

Epidemiology of Urinary Pathogens and Antibiotic Resistance Trends: A Retrospective Analysis Stratified by Age and Sex from a Large Tertiary Hospital in Saudi Arabia

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Background: Urinary tract infections (UTIs) are among the most prevalent bacterial infections worldwide, with notable variations in antimicrobial resistance (AMR) patterns influenced by age and sex. Local surveillance of resistance trends is essential for optimizing empirical treatment.

Methods: This retrospective study analyzed urine culture data collected over a span of 7-year (2017–2023) from a tertiary hospital in Saudi Arabia. The distribution of Pathogens and patterns of AMR were examined based on sex, age group, and year. Logistic regression was used to assess predictors of resistance.

Results: The analysis included 3,201 urinary isolates from patients with culture-confirmed UTIs. *E. coli* was the predominant pathogen in most years, reaching up to 47.5%, but noted a decline in 2020 to 22.7% and further to 22% in 2023. In contrast, *K. pneumoniae* exhibited steady increase, peaking at 43.1% in 2023. The prevalence of antibiotic resistance to *E. coli* was notably higher among older males (>19 years), with exception of nitrofurantoin in younger males and ampicillin, ciprofloxacin, and sulfamethoxazole-trimethoprim in younger females (≤18 years). In *K. pneumoniae*, younger males exhibited increased resistance to ampicillin, amoxicillin, and 3rd-generation cephalosporins, while females showed overall higher resistance levels, with the exception of ampicillin and nitrofurantoin, where younger females showed greater resistance. Male sex was significantly associated with resistance in *E. coli* to ampicillin (OR: 1.53, $p=0.021$), ciprofloxacin (OR: 1.47, $p=0.026$), imipenem (OR: 5.83, $p=0.009$), and in *K. pneumoniae* to gentamicin (OR: 1.85, $p=0.001$), ceftriaxone (OR: 2.44, $p=0.008$), ceftazidime (OR: 1.64, $p=0.006$), and imipenem (OR: 1.95, $p=0.001$). Age was inversely associated with imipenem resistance in *E. coli* (OR: 0.97, $p=0.007$).

Conclusion: This study demonstrates significant variability in UTI pathogens and their resistance patterns based on sex and age. The findings support the need for targeted empirical treatment protocols and underscore the importance of ongoing monitoring of AMR.

Plain Language Summary: Urinary tract infections (UTIs) are common and often treated with antibiotics. However, growing resistance to antibiotics makes treatment harder, especially when bacteria no longer respond to commonly used drugs. In this study, we analyzed 7 years of lab data from a large hospital in Saudi Arabia to understand which bacteria are causing UTIs and how resistant they are to antibiotics, especially among different age groups and between males and females.

We found that *E. coli* and *Klebsiella pneumoniae* were the most common bacteria causing UTIs. Over time, *Klebsiella* infections increased and even became more common than *E. coli* in some years. Antibiotic resistance patterns were different depending on the patient's age and sex. For example, older males had higher resistance to many antibiotics, while younger patients also showed resistance to certain drugs. We also found that male patients were more likely to have infections resistant to multiple antibiotics.

These results show the importance of regularly monitoring local bacteria and their resistance to help doctors choose the right treatment. Understanding how resistance varies by age and sex can lead to more effective care and help reduce antibiotic misuse.

Keywords: urine, resistance, *E. coli*, *K. pneumoniae*, antibiotics

Introduction

Urinary tract infections (UTIs) are among the most common bacterial infections globally, contributing substantially to antibiotic use, resistance, and healthcare burden.¹ In Saudi Arabia, UTIs are frequently encountered in both outpatient and inpatient settings, with growing concerns about resistance patterns.^{2,3} The management of UTI is becoming more complicated due to the emergence of antimicrobial resistant strains, especially among elderly patients or patients with underlying health conditions.⁴ Epidemiological patterns of UTI differ by sex and age. In adults, UTIs are primarily caused by *Escherichia coli*, and UTIs caused by multidrug-resistant (MDR) organism are more prevalent among patients >50 years.⁵ Females, especially during reproductive years, are more susceptible due to anatomical factors.⁶ In contrast, men over 50 are at increased risk for complicated UTIs related to prostatic and comorbid conditions.⁷ Children are also vulnerable, with higher incidence reported among girls under seven years.⁸

The rise of multidrug-resistant (MDR) uropathogens, particularly *E. coli* and *K. pneumoniae*, poses a growing threat. Resistance to first-line agents like ciprofloxacin and trimethoprim-sulfamethoxazole (SXT) has been widely reported, with age and sex influencing resistance patterns. Also, *Klebsiella pneumoniae* have been previously reported to exhibit a high resistance rate to both SXT and cefuroxime (CXM).⁵ Notably, antibiotic resistance patterns can be influenced by both sex and age. Patients over 50 years, have previously demonstrated higher resistance rates to fluoroquinolones and cephalosporins.⁹ According to a large-scale study from the USA, females over 50 years had higher risk of resistance to ciprofloxacin, ceftriaxone, and amoxicillin-clavulanate. While men had lower risk of resistance to amoxicillin-clavulanate but higher resistance to ciprofloxacin.¹⁰ While the presence of bacterial organisms in the urine does not always indicate an active infectious process in the absence of symptoms, asymptomatic bacteriuria can be concerning in certain populations requiring treatment for complete eradication, such as in pregnancy and men undergoing transurethral resection of the prostate.¹¹

This study aims to evaluate sex- and age-stratified trends in uropathogen distribution and antimicrobial resistance using a 7-year dataset from a large tertiary hospital in Saudi Arabia. These insights can inform empirical treatment guidelines and stewardship strategies tailored to demographic risk profiles.

Methods

Study Design and Patient Population

We performed a 7-year retrospective analysis of antibiotic susceptibility test results of urinary isolates of outpatients and inpatients without age or sex restriction. Data were obtained from the clinical microbiology laboratory of Al-Noor Hospital in Makkah, Saudi Arabia (a 500-bed tertiary public hospital) from January 2017 to December 2023. Only samples with positive urine cultures yielding identifiable bacterial organisms were included, regardless of the bacterial count and the presence of urinary symptoms, across various clinical settings, including clinics, wards, emergency department, and intensive care units. Exclusion criteria included missing or incomplete data on microbial growth, sample contamination, or duplicate results. This study complies with the Declaration of Helsinki. Ethical approval from the Institutional Review Board (IRB) of Um AlQura University was obtained (approval No. HAPO-02-K-012-2025-04-2653).

Bacterial Isolates and Antibiotic Susceptibility Testing

The analysis focused on the most commonly identified uropathogens isolated from urine cultures during the study period. These included *E. coli*, *K. pneumoniae*, *Pseudomonas aeruginosa*, *Proteus spp.*, and *Enterococcus spp.* The selection of these organisms was driven by their clinical significance in urinary tract infections and their prevalence within the

dataset. Inclusion was limited to bacterial species with sufficient number of isolates to facilitate a meaningful analysis of resistance patterns. Data collection was conducted in strict adherence to ethical standards during the entirety of the study. The identification of microbes was performed following established laboratory protocols. The bacterial isolates from patient urine samples were cultured on different agar media, including blood agar (Oxoid, Hampshire, UK, CM0259) and MacConkey agar plates (Oxoid, CM0007), and then incubated in a standard incubator at 35–37 °C for 18–24 hours. After the incubation period, bacterial colonies were identified utilizing the Vitek-2 automated system (bioMérieux, Marcy-l'Étoile, France) with GN-21341 and GP-21342 cards for identification. Antibiotic susceptibility testing was carried out using Vitek-2 automated system (bioMérieux, Marcy-l'Étoile, France) with N291, N292, N204, and ASTP605/AST-P516 cards for antimicrobial susceptibility testing. Additionally, the Microscan WalkAway automated system (Negative Breakpoint Combo 50, NBC 50, Beckman Coulter, Brea, CA, USA) was employed, adhering to the manufacturer's guidelines. The analysis of the MIC data adhered to the criteria established by the Clinical Laboratory Standards Institute (CLSI).¹²

Data Analysis

Descriptive statistics were used to summarize the distribution of bacterial species and resistance patterns across sex and age groups. Patient age at the time of culture was categorized into three groups: <18 years, 18–50 years, and >50 years, to allow comparison across pediatric, adult, and older populations. The proportion of resistant isolates was calculated for each antibiotic within these age and sex categories. To assess overall differences in antibiotic resistance rates between males and females, Fisher's exact test was applied to each antibiotic separately. To further evaluate the association between patient sex and age with resistance to specific antibiotics, logistic regression analyses were performed. In each model, the dependent variable was resistance status to the specific antibiotic (ie., non-susceptible vs. susceptible), and the independent variables were sex (male vs. female) and age (as a continuous variable). Logistic regression models were applied only to selected bacterial species that had sufficient isolate counts and resistance events to ensure meaningful statistical inference; other less frequent pathogens were excluded from regression analyses. Therefore, Logistic regression models were only included in the final analysis if they demonstrated statistical significance of the Omnibus test ($p < 0.05$) and showed adequate fit to the data as indicated by the Hosmer–Lemeshow test ($p > 0.05$). Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). A p -value of < 0.05 was considered statistically significant. All analyses were conducted using Stata version 17.0 (StataCorp LLC, College Station, TX, USA).

Results

Sample Selection and Inclusion Flow

The initial dataset included 104,779 isolates, of which 98,732 were excluded due to being non-urine cultures or having missing organism, culture, or antibiotic data (Figure 1). An additional 2,846 isolates were excluded due to duplicate entries or non-relevant organisms. Through the analysis of all eligible urinary isolates collected over the 7-year study period, the resulting subset comprised 3,201 isolates from patients with positive urine cultures with annual isolate counts ranging between 304 in 2020 and 577 in 2018 (Table 1).

Patient and Pathogen Demographics

The sample sizes for males and females were nearly equal, comprising 1,571 isolates from males and 1,630 from females (Table 1). The distribution of patient sex per year shows a difference before and after 2020, with a higher percentage of females recorded prior to 2020. However, following 2020, the proportion of male positive urine samples increased steadily, reaching 61% in 2023. Throughout the years, the majority of isolates (>50%) were identified in patients aged over 50. The trend observed was consistent across males and females, with a notable increase in the proportion of isolates from younger age groups (19–50 years) among males in 2020 (42.5%) and 2023 (31.2%). *E. coli* and *K. pneumoniae* have consistently been identified as the leading causative agents of urinary tract infections, representing over 60% of all samples analyzed annually (Table 1). While *E. coli* accounted for over 40% of isolates in most years, its proportion declined significantly in 2020 and 2023 (22.7% and 22%, respectively) (Table 1). In contrast, *K. pneumoniae* showed

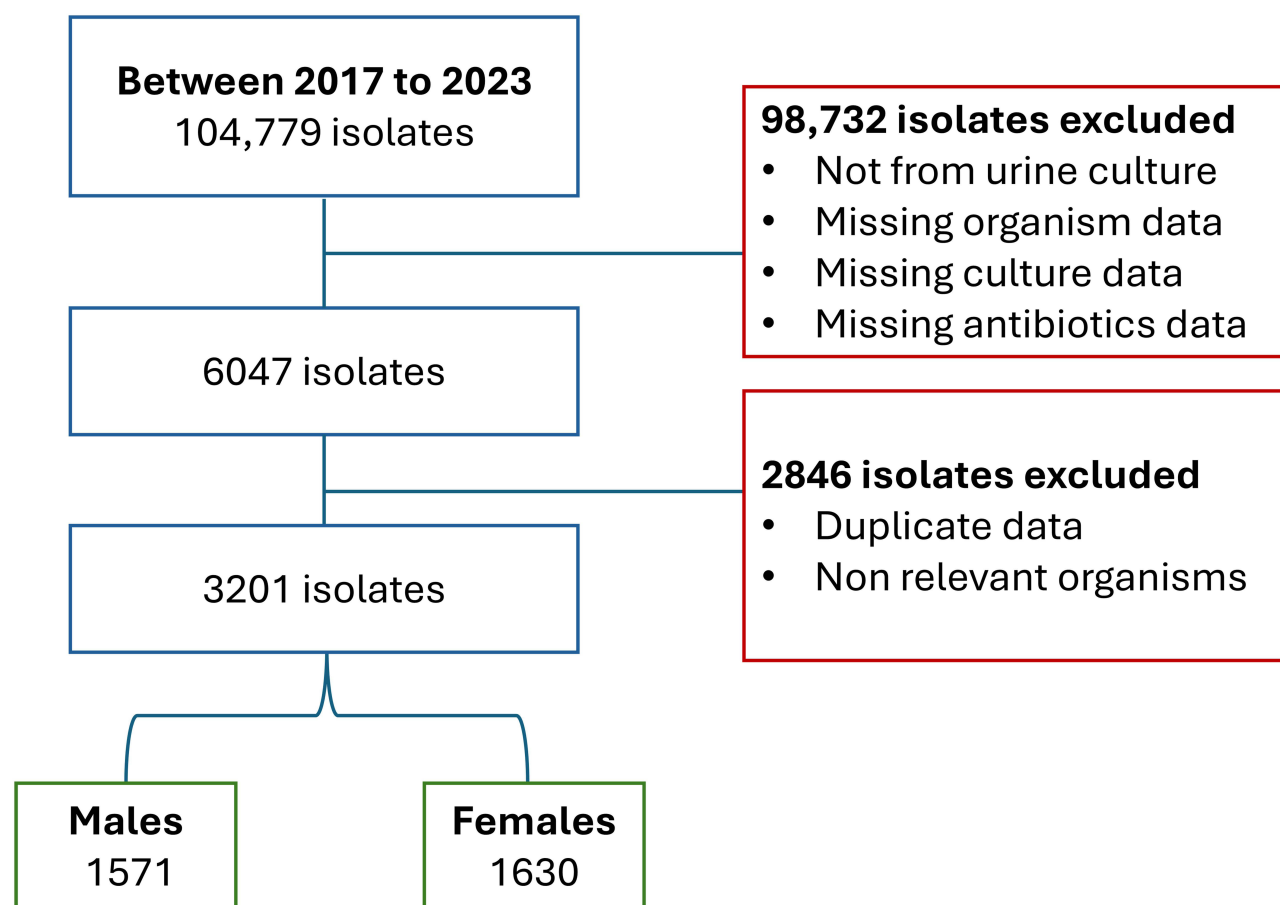


Figure 1 Flowchart of urine culture isolate selection and reasons for exclusion.

a relative increase over time, comprising 43.1% of isolates in 2023. Other organisms such as *P. aeruginosa* and *Enterobacter* spp. showed marked increases in certain years, with *P. aeruginosa* rising to 18.4% in 2020 and 16.7% in 2023. The distribution of urinary pathogens by sex showed distinct patterns (Figure 2). *K. pneumoniae* was the leading pathogen in males in several years (eg, 2017, 2020, 2023) (Figure 2a), peaking at 40.94% in 2020. Notably, *P. aeruginosa* and *Enterobacter* spp. showed a marked rise in males during 2020 and 2023, while their proportions remained lower in females. While *E. coli* consistently dominated among females across all years (Figure 2b), reaching its peak in 2022 (56.25%) but dropping significantly during 2020 (24.14%), coinciding with the COVID-19 pandemic.

Difference in Antimicrobial Resistance by Sex and Age-Group

Significant sex-based differences in resistance rates were noted for several antibiotic-pathogen combinations (Table 2). Among *E. coli* isolates, resistance rates to ampicillin (AMP) and ciprofloxacin (CIP) were significantly higher in males compared to females ($P = 0.027$ and $P = 0.028$, respectively). Additionally, the resistance rates to imipenem (IPM) and meropenem (MEM) were also higher among male patients ($P = 0.020$ and $P = 0.050$). Furthermore, in the case of *K. pneumoniae*, there was a notable increase in resistance among males against various agents, including amikacin (AMK) ($P = 0.011$), CXM ($P = 0.008$), ceftriaxone (CRO) ($P = 0.008$), ceftazidime (CAZ) ($P = 0.007$), CIP ($P = 0.001$), gentamicin (GEN) ($P = 0.001$), imipenem (IPM) ($P = 0.001$), meropenem (MEM) ($P = 0.011$), and SXT ($P = 0.005$). No statistically significant differences were observed between sexes in the distribution of antibiotic resistance by *P. aeruginosa*, *Enterococcus* spp., *Enterobacter* spp., or *P. mirabilis*, although numerically higher resistance rates against certain antibiotics were noted in males exhibited by several organisms.

Table 1 Distribution of Urinary Bacterial Isolates Across 7 years by Sex and Age Group; n (%)

Isolates per year (n)	2017	2018	2019	2020	2021	2022	2023
	402	577	463	304	533	509	413
Sex							
Male (%)	175 (43.5)	238 (41.2)	206 (44.4)	155 (50.9)	261 (48.9)	280 (55)	256 (61.9)
Female (%)	227 (56.4)	339 (58.7)	257 (55.5)	149 (49)	272 (51)	229 (44.9)	157 (38)
Age group (%)							
0 to ≤18 (Male)	3 (1.7)	2 (0.8)	2 (0.9)	2 (1.2)	7 (2.6)	10 (3.5)	6 (2.3)
0 to ≤18 (Female)	1 (0.44)	2 (0.56)	3 (1.1)	1 (0.6)	10 (3.6)	11 (4.8)	1 (0.64)
19 to ≤50 (Male)	20 (11.4)	34 (14.2)	31 (15)	66 (42.5)	60 (22.9)	55 (19.6)	80 (31.2)
19 to ≤50 (Female)	41 (18)	51 (15)	44 (17.1)	66 (44.3)	64 (23.5)	53 (23.1)	37 (23.5)
>50 (Male)	152 (86.8)	202 (84.8)	173 (83.9)	87 (56.1)	194 (74.3)	215 (76.7)	170 (66.4)
>50 (Female)	185 (81.5)	286 (84.3)	210 (81.7)	82 (55)	198 (72.7)	165 (72)	119 (75.8)
Organism (%)							
<i>Escherichia coli</i>	171 (42.5)	230 (39.9)	185 (39.9)	69 (22.7)	186 (34.9)	242 (47.5)	91 (22)
<i>Klebsiella pneumoniae</i>	113 (28.1)	184 (31.9)	136 (29.3)	121 (39.8)	153 (28.7)	154 (30.2)	178 (43.1)
<i>Proteus mirabilis</i>	6 (1.4)	12 (2.1)	9 (1.9)	6 (1.9)	20 (3.7)	25 (4.9)	19 (4.6)
<i>Pseudomonas aeruginosa</i>	26 (6.4)	36 (6.2)	32 (6.9)	56 (18.4)	38 (7.1)	40 (7.8)	69 (16.7)
<i>Enterobacter</i> spp.	6 (1.4)	8 (1.4)	11 (2.3)	31 (10.2)	18 (3.3)	16 (3.1)	40 (9.6)
<i>Enterococcus</i> spp.	25 (6.2)	22 (3.8)	29 (6.2)	11 (3.6)	49 (9.1)	26 (5.1)	11 (2.6)

Age-related patterns indicated that older males (>19 years) exhibited generally higher resistance rates to multiple antibiotics for *E. coli*. However, nitrofurantoin (NIT) demonstrated a higher resistance rate in younger male patients (≤18 years). Younger female patients (<18 years) exhibited heightened resistance to AMP, CIP, and SXT antibiotics against

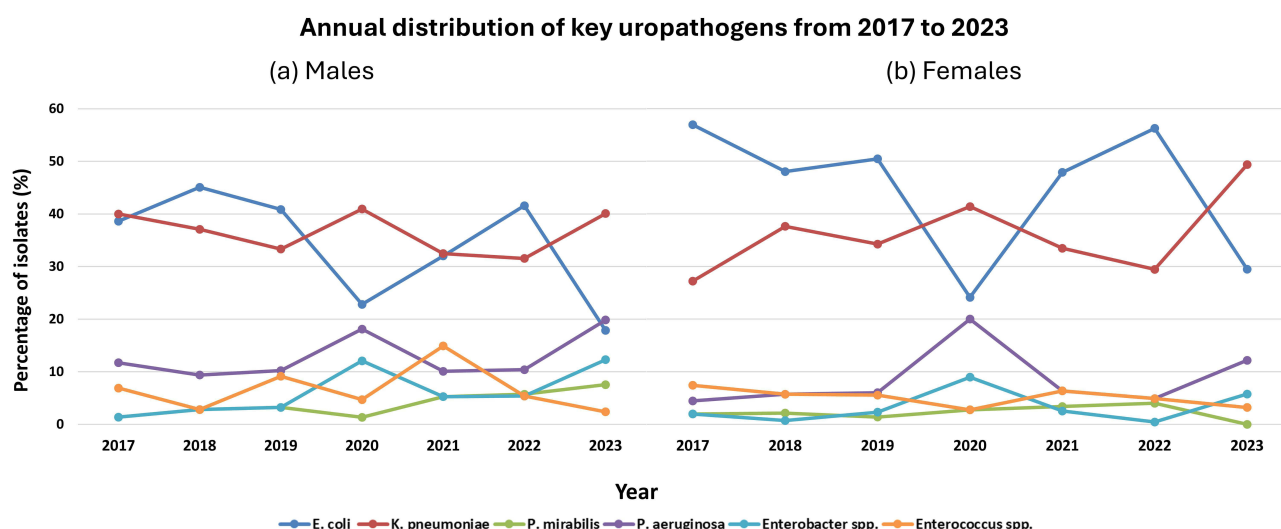

Figure 2 Percentage of uropathogens distribution by sex from 2017 and 2023; (a) distribution in males, (b) distribution in females.

Table 2 Heatmap of Antibiotic Resistance Patterns by Pathogen, Age Group, and Sex in Urine Cultures (2017–2023)

Bacteria	ABX	Males				Females				P-value*
		≤18 n= 6	19-50 n= 71	>50 n= 419	Total n= 496	≤18 n= 19	19-50 n= 153	>50 n= 506	Total n= 678	
<i>E. coli</i> (n=1174)	AMX	0.0	2 (2.8)	10 (2.4)	12 (2.4)	0.0	0.0	9 (1.8)	9 (1.3)	0.185
	AMP	0.0	11 (15.5)	59 (14.1)	70 (14.1)	1 (5.3)	20 (13.1)	46 (9.1)	67 (9.9)	0.027
	CRO	0.0	4 (5.6)	6 (1.4)	10 (2)	0.0	4 (2.6)	7 (1.4)	11 (1.6)	0.660
	CIP	0.0	12 (16.9)	65 (15.5)	77 (15.5)	4 (21.1)	15 (9.8)	56 (11.1)	75 (11.1)	0.028
	GEN	0.0	3 (4.2)	26 (6.2)	29 (5.8)	0.0	1 (0.7)	26 (5.1)	27 (4.0)	0.165
	IPM	0.0	4 (5.6)	6 (1.4)	10 (2)	0.0	1 (0.7)	2 (0.4)	3 (0.4)	0.020
	MEM	0.0	3 (4.2)	11 (2.6)	14 (2.8)	0.0	0.0	8 (1.6)	8 (1.2)	0.050
	NIT	1 (16.7)	1 (1.4)	7 (1.7)	9 (1.8)	0.0	1 (0.7)	9 (1.8)	10 (1.5)	0.648
	SXT	0.0	7 (9.9)	45 (10.7)	52 (10.5)	3 (15.8)	8 (5.2)	62 (12.3)	73 (10.8)	0.924
<i>K. Pneumoniae</i> (n=1039)	ABX	≤18 n= 13	19-50 n= 118	>50 n= 392	Total n= 523	≤18 n= 5	19-50 n= 102	>50 n= 409	Total n= 516	P-value*
	AMK	4 (30.8)	20 (17)	61 (15.6)	85 (16.3)	0.0	13 (12.8)	43 (10.5)	56 (10.9)	0.011
	AMX	2 (15.4)	6 (5.1)	16 (4.1)	24 (4.6)	0.0	1 (1)	21 (5.1)	22 (4.3)	0.880
	AMP	4 (30.8)	17 (14.4)	64 (16.3)	85 (16.3)	1 (20)	12 (11.8)	56 (13.7)	69 (13.4)	0.221
	CEF	2 (15.4)	2 (1.7)	24 (6.1)	28 (5.4)	0.0	4 (3.9)	7 (1.7)	11 (2.1)	0.008
	FEP	4 (30.8)	26 (22)	93 (23.7)	123 (23.5)	0.0	22 (21.6)	74 (18.1)	74 (18.6)	0.057
	FOX	3 (23.1)	5 (4.2)	34 (8.7)	42 (8)	0.0	5 (4.9)	21 (5.1)	26 (5)	0.060
	CRO	2 (15.4)	3 (2.5)	26 (6.6)	31 (5.9)	0.0	4 (3.9)	9 (2.2)	13 (2.5)	0.008
	CAZ	4 (30.8)	21 (17.8)	68 (17.4)	93 (17.8)	0.0	15 (14.7)	45 (11)	60 (11.6)	0.007
	CIP	4 (30.8)	22 (18.6)	80 (20.4)	106 (20.3)	0.0	12 (11.8)	54 (13.2)	66 (12.8)	0.001
	GEN	4 (30.8)	25 (21.2)	69 (17.6)	98 (18.7)	0.0	14 (13.7)	43 (10.5)	57 (11)	0.001
	IPM	4 (30.8)	16 (13.6)	54 (13.8)	74 (14.1)	0.0	9 (8.8)	31 (7.6)	40 (7.8)	0.001
	MEM	4 (30.8)	25 (21.2)	77 (19.6)	106 (20.3)	0.0	17 (16.7)	56 (13.7)	73 (14.1)	0.011
	NIT	3 (23.1)	7 (5.9)	37 (9.4)	47 (9.0)	1 (20)	11 (10.8)	23 (5.6)	35 (6.8)	0.206
	TZP	1 (7.7)	7 (5.9)	11 (2.8)	19 (3.6)	0.0	0.0	16 (3.9)	16 (3.1)	0.732
	TGC	2 (15.4)	9 (7.6)	37 (9.4)	48 (9.2)	0.0	8 (7.8)	26 (6.4)	34 (6.6)	0.135
	SXT	4 (30.8)	27 (22.9)	93 (23.7)	124 (23.7)	0.0	20 (19.6)	66 (16.1)	86 (16.7)	0.005

(Continued)

Table 2 (Continued).

Bacteria	ABX	Males				Females				P-value*
		≤18 n= 6	19-50 n= 71	>50 n= 419	Total n= 496	≤18 n= 19	19-50 n= 153	>50 n= 506	Total n= 678	
<i>P. aeruginosa</i> (n=297)	ABX	≤18 n= 5	19-50 n= 56	>50 n= 124	Total n= 185	≤18 n= 2	19-50 n= 29	>50 n= 81	Total n= 112	P-value*
	AMK	1 (20)	2 (3.6)	8 (6.5)	11 (5.9)	0.0	1 (3.5)	2 (2.5)	3 (2.7)	0.264
	ATM	0.0	0.0	6 (4.8)	6 (3.2)	0.0	1 (3.5)	1 (1.2)	2 (1.8)	0.715
	CAZ	1 (20)	5 (8.9)	14 (11.3)	20 (10.8)	1 (50)	4 (13.8)	5 (6.2)	10 (8.9)	0.693
	LVX	0.0	5 (8.9)	7 (5.7)	12 (6.5)	0.0	2 (6.9)	0.0	2 (1.8)	0.089
	CIP	1 (20)	6 (10.7)	10 (8.1)	17 (9.2)	0.0	4 (13.8)	3 (3.7)	7 (6.3)	0.511
	CST	0.0	4 (7.1)	11 (8.9)	15 (8.1)	0.0	5 (17.2)	3 (3.7)	8 (7.1)	0.826
	FEP	1 (20)	2 (3.6)	10 (8.1)	13 (7)	1 (50)	2 (6.9)	3 (3.7)	6 (5.4)	0.633
	GEN	1 (20)	4 (7.1)	13 (10.5)	18 (9.7)	0.0	3 (10.3)	4 (4.9)	7 (6.3)	0.390
	IPM	1 (20)	4 (7.1)	7 (5.7)	12 (6.5)	0.0	1 (3.5)	1 (1.2)	2 (1.8)	0.089
	MEM	1 (20)	7 (12.5)	13 (10.5)	21 (11.4)	0.0	4 (13.8)	3 (3.7)	7 (6.3)	0.158
	TOB	0.0	0.0	4 (3.2)	4 (2.2)	0.0	1 (3.5)	1 (1.2)	2 (1.8)	1.000
	TZP	0.0	6 (10.7)	12 (9.7)	18 (9.7)	1 (50)	3 (10.3)	5 (6.2)	9 (8)	0.682
<i>Enterococcus</i> spp. (n=173)	ABX	≤18 n= 1	19-50 n= 24	>50 n= 70	Total n= 95	≤18 n= 2	19-50 n= 19	>50 n= 78	Total n= 112	P-value*
	AMK	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
	AMP	0.0	0.0	4 (5.7)	4 (4.2)	0.0	0.0	3 (5.3)	3 (3.8)	1.000
	SAM	0.0	1 (4.2)	0.0	1 (1.1)	0.0	0.0	0.0	0.0	1.000
	CAZ	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
	LVX	0.0	3 (12.5)	7 (10)	10 (10.5)	1 (50)	1 (5.3)	4 (7)	6 (7.7)	0.604
	CIP	0.0	2 (8.3)	6 (8.6)	8 (8.4)	1 (50)	1 (5.3)	3 (5.3)	5 (6.4)	0.774
	DAP	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
	ERY	0.0	6 (25)	7 (10)	13 (13.7)	1 (50)	3 (15.8)	3 (5.3)	7 (9)	0.474
	FEP	0.0	1 (4.2)	0.0	1 (1.1)	0.0	0.0	0.0	0.0	1.000
	LZD	0.0	1 (4.2)	0.0	1 (1.1)	0.0	0.0	0.0	0.0	1.000
	MEM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
	PEN	0.0	0.0	4 (5.7)	4 (4.2)	0.0	1 (5.3)	3 (5.3)	4 (5.1)	1.000
	TEC	0.0	1 (4.2)	2 (2.9)	3 (3.2)	0.0	0.0	3 (5.3)	3 (3.8)	1.000
	TET	0.0	2 (8.3)	3 (4.3)	5 (5.3)	1 (50)	2 (10.5)	4 (7)	7 (9)	0.380
	TOB	0.0	1 (4.2)	0.0	1 (1.1)	0.0	0.0	0.0	0.0	1.000
	VAN	0.0	1 (4.2)	4 (5.7)	5 (5.3)	0.0	0.0	3 (5.3)	3 (3.8)	0.731

(Continued)

Table 2 (Continued).

Bacteria	ABX	Males				Females				P-value*
		≤18 n= 6	19-50 n= 71	>50 n= 419	Total n= 496	≤18 n= 19	19-50 n= 153	>50 n= 506	Total n= 678	
<i>Enterobacter</i> spp. (n=130)	ABX	≤18 n= 1	19-50 n= 30	>50 n= 59	Total n= 90	≤18 n= 0	19-50 n= 16	>50 n= 24	Total n= 40	P-value*
	AMX	0.0	3 (10)	5 (8.5)	8 (8.9)	0.0	0.0	0.0	0.0	0.106
	CAZ	0.0	7 (23.3)	8 (13.6)	15 (16.7)	0.0	0.0	2 (8.3)	5.0	0.091
	CEF	0.0	0.0	4 (6.8)	4 (4.4)	0.0	0.0	0.0	0.0	0.311
	CIP	0.0	6 (20)	12 (20.3)	18 (20)	0.0	0.0	3 (12.5)	3 (7.5)	0.119
	CRO	0.0	0.0	2 (3.4)	2 (2.2)	0.0	0.0	0.0	0.0	1.000
	FEP	0.0	7 (23.3)	10 (17)	17 (18.9)	0.0	1 (6.3)	4 (16.7)	5 (12.5)	0.454
	CFX	0.0	2 (6.7)	6 (10.2)	8 (8.9)	0.0	0.0	0.0	0.0	0.106
	AMK	0.0	7 (23.3)	7 (11.9)	14 (15.6)	0.0	0.0	3 (12.5)	3 (7.5)	0.268
	GEN	0.0	7 (23.3)	7 (11.9)	14 (15.6)	0.0	1 (6.3)	3 (12.5)	4 (10)	0.583
	IPM	0.0	4 (13.3)	3 (5.1)	7 (7.8)	0.0	0.0	2 (8.3)	2 (5)	0.721
	MEM	0.0	9 (30)	7 (11.9)	16 (17.8)	0.0	0.0	3 (12.5)	3 (7.5)	0.179
	NIT	0.0	1 (3.3)	7 (11.9)	8 (8.9)	0.0	1 (6.3)	1 (4.2)	2 (5)	0.723
	SXT	0.0	7 (23.3)	11 (18.6)	18 (20)	0.0	1 (6.3)	3 (12.5)	4 (10)	0.209
	TGC	0.0	2 (6.7)	5 (8.5)	7 (7.8)	0.0	0.0	2 (8.3)	2 (5)	0.721
	TZP	0.0	2 (6.7)	1 (1.7)	3 (3.3)	0.0	0.0	0.0	0.0	0.552
<i>P. mirabilis</i> (n=97)	ABX	≤18 n= 3	19-50 n= 20	>50 n= 40	Total n= 63	≤18 n= 1	19-50 n= 6	>50 n= 27	Total n= 34	P-value*
	AMP	1 (33.3)	3 (15)	9 (22.5)	20.6	0.0	0.0	3 (11.1)	3 (8.8)	0.162
	AMX	0.0	2 (10)	5 (12.5)	7 (11.1)	0.0	0.0	0.0	0.0	0.092
	CAZ	0.0	2 (10)	6 (15)	8 (12.7)	0.0	0.0	1 (3.7)	1 (2.9)	0.154
	CFZ	0.0	2 (10)	9 (22.5)	11 (17.5)	0.0	0.0	2 (7.4)	2 (5.9)	0.131
	CIP	1 (33.3)	2 (10)	9 (22.5)	12 (19)	0.0	0.0	3 (11.1)	3 (8.8)	0.245
	CTX	0.0	1 (5)	5 (12.5)	6 (9.5)	0.0	0.0	0.0	0.0	0.088
	FOF	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
	AMK	0.0	1 (5)	3 (7.5)	4 (6.3)	0.0	0.0	0.0	0.0	0.294
	GEN	0.0	4 (20)	10 (25)	14 (22.2)	0.0	0.0	3 (11.1)	8.8	0.160
	IPM	0.0	0.0	2 (5)	2 (3.2)	0.0	0.0	0.0	0.0	0.540
	MEM	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
	ETP	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
	NIT	2 (66.7)	3 (15)	4 (10)	9 (14.3)	0.0	0.0	1 (3.7)	1 (2.9)	0.158

(Continued)

Table 2 (Continued).

Bacteria	ABX	Males				Females				P-value*
		≤18 n= 6	19-50 n= 71	>50 n= 419	Total n= 496	≤18 n= 19	19-50 n= 153	>50 n= 506	Total n= 678	
	SXT	1 (33.3)	2 (10)	9 (22.5)	12 (19)	0.0	0.0	6 (22.2)	6 (17.6)	1.000
	TZP	0.0	0.0	1 (2.5)	1 (1.6)	0.0	0.0	0.0	0.0	1.000

Notes: *The P-value indicates the significant differences between the total resistance between males and females. All antibiotic abbreviations used follow the standard nomenclature recommended by the American Society for Microbiology (ASM): ABX- Antibiotic, AMK – Amikacin, AMX – Amoxicillin, AMP – Ampicillin, SAM – Ampicillin-Sulbactam, ATM – Aztreonam, CAZ – Ceftazidime, CFZ – Cefazolin, CRO – Ceftriaxone, CXM – Cefuroxime, LEX – Cephalixin, FOX – Cefoxitin, CIP – Ciprofloxacin, FEP – Cefepime, CST – Colistin, CTM – Cefmetazole, CTX – Cefotaxime, DAP – Daptomycin, ERY – Erythromycin, ETP – Ertapenem, FOF – Fosfomycin, GEN – Gentamicin, IPM – Imipenem, LZD – Linezolid, LVX – Levofloxacin, MEM – Meropenem, NIT – Nitrofurantoin, PEN – Penicillin, SXT – Trimethoprim-Sulfamethoxazole (Bactrim), TEC – Teicoplanin, TET – Tetracycline, TGC – Tigecycline, TOB – Tobramycin, TZP – Piperacillin-Tazobactam, VAN – Vancomycin.

E. coli when compared to older female age groups (Table 2). The analysis of ABX sensitivity to *K. pneumoniae*, reveals that younger male patients (≤18 years) exhibit higher resistance rates to AMP, AMX, and 3rd generation cephalosporins (CTX, CAZ, CRO, and FEP) compared to older patients, indicating the presence of Extended-spectrum beta-lactamase (ESBL) producing *K. pneumoniae*. Female patients exhibited a generally elevated resistance rate to the majority of the ABX with the notable exceptions of AMP and NIT, where younger patients (≤18 years) demonstrated higher resistance rates compared to older patients. Moreover, the findings regarding ABX sensitivity for *P. aeruginosa* indicated that younger male patients (≤18 years) had higher rates of resistance to aminoglycosides and carbapenems compared to older patients (Table 2). While adult female patients (19–50 years) exhibited a higher resistance rate to most ABX compared to older patients (>50 years). The sensitivity results for *Enterococcus* spp, revealed a limited number of resistance cases to vancomycin (VAN), suggesting the presence of Vancomycin-Resistant Enterococci (VRE) at rates of 5.3% in males and 3.8% in females.

Factors Associated with Antibiotic Resistance

Logistic regression analyses revealed that male sex was significantly associated with increased odds of antimicrobial resistance across multiple pathogens and antibiotics (Table 3). In the analysis of *E. coli* isolates, males exhibited higher odds of resistance to ampicillin (OR: 1.53; 95% CI: 1.07–2.19; $p = 0.021$), ciprofloxacin (OR: 1.47; 95% CI: 1.05–2.09; $p = 0.026$), and imipenem (OR: 5.83; 95% CI: 1.56–21.68; $p = 0.009$). The analysis revealed a significant association between age and imipenem resistance in *E. coli* (OR: 0.97; 95% CI: 0.94–0.99; $p = 0.007$), indicating a slight decrease in resistance with increasing age.

For *K. pneumoniae*, male sex remained a strong predictor of resistance across several antibiotics: amikacin (OR: 1.59; $p = 0.012$), gentamicin (OR: 1.85; $p = 0.001$), cefalotin (OR: 2.60; $p = 0.008$), ceftriaxone (OR: 2.44; $p = 0.008$), ciprofloxacin (OR: 1.73; $p = 0.001$), ceftazidime (OR: 1.64; $p = 0.006$), imipenem (OR: 1.95; $p = 0.001$), meropenem (OR: 1.53; $p = 0.010$), and trimethoprim-sulfamethoxazole (bactrim) (OR: 1.55; $p = 0.005$). The analysis revealed that age did not exhibit a statistically significant association with resistance to most antibiotics in *K. pneumoniae*. Overall, the findings suggest that male sex serves as an independent predictor of antibiotic resistance in both *E. coli* and *K. pneumoniae*, whereas age appears to have limited influence except in specific cases.

Discussion

In this retrospective study, we have investigated the age- and sex-differences in the distribution of patients with urinary organisms and antibiotic resistance patterns over a period of seven years at a large tertiary care hospital in Saudi Arabia. We found that males, in particular those over 50 years or more, had a higher rate of organism isolation from the urinary tract over time, and that *E. coli* and *K. pneumoniae* remained the predominant uropathogens. Importantly, the number of resistant uropathogens were higher in male patients regardless of bacterial species, while age was not associated with

Table 3 Results of Logistic Regression for the Association of Sex and Age with Antimicrobial Resistance

		OR (95% CI)	P value
<i>E. coli</i>	Ampicillin		
	Female	Ref	
	Male	1.53 (1.07; 2.19)	0.021
	Age	0.99 (0.98; 1.00)	0.438
	Ciprofloxacin		
	Female	Ref	
	Male	1.47 (1.05; 2.09)	0.026
	Age	0.98 (0.99; 1.01)	0.961
	Imipenem		
	Female	Ref	
	Male	5.83 (1.56; 21.68)	0.009
	Age	0.97 (0.94; 0.99)	0.007
<i>K. pneumoniae</i>	Amikacin		
	Female	Ref	
	Male	1.59 (1.10; 2.28)	0.012
	Age	0.99 (0.98; 1.00)	0.529
	Gentamicin		
	Female	Ref	
	Male	1.85 (1.30; 2.63)	0.001
	Age	0.99 (0.98; 1.00)	0.410
	Cefalothin		
	Female	Ref	
	Male	2.60 (1.28; 5.28)	0.008
	Age	1.00 (0.98; 1.02)	0.430
	Ceftriaxone		
	Female	Ref	
	Male	2.44 (1.26; 4.72)	0.008
	Age	1.00 (0.99; 1.02)	0.317
	Ciprofloxacin		
	Female	Ref	
	Male	1.73 (1.24; 2.42)	0.001
	Age	1.00 (0.99; 1.00)	0.856

(Continued)

Table 3 (Continued).

	OR (95% CI)	P value
Ceftazidime		
Female	Ref	
Male	1.64 (1.15; 2.33)	0.006
Age	0.99 (0.98; 1.00)	0.683
Imipenem/Imipenem		
Female	Ref	
Male	1.95 (1.30; 2.93)	0.001
Age	0.99 (0.98; 1.00)	0.573
Meropenem		
Female	Ref	
Male	1.53 (1.10; 2.13)	0.010
Age	0.99 (0.98; 1.00)	0.229
Trimethoprim/sulfamethoxazole		
Female	Ref	
Male	1.55 (1.14; 2.11)	0.005
Age	0.99 (0.98; 1.00)	0.734

bacterial resistance patterns. Overall, these trends reveal important implications for empirical therapy for patients with symptoms suggestive of a UTI, infection control, and antimicrobial stewardship.

A large epidemiological study conducted across the Middle East and North Africa by Amiriet al analyzed UTI incidence trend over 22 years¹³ They found that the burden of UTIs in the Middle East and North Africa has increased over the past three decades, particularly among older adults. Although overall rates have remained relatively stable when adjusted for age, UTIs continue to contribute significantly to morbidity and mortality. The predominance of *E. coli* as the most common urinary pathogen aligns with both local and international literature. In our study, *E. coli* accounted for 22–47.5% of urinary pathogens annually. This is similar to earlier studies from Saudi Arabia, such as the study by Al Hazni et al³ where *E. coli* accounted for approximately 48% of all urinary isolates, and Almutawif et al,¹⁴ who reported a prevalence of approximately 30% for UTIs caused by *E. coli*. A recent systematic review on the epidemiology of complicated UTIs that included 118 study (mainly from the USA) reported that *E. coli* was identified as the most common causative pathogen in complicated UTIs, including pyelonephritis, with a prevalence ranging from 18% to 88.4% in inpatient settings and 26.8% to 86.4% in outpatient settings.

Overall and regardless of sex and age, *K. pneumoniae* came second after *E. coli* as the most common organism isolated from the urine, except during the year 2020 and 2023. The notable decline in *E. coli* prevalence observed in 2020 likely reflects broader shifts in healthcare utilization during the COVID-19 pandemic and shifts toward more hospital-acquired pathogens like *K. pneumoniae*. It is also worth noting that our analysis was based on data from Al Noor tertiary hospital in Makkah that plays a critical role during Hajj (Islamic pilgrimage) season which was dramatically scaled down to limited number of pilgrims in 2020. Therefore, observing this decline in *E. coli* isolation during the pandemic is not surprising, especially with travel restrictions, infection control protocols and social distancing measures being applied. Earlier studies have explored the impact of COVID-19 pandemic on the prevalence of certain uropathogens. For instance, a nationwide study in Finland found a noticeable decline in ESBL-producing *E. coli* in urine and blood infections during

the COVID-19 pandemic.¹⁵ This decline was observed across age groups, sexes, and both community and healthcare settings in several countries, including France, Canada, and Australia.^{16–18} Despite the declining trend in *E. coli* prevalence during 2020, there has been an increase in the rate of *K. pneumoniae* in urine cultures. Studies from multiple countries reported a marked increase in MDR *K. pneumoniae* infections, including UTIs, during the pandemic, consistent with our findings. For example, a study from a large Italian hospital showed that the incidence of MDR *K. pneumoniae* (notably carbapenemase-producing strains) rose during later pandemic waves, particularly among critically ill patients.¹⁹ In Romania, resistance rates of *K. pneumoniae* increased for most antibiotics between 2019 and 2021, with recent antibiotic use and hospital contact as key risk factors.²⁰ In Kenya, 92% of *K. pneumoniae* isolates from ICU patients with UTIs were MDR.²¹ However, in the study by Altamimi et al,²² despite reporting a significant reduction in resistance rates among *E. coli* and *K. pneumoniae* isolates, the authors did report that *K. pneumoniae* surpassed *E. coli* as the leading UTI pathogen during COVID-19 pandemic, which contrasts our findings. Their main observation involved a reduction in resistance rates, not a change in pathogen dominance. Variation in UTI pathogen prevalence between studies is expected and reflects differences in healthcare practices and local epidemiology. These factors can shift the balance between *E. coli* and *K. pneumoniae* as the leading UTI pathogens in different settings and time periods. Overall, the pandemic had a unique impact on UTI bacterial trends emphasizing the need for ongoing surveillance and research in this area.

Our analysis for UTIs revealed notable age- and sex-based differences in antimicrobial resistance among key uropathogens. In *E. coli*, adult male patients (>19 years) exhibited higher resistance to most antibiotics, for nitrofurantoin, which showed greater resistance in younger males (≤18 years). Similarly, younger females had higher resistance rates to ampicillin, ciprofloxacin, and trimethoprim-sulfamethoxazole. Multiple studies confirm that antimicrobial resistance in *E. coli* increases with age, particularly in males. Older males (>50 or >60 years) show higher resistance rates to several antibiotics, including ciprofloxacin and amoxicillin-clavulanate, compared to younger males and females.^{10,23,24} While most studies report low overall resistance to nitrofurantoin, some data suggest that resistance patterns can vary by age and sex. For example, a study found moderate resistance rates (12–30%) to nitrofurantoin, with some age and sex variation, but did not specifically highlight higher resistance in younger males.²⁵ As for younger female patients similar to what we have found, earlier research found that females under 50 or 60 years are more likely to be infected with *E. coli* and, in some settings, have higher resistance rates to ampicillin, ciprofloxacin, and trimethoprim-sulfamethoxazole compared to older females or males.^{10,23,25} Overall there is a strong evidence that age and sex significantly influence antimicrobial resistance patterns in urinary *E. coli* isolates, with older males and younger females are more prone to harbor organisms resistant to key antibiotics. These trends support the need for strategies that age- and sex-specific empirical treatment strategies.

Age- and sex-specific resistance trends in *K. pneumoniae* indicated a concerning pattern of higher resistance among younger male patients (≤18 years), particularly against ampicillin, amoxicillin, and third-generation cephalosporins (CTX, CAZ, CRO, and FEP), suggesting the presence of ESBL-producing strains in this age group. In contrast, female patients showed an overall higher resistance to most tested antibiotics, with the exception of ampicillin and nitrofurantoin, where resistance was notably higher in younger females. Previous studies confirm that male sex is a significant risk factor for MDR and ESBL-producing *K. pneumoniae* infections. Several studies confirm that male sex is a significant risk factor for multidrug-resistant (MDR) and ESBL-producing *K. pneumoniae* infections.^{26–28} Age-specific data show that children and adolescents can have high rates of *K. pneumoniae* UTI and resistance, especially in males, though most studies report the highest prevalence in very young (1–9 years) or middle-aged males.^{26,27} Resistance to third-generation cephalosporins and ampicillin is common in *K. pneumoniae*, and high rates in younger males may indicate ESBL production, though most studies do not provide detailed breakdowns by both age and sex for these antibiotics.^{26,27,29} Although current research suggests that male sex and younger age are associated with increased resistance in *K. pneumoniae* UTIs—particularly for MDR and ESBL-producing strains—and that females may exhibit higher resistance to certain antibiotics, detailed age- and sex-specific resistance patterns for individual drugs remain under-reported, underscoring the need for more granular surveillance. An 11-year review of antibiotic resistance trend in Saudi Arabia showed a lower rate of ESBL-producing *E. coli* and *K. pneumoniae* isolation in 2020 reaching less than 30%, which corroborates with our findings. Notably, however, *K. pneumoniae* labeled as CRE was isolated at a rate of

approximately 70% compared with CRE *E. coli* which was isolated at a rate of less than 10%. This probably reflects the overuse of broad-spectrum antibiotics during the COVID-19 pandemic which was reported in a large global study.^{30,31}

The third most common uropathogen identified in our study was *P. aeruginosa*. No differences were observed in the distribution of antibiotic resistance between age and sex groups. However, the notable higher prevalence of resistance to aminoglycosides and β -lactams, including carbapenems, among isolates collected from male patients aged ≤ 18 years was probably due to denominator issue as the number of isolates in this group was only five. The MDR pattern demonstrated by *P. aeruginosa* in this study reflects what was reported from several antimicrobial resistance surveillance studies from Saudi Arabia, where the average prevalence of MDR *P. aeruginosa* varied between 10% and 60% over the last 10 years.³¹ A lack of difference in antibiotic resistance with regards to age and sex was also seen among the remaining isolates, *Enterococci* spp., *Enterobacter* spp., and *P. mirabilis*, which could be due to lower isolation rates compared with *E. coli* and *K. pneumoniae*, which has been documented in previous epidemiological studies from Saudi Arabia and globally.^{3,32}

A major strength of this study is the inclusion of a large number of urinary isolates over a 7-year period, providing a robust dataset to analyze temporal trends and stratify resistance patterns by age and sex. The study also highlights resistance data for commonly encountered uropathogens, offering granular insight into differences not only between organisms but also across patient demographics. However, the study has some limitations that demand careful interpretation of results. As a single-center retrospective analysis, generalizability to other settings may be limited. Despite the large sample size, the analysis was constrained by the limited availability of patient-level clinical data, including information on urinary symptoms, which limited our ability to distinguish between symptomatic UTIs and asymptomatic bacteriuria—an important consideration when interpreting resistance findings and their therapeutic implications. Due to the retrospective design and reliance on microbiology records, we were unable to stratify isolates by clinical context, including community- versus hospital-acquired infections, presence of urinary catheterization, or classification into complicated versus uncomplicated UTI. These factors may influence the observed patterns and should be considered in future prospective studies. Additionally, while resistance patterns to third-generation cephalosporins (eg, ceftriaxone, cefotaxime) were observed, we could not definitively determine extended-spectrum β -lactamase (ESBL) or carbapenemase production, as phenotypic confirmatory tests (eg, clavulanate synergy) or molecular assays were not performed. As such, resistance mechanisms were inferred based on antibiotic susceptibility data rather than confirmed by standardized ESBL detection methods.

Conclusion

This 7-year retrospective analysis from a tertiary care hospital in Saudi Arabia highlights evolving uropathogen trends and antimicrobial resistance patterns, with notable differences by age and sex. *E. coli* and *K. pneumoniae* remain the most common pathogens, yet significant resistance variability exists across patient subgroups and antibiotics. These findings underscore the importance of tailored empirical therapy guided by local surveillance and patient demographics, along with ongoing efforts in antimicrobial stewardship and resistance monitoring. Recognizing age- and sex-related resistance variations can support more targeted antibiotic choices, improving outcomes and limiting further resistance. The observed shifts during the COVID-19 period further emphasize the need for continuous surveillance. Future studies should investigate the underlying drivers and validate these findings in broader, multicenter cohorts with clinical correlates and resistance mechanism confirmation.

Data Sharing Statement

The data underlying this study are derived from a tertiary hospital database and contain anonymized patient information. Due to ethical and legal restrictions, these data cannot be shared publicly. Access to the data may be granted upon reasonable request and with prior approval from the hospital's ethical review board. Interested researchers may contact the corresponding author to initiate the request and obtain guidance on submitting the necessary ethical approval.

Ethics Statement

The study utilized anonymized data extracted from hospital records, and individual patient consent was not required as per the IRB guidelines, given the retrospective nature of the study and the use of fully de-identified data.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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