured on blood agar and MacConkey agar by standard laboratory procedures and incubated in an aerobic environment at 35-37°C for 18-24 h, and significant growth was considered according to the standard operating procedure of the respective lab. Identification was based on col-

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ony morphology, Gram's staining, lactose fermentation in MacConkey agar and various conventional biochemical tests, which include indole, citrate, urease, motility and triple sugar iron reaction. If identified, verification was done by the automated identification system (VITEK 2 Compact automated identification system, bioMérieux, France). Quality control procedures include the use of *E.coli* ATCC 25922 as the standard reference strain.

Antimicrobial susceptibility testing. Antimicrobial susceptibility testing was done using the Kirby–Bauer disk diffusion method on Mueller–Hinton agar and/or automated susceptibility testing systems, as per laboratory availability. The Clinical and Laboratory Standards Institute recommendations were followed for the interpretation of results. A broad antibiotic panel was performed to examine the usage of common oral and parenteral agents for community-acquired UTIs, such as beta-lactams, beta-lactam/beta-lactamase inhibitor combinations, cephalosporins, fluoroquinolones, trimethoprim-sulfamethoxazole, nitrofurantoin, fosfomycin, aminoglycosides, and carbapenems as appropriate. Quality control was carried out using standard reference strains following laboratory protocols. As for Antimicrobial Susceptibility Quality Control, *E. coli* ATCC 25922 was used routinely. During ESBL confirmation processes, *K. pneumoniae* ATCC 700603 was employed as a positive ESBL control.

Phenotypic detection of ESBL and AmpC. ESBL screening was based on reduced susceptibility to third-generation cephalosporins. Phenotypic confirmation was performed using a clavulanate-based confirmatory test, such as the combination disk method with cephalosporin disks with and without clavulanic acid. An increase in inhibition zone diameter in the presence of clavulanic acid was interpreted as phenotypic evidence of ESBL production according to standard laboratory criteria. AmpC screening was based on cefoxitin non-susceptibility and resistance patterns suggestive of AmpC beta-lactamase production. Phenotypic confirmation was performed using an inhibitor-based method, such as boronic acid or cloxacillin-based testing, depending on local laboratory availability. Isolates were classified as AmpC-positive when confirmatory testing supported AmpC production.

Definitions of outcomes. Empirical therapy mismatch was defined as initial antibiotic therapy given within the first 24–48 hours that was inactive against the isolated organism according to antimicrobial susceptibility testing. Isolates reported as resistant or non-susceptible to the empirical agent were classified as mismatched.

Treatment failure was assessed within 14 days after treatment initiation. It was defined as one or more of the following: persistent or worsening urinary symptoms after at least 72 hours of therapy, need for antibiotic change or escalation due to poor clinical response, UTI-related hospital admission, or repeat positive urine culture with persistent symptoms. Recurrence was defined as a new symptomatic UTI episode after initial clinical improvement or resolution. Recurrence was assessed at 30 days and 90 days after the index episode.

Short-term outcomes were assessed using medical records, prescription records, emergency or outpatient revisits, and hospitalization data. Recurrence at 30 and 90 days was assessed through review of hospital and clinic records and, when available, structured telephone follow-up.

Patients with insufficient follow-up information were included in baseline and microbiological analyses but were excluded from outcome-specific analyses when the relevant outcome could not be confirmed. The main outcome variables were empirical therapy mismatch, treatment failure within 14 days, and recurrence within 30 and 90 days. The main explanatory variables included ESBL phenotype, AmpC phenotype, prior antibiotic exposure within 90 days, prior UTI within 12 months, clinical syndrome, age, and sex.

Statistical analysis. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages; continuous variables were presented as mean and standard deviation (M ± SD) for normally distributed data or median and interquartile range [Me (Q25-Q75)] for non-normally distributed data. The normality of continuous variables was assessed using the Shapiro–Wilk test. For comparisons between two groups, normally distributed continuous variables were analyzed using the independent-samples t-test, while non-normally distributed variables were analyzed using the Mann–Whitney U test. Categorical variables were compared using the chi-square test or Fisher's exact test when the expected cell count was less than 5.

Univariable logistic regression analysis was used to evaluate factors associated with empirical therapy mismatch and treatment failure. Variables with clinical relevance and/or a p-value <0.20 in univariable analysis were considered for multivariable logistic regression. Because of the limited number of outcome events, multivariable models were kept parsimonious to avoid overfitting. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported. A two-sided p-value <0.05 was considered statistically significant.

Results. *Baseline characteristics*. A total of 150 non-duplicate episodes of community-acquired UTIs were included. *E. coli* was the predominant pathogen, and most patients were female. Uncomplicated cystitis was the most common presentation. Recent antibiotic exposure and prior UTI were frequent among participants. Detailed baseline characteristics are shown in Table 1.

Table 1

Characteristics of the study cohort

Characteristic	Total (n = 150)	*E. coli* (n = 115)	*K. pneumoniae* (n = 35)	*p*-value
Age, years, mean ± SD	39.8 ± 16.2	38.9 ± 15.8	42.8 ± 17.3	0.233
Female sex, n (%)	112 (74.7)	89 (77.4)	23 (65.7)	0.168
Al-Hilla Surgical Hospital, n (%)	55 (36.7)	41 (35.7)	14 (40.0)	0.831
Al-Imam Al-Sadiq Hospital, n (%)	60 (40.0)	46 (40.0)	14 (40.0)	
Outpatient clinics, n (%)	35 (23.3)	28 (24.3)	7 (20.0)	
Uncomplicated cystitis, n (%)	78 (52.0)	63 (54.8)	15 (42.9)	0.454
Complicated UTIs, n (%)	49 (32.7)	35 (30.4)	14 (40.0)	
Pyelonephritis, n (%)	23 (15.3)	17 (14.8)	6 (17.1)	
Diabetes mellitus, n (%)	41 (27.3)	29 (25.2)	12 (34.3)	0.283
CKD, n (%)	14 (9.3)	10 (8.7)	4 (11.4)	0.815
Urologic abnormality/obstruction, n (%)	26 (17.3)	18 (15.7)	8 (22.9)	0.293
Catheter/instrumentation ≤90 days, n (%)	18 (12.0)	12 (10.4)	6 (17.1)	0.747
Antibiotics in the prior 90 days, n (%)	54 (36.0)	39 (33.9)	15 (42.9)	0.323
Prior UTIs in the last 12 months, n (%)	47 (31.3)	34 (29.6)	13 (37.1)	0.372

Abbreviations: CKD, chronic kidney disease.

Phenotypic ESBL, AmpC, and multidrug-resistant distribution. Phenotypic ESBL, AmpC, and MDR were common among the isolates. Overall, 36.0% of isolates were ESBL/AmpC-positive, including six isolates positive for both phenotypes. MDR was detected in nearly one-third of isolates. The distribution by organism is shown in Table 2.

Table 2

Phenotypic ESBL, AmpC, and MDR distribution by organism

Microbiology outcome	Total (n = 150)	*E. coli* (n = 115)	*K. pneumoniae* (n = 35)	*p*-value
ESBL positive, n (%)	44 (29.3)	32 (27.8)	12 (34.3)	0.463
AmpC positive, n (%)	16 (10.7)	9 (7.8)	7 (20.0)	0.061
ESBL and AmpC co-positive, n (%)	6 (4.0)	3 (2.6)	3 (8.6)	–
ESBL and/or AmpC positive, n (%)	54 (36.0)	38 (33.0)	16 (45.7)	0.179
MDR, n (%)	48 (32.0)	34 (29.6)	14 (40.0)	0.257

Abbreviations: ESBL, extended-spectrum beta-lactamase; AmpC, AmpC beta-lactamase; MDR, multidrug resistance.

Antimicrobial susceptibility profile. Fosfomycin and nitrofurantoin showed the highest activity among oral agents, particularly against *E. coli*, whereas susceptibility to TMP-SMX and fluoroquinolones was limited. Among parenteral agents, amikacin and meropenem/imipenem showed the highest susceptibility rates (Table 3).

Table 3

Antimicrobial susceptibility profile

Antibiotic	Total susceptible n/N (%)	*E. coli* susceptible n/N (%)	*K. pneumoniae* susceptible n/N (%)	*p*-value
Nitrofurantoin	111/150 (74.0)	96/115 (83.5)	15/35 (42.9)	<0.001
Fosfomycin	132/150 (88.0)	106/115 (92.2)	26/35 (74.3)	0.014
TMP-SMX	69/150 (46.0)	55/115 (47.8)	14/35 (40.0)	0.442

Continuation of Table 3

Antibiotic	Total susceptible n/N (%)	*E. coli* susceptible n/N (%)	*K. pneumoniae* susceptible n/N (%)	*p*-value
Fluoroquinolone	76/150 (50.7)	60/115 (52.2)	16/35 (45.7)	0.562
Amoxicillin-clavulanate	85/150 (56.7)	67/115 (58.3)	18/35 (51.4)	0.561
Ceftriaxone/Cefotaxime	97/150 (64.7)	75/115 (65.2)	22/35 (62.9)	0.843
Cefepime	107/150 (71.3)	82/115 (71.3)	25/35 (71.4)	1.00
Piperacillin-tazobactam	131/150 (87.3)	101/115 (87.8)	30/35 (85.7)	0.772
Gentamicin	127/150 (84.7)	98/115 (85.2)	29/35 (82.9)	0.791
Amikacin	144/150 (96.0)	111/115 (96.5)	33/35 (94.3)	0.628
Meropenem/Imipenem	149/150 (99.3)	114/115 (99.1)	35/35 (100.0)	1.00

Abbreviations: TMP-SMX, trimethoprim-sulfamethoxazole; n, number of susceptible isolates; N, total number of tested isolates.

Empirical therapy and mismatch. Nitrofurantoin, fluoroquinolones, and third-generation cephalosporins were the most commonly used empirical regimens. Empirical therapy mismatch occurred in 42 episodes (28.0%), with the highest mismatch rates observed for third-generation cephalosporins and TMP-SMX. Detailed regimen-specific results are shown in Table 4.

Table 4

Empirical antibiotic therapy and overall mismatch

Empirical regimen	Total n (%)	Active in vitro n (%)	Inactive / mismatch n (%)
Nitrofurantoin	36 (24.0)	31 (86.1)	5 (13.9)
Fosfomycin	12 (8.0)	11 (91.7)	1 (8.3)
TMP-SMX	10 (6.7)	5 (50.0)	5 (50.0)
Fluoroquinolone	28 (18.7)	18 (64.3)	10 (35.7)
Amoxicillin-clavulanate	18 (12.0)	12 (66.7)	6 (33.3)
Third-generation cephalosporin	28 (18.7)	14 (50.0)	14 (50.0)
Piperacillin-tazobactam	10 (6.7)	9 (90.0)	1 (10.0)
Carbapenem	6 (4.0)	6 (100.0)	0 (0.0)
Other / combination therapy	2 (1.3)	2 (100.0)	0 (0.0)
Total	150 (100.0)	108 (72.0)	42 (28.0)

Abbreviations: TMP-SMX, trimethoprim-sulfamethoxazole; n, number of episodes.

Note: Active in vitro means that the isolated organism was susceptible to the empirical antibiotic according to antimicrobial susceptibility testing. Inactive/mismatch means that the empirical antibiotic was not active against the isolated organism.

Clinical outcomes. ESBL/AmpC-positive infections showed poorer outcomes, including higher rates of treatment failure, antibiotic escalation, and recurrence. Hospitalization was also more frequent in this group, but the difference was not statistically significant. Detailed comparisons are shown in Table 5.

Table 5

Clinical outcomes according to ESBL/AmpC status

Outcome	Total (n =150)	ESBL/AmpC positive (n = 54)	ESBL/AmpC negative (n = 96)	*p*-value
Treatment failure ≤14 days, n (%)	22 (14.7)	14 (25.9)	8 (8.3)	0.003
Antibiotic escalation/change, n (%)	18 (12.0)	12 (22.2)	6 (6.3)	0.004
UTI-related hospitalization, n (%)	9 (6.0)	6 (11.1)	3 (3.1)	0.071

Continuation of Table 5

Outcome	Total (n =150)	ESBL/AmpC positive (n = 54)	ESBL/AmpC negative (n = 96)	p-value
Recurrence ≤30 days, n (%)	19 (12.7)	11 (20.4)	8 (8.3)	0.033
Recurrence ≤90 days, n (%)	31 (20.7)	16 (29.6)	15 (15.6)	0.042

Abbreviations: ESBL, extended-spectrum beta-lactamase; AmpC, AmpC beta-lactamase; UTI, urinary tract infection; n, number of episodes; N, total number of episodes.

Note: ESBL/AmpC-positive episodes included isolates positive for ESBL and/or AmpC phenotype. Fisher's exact test was used for hospitalization because of small expected counts. For the other outcomes, Pearson's chi-square test was used.

Factors associated with empirical therapy mismatch. ESBL phenotype and recent antibiotic exposure were the main factors associated with empirical therapy mismatch. Patients with ESBL-positive isolates were more likely to receive inactive empirical therapy. Previous antibiotic use within 90 days also increased the risk of mismatch. AmpC showed a positive association in the crude analysis, but this association became weaker after adjustment. The full regression results are shown in Table 6.

Table 6

Predictors of empirical therapy mismatch

Predictor	Univariable OR (95% CI)	p-value	Multivariable aOR (95% CI)	p-value
ESBL phenotype	5.02 (2.40–10.50)	<0.001	4.10 (1.90–8.90)	<0.001
AmpC phenotype	3.15 (1.10–8.99)	0.032	2.70 (0.88–8.30)	0.081
Prior antibiotics ≤90 days	2.45 (1.20–4.98)	0.013	2.05 (1.00–4.20)	0.049
Prior UTI ≤12 months	1.62 (0.78–3.36)	0.20	1.35 (0.62–2.95)	0.452
Complicated UTI/pyelonephritis	1.88 (0.92–3.84)	0.083	1.70 (0.80–3.62)	0.173
Age, per 10-year increase	1.10 (0.92–1.31)	0.30	1.08 (0.90–1.30)	0.412
Male sex	1.28 (0.60–2.72)	0.52	1.15 (0.50–2.64)	0.745

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; ESBL, extended-spectrum beta-lactamase; AmpC, AmpC beta-lactamase; UTI, urinary tract infection.

Factors associated with treatment failure. Empirical therapy mismatch was the strongest factor associated with treatment failure within 14 days. Patients who received inactive empirical therapy had a higher risk of early failure. ESBL/AmpC-positive infection and complicated UTI or pyelonephritis were associated with failure in the crude analysis, but their effects were reduced after adjustment. The detailed regression results are presented in Table 7.

Table 7

Predictors of treatment failure within 14 days

Predictor	Univariable OR (95% CI)	p-value	Multivariable aOR (95% CI)	p-value
Empirical therapy mismatch	4.05 (1.70–9.68)	0.002	3.02 (1.20–7.60)	0.019
ESBL and/or AmpC positive	3.84 (1.55–9.52)	0.004	2.45 (0.95–6.30)	0.064
Complicated UTI/pyelonephritis	2.90 (1.15–7.30)	0.024	2.10 (0.80–5.50)	0.133
Prior antibiotics ≤90 days	2.20 (0.92–5.30)	0.076	1.70 (0.68–4.20)	0.265
Diabetes mellitus	2.05 (0.85–4.95)	0.11	1.80 (0.70–4.60)	0.226
Age, per 10-year increase	1.18 (0.95–1.46)	0.13	1.12 (0.89–1.40)	0.331

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; ESBL, extended-spectrum beta-lactamase; AmpC, AmpC beta-lactamase; UTI, urinary tract infection.

Discussion. This study shows that community-acquired UTI in Babylon is not a simple low-risk infection in a considerable proportion of patients. A large part of the isolates carried ESBL and/or AmpC phenotypes, and this was clinically relevant because resistance was linked to empirical treatment mismatch and poorer outcomes.

The most important finding was the high rate of empirical therapy mismatch. Almost one-third of patients received an initial antibiotic that was inactive against the isolated organism. This finding has direct clinical importance. Inactive empirical therapy can delay symptom control, increase the need for antibiotic change, and contribute to early treatment failure. Therefore, mismatch should be considered a modifiable risk factor rather than only a microbiological observation. The high frequency of ESBL and AmpC phenotypes provides a plausible explanation for this mismatch. ESBL-producing isolates are resistant to many penicillins and cephalosporins, while AmpC production may further reduce the activity of several beta-lactam agents [9, 10]. When these phenotypes are common in the community, empirical use of third-generation cephalosporins or other commonly prescribed oral agents becomes less reliable. This explains why mismatch was especially frequent with agents that showed lower susceptibility in the antibiogram [10, 11].

Recent antibiotic exposure was another important factor associated with mismatch. This is biologically expected. Previous antibiotic use creates selective pressure and may increase colonization or infection with resistant Enterobacterales [12, 13]. In clinical practice, this means that a recent history of antibiotic use should be actively checked before choosing empirical therapy. Patients with recent antibiotic exposure may need earlier urine culture, closer follow-up, and faster adjustment once susceptibility results become available [13]. The susceptibility pattern also has practical implications. Activity of fosfomycin and nitrofurantoin was superior to fluoroquinolones and TMP-SMX, primarily in cases of *E. coli*. These antibiotics should not be considered a panacea, though. Nitrofurantoin is primarily indicated for lower UTI and contraindicated in suspected pyelonephritis [14]. Fosfomycin may have some niche indication in cystitis, but has a more limited role in complicated infection and in *K. pneumoniae* infections. Decision about drug usage should be organism, clinical syndrome and severity dependent along with local susceptibility patterns [10, 14].

The clinical outcome findings support the microbiological results. ESBL/AmpC-positive infections were associated with more treatment failure, antibiotic escalation, and recurrence. This suggests that resistance phenotypes are not only laboratory markers [15]. They affect patient management and may increase the burden on outpatient and hospital services. From a stewardship perspective, the goal should not be broader empirical therapy for all patients, but better risk stratification to identify patients who are more likely to have resistant infection [7, 13]. Integration of the microbiology, empirical antibiotic selection, and follow-up outcomes provided actionable information for local prescribing guidelines in Babylon.

The results are similar to broader observations reported in the literature regarding the rise of ESBL-producing Enterobacterales in community-acquired UTI and decreasing reliability of fluoroquinolones and TMP-SMX in many areas [4–7]. These observations were also confirmed by others who demonstrated a correlation between empirical discordance and worse clinical outcome [4, 7, 8]. It is still vital, though, to use local data, as antibiotic resistance patterns and physician ordering habits differ not only between countries and regions but between individual centers. We can recommend to applied molecular technique to investigate the results, In general the molecular technique such as PCR is widely applied in medicine filed; it used to diagnose urinary tract and another medical disorders [16-26].

This study has several limitations. First, the study was conducted in a small population in Babylon, Iraq, and the results may not be generalizable to other governorates or healthcare institutions. Second, only *E. coli* and *K. pneumoniae* isolates were examined, not representative of all causes of community-acquired UTIs. Third, ESBL and AmpC were detected by phenotypic methods only. Molecular confirmation of resistance genes was not performed. Therefore, the study could not identify specific resistance genes or distinguish between different ESBL and AmpC mechanisms. Co-production of resistance mechanisms may also have affected phenotypic interpretation. Fourth, the data were collected using existing clinical records, and such limitations were seen regarding antibiotic dose, duration, compliance, previous culture, symptom severity, kidney function, and exposure to health care settings, all of which may have influenced treatment failure and recurrence. Fifth, follow-up outcomes may have been underestimated. Some patients may have received further treatment in other hospitals, private clinics, or pharmacies without returning to the participating centers. Recurrence was also assessed clinically, and molecular typing was not performed. Therefore, the study could not distinguish relapse caused by the same strain from reinfection with a new strain. Sixth, the number of treatment failure events was limited. This reduces the stability of regression models and increases the risk of overfitting. For this reason, adjusted associations should be interpreted cautiously. Finally, this study was observational. It can show associations between resistance phenotypes, empirical therapy mismatch, and clinical outcomes, but it cannot prove causality. Larger prospective studies with standardized follow-up, molecular resistance testing, and external validation are needed to confirm these findings and improve empirical treatment algorithms.

Conclusions. In conclusion, this study implies that phenotypic ESBL and AmpC can serve as a significant risk factor for the incidence of empirical therapy mismatch and poorer outcomes in patients presenting with community- acquired UTIs. Our results argue in favor of consistent use of local antibiograms, timely obtaining of urine cultures in at-risk individuals and prompt modification of therapy guided by culture data. Well-designed, prospective studies from multiple sites across Iraq are needed to confirm these results and to develop actionable risk-guided empirical treatment algorithms.

Ethics approval and consent to participate. The study protocol was reviewed and approved by the College of Health and Medical Technologies, University of Hilla, Babylon, Iraq (Reference No. 48 B, dated 25/12/2024). The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from participants when required by the approved study protocol.

Consent for publication. Not applicable. The manuscript does not contain any identifiable individual patient data, images, or personal clinical details.

Availability of data and materials. The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of interest. The authors declare that they have no competing interests.

Funding. No specific funding was received for this study.

Authors' contributions. All the authors contributed to proposing the research plan, writing the manuscript, analyzing the results statistically, and implementing the research plan.

Use of artificial intelligence tools. No artificial intelligence tools were used for data collection, laboratory analysis, statistical analysis, or interpretation of the study findings.

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