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ORIGINAL RESEARCH

Prevalence of Urinary Tract Infections Caused by Extended-Spectrum β-Lactamase *Escherichia coli*, a Tertiary Center Nine-Year Comparison

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Purpose: This study used data collected nine years apart (2014 and 2023) to compare the prevalence of *Escherichia coli* that produces extended-spectrum β-lactamase (ESBL) among patients with urinary tract infections at a tertiary care center. Additionally, it aimed to assess how ESBL prevalence varied by gender and age group.

Patients and Methods: Urine culture data from 2014 and 2023 were used in this two-point cross-sectional investigation. Data on demographics and microbiology were retrieved and examined. Chi-square tests were used in conjunction with prevalence ratios and phi coefficient tests for statistical comparison.

Results: The overall prevalence of ESBL-positive *E. coli* in 2500 patients rose from 43.7% to 58.9% between 2014 and 2023. The rise was even more noticeable in male patients PR = 1.50 and pediatric patients 41% to 65.4%, PR = 1.55. All age groups showed statistically significant increases in ESBL-positive, however, the level of statistical power varied.

Conclusion: There has been a rise in ESBL-producing *E. coli* UTIs over the previous ten years, particularly in male children. These results emphasize how urgent it is to improve responsible antibiotic use must be improved to reduce future antimicrobial resistance.

Keywords: urinary tract infection, ESBL-producing *E. coli*, antimicrobial resistance, pediatric UTI, gender differences, Jordan, β-lactamase, multidrug resistance

Introduction

A bacterial urinary tract infection (UTI) is defined as the detection of a pure growth of more than 10^5 colony-forming units (CFU) of bacteria per milliliter (mL) of urine. It is one of the most prevalent bacterial illnesses in the pediatric age group, where up to 11.3% of girls and 3.6% of boys will have experienced a UTI by the age of 16[1,2] Up to 90% of pediatric UTIs are caused by *Escherichia coli*, with *Klebsiella, Proteus*, and *Enterococcus* species closely behind.[3] Over the past 70 years, β-lactam antibiotics have been widely used as therapeutic agents, particularly for treating urinary tract infections.[4]

The β-lactam class makes up nearly two-thirds of hospital prescriptions and is crucial to 21st-century medical practice. As a result, major bacterial pathogens, particularly Gram-negative species, are rapidly developing pan-drug resistance phenotypes, increasing the alarming levels of antibacterial resistance. If this medical problem is not adequately addressed, the burden and mortality linked to infectious diseases, particularly hospital-acquired bacterial infections, will subsequently increase.[5] This growing resistance poses a particular challenge in pediatric populations, where therapeutic options are already limited due to age-related drug restrictions and safety concerns.

One of the most common mechanisms of antibiotic resistance in bacteria is mediated by β-lactam-inactivating β-lactamases, which have become abundant in recent years. Since their initial discovery in the early 1980s, shortly after the

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introduction of β-lactam antibiotics, extended-spectrum β-lactamase (ESBL)-producing microbes have proliferated globally.[6] The Enterobacteriaceae family, which includes *E. coli, Klebsiella pneumoniae*, and *Klebsiella oxytoca*, is the principal pathogen causing UTIs in children.[7] The primary mechanism of bacterial resistance to the β-lactam class of antibiotics is the generation of β-lactamases, hydrolytic enzymes that can render the antibiotics inactive before they reach the cytoplasmic membrane's penicillin-binding proteins.[8]

In the past few years, there has been a dramatic increase in the ESBL-positive bacteria detected in urine cultures, especially in the pediatric age group.[9] A study by Dr. Collingwood investigated the prevalence of ESBL in the pediatric age group in the US. The prevalence of community-acquired ESBL-*E. coli* UTIs have seen a significant increase throughout the six-year study, from 0.97% in 2015 to 3.54% in 2020, with an average annual rise of 0.51%.[10] This has raised many concerns regarding the difficulty of diagnosis, treatment, and infection control challenges caused by the uprising of ESBL-resistant organisms. This phenomenon has caused limitations in the effective treatments available and delays in starting the right treatment, particularly in empirical treatment settings where traditional antibiotics might no longer work.[11] Furthermore, routine laboratory tests might not be able to diagnose ESBL production right away. In these cases, advanced molecular or phenotypic testing, which may not be accessible in all healthcare settings, may be necessary for confirmation, which will further hinder the likelihood of a successful treatment.

This study is novel in that it compares ESBL-producing uropathogens in pediatric/adult bacterial UTI cases at a single tertiary care facility over nine years, providing important information about changing resistance patterns over time. Such information is essential for developing infection control plans and local treatment guidelines.

The primary objective of this study was to compare the prevalence rates of ESBL-producing organisms among urinary tract infection (UTI) patients at King Abdullah University Hospital (KAUH), using data collected ten years apart, in 2014 and 2023.

Materials and Methods

A two-point cross-sectional study was conducted at King Abdullah University Hospital (KAUH). The hospital's infection control committee often maintains records of both the organisms' antibiotic susceptibility and positive cultures, including urine cultures. This recording system started in KAUH in 2014; thus, this year was chosen as a comparison point. Data were collected over two distinct periods: from January 1, 2014, to December 31, 2014 and from January 1, 2023, to December 31, 2023. All the urine culture results from the years 2014 and 2023 were extracted from the hospital database. All potentially eligible hospitalized adult and pediatric patients with at least one ESBL-positive UTI episode were identified during the two study points. The prevalence of ESBL-producing organisms (*E. coli*) among all positive urine cultures was compared. Urine samples were collected per midstream clean catch or bladder catheterization, and urine cultures were made on conventional media (MacConkey agar) and incubated at 37°C for 24–48 hours. Bacterial identification and susceptibility testing were performed using the VITEK 2 automated system (bioMérieux, France) with interpretation according to the Clinical and Laboratory Standards Institute (CLSI) M100™ guidelines corresponding to each study year (CLSI M100™ for 2014 and CLSI M100™ for 2023).[12,13] ESBL production was identified by the combined disk method using cefotaxime and ceftazidime, with and without clavulanic acid; ≥5 mm increase in inhibition zone was noted for the activity of ESBL. The confirmatory ESBL testing methodology (combined disk method and interpretation criteria) was identical in both study periods to ensure consistency and comparability of results over time. Annual results were compared to CLSI standards for susceptibility and resistance for clinical significance. All susceptibility interpretations and resistance classifications were standardized according to the CLSI M100™ document applicable to each respective year to ensure methodological consistency and comparability over time. Annual comparison was standardized to laboratory criteria and reporting criteria; 2014 and 2023 had similar criteria over time applied to them, with no significant change in sample collection parameters, patient inclusion, processing of specimens, or access to laboratories. The required information for each patient was obtained by reviewing patients' files and computerized laboratory results: age, gender, ESBL status, organism (*E. coli*), and test dates. During our data collection, there were many duplicate cultures for the same patient, in which only the most recent culture was included in our analysis, and any other duplicates were excluded to ensure that each patient was counted once. This study was compliant with the ethical standards set by our ethics institution committee, since there was no breach of privacy and confidentiality guidelines.

Only microbiological culture data were collected; personal identifiers were not included. Data was analyzed using IBM SPSS Statistics version 25.0.0.0. The collected information was grouped into three main groups: combined, adult, and pediatric age groups, after analyzing the basic descriptive statistics of the population, multiple comparative tests were conducted most notably; Chi square test, Prevalence Ratio (PR), P-value, and Phi coefficients to ascertain the correlation between the variables.

Results

A total of 2500 participants were included in the study. With 1096 (43.84%) in the year 2014 and 1404 (56.16%) in the year 2023. The mean age for the participants was estimated to be 51. Of which there were 1845 (73.8%) females, 655 (26.2%) males, as shown in Figure 1. Moreover, 324 (12.96%) were aged 0–18 years old, and 2176 (87.04%) were aged more than 18.

In 2014, 479 (43.7%) participants tested positive for ESBL, while 617 (56.3%) of the participants tested negative for ESBL in the same year. In 2023, 827 (58.9%) participants were positive for ESBL and 577 (41.1%) were negative. As illustrated in Figure 2.

We stratified the data into 3 groups according to age. A combined group to include both age groups, an Adult (>18) and a Pediatric group (0–18). The Chi-square, Phi, and prevalence ratio tests were done for each individual group to ascertain the magnitude of the association*.

In the combined group, the comparison between the years 2014 and 2023 yielded a p-value (<0.001), the prevalence ratio of the positive ESBL to the negative ESBL cases was 0.710 in 2014 and 1.310 in 2023, signifying a higher likelihood for a positive ESBL result in 2023. The phi test resulted in a value of 0.151, which indicates weak but statistically significant association.

In the adult age group, the comparison between the year 2014 and 2023 returned a p-value (<0.001), the prevalence ratio of the positive ESBL to the negative ESBL cases was 0.733 in 2014 and 1.279 in 2023, highlighting a higher likelihood for a positive ESBL result in 2023. The phi test resulted in a value of 0.137, which indicates weak but statistically significant association.

In the pediatric age group, the comparison between the years 2014 and 2023 yielded a p-value (<0.001), the prevalence ratio of the positive ESBL to the negative ESBL cases was 0.570 in 2014 and 1.550 in 2023, demonstrating a higher likelihood for a positive ESBL result in 2023. The phi test resulted in a value of 0.243, which indicates moderate association. Additional details are provided in Tables 1 and 2.

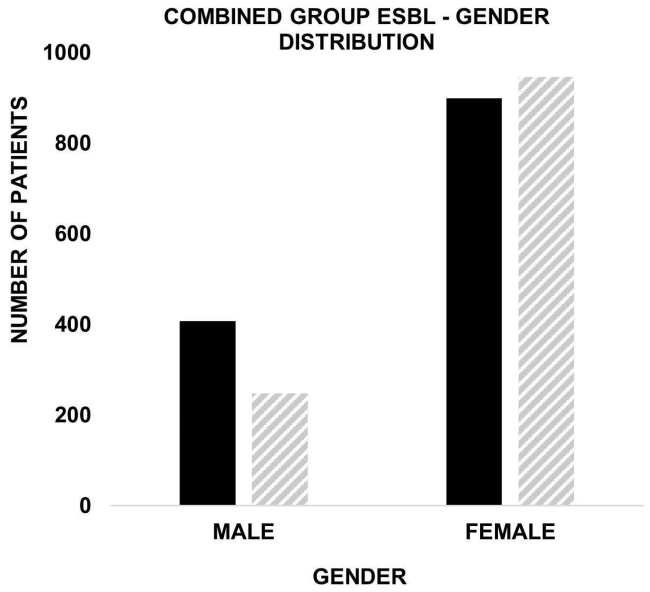

Figure 1 Combined group ESBL-Gender distribution. A bar chat displaying the distribution of ESBL positive and negative cases between genders. Fully shaded column - ESBL positive, Striped lightly shaded column - ESBL negative.

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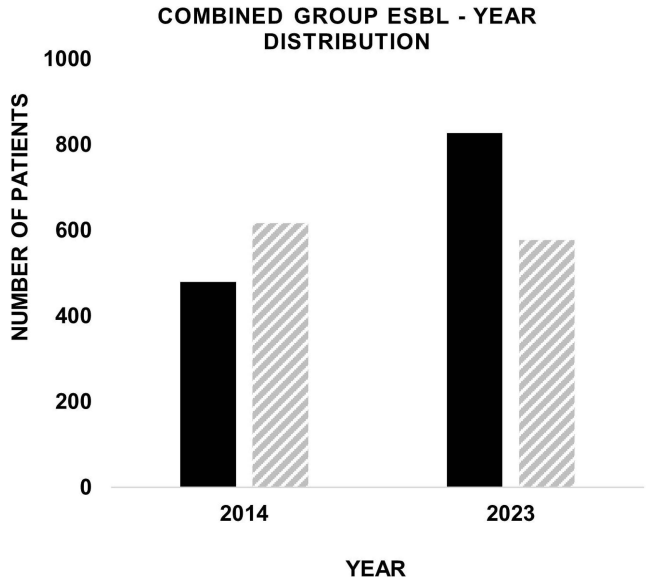

Figure 2 Combined group ESBL-Year distribution. A bar chat displaying the distribution of ESBL positive and negative cases in the years 2013 and 2024. Fully shaded column - ESBL positive, Striped lightly shaded column - ESBL negative.

Additionally, we performed the Chi-square, Phi, and prevalence ratio tests in the combined age group to look for association between gender and ESBL, the results were a p-value of (<0.001), the prevalence ratio of the positive ESBL to the negative ESBL cases was 1.502 in males and 0.869 in females indicating a higher likelihood for a positive ESBL result in males. The phi test revealed a value of 0.118, which indicates weak but statistically significant association.

In the adult age group, the comparison between males and females yielded a p-value (<0.001), the prevalence ratio of the positive ESBL to the negative ESBL cases was 1.502 for males and 0.858 for females, highlighting a higher likelihood for

Table 1 Chi Square Test 2014 ESBL Distribution

	n	*df*	*PR*[a]	95% CI		*p*[b]
				LL	*UL*	
Group						
Combined Group	1096	1.00	0.71	0.65	0.78	**<0.001**
Adult Group (>18)	957	1.00	0.73	0.67	0.81	**<0.001**
Pediatric Group (0–18)	139	1.00	0.57	0.44	0.74	**<0.001**

Notes: p values bolded if <0.05. [a]Prevalence Ratio for Cohort year = 2014. [b]Pearson Chi-Square Year 2014/2023 Comparison.

Table 2 Chi Square Test 2023 ESBL Distribution

	n	*df*	*PR*[a]	95% CI		*p*[b]
				LL	*UL*	
Group						
Combined Group	1404	1.00	1.31	1.22	1.41	**<0.001**
Adult Group (>18)	1219	1.00	1.28	1.18	1.38	**<0.001**
Pediatric Group (0–18)	185	1.00	1.55	1.26	1.91	**<0.001**

Notes: p values bolded if <0.05. [a]Prevalence Ratio for Cohort year = 2023. [b]Pearson Chi-Square Year 2014/2023 Comparison.

Table 3 Chi Square Test ESBL Correlated with Gender

	n	*df*	*PR*[a]	95% CI		*p*[b]
				LL	*UL*	
Group						
Combined Group	2500	1.00	1.50	1.308	1.721	**<0.001**
Adult Group (>18)	2176	1.00	1.50	1.305	1.728	**<0.001**
Pediatric Group (0–18)	324	1.00	1.64	0.938	2.868	0.077

Notes: p values bolded if <0.05. [a]Prevalence Ratio for male gender [b]Pearson Chi-Square gender correlation.

a positive ESBL result in males. The phi test resulted in a value of 0.124, which indicates weak but statistically significant association.

In the pediatric age group, the comparison between males and females returned a p-value (0.077), the prevalence ratio of the positive ESBL to the negative ESBL cases was 1.639 for males and 0.921 for females, highlighting a higher likelihood for a positive ESBL result in males. The phi test resulted in a value of 0.098, which indicates a negligible association. For the details of the gender based comparison please refer to Table 3.

* Phi coefficient is a measure of the degree of association (effect size) between two binary (dichotomous) variables. Phi coefficients were used to quantify the magnitude of the associations demonstrated in the significant p values above.

Discussion

Emerging extended-Spectrum-β-lactamase (ESBL) infections and antimicrobial resistance are now considered a serious concern in public health.[10] Resistance is explained by ESBLs' ability to inactivate β-lactam antibiotics (penicillin and cephalosporin) through several mechanisms, in which the periplasm of Gram-negative bacteria releases β-lactamase, which has a greater affinity towards β-lactam antibiotics than the affinity of β-lactam antibiotics to their targets. The gene coding for β-lactamase may be found in extra-chromosomal mobile genetic elements such as integrins, plasmids, transposon, or immobile genetic chromosomes (as seen in *Enterobacter* species). However, resistance genes evolve either by gene-level mutations or by the acquisition of resistant genes from other bacteria of the same or different species.[14]

According to our data, we noticed a considerable and statistically significant increase in the prevalence of ESBL-positive cultures between 2014 and 2023, and this trend held true for all three groups ($p < 0.001$). The percentage of an ESBL-positive result in our pediatric age group increased significantly from 41% in 2014 to 65.41% in 2023. This substantial rise in prevalence is consistent with a study conducted by Dr Collingwood, which reported an increase in the prevalence of ESBL-positive cultures from 0.97% in 2015 to 3.54% in 2020, on average by 0.51% yearly.[10]

Our findings regarding pediatric patients are concordant with a study that was conducted on Thai children, where ESBL UTIs prevalence (including *E. coli* and *Klebsiella pneumoniae*) showed an interestingly marked increase from 2004 to 2008 before plateauing at around 30–40% per year.[15] Similarly, another study performed in Primary Children's Medical Center (PMC; salt lake city, UT) also demonstrated a significant rise in rates of ESBL production (*E. coli, K. pneumoniae* and *K. oxytoca*) among general clinical isolates, increasing from 0.53% to 1.4% in the first and second halves of the study period, respectively.[16]

We also observed an analogous pattern across both adults and combined age groups. For adults, the prevalence of positive ESBL *E. coli* cultures rose significantly from 44.10% in 2014 to 57.92% in 2023. On the other hand, the combined age group also demonstrated an increase in ESBL *E. coli* positive cultures from 43.70% in 2014 to 58.90% in 2023.

The rise in Prevalence is consistent with findings from a study conducted at Saint George Hospital University Medical Center, which reported a noteworthy rise in rates of ESBL *E. coli* urinary isolates from 2.1% in 2000 to 16.8% in 2009.[17] In addition, broader analysis performed in a major tertiary care center in the same country, along with related studies

conducted during the same period, demonstrated a substantial rise in rates of ESBL-producing isolates across multiple organisms and clinical specimens from 2000 to 2011.[18]

Our findings concerning the increasing rates of ESBL aligned with studies carried out in the West. One study conducted in the United States demonstrated a significant increase in the rate of ESBL-*E. coli* positive urine cultures from 7.8% in 2010 to 18.3% in 2014 ($p < 0.0001$).[19] In France, a retrospective survey also illustrated a noticeable rise in the percentage of ESBL-producing *E. coli* urine isolates from 2.0% in 2010 to 3.3% in 2013 ($P < 0.001$),[20] which is consistent with earlier findings from France that showed an increase in the percentage of ESBL isolates from 0.3% to 1.1% between 1999 and 2006.[21,22] A comparable upward trend has been documented in Netherlands too, where the prevalence of ESBL producing *E. coli* increased from 0.1% in 2004 to 2.2% in 2014.[23]

Our pediatric age group showed the most remarkable increase in ESBL-positive cultures, indicating a significant rise in the trend of antimicrobial resistance patterns which might be due to high prescription rates and inappropriate antibiotic use. Previous research in Jordan reported that the purchase of antibiotics without a prescription was (46%) either via self-medication (23.2%) or pharmacist recommendation (23.1%).[24] This marked increase in the rate of positive cultures could result in increased antibiotic use, which may raise concerns for future resistance.

Our gender-based analysis also revealed a significant association where males are more prone to have ESBL-positive cultures than females in the three groups (combined, adults and pediatrics). This finding regarding the pediatrics age group aligns with one study reporting that although females have an increased predisposition to UTIs, male gender was an independent risk factor for ESBL *E. coli* UTI.[25] Broader evidence in the literature shows that UTIs overall tend to be more common in male children.[26,27] Additionally, one study specifically reported a similar predominance of UTI in general among male children aged 0–10 years.[28] However, findings from Colombia contrasted with our results showing a predominance of ESBL positive urine isolates in previously healthy girls of preschool age.[29]

A similar male predominance has also been reported in adult populations. A study conducted in Turkey showed that male gender was an independent risk factor for acquiring ESBL-producing *E. coli* and *K. pneumoniae* UTIs in hospitalized older adults.[30] Similarly, in France previously published results showed that the proportion of ESBL producing *E. coli* isolates was higher in males (4.8%) than in females (3%) and increased with age from 2% for patients under 20 years to 5.4% for those aged older than 80 years.[20]

The reason for this male predominance remains unclear and warrants further investigation to determine the underlying causes, but one of the reasons might be that elderly males may develop more complicated/inpatient UTI.[31] Additionally, a higher prevalence of comorbidities in males could contribute to this observation. However, this explanation is hypothesis-generating, and differences are likely to be multifactorial, influenced by clinical and epidemiological factors rather than gender alone.

Our study has some limitations. For instance, the study population was restricted to a single center, which serves northern Jordan, so the results may not represent the change in ESBL-positive culture patterns in other areas of the country. It was a two-point cross-sectional study; therefore, histories of previous antibiotic and prophylactic therapy were not available. However, the history of antibiotic therapy in our community is usually unreliable, due to the wide availability of antimicrobials obtained from pharmacies across the country that fail to have any records, and whether the patient completes the course of antibiotics is also unknown.

Conclusion

In conclusion, the findings of our study confirmed the increasing trend in the emergence of ESBL-positive urine cultures between 2014 and 2023 in our region. This increase was particularly notable among males and pediatric patients, where resistance appeared to be emerging more strongly. The rise in prevalence may reflect an increase in broad-spectrum antibiotic misuse, facilitating an increase in rates of ESBL-producing strains in the community. These results highlight the need for ongoing antimicrobial stewardship and surveillance, as well as the establishment of antibiotic guidelines to manage complex multidrug-resistant infections among age-specific groups. The implementation of effective infection control programs and the evaluation of such programs' effectiveness in halting the spread of resistance are also recommended.

Abbreviations

UTI, Urinary Tract Infection; ESBL, Extended-Spectrum β-lactamase; KAUH, King Abdullah University Hospital.

Data Sharing Statement

The dataset analyzed during this study was obtained from KAUH. The data are anonymized and not publicly available due to institutional privacy regulations but are available from the corresponding authors (Mohammad Tayyem) upon reasonable request and with permission from KAUH.

Ethics Approval and Consent to Participate

The need for informed consent was waived by the IRB and Ethics committee at KAUH, reference number 91/164/2023, due to the anonymized retrospective nature of the study. The study was conducted in accordance with local and national ethical guidelines and considerations. This study was approved by the ethics committee at KAUH and complies with the Declaration of Helsinki.

Consent for Publication

All authors have reviewed the final manuscript and consent to its publication.

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Disclosure

The authors declare that they have no competing interests in this work.

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