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ORIGINAL ARTICLE

Age-related Trends in Multidrug Resistance and Extended-spectrum Beta-lactamase Production among Patients with Community-acquired Urinary Tract Infections

MURAD ALI[1], SYED QASIM SHAH[2], AMJAD ALI[3], SARA SHAMSHAD[4], HUMAIRA ZAKIR[5], HAMIDULLAH[6]
[1]*Assistant Professor of Medicine, Mardan Medical Complex, Mardan*
[2]*District Medical Specialist, Tehsil Headquarter Hospital, Takht Bhai Mardan*
[3]*Professor of Medicine, Mardan Medical Complex, Mardan*
[4]*WMO, Mumtaz Bakhtawar Hospital, Raiwand Road Lahore*
[5]*Assistant Professor of Medicine, Altibri Medical College and Hospital, Karachi*
[6]*Assistant Professor of Medicine, Bacha Khan Medical College, Swabi*
Correspondence to: Syed Qasim Shah, Email: drsyedqasimshah@gmail.com

ABSTRACT

Background: Urinary tract infections (UTIs) are among the most common community-acquired infections worldwide. The increasing prevalence of multidrug-resistant (MDR) organisms and extended-spectrum beta-lactamase (ESBL) producers in these infections has become a major public health concern, especially in regions with unregulated antibiotic use.

Objective: This study aimed to determine the frequency of EDR and ESBL expression among bacterial isolates from patients with community-acquired UTIs, and to explore the association of resistance with age and clinical history.

Methods: An observational study was conducted over 11 months at Mardan Medical Complex, Mardan including 167 patients presenting with symptoms of UTI from May 2022 to March 2023. 'Midstream urine samples were collected and cultured using standard microbiological procedures'. 'Antibiotic susceptibility testing was performed using the Kirby-Bauer disk diffusion method following CLSI guidelines'. ESBL production was confirmed using the combination disk method. Clinical and demographic data were analyzed to identify factors associated with resistance.

Results: Escherichia coli was the most frequently isolated organism (62.3%), followed by Klebsiella pneumoniae (17.4%). Overall, 71.9% of isolates were found to be multidrug-resistant, and 50.9% produced ESBLs. Older age, comorbidities, and recent antibiotic use were significantly associated with both MDR and ESBL positivity ($p < 0.05$). Resistance was particularly high against ciprofloxacin, trimethoprim-sulfamethoxazole, and ceftriaxone, while carbapenems remained largely effective.

Conclusion: The study highlights a high burden of MDR and ESBL-producing pathogens in community-acquired UTIs. These findings underscore the urgent need for rational antibiotic use and local surveillance data to guide empirical therapy. Age and clinical history should be considered when selecting treatment in outpatient settings.

Keywords: Urinary tract infection, EDR, ESBL, community-acquired infection, Escherichia coli, antibiotic resistance, Pakistan, uropathogens

INTRODUCTION

Urinary tract infections (UTIs) remain one of the most frequently encountered bacterial infections across all age groups, affecting millions of individuals worldwide each year. They represent a considerable percentage of outpatient clinic visits, especially by female patients, the elderly, and those with chronic health issues. Although most primary care UTIs can be managed with oral antibiotics, the growing pattern of resistance to antibiotics makes even straightforward infections more difficult to treat[1].

A rise in multidrug-resistant (MDR) bacteria is one of the most troubling issues that needed attention in recent years. MDR, which includes fluoroquinolones, beta-lactams, and trimethoprim-sulfamethoxazole, is becoming increasingly difficult to treat as multiple commonly used antibiotics fail to effectively work against it. With limited treatment choices available, the risk of treatment failure, complications, and prolonged illness increases[2]. 'The emergence of ESBL producing organisms has raised concern'. These enzymes are largely made by Gram negatives like Escherichia coli and Klebsiella pneumoniae which makes them resistant to penicillins and cephalosporins, often requiring stronger broad-spectrum agents such as carbapenems[3].

Historically, ESBLs and multidrug-resistant (MDR) organisms were regarded as related to infections acquired within a hospital setting. Recently, however, some studies suggest these resistant organisms are becoming more prevalent in the community, these include access to antibiotics without prescriptions, self-treatment, non-compliance to prescribed regimens, and inadequate control of the spread of infections. In areas such as Pakistan, where there are weak regulations on antibiotics and low levels of education and knowledge, the extent of resistance in community-acquired UTIs is particularly concerning[4].

Age is a crucial factor for assessing the risk and susceptibility patterns of an infection. The elderly population suffers from comorbidities, prior exposure to antibiotics, and higher frequency of healthcare interactions which cumulatively make them more susceptible to resistant infections. Understanding the disparate patterns of resistance could optimize the use of antibiotics at the ecosystem level adjust local policies[5].

Considering these issues, 'the purpose of the study was to assess the prevalence of EDR and the expression of ESBL with age in community-acquired UTIs'. The study aims to enhance knowledge of current resistance patterns and aid in formulating better, more informed treatment plans in community healthcare by identifying the prevalent causative organisms and their resistance patterns.

METHODOLOGY

This 'observational study' was carried out at the Mardan Medical Complex in Mardan, Khyber Pakhtunkhwa, from May 2022 to March 2023. The study was conducted over a period of eleven months in order to gather enough data to assess the trends of antibiotic resistance among patients with community-acquired urinary tract infections (UTIs). Ethical clearance for the study was secured from the institutional review board of Mardan Medical Complex before data collection commenced. Participants were guaranteed confidentiality, their names and other identifying information were removed throughout the study.

A total of 167 patients were enrolled using a non-probability consecutive sampling technique. All participants included in the study were diagnosed with community-acquired UTIs based on clinical symptoms and laboratory confirmation through urine culture. Patients were selected irrespective of gender and included across various age groups to observe age-related trends in resistance patterns.

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The inclusion criteria were as follows: patients of any age and gender presenting with symptoms of UTI, such as dysuria, urgency, increased frequency of urination, lower abdominal pain, or fever, who had not been hospitalized or undergone any invasive procedures in the 48 hours prior to symptom onset. Only those whose urine cultures showed significant bacterial growth (≥10^5 CFU/mL) were included. Patients with hospital-acquired infections, those already on long-term antibiotic therapy, and individuals with known structural urinary tract abnormalities were excluded to ensure the focus remained on community-acquired cases.

'After obtaining informed consent, detailed clinical and demographic data were recorded, including age, gender, residential background, history of recurrent UTIs, previous antibiotic use within the past three months, presence of comorbid conditions, and any recent history of catheterization or hospitalization'. Midstream urine samples were collected under aseptic conditions from each participant. Samples were immediately transported to the hospital's microbiology laboratory for analysis.

Urine cultures were performed using standard microbiological techniques. The identification of bacterial isolates was carried out using colony morphology, Gram staining, and biochemical testing. 'Antibiotic susceptibility was determined by the Kirby-Bauer disk diffusion method in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines'. 'The antibiotics tested included commonly prescribed agents such as ciprofloxacin, nitrofurantoin, ceftriaxone, trimethoprim-sulfamethoxazole, fosfomycin, and carbapenems like imipenem and meropenem'.

EDR was defined as non-susceptibility to at least one agent in three or more antimicrobial categories. For the detection of ESBL production, confirmatory testing was done using the combination disk method, comparing the zone sizes around cefotaxime and ceftazidime disks with and without clavulanic acid. 'A ≥5 mm increase in zone diameter in the presence of clavulanic acid was considered positive for ESBL production'.

All data were entered and analyzed using SPSS version 25. Categorical variables were expressed as frequencies and percentages. The chi-square test was applied to determine associations between MDR/ESBL presence and variables such as age, gender, comorbidities, prior antibiotic use, and history of catheterization. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study involved 167 patients diagnosed with 'community-acquired urinary tract infections (UTIs)'. Among these patients, the most represented age group was 51–70 years, followed by those aged 31–50 years. The majority were female, accounting for almost 60% of the total sample. A greater proportion of participants belonged to urban areas. Over half of the patients had at least one comorbidity, suggesting a significant underlying health burden in this population. These demographic patterns reflect the common trends seen in UTI susceptibility, with older age and female gender being known risk factors.

Table 1: Demographic Characteristics of Patients with Community-Acquired UTI (n=167)

Variable	Frequency (n)	Percentage (%)
Age Group		
<18 years	22	13.2%
18–30 years	36	21.6%
31–50 years	40	24.0%
51–70 years	41	24.6%
>70 years	28	16.8%
Gender		
Male	67	40.1%
Female	100	59.9%
Residence		
Urban	94	56.3%
Rural	73	43.7%
Comorbidities		
Yes	89	53.3%
No	78	46.7%

Clinically, most patients presented with symptomatic UTI, and nearly 40% had a previous history of the condition. Prior antibiotic use was documented in 43.7% of participants, which may have contributed to resistance patterns observed later. A quarter of the sample had undergone catheterization, and 19.2% had been hospitalized in the preceding six months. These clinical backgrounds are important, as recurrent infections and recent medical interventions are known contributors to antimicrobial resistance.

Table 2: Clinical Characteristics of Study Participants

Variable	Frequency (n)	Percentage (%)
First UTI Episode	101	60.5%
Recurrent UTI	66	39.5%
Prior Antibiotic Use (Last 3 Months)	73	43.7%
History of Catheterization	41	24.6%
Hospitalization in Last 6 Months	32	19.2%
Symptomatic UTI	151	90.4%
Asymptomatic	16	9.6%

Microbiological analysis revealed Escherichia coli as the most frequently isolated uropathogen, accounting for over 60% of the isolates. 'Klebsiella pneumoniae was the second most common. A high proportion of these isolates were multidrug-resistant (MDR), particularly E. coli and Klebsiella'. ESBL production was also common among these organisms. This finding 'underscores the growing concern of resistance in commonly encountered uropathogens within the community setting'.

Table 3: Distribution of Isolated Uropathogens and Their Resistance Patterns

Organism Isolated	Frequency (n)	Percentage (%)	MDR (%)	ESBL Positive (%)
Escherichia coli	104	62.3%	81 (77.9%)	63 (60.6%)
Klebsiella pneumoniae	29	17.4%	21 (72.4%)	19 (65.5%)
Pseudomonas aeruginosa	12	7.2%	9 (75.0%)	2 (16.7%)
Proteus spp.	9	5.4%	6 (66.7%)	1 (11.1%)
Enterococcus spp.	13	7.8%	3 (23.1%)	0 (0.0%)

Table 4: 'Antibiotic Resistance Patterns of Isolates (n=167)'

Antibiotic	Resistant n (%)
Ciprofloxacin	118 (70.7%)
Nitrofurantoin	29 (17.4%)
Trimethoprim-Sulfamethoxazole	109 (65.3%)
Amoxicillin-Clavulanate	91 (54.5%)
Ceftriaxone	103 (61.7%)
Fosfomycin	19 (11.4%)
Imipenem	6 (3.6%)
Meropenem	4 (2.4%)

When analyzing antibiotic resistance patterns, a worrying trend emerged. The majority of uropathogens exhibited resistance to fluoroquinolones and cephalosporins, with 70.7% of isolates resistant to ciprofloxacin and 61.7% to ceftriaxone. Trimethoprim-sulfamethoxazole and amoxicillin-clavulanate also showed high resistance rates. In contrast, carbapenems such as imipenem and meropenem maintained excellent efficacy, though their use in community settings should remain restricted to prevent future resistance development.

Statistical analysis showed significant associations between EDR and several variables. Patients aged 50 years and above, as well as those with comorbidities or recent antibiotic use, had significantly higher rates of MDR and ESBL-producing infections. There was no significant difference with regard to gender or residence. These associations highlight the role of advancing age and medical history in the development of resistant infections, underscoring the need for targeted antibiotic stewardship in these high-risk groups.

Table 5: Association of Demographic and Clinical Variables with MDR and ESBL Production

Variable	MDR Present (n=120)	MDR Absent (n=47)	p-value	ESBL Positive (n=85)	ESBL Negative (n=82)	p-value
Age ≥50 years	59	10	0.012*	51	18	0.009*
Female Gender	76	24	0.415	49	51	0.104
Urban Residence	72	22	0.661	47	47	0.881
Comorbidities Present	79	10	0.003*	58	31	0.001*
Prior Antibiotic Use	61	12	0.020*	49	24	0.005*
Catheterization History	34	7	0.341	21	20	0.557
Recurrent UTI	52	14	0.279	33	33	0.623

*Statistically significant at $p < 0.05$

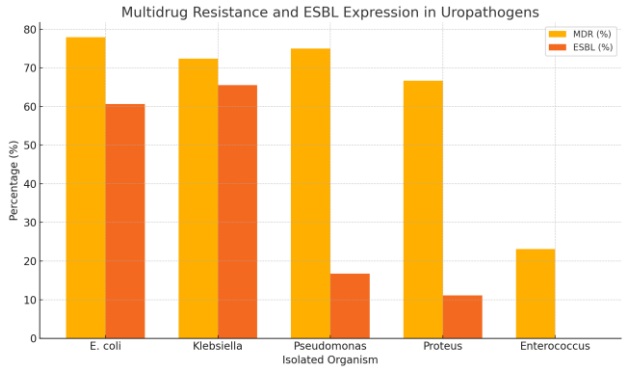

Figure 1: The graph shows that E. coli and Klebsiella have the highest rates of both EDR and ESBL production, making them the most resistant uropathogens in the study. Pseudomonas also shows high MDR but lower ESBL expression. In contrast, Enterococcus has the lowest resistance levels overall. These trends highlight the growing concern of resistant E. coli and Klebsiella strains in community-acquired urinary tract infections.

DISCUSSION

Urinary tract infections continue to be one of the most frequent reasons for outpatient visits, particularly in the adult and elderly population. This study highlights a growing concern in the management of community-acquired UTIs antibiotic resistance, 'especially EDR (MDR) and ESBL production'. Our findings indicate that more than 70% of the isolated uropathogens were multidrug resistant, and over half were ESBL producers. These resistance trends pose significant challenges in empirical antibiotic selection and call for urgent reassessment of prescribing practices (6-8).

Escherichia coli remained the most commonly isolated organism, consistent with numerous previous reports, including studies which identified E. coli as the leading cause of community-acquired UTIs in Pakistan. In our study, 77.9% of E. coli isolates were multidrug resistant, and 60.6% produced ESBLs(9-11). These figures are slightly higher than those reported in a multicenter surveillance studies, where ESBL production among E. coli was found to be 51%, suggesting a regional variation or a possible rise in resistance over time(12-14).

'Klebsiella pneumoniae was the second most common pathogen in our analysis'. Over 70% of Klebsiella isolates demonstrated MDR, while 65.5% showed ESBL production. These findings align with the studies that also documented increasing resistance in Klebsiella isolates, particularly in community settings (15-17). The similarity in resistance profiles between E. coli and Klebsiella suggests the potential horizontal transfer of resistance genes, especially in environments with uncontrolled antibiotic use.

The relationship between age and resistance was also notable in our findings. Patients aged 50 years and above had markedly greater rates of both MDR and ESBL-positive infections. This may be related to an accumulation of age-related comorbidities, greater prior exposure to antibiotics, and more frequent interactions with the healthcare system, which are described as risk factors in the literature (18, 19). Similarly, our data revealed that patients with diabetes and chronic kidney disease as comorbid conditions were substantially more likely to possess resistant organisms. An additional concerning risk factor was antecedent antibiotic use within the preceding three months, which has consistently been documented in local and international studies (20).

Antibiotic susceptibility testing showed that fluoroquinolones, third-generation cephalosporins and trimethoprim-sulfamethoxazole had little to no susceptibility, with more than 60 percent of strains resistant. This is consistent with the increasing worrying trend towards loss of effectiveness these previously dependable drugs face. However, carbapenems have shown outstanding activity, with less than 4 percent resistance of imipenem and meropenem. While this is a positive finding, the broad spectrum of activity of carbapenems should be conserved to avoid accelerating the escalation of resistance (21, 22).

Our research highlights the importance of implementing antimicrobial control measures in community healthcare settings. Empirical treatment plans should be modified according to the specific resistance trends of the area instead of using obsolete or nonspecific protocols. Furthermore, increasing awareness among healthcare professionals and the general public regarding the judicious use of antibiotics is essential.

CONCLUSION

'The study reveals a high prevalence of EDR and ESBL production among community-acquired uropathogens, particularly Escherichia coli and Klebsiella pneumoniae'. Older age, comorbidities, and recent antibiotic use were significantly associated with resistant infections. The findings emphasize the importance of local surveillance data to guide empirical therapy and the need to strengthen antimicrobial stewardship strategies to prevent further resistance development in the community.

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