



Prevalence of Aminoglycoside Resistance among *Escherichia coli* Isolated from UTI Patients in Sana'a City, Yemen

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ABSTRACT

Background:

Antimicrobial resistance is a critical global threat, particularly in urinary tract infections (UTIs) caused by *Escherichia coli*. The rise in aminoglycoside-resistant strains complicates treatment. This study investigated the prevalence of aminoglycoside resistance among *E. coli* isolated from patients with UTI in Sana'a city, Yemen.

Methods:

A cross-sectional study was conducted on 378 patients at Al-Kuwait University Hospital in Sana'a City. Midstream morning urine samples were cultured, and *E. coli* isolates were identified using standard methods. Antimicrobial susceptibility was assessed using the Kirby-Bauer disk diffusion method according to the CLSI (2019) guidelines. Aminoglycoside resistance was phenotypically detected.

Results:

Among the 378 samples, 167 *E. coli* isolates were identified (44.18%), of which 41 (24.6%) exhibited resistance to at least one clinically critical aminoglycoside (gentamicin, tobramycin, or amikacin). The risk factors for resistance included catheterization, hospitalization, and older age.

Conclusion:

The high prevalence of aminoglycoside-resistant *E. coli* strains in Yemen underscores the need for enhanced molecular surveillance and antimicrobial stewardship.

ARTICLE INFO

Keywords:

Escherichia coli, aminoglycosides, antimicrobial resistance, urinary tract infection, Yemen.

Article History:

Received: 31-July-2023,

Revised: 7-August-2025,

Accepted: 18-September-2025,

Available online: 28-October-2025.

1. INTRODUCTION

Aminoglycosides (AGs) are a class of bactericidal antibiotics primarily derived from soil actinomycetes, with streptomycin being the first AG discovered and used against tuberculosis and gram-negative infections [1]. Over time, natural and semi-synthetic derivatives, such as gentamicin, tobramycin, amikacin, and neomycin, have been developed to enhance antimicrobial efficacy and overcome resistance [2]. These antibiotics share a core structure consisting of an aminocyclitol ring linked to amino sugars via glycosidic bonds, although some, such as spectinomycin, lack the amino sugar linkage [3]. They are classified based on their 2-deoxystreptamine (DOS)

ring substitutions: 4,6-disubstituted (e.g., gentamicin, tobramycin, amikacin), 4,5-disubstituted (e.g., neomycin), and 4-monosubstituted DOS agents (e.g., apramycin), with the first being widely used intravenously or via nebulization for serious infections [4–7].

Aminoglycosides exhibit broad-spectrum activity against both Gram-positive and Gram-negative bacteria, particularly Enterobacteriaceae such as *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus spp.*, and *Serratia spp.* [8, 9]. They are also effective against *Pseudomonas aeruginosa*, *Staphylococcus aureus* (including MRSA), and certain mycobacteria, such as *Mycobacterium tuberculosis* [10–12]. Their clinical utility is enhanced by synergistic effects when combined with cell wall-active



antibiotics, such as β -lactams, which improve efficacy against both susceptible and multidrug-resistant (MDR) isolates [13]. This synergy is widely exploited for the treatment of severe systemic infections, especially in hospital settings.

The primary mechanism of action involves high-affinity binding to the A-site of 16S rRNA in the bacterial 30S ribosomal subunit, disrupting protein synthesis by inducing mRNA misreading and inhibiting translation initiation or elongation [14–17]. This leads to the production of defective proteins that integrate into the cell membrane, increasing permeability and promoting further antibiotic uptake in a self-amplifying cycle [10, 14]. Aminoglycoside entry occurs in stages: initial electrostatic interaction with the negatively charged cell surface, displacement of stabilizing Mg^{2+} ions, and subsequent energy-dependent uptake into the cytoplasm [18]. These antibiotics are rapidly bactericidal and exhibit a prolonged post-antibiotic effect (PAE), which correlates with the time required for bacterial recovery [19, 20].

Despite their efficacy, their clinical use is limited by significant toxicities, primarily nephrotoxicity and ototoxicity [21, 22]. Nephrotoxicity results from AG accumulation in renal proximal tubular cells, leading to acute kidney injury [23], whereas ototoxicity involves damage to cochlear or vestibular hair cells, potentially causing hearing loss or balance disorders, with risk influenced by dose and genetic factors [24, 25]. Inhalation delivery reduces systemic absorption and toxicity [26]. Resistance arises through multiple mechanisms, including enzymatic modification (e.g., acetyltransferases and phosphotransferases), efflux pumps, reduced permeability, and ribosomal target modifications [27]. Enzymatic inactivation remains the most common and widespread resistance mechanism in clinical isolates.

In Yemen, the empirical treatment of urinary tract infections (UTIs) relies heavily on aminoglycosides. However, the rising resistance among uropathogens, particularly uropathogenic *Escherichia coli*, threatens their effectiveness. Local data on aminoglycoside resistance patterns in *E. coli* from patients with UTI in Sana'a City are limited. The findings are expected to inform empirical therapy and guide clinical management and antimicrobial stewardship policies in Yemen. This study aimed to investigate the following:

- The prevalence of *E. coli* in UTI infections in Sana'a city.
- The prevalence of aminoglycoside resistance among UTI *E. coli*.
- Risk factors associated with UPEC resistance to aminoglycosides.

2. MATERIALS AND METHODS

2.1. STUDY DESIGN AND POPULATION

This cross-sectional study was conducted among patients attending the outpatient and inpatient departments of Al-Kuwait University Hospital in Sana'a, Yemen. A total of 378 urine samples were collected from patients of both sexes and all age groups who presented with clinical symptoms suggestive of a urinary tract infection (UTI). Patients who had received antibiotics in the past 48 h or had contaminated samples were excluded.

2.2. SAMPLE COLLECTION AND CULTURE

Clean-catch midstream urine specimens were aseptically collected in sterile, wide-mouthed containers and processed within two hours of collection. Each sample was cultured on blood agar and MacConkey agar using a calibrated loop to deliver 0.001 mL of urine. The plates were incubated at 37 °C for 24 h. A colony count of $\geq 10^5$ CFU/mL was considered significant. Only one isolation per patient was included in the study.

2.3. IDENTIFICATION OF ISOLATES

Bacterial isolates were preliminarily identified by Gram staining and colony morphology, followed by biochemical identification using standard tests, including indole, citrate utilization, urease production, triple sugar iron agar, and oxidase (Kaur *et al.*, 2021).

2.4. ANTIMICROBIAL SUSCEPTIBILITY TESTING

Antibiotic susceptibility was assessed using the modified Kirby-Bauer disk diffusion method, in accordance with the Clinical and Laboratory Standards Institute (CLSI) 2019 guidelines. The antibiotics tested included aminoglycosides (gentamicin, amikacin, and tobramycin), and the zones of inhibition were interpreted according to CLSI breakpoints.

3. RESULTS

3.1. CULTURE AND IDENTIFICATION OF ISOLATES

Of the 378 urine samples analyzed, 274 (72.5%) showed significant bacterial growth, whereas 104 (27.5%) exhibited either non-significant or no growth. Among the culture-positive samples, *Escherichia coli* was the most frequently isolated pathogen, accounting for 167 (44.18 %) of the isolates. Other organisms included *Klebsiella* spp. (66 cases, 17.46%), *Pseudomonas* spp. (25 cases, 6.61%), and *Staphylococcus saprophyticus*, *Proteus* spp., and *Candida* spp., each isolated in four cases (1.1% respectively). Less frequent isolates included *Streptococcus* sp. and *Enterobacter* sp., each

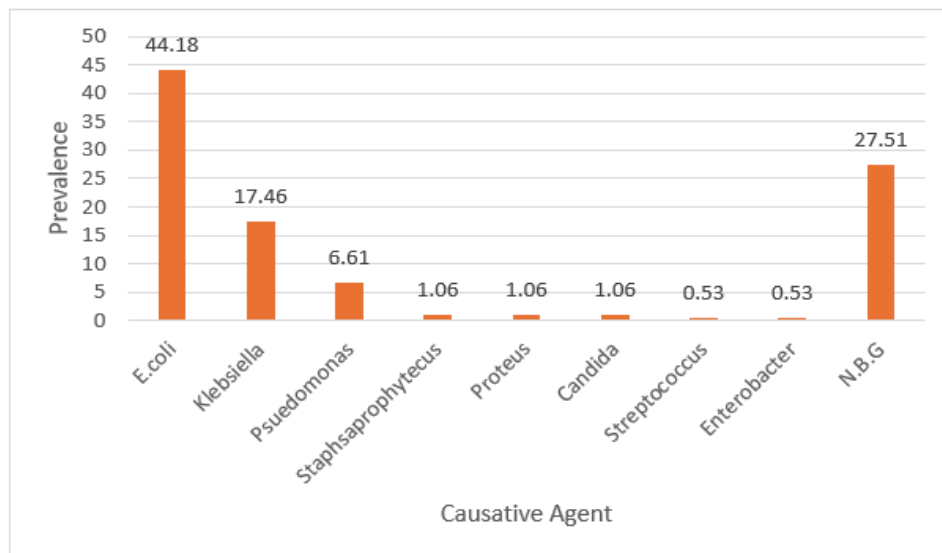


Figure 1

detected in 2 cases (0.5%)

3.2. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

The prevalence of culture-positive UTIs was higher among elderly patients (≥ 60 years), representing 27.8% ($n=105$) of the positive cases. The most commonly reported symptom was burning urination, observed in 217 patients (79.2%), followed by fever in 144 patients (52.5%), dysuria in 141 patients (51.5%), and flank pain in 134 patients (48.9%).

3.3. THE MOST FREQUENT RISK FACTORS ASSOCIATED WITH POSITIVE GROWTH CULTURE

Among the 274 positive growth cultures, risk factor analysis revealed notable prevalence rates among key variables. Older age (≥ 60 years) was the most common characteristic, affecting 38.3% ($n=105$) of the population. Recent catheterization was reported in 25.18% ($n=69$) of cases, while diabetes and kidney disorders were present in 24.45% ($n=67$) and 15.33% ($n=42$) of participants, respectively. Less frequent risk factors included kidney calculi (11.68%, $n=32$) and hospitalization/ICU admission (9.85%, $n=27$).

3.4. ANTIMICROBIAL RESISTANCE PROFILE

The antimicrobial susceptibility profile of UPEC isolates to the clinically used aminoglycoside antibiotics is presented in table. Among the tested agents, amikacin demonstrated the highest efficacy, with 146 (87.43%) sensitive and only 16 (9.58 %) resistant isolates, indicating its continued reliability for treating UPEC infections.

In contrast, gentamicin and tobramycin showed lower sensitivity rates of 73.05% (122 isolates) and 69.46% (116 isolates), respectively, with correspondingly higher resistance rates of 18.56% (31 isolates) and 24.55% (41 isolates). Moderate susceptibility was observed in a small proportion of isolates: 5 (2.99%) for amikacin, 14 (8.38%) for gentamicin, and 10 (5.99%) for tobramycin, respectively. These findings suggest a significant level of resistance to gentamicin and tobramycin among UPEC strains, potentially limiting their clinical utility. These data underscore the importance of amikacin as a more effective aminoglycoside option in the study region and highlight the need for continuous antimicrobial surveillance to guide empirical therapy and combat the rising challenge of antibiotic resistance in urinary tract infections.

3.5. RISK FACTORS FOR AGs RESISTANCE

The association between various risk factors and phenotypic resistance to aminoglycosides (AG) among *Escherichia coli* isolates is presented in Table 3.6. Older age and recent catheterization were significantly associated with increased odds of AMG resistance, with odds ratios (OR) of 4.71 (95% CI: 1.77–12.53; $\chi^2 = 10.11$, $p = 0.001$) and 6.85 (95% CI: 2.51–18.74; $\chi^2 = 15.14$, $p < 0.001$), respectively. Similarly, hospitalization or ICU admission was strongly linked to resistance, with an OR of 6.07 (95% CI: 2.24–16.40; $\chi^2 = 13.52$, $p < 0.001$). In contrast, diabetes mellitus, kidney disorders, and urinary calculi were not significantly associated with AMG resistance ($p > 0.05$), with ORs of 1.20 (95% CI: 0.47–3.08), 0.76 (95% CI: 0.27–2.14), and 1.80 (95% CI: 0.54–6.02), respectively. These findings suggest that older age, recent catheterization, and hospitalization are significant predictors of aminoglycoside resistance, highlighting the

**Table 1.** The most frequent risk factors among UTI patients show growth culture (n = 274)

Risk factors		Numbers	(%)
Older age	Yes	105	38.3
	No	169	61.7
Recent Catheterization	Yes	69	25.18
	No	205	74.82
Diabetic	Yes	67	24.45
	No	207	75.55
Kidney Disorder	Yes	42	15.33
	No	232	84.67
Calculi	Yes	32	11.68
	No	242	88.32
Hospitalization /ICU	Yes	27	9.85
	No	247	90.15
Total		274	100%

Table 2. AGs Antibiotic Susceptibility Testing of UTI *E. coli* isolates

Antibiotics group		UPEC					
		Sensitive		Moderate		Resistance	
		No.	%	No.	%	No.	%
Aminoglycosides	Amikacin	146	87.43	5	2.99	16	9.58
	Gentamycin	122	73.05	14	8.38	31	18.56
	Tobramycin	116	69.46	10	5.99	41	24.55
Total		167					

Table 3. Risk factors associated with aminoglycoside resistance

Risk factors		Phenotypically Resistance to AMG		OR	CI	X ²	p
		No.	%				
Older age	Yes	98	58.9	4.71	1.77–12.53	10.11	0.001
	No	69	41				
Recent Catheterization	Yes	105	62.9	6.85	2.51–18.74	15.14	<0.001
	No	62	37.1				
Diabetic	Yes	60	35.9	1.20	0.47–3.08	0.14	0.705
	No	107	64.1				
Kidney Disorder	Yes	34	20.4	0.76	0.27–2.14	0.28	0.596
	No	133	79.6				
Calculi	Yes	34	20.4	1.80	0.54–6.02	0.94	0.332
	No	133	79.6				
Hospitalization /ICU	Yes	26	15.6	6.07	2.24–16.40	13.52	<0.001
	No	141	84.4				
Total		167					

importance of infection control measures and prudent antibiotic use in healthcare facilities.

4. DISCUSSION

The present study highlights the high prevalence of urinary tract infections (UTI) in Sana'a city, Yemen, with a marked predominance among female patients, consistent with findings from previous studies in Saudi Arabia [28, 29]. This gender disparity is attributed to anatomical and physiological factors, including a shorter urethra, closer proximity of the anus to the urethral meatus, and a more humid perineal environment in females, all of which facilitate bacterial ascension. In contrast, males benefit from the antimicrobial properties of prostatic secretions, which offer relative protection [30]. A significant proportion of UTI cases was observed in elderly patients (≥ 60 years), aligning with a prior study in Yemen [31]. This increased susceptibility in older adults may be linked to age-related immune decline, higher rates of hospitalization, and the frequent use of urinary catheters. Indeed, older age and recent catheterization emerged as the leading risk factors for UTI in this cohort [32, 33]. Diabetes mellitus was also prevalent (24.45%), consistent with its well-documented role in predisposing individuals to UTIs owing to impaired immune function and glycosuria [34]. The most common clinical symptoms—burning urination (79.2%), fever (52.55%), dysuria (51.46%), and flank pain (48.91%)—are typical of acute UTIs and are consistent with previous reports

[35].

Among the 378 urine samples analyzed, gram-negative bacteria were the predominant uropathogens, with *Escherichia coli* being the most frequently isolated organism (44.18%), followed by *Klebsiella spp.* (17.46%), and *Pseudomonas* (6.61%). This distribution is consistent with global and regional epidemiological trends, in which *E. coli* remains the leading cause of both community- and hospital-acquired UTIs [36, 37]. Similar high prevalence rates of *E. coli* have been reported in Yemen [38, 39], Iraq [40], Egypt [41], and the USA [42]. The slightly lower *E. coli* prevalence compared to some Saudi studies [43] may reflect regional variations in antibiotic use, infection control practices, and healthcare infrastructure [44].

Antimicrobial susceptibility testing revealed a tiered pattern of efficacy for aminoglycosides. Amikacin demonstrated high sensitivity (87.43%), indicating its continued utility in treating resistant infections, whereas gentamicin and tobramycin showed lower sensitivity (73.05% and 69.46%, respectively) and higher resistance rates (18.56% and 24.55%, respectively). These resistance levels are higher than those reported in Spain [45] and Norway [46], suggesting increasing regional resistance trends, possibly due to widespread empirical use and limited antibiotic use.

Critically, older age (≥ 65 years), recent catheterization, and hospitalization/ICU admission were identified as significant predictors of aminoglycoside resistance, underscoring the role of healthcare exposure in the develop-



ment of multidrug resistance. These findings are consistent with studies linking invasive procedures and hospital stays to the selection and spread of resistant strains [47–53]. Collectively, these results emphasize the urgent need for improved infection control, judicious antibiotic use, and continuous surveillance to combat the rising burden of antimicrobial resistance in resource-limited settings worldwide.

5. CONCLUSION AND RECOMMENDATIONS:

The high prevalence of aminoglycoside resistance among *Escherichia coli* isolates from patients with UTI in Sana'a city highlights the growing challenge of antimicrobial resistance in clinical practice. This resistance is particularly evident against key aminoglycosides, such as gentamicin and amikacin, limiting effective treatment options and increasing the risk of therapeutic failure. To address this public health concern, local healthcare facilities should implement routine antimicrobial susceptibility testing to guide evidence-based prescribing. National and institutional antimicrobial stewardship programs should be strengthened to regulate the use of antibiotics. Furthermore, expanded surveillance of resistance patterns across different regions of Yemen is urgently needed to monitor emerging trends and to inform empirical treatment guidelines.

6. CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest. No financial or personal relationships influenced the work reported in this manuscript. This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

7. AUTHORS' CONTRIBUTIONS

Siham Al-Arosi has collected the clinical samples, performed all diagnostic and laboratory procedures, analyzed the data, and written the manuscript. Prof. Saleh and Prof. Ahmed supervised the research and provided guidance throughout the study and manuscript preparation. All the authors have read and approved the final version of the manuscript.

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