Original Article

Patterns of antibiotic resistance in uropathogens isolated from pediatric patients

A multicenter study

Zeyad A. Almatroudi, *Medical Student,* ***Abdullah M. Almazrou,*** *Medical Student,* ***Abdullah H. Aljomoai,*** *Medical Student,* ***Zaid M. Alsulami,*** *Medical Student,* ***Abdulaziz M. Alotaibi,*** *Medical Student,* ***Abdulmohsen A. Almutairi,*** *Medical Student,* ***Aiman El-Saed,*** *MD, PhD,* ***Faisal A. Alsehli,*** *PharmD, MSc,* ***Majid M. Alshamrani,*** *MD.*

ABSTRACT

الأهداف: تقييم أنماط مقاومة المضادات الحيوية في مسببات الأمراض البولية الشائعة المعزولة من مرضى الأطفال.

المنهجية: اشتملت هذه الدراسة مراجعةً رجعيةً لبيانات مسببات الأمراض البولية المسببة لالتهابات المسالك البولية المصحوبة بأعراض والمكتسبة من المجتمع لأول مرة. جُمعت بيانات هذه الدراسة من مستشفى رعاية ثالثية وأربعة مراكز رعاية أولية في الرياض، المملكة العربية السعودية، وتغطي الفترة من 2017 إلى 2022م. كان تشخيص التهابات المسالك البولية متوافقًا مع إرشادات الأكاديمية الأمريكية لطب الأطفال.

النتائج: جُمعت العينات المعزولة من 610 مرضى، منهم 101 (16.6%) من الذكور و509 (83.4%) من الإناث. كانت الأنواع الثلاثة الأكثر شيوعًا المعزولة هي الإشريكية القولونية (E. coli؛ 50.5% لدى الذكور و82.7% لدى الإناث)، والكلبسيلة الرئوية (*K. pneumoniae*؛ 82.7% لدى الذكور و10.4% لدى الإناث)، ثم بروتيوس ميرابيليس (5.9% لدى الذكور و2.9% لدى الإناث). كانت الإشريكية القولونية أكثر انتشارًا لدى الإناث منها لدى الذكور (p<0.001). كما عُزلت الإشريكية القولونية المقاومة للأدوية المتعددة من الذكور أكثر من الإناث (39.2% مقابل 23.5%، p=0.014). لوحظ اتجاه مماثل، وإن كان غير ذي دلالة إحصائية، في بكتيريا كلوستريديوم نيوموني المقاومة للأدوية المتعددة (48.1% مقابل 30.8%، p=0.128)، وفي بكتيريا الإشريكية القولونية المنتجة لبيتا لاكتاماز ممتد الطيف (ESBL) (13.7% مقابل 11.9%، قيمة الاحتمال p=0.701)، وفي بكتيريا كلوستريديوم نيوموني المنتجة لبيتا لاكتاماز ممتد الطيف (ESBL) (18.5% مقابل 7.7%، قيمة الاحتمال p=0.151).

الخلاصة: وجدنا أن مراقبة مقاومة مسببات الأمراض البولية يجب أن تُميز بين العزلات المأخوذة من مرضى ذكور وإناث. كما تشير هذه الدراسة إلى احتمال زيادة عزلات الإشريكية القولونية المنتجة لبيتا لاكتاماز ممتد الطيف، وزيادة عزلات الإشريكية القولونية المقاومة للأدوية المتعددة.

Objectives: To evaluate the antibiotic resistance patterns in common uropathogens isolated from pediatric patients.

Methods: This was a retrospective chart review on the uropathogens causing first-time, community-acquired, symptomatic urinary tract infection (UTI). The data for this study was collected from one tertiary care hospital and 4 primary care centers in Riyadh, Saudi Arabia, with data spanning from 2017-2022. Diagnosis of UTIs was in line with the guidelines of the American Academy of Pediatrics.

Results: Isolates were gathered from 610 patients, 101 (16.6%) of whom were male and 509 (83.4%) were female. The 3 most common species isolated were *Escherichia coli* (*E. coli*; 50.5% in males and 82.7% in females), *Klebsiella pneumoniae* (*K. pneumoniae*; 28.7% males and 10.4% females), and then *Proteus mirabilis* (5.9% males and 2.9% in females). *Escherichia coli* was more prevalent in females than in males ($p<0.001$). Multidrugresistant *E. coli* was isolated more often from males than in females (39.2% versus 23.5%, $p=0.014$). A similar but non-significant trend was observed in multidrug-resistant *K. pneumoniae* (48.1% versus 30.8%, $p=0.128$), extended-spectrum beta-lactamase (ESBL) producing *E. coli* (13.7% versus 11.9%, $p=0.701$), and ESBL-producing *K. pneumoniae* (18.5% versus 7.7%, $p=0.151$).

Conclusion: Our study indicates that surveillance of uropathogen resistance should differentiate between isolates gathered from male and female patients. This study also indicates a possible increase in ESBL-producing *E. coli* isolates, and an increase in multidrug-resistant *E. coli* isolates.

Keywords: antibiotic resistance, multidrug-resistance, urinary tract infection, pediatrics, extended-spectrum beta-lactamase

Saudi Med J 2025; Vol. 46 (4): 418-424
doi: 10.15537/smj.2025.46.4.20241083

From the College of Medicine (Almatroudi, Almazrou, Aljomoai, Alsulami, Alotaibi, Almutairi, Alsehli), King Saud bin Abdulaziz University for Health Sciences, from the Department of Neonatal Intensive Care (Alsehli); and from the Department of Infection Prevention and Control (El-Saed, Alshamrani), King Abdulaziz Medical City, Riyadh, Kingdom of Saudi Arabia.

Received 25th December 2024. Accepted 17th March 2025.

Address correspondence and reprint request to: Dr. Zeyad A. Almatroudi, College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Kingdom of Saudi Arabia.
E-mail: ZeyadAlmatroudi@outlook.com
ORCID ID: https://orcid.org/0009-0009-4849-7144.

The misuse and overuse of antibiotics has led to bacteria developing mechanisms to overcome the efficacy of antibiotics; this is known as antibiotic resistance. Antibiotic resistance is an emerging threat that is affecting public health. In 2019, infections with bacteria that were antibiotic resistant were responsible for over one million fatalities worldwide and approximately 2,500 deaths in Saudi Arabia.[1,2] It is also estimated that 33,110 deaths in the European Union in 2015 can be attributed to infections with bacteria that were resistant to antimicrobials.[3]

Antibiotic resistance is especially dangerous for pediatric patients, as infection with multidrug-resistant (MDR) bacteria increases morbidity and mortality, and the mortality rate due to antibiotic resistant bacteria will only increase without proper intervention.[4] The effect of antibiotic-resistant bacteria is even more apparent in urinary tract infections (UTIs) in children, where up to 83% of the causative uropathogens were found to be resistant to first-line treatment options. In contrast, up to 58% of the causative uropathogens in adults were resistant to first-line treatment options.[5,6] It was also found that pediatric patients up to 5 years old were most susceptible to infections with multidrug-resistant bacteria out of any other age group.[7]

While there are some local studies on antimicrobial resistance, most of them are limited to specific pathogens (namely, *Escherichia coli* [*E. coli*]), and many more do not differentiate between adult and pediatric patients nor between isolates gathered from male and female patients. Despite some local studies on antibiotic resistance, the consumption of antibiotics continues to be higher than the international average.[8,9] The importance of gathering statistics on antibiotic resistant bacteria is clear now more than ever, as infections that were once easy to treat, now require extensive testing and more complex treatment strategies.[10]

Studies on antibiotic resistance are insufficient in Saudi Arabia, but resistance patterns of infections in pediatric patients are especially sparse. Local studies on cases of antibiotic resistance in pediatrics are primarily focused on the resistance of a specific pathogen rather than a more comprehensive view of the resistance patterns within an infectious disease entity. This study aimed to evaluate resistance patterns of the causative pathogens of UTIs affecting pediatric patients at a hospital network in Riyadh, Saudi Arabia.

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

Methods. This study was a retrospective chart review that investigated the causative uropathogens and their respective resistance to antibiotics in first-time, community-acquired urinary tract infection (CAUTI). The study was carried out in 5 centers under the umbrella of the Ministry of National Guard Health Affairs, all of which were in Riyadh, Saudi Arabia. Our study focused on patients treated in the emergency department and outpatient care. The data gathered spanned over a 6-year period from 2017-2022. The data collected included patient diagnoses, medications prescribed, cultures of the organisms isolated, and testing of their respective susceptibility to antibiotics.

In accordance with the guidelines of the American Academy of Pediatrics, the following guidelines were used as the definition of UTI: growth of 1,000 colony-forming units (CFUs) per mL from suprapubic aspiration, 50,000 CFUs/mL for catheter samples, or 100,000 CFUs/mL for clean catch samples.[11]

Patients aged 0-15 with a first-time diagnosis of symptomatic UTI with bacteria as the causative pathogen were included. Organ transplant patients and stem cell transplant patients, along with healthcare-associated infections, were excluded.

King Abdullah International Medical Research Center, Riyadh, Saudi Arabia, provided a complete data set from the centers, including patient diagnosis, medications prescribed, culture results, and culture sensitivity results.

Statistical analysis. OpenEpi was used to carry out Chi-square tests to assess the differences between isolates gathered from male versus female patients, and a *p*-value of <0.05 was considered significant.

Results. Out of the isolates gathered, 610 fit the inclusion criteria, 509 (83.4%) of which were from female patients, whereas only 101 (16.5%) were from male patients. When including both genders, 389 (63.7%) were 5 years old or younger. There were 172 patients less than one year old; and of those, 125 (72.7%) were female, whereas only 47 (27.3%) were male ($p<0.001$, Table 1).

Escherichia coli was most common, with 421 (82.7%) isolates from female and 51 (50.5%) from

Table 1 - Age distribution of patients, stratified by gender.

Age groups (in years)	Males (n=101)	Females (n=509)	*P*-values
<1	47 (46.6)	125 (24.6)	<0.001
1-5	27 (26.7)	190 (37.3)	0.042
6-15	27 (26.7)	194 (38.1)	0.029

Values are presented as numbers and percentages (%).

male patients. Second most prevalent was *Klebsiella pneumoniae* (*K. pneumoniae*) with 52 (10.2%) isolates from female patients and 27 (26.7%) from male patients, and third most common, *Proteus mirabilis* (*P. mirabilis*) with 15 (2.9%) isolates from female patients and 6 (5.9%) from male patients (Table 2).

Table 2 includes one more *Klebsiella* isolate from female patients, and 2 more *Klebsiella* isolates from male patients, and these were *Klebsiella oxytoca* (*K. oxytoca*) isolates. Therefore, the *Klebsiella* isolates gathered were 52 *K. pneumoniae* and one *K. oxytoca* isolates from females, and 27 *K. pneumoniae* and 2 *K. oxytoca* specimens from males.

When comparing the ratio of *E. coli* to non-*E. coli* isolates affecting male and female individuals, it was found that males were more likely to present with non-*E. coli* UTI ($p<0.001$, Table 3).

From the isolates collected from females, *E. coli* was shown to be highly sensitive to nitrofurantoin, with 392 (96.3%) tested isolates being sensitive; only 2 (0.5%) resistant and 13 (3.2%) intermediate susceptibility isolates were found. Trimethoprim/sulfamethoxazole (TMP/SMX) showed lesser efficacy, with 260 (63.1%) of the tested isolates being sensitive and 152 (36.9%) being resistant. The isolates collected showed similar susceptibility to ceftriaxone with 324 (78.6%) and ciprofloxacin with 305 (76.6%) tested isolates being sensitive to both, while 87 (21.1%) tested specimens were resistant to ceftriaxone and 62 (15.6%) were resistant to ciprofloxacin; however, where the tested isolates only included one that had intermediate susceptibility to ceftriaxone, 31 (7.8%) of the isolates tested for ciprofloxacin sensitivity showed intermediate susceptibility. A total of 324 samples were tested for ampicillin susceptibility, 199 (61.4%) were resistant, one was of intermediate susceptibility, and 124 (38.3%) isolates were sensitive (Table 4).

Escherichia coli isolates from males tested for nitrofurantoin showed promising susceptibility, with 41 (97.6%) sensitive isolates and one (2.3%) isolate with intermediate susceptibility. Of the isolates tested for TMP/SMX susceptibility, 23 (52.3%) were sensitive, and 21 (47.7%) were resistant. Isolates tested for ceftriaxone susceptibility showed 29 (63%) sensitive isolates and 17 (37%) resistant isolates and ciprofloxacin susceptibility showed 20 (47.6%) sensitive isolates and 16 (38.1%) resistant isolates; although, 6 (14.3%) isolates had intermediate susceptibility to ciprofloxacin. A total of 41 isolates were tested for ampicillin susceptibility, 32 (78%) were resistant, 8 (19.5%) were sensitive, and one isolate had intermediate susceptibility to ampicillin (Table 4).

There were 52 *K. pneumoniae* isolates collected from female patients, 49 of which were tested for ampicillin susceptibility; all 49 tested isolates were resistant to ampicillin. A total of 44 *K. pneumoniae* isolates were tested for nitrofurantoin susceptibility, 17 (38.6%) isolates were sensitive, 5 (11.4%) were resistant, and 22 (50%) were of intermediate susceptibility to nitrofurantoin. A total of 44 isolates were also tested for TMP/SMX susceptibility, 35 (79.6%) of which were sensitive, whereas 9 (20.4%) isolates were resistant to TMP/SMX. Of the isolates tested for ceftriaxone susceptibility, 38 (80.8%) were sensitive, and 9 (19.1%) were resistant. 30 (69.7%) of isolates tested for ciprofloxacin susceptibility were sensitive, 6 (13.9%) were resistant, and an additional 7 (16.3%) were of intermediate susceptibility, unlike ceftriaxone (Table 4)

In the case of *K. pneumoniae*, only 27 specimens were gathered from males, 25 of which were tested for ampicillin susceptibility and were all resistant. Of the 20 isolates tested for nitrofurantoin susceptibility, 7 (35%) were sensitive, one was resistant, and 12 (60%) were of intermediate susceptibility to nitrofurantoin. A total of

Table 2 - Distribution of uropathogen species, stratified by gender.

Species ↓	Males	Females	Total by species
Escherichia coli	51 (50.5)	421 (82.7)	472 (77.4)
Klebsiella species	29 (28.7)	53 (10.4)	82 (13.4)
Proteus mirabilis	6 (5.9)	15 (2.9)	21 (3.4)
Pseudomonas aeruginosa	5 (4.9)	4 (0.8)	9 (1.5)
Citrobacter koseri	1 (1.0)	4 (0.8)	5 (0.8)
Enterococcus species	2 (2.0)	4 (0.8)	6 (0.9)
Enterobacter cloacae	4 (4.0)	2 (0.4)	6 (0.9)
Salmonella species	2 (2.0)	2 (0.4)	4 (0.7)
Achromobacter xylosoxidans	1 (1.0)	0 (0.0)	1 (0.2)
MRSA	0 (0.0)	1 (0.2)	1 (0.2)
Myroides species	0 (0.0)	1 (0.2)	1 (0.2)
Acinetobacter baumannii	0 (0.0)	1 (0.2)	1 (0.2)
Streptococcus agalactiae	0 (0.0)	1 (0.2)	1 (0.2)
Total by gender	101 (100)	509 (100)	610 (100)

Values are presented as numbers and percentages (%).
MRSA: Methicillin-resistant *Staphylococcus aureus*

Table 3 - *Escherichia coli* verses non-*Escherichia coli* isolates, stratified by gender ($p<0.001$).

Species ↓	Males (n=101)	Females (n=509)
E. coli	51 (50.5)	421 (82.7)
Non-*E. coli*	50 (49.5)	88 (17.3)

Values are presented as numbers and percentages (%).
E. coli: *Escherichia coli*

Table 4 - Resistance patterns of *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis* isolates, stratified by gender.

Species	Antibiotic ↓	Males		Females		*P*-values
		No. of isolates tested	Non-susceptible	No. of isolates tested	Non-susceptible	
E. coli	Ampicillin	41	33 (80.5)*	324	200 (61.7)	0.018
	Ceftriaxone	46	17 (37.0)*	412	88 (21.4)	0.016
	Ciprofloxacin	42	22 (52.4)*	398	93 (23.4)	<0.001
	Imipenem	17	0 (0.0)*	88	0 (0.0)	N/A
	Meropenem	17	0 (0.0)*	89	0 (0.0)	N/A
	Nitrofurantoin	42	1 (2.4)*	407	15 (3.7)	0.664
	TZP	8	0 (0.0)*	54	3 (5.6)	0.494
	TMP/SMX	44	21 (47.7)*	412	152 (36.9)	0.159
	Gentamicin	26	0 (0.0)*	122	9 (7.4)	0.153
	Amox-clav	9	2 (22.2)*	62	18 (29.0)	0.671
K. pneumoniae	Ampicillin	25	25 (100)	49	49 (100)	N/A
	Ceftriaxone	26	10 (38.5)	47	9 (19.1)	0.071
	Ciprofloxacin	19	10 (52.6)	43	13 (30.2)	0.092
	Imipenem	10	0 (0.0)	9	0 (0.0)	N/A
	Meropenem	10	0 (0.0)	9	0 (0.0)	N/A
	Nitrofurantoin	20	13 (65.0)	44	27 (61.4)	0.780
	TZP	5	1 (20.0)	4	0 (0.0)	0.342
	TMP/SMX	19	14 (73.7)	44	9 (20.4)	<0.001
	Gentamicin	21	1 (4.8)	22	2 (9.1)	0.577
	Amox-clav	6	1 (16.7)	6	1 (16.7)	1
P. mirabilis	Ampicillin	5	2 (40.0)	13	6 (46.1)	0.882
	Ceftriaxone	6	1 (16.7)	15	2 (13.3)	0.865
	Ciprofloxacin	6	1 (16.7)	15	2 (13.3)	0.865
	Imipenem	1	0 (0.0)	1	1 (100)	0.386
	Meropenem	2	0 (0.0)	2	0 (0.0)	N/A
	Nitrofurantoin	6	6 (100)	15	15 (100)	1
	TMP/SMX	6	2 (33.3)	15	4 (26.7)	0.821
	Gentamicin	4	0 (0.0)	3	1 (33.3)	0.286
	Amox-clav	1	1 (100)	3	1 (33.3)	0.540

Values are presented as numbers and percentages (%). *Non-susceptibility includes resistant and intermediate susceptibility isolates. *E. coli*: *Escherichia coli*, *K. pneumoniae*: *Klebsiella pneumoniae*, *P. mirabilis*: *Proteus mirabilis*, TZP: piperacillin-tazobactam, TMP/SMX: trimethoprim-sulfamethoxazole, Amox-clav: amoxicillin and clavulanate, N/A: not available

19 isolates were tested for TMP/SMX susceptibility, 5 (26.3%) isolates were sensitive, whereas 14 (73.7%) were resistant. All but one isolate were tested for ceftriaxone susceptibility, 16 (61.5%) isolates were sensitive, but 10 (38.4%) were resistant. A total of 19 isolates were tested for ciprofloxacin susceptibility, 9 (47.3%) isolates were sensitive, 6 (31.5%) were resistant, and 4 (21%) were of intermediate susceptibility to ciprofloxacin. Gentamicin susceptibility was also tested, 20 (95.2%) isolates were sensitive, and one isolate was resistant (Table 4).

A total of 15 isolates of *P. mirabilis* were collected from females, all of which were tested for nitrofurantoin susceptibility, all 15 were resistant to nitrofurantoin. All 15 isolates were also tested for TMP/SMX susceptibility, 11 (73.3%) were sensitive, and 4 (26.6%) were resistant. The isolates were also tested for ceftriaxone and ciprofloxacin; the isolates had the same susceptibility to both, with 13 (86.6%) isolates sensitive and 2 (13.3%) isolates resistant to ceftriaxone and ciprofloxacin (Table 4).

A multidrug-resistant isolate was defined as an isolate with non-susceptibility (whether resistance or intermediate susceptibility) to at least one antibiotic agent within 3 or more separate antibiotic categories.[12] With that in mind 99 (23.5%) of the 421 *E. coli* isolates gathered from females were MDR, compared to the 20 (39.2%) out of a total of 51 *E. coli* isolates gathered from males (p=0.014). *Klebsiella pneumoniae* isolates gathered from females had 16 (30.8%) MDR isolates out of the 52 total isolates collected, whereas *K. pneumoniae* isolates from males had 13 (48.1%) MDR isolates out of the 27 total isolates (p=0.128, Figure 1).

Extended spectrum beta-lactamase (ESBL)-producing isolates were found among the *E. coli* and *K. pneumoniae* specimens collected from both males and females. From the 421 *E. coli* isolates gathered from females, 50 (11.9%) of them were found to be ESBL-producing *E. coli* isolates, whereas of the 51 *E. coli* isolates gathered from males, 7 (13.7%) of them were ESBL-producing isolates (p=0.701). On the other hand, of the 52 *K. pneumoniae* isolates collected from females, 4 (7.7%) were ESBL-producing, compared to the *K. pneumoniae* isolates gathered from males which contained 5 (18.5%) ESBL-producing isolates out of the 27 isolates in total (p=0.151, **Figure 1**).

A statistically significant difference was found between the amount of non-*E. coli* isolates causing UTI in males compared to females, with males being more likely to have a non-*E. coli* UTI (p<0.001). When comparing the *E. coli* isolates gathered from males and females, specimens from males were more likely to be resistant/intermediate susceptibility to ampicillin (p=0.018), ceftriaxone (p=0.016), and ciprofloxacin (p<0.001).

When comparing the ESBL-producing *E. coli* isolates gathered from males and females, no statistically significant difference was found (p=0.701). However, it was found that MDR *E. coli* isolates affected males more (p=0.014).

Regarding *K. pnemoniae* isolates, a proportionally larger number of isolates gathered from male patients were non-susceptible to ceftriaxone (p=0.071) and ciprofloxacin (p=0.092) compared to isolates gathered from females. However, the results are not statistically significant, which may change if the sample size for *K. pneumoniae* isolates increases. Interestingly, TMP/SMX resistant *K. pnemoniae* isolates were more commonly isolated from male patients (p<0.001) which must be validated and studied. Again, no difference was found between the susceptibility of *K. pnemoniae* isolates gathered from males compared to females when it came to imipenem, meropenem, nitrofurantoin, piperacillin-tazobactam (TZP), gentamicin, or amoxicillin/clavulanate. However, it is important to note that these results may change with a larger sample size of *K. pnemoniae* isolates.

Proportionally speaking, more of the *K. pneumoniae* isolates gathered from males were ESBL-producing (p=0.151) and MDR (p=0.128) than isolates gathered from females, but a larger sample size of *K. pneumoniae* is needed to validate these claims.

Discussion. When comparing the species gathered, UTI due to *E. coli* was most common, with 77.4% of isolates being *E. coli*, close to the 75.7% that a comparable study found.[6] An interesting finding brought up by Hameed et al[5] was that non-*E. coli* isolates were proportionally more common in male patients; our study reinforces this finding; 49.5% of the isolates gathered from males were non-*E. coli* species, compared to 17.3% of non-*E. coli* isolates from females (p<0.001, **Table 3**).

Comparing the number of MDR isolates found in our study to those found in other studies proved somewhat difficult due to the differences in defining MDR. Nevertheless, Alanazi et al[6] using the same definition for MDR that our study used, found that from January to March of 2008, 22.7% of the *E. coli* isolates gathered were MDR, compared to 25.2% that we found in this study, possibly indicating a 2.5% increase in MDR CAUTIs in pediatric patients over a decade.

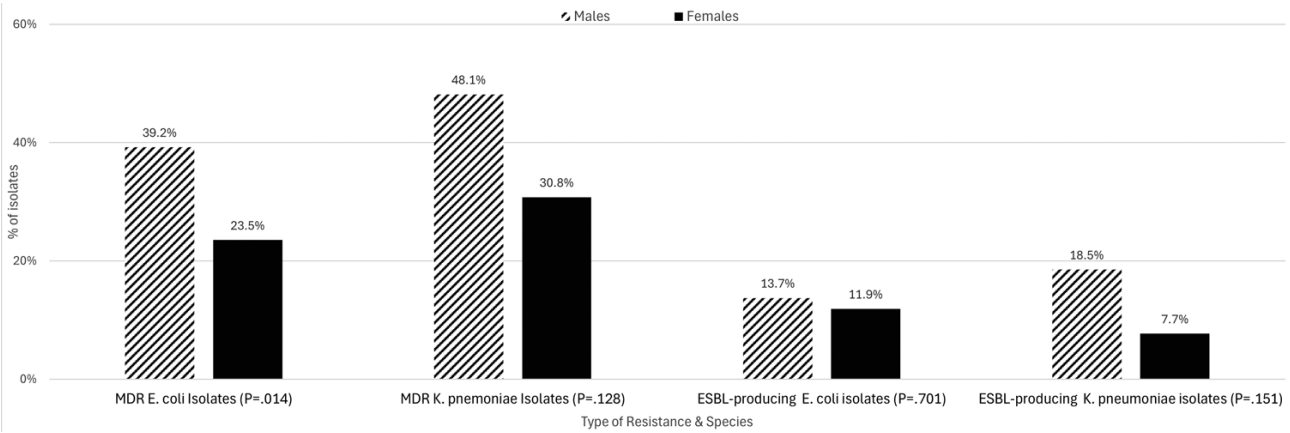

Figure 1 - Multidrug-resistant and extended-spectrum beta lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* isolates, stratified by gender. MDR: multidrug-resistant, E. coli: *Escherichia coli*, K. pnemoniae: *Klebsiella pneumoniae*, ESBL: extended-spectrum beta lactamase

Alqasim et al[13] observed that 67% of *E. coli* specimens gathered from inpatients (most of whom were adults) hospitalized in a tertiary hospital were MDR, compared to the 25.2% that our study found in the outpatient/emergency department setting in pediatric patients. This highlights the need for a study to provide insight into the resistance patterns of antibiotics to uropathogens in pediatric inpatients possibly with hospital-acquired infection.

While our study found that 57 (12.1%) of the *E. coli* samples were ESBL-producing, Alanazi et al[6] found that only 3.2% of the *E. coli* isolates gathered from pediatric patients from January to March 2008 were ESBL-producing. The previously mentioned study was carried out at King Abdullah Medical City, Riyadh, Saudi Arabia (one of the centers we studied), suggesting that there may have been a significant increase in the amount of ESBL-producing *E. coli* isolates. However, it is important to consider the possibility that changes in surveillance intensity and infection control policies over the decade between the studied periods could have led to this increase.

Study limitations. Since this study was carried out in a limited number of centers in one city, our data may not be representative of the entire pediatric population of Saudi Arabia. The fact that the study was carried out in one city also limited the total number of cases and therefore the number of non-*E. coli* isolates and thus limited our ability to infer on non-*E. coli* isolates. The retrospective study design was also a limiting factor as we found that not all specimens were tested for the susceptibility of all possible antibiotics.

In conclusion, the possibility of a 9% increase in ESBL-producing *E. coli* isolates over a decade is alarming when comparing what our study found to the findings of Alanazi et al[6] and requires further investigation and monitoring. The same can be said on the possible 2.5% increase in MDR *E. coli* isolates.

We found that the susceptibility of an isolate often depended on the gender of the individual from whom the isolate was collected. In the case of *K. pneumoniae*, isolates gathered from males were significantly less susceptible to TMP/SMX (p<0.001); the same could be said for the susceptibility of *E. coli* isolates to ampicillin (p=0.018), ceftriaxone (p=0.016), and ciprofloxacin (p<0.001). This finding indicates that routine surveillance of uropathogens should distinguish between susceptibility of isolates gathered from males versus those gathered from females, as the susceptibility of an isolate to antibiotics may differ depending on the patient's gender.

Nitrofurantoin, TZP, and gentamicin remain excellent choices for *E. coli* UTI with >95% sensitivity to each. Susceptibility to TMP/SMX is not ideal, with 62.1% of the *E. coli* isolates being sensitive. On the other hand, only 36.2% of the *E. coli* isolates were sensitive to ampicillin.

While our study's sample size regarding *E. coli* isolates was enough to draw inferences and judgements to compare isolates collected from males to those gathered from females, the same could not be said for *K. pneumoniae* isolates or *P. mirabilis* isolates. Future studies on the antibiotic resistance patterns of uropathogens must include a much larger sample size, preferably one from multiple hospitals within an area (as opposed to a single city), or ideally, all the hospitals within a region. This would enable the comparison to other regions in Saudi Arabia and would also allow for a large enough sample size of each of the uropathogens to draw significant inferences.

Acknowledgment. *The authors gratefully acknowledge Sofia Fields Author Services (www.sofiafields.com) for their English language editing.*

References

1. Murray CJl, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. ***Lancet*** 2022; 399: 629-655.
2. IHME. The burden of antimicrobial resistance (AMR) in Saudi Arabia. [Updated 2019; Accessed 2024 Nov 27]. Available from: https://www.healthdata.org/sites/default/files/files/Projects/GRAM/Saudi_Arabia_0.pdf
3. Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. ***Lancet Infect Dis*** 2019; 19: 56-66.
4. Meropol SB, Haupt AA, Debanne SM. Incidence and outcomes of infections caused by multidrug-resistant *Enterobacteriaceae* in children, 2007-2015. ***J Pediatric Infect Dis Soc*** 2018; 7: 36-45.
5. Hameed T, Al Nafeesah A, Chishti S, Al Shaalan M, Al Fakeeh K. Community-acquired urinary tract infections in children: resistance patterns of uropathogens in a tertiary care center in Saudi Arabia. ***Int J Pediatr Adolesc Med*** 2019; 6: 51-54.
6. Alanazi MQ, Alqahtani FY, Aleanizy FS. An evaluation of *E. coli* in urinary tract infection in emergency department at KAMC in Riyadh, Saudi Arabia: retrospective study. ***Ann Clin Microbiol Antimicrob*** 2018; 17: 3.
7. Bamshmous YS, Alwagdani SM, Albarakati MM, Alkouwait MJ, AlThwebi SM. Infection with gram-negative bacteria among children at a tertiary hospital in Jeddah, Saudi Arabia. ***Saudi J Kidney Dis Transpl*** 2021; 32: 1593-1599.

8. Balkhy HH, El-Saed A, AlShehri A, Alshaalan M, Hijazi O, El-Metwally A, et al. Antimicrobial consumption in 3 pediatric and neonatal intensive care units in Saudi Arabia: 33-month surveillance study. ***Ann Clin Microbiol Antimicrob*** 2019; 18: 20.
9. Bin Abdulhak AA, Altannir MA, Almansor MA, Almohaya MS, Onazi AS, Marei MA, et al. Non prescribed sale of antibiotics in Riyadh, Saudi Arabia: a cross sectional study. ***BMC Public Health*** 2011; 11: 538.
10. Zowawi HM. Antimicrobial resistance in Saudi Arabia. An urgent call for an immediate action. ***Saudi Med J*** 2016; 37: 935-940.
11. Mattoo TK, Shaikh N, Nelson CP. Contemporary management of urinary tract infection in children. ***Pediatrics*** 2021; 147: e2020012138.
12. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. ***Clin Microbiol Infect*** 2012; 18: 268-281.
13. Alqasim A, Abu Jaffal A, Alyousef AA. Prevalence of multidrug resistance and extended-spectrum β-lactamase carriage of clinical uropathogenic *Escherichia coli* isolates in Riyadh, Saudi Arabia. ***Int J Microbiol*** 2018; 2018: 3026851.