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The prevalence of multiple drug-resistant urinary tract infections among critically ill patients in tertiary hospital

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Abstract

Introduction: Multidrug-resistant -urinary tract infection (MDR-UTI) is considered a significant source of in-hospital mortality and morbidity in critically ill patients in intensive care units (ICUs).
Objectives: This study aimed to evaluate the prevalence and risk factors of MDR-UTI among critically ill Egyptian patients. In addition, the study aimed to determine the potential risk factors in various ICUs at Ain Shams University Hospital, Cairo, Egypt.
Patients and Methods: The current cross-sectional study included 383 adult patients with positive urine cultures enrolled from different medical and surgical ICUs within a 6-month duration. MDR-UTI was defined as isolates that exhibited resistance or intermediate susceptibility to ≥3 of the antimicrobial categories. Antibiotic resistance rates and patterns were identified using the disc diffusion method and automated antimicrobial susceptibility testing by Vitek 2. Full clinical evaluation and biochemical analysis were done. Healthcare-associated risks were surveyed, including chronic indwelling urinary catheters, hospitalization for at least 48 hours, regular hemodialysis, or undergoing urological procedures within the past three months.
Results: MDR-UTI prevalence was observed in approximately 173 patients, accounting for 45.2% of the total. The mean age of studied patients was 63.07 ±17.82 years, with 53.3% being females. Additionally, the average duration of hospitalization was 3.32 ±3.08 days. There was a highly statistically significant relation between MDR-UTI results and hospitalization for at least 48 hours. *Enterococcus* and *Klebsiella* were significantly more prevalent among MDR-UTI cases (41.6% and 46.8 % respectively). *Escherichia coli* was the predominant uropathogenic microorganism in patients with non-MDR UTI, accounting for 49.0% of cases. Penicillin was the most prevalent antimicrobial resistance. The presence of chronic indwelling urinary catheters is the most common healthcare-associated risk factor for MDR UTI, with a 78% prevalence. At the time of admission to the ICU, 59% of the patients with MDR-UTI had septic shock, while 18.5% had acute kidney injury (AKI).
Conclusion: The prevalence of MDR-UTI was 45.2% among critically ill patients in the ICUs of Ain Shams University Hospital. *Klebsiella* and *Enterococcus* were the most common uropathogenic among MDR UTIs, with resistance mainly to penicillins and carbapenems. The hospital stay >48 hours, hemodialysis, and urological procedures were the most significant risk factors for MDR-UTI. Patients with septic shock and AKI were significantly associated with the presence of MDR-UTI.

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Introduction

Multidrug-resistant infections are considered a significant source of mortality and morbidity in critically ill patients in intensive care units (ICUs). Numerous independent risk factors for multidrug-resistant (MDR) have been identified, and it is crucial to administer the appropriate antibiotics for treatment. Utilizing conventional and novel antibiotic combinations is usually a viable in vitro approach against highly antimicrobial-resistant strains (1).

The prevalence of urinary tract infections (UTIs) has been estimated to be around 150 million persons per year (2). UTI is classified as asymptomatic bacteriuria, symptomatic UTI, and UTI-related septicemia. The diagnosis of UTI is determined based on a basic laboratory test in which bacteriuria ≥10^5 CFU/mL. Suggestive symptoms of UTI include increased frequency of urination, dysuria, presence or absence of vaginal discharge, urgency, backache, and hematuria (3).

Dipstick urinalysis is widely available and beneficial. However, it is important to note that a negative result from dipstick urinalysis does not necessarily rule out the presence of UTI. The preferred diagnostic test is urine culture (4).

Prompt management of UTI is crucial to prevent complications, such as deterioration

Key point

Multidrug-resistant (MDR) infections are an increasingly significant concern worldwide. In addition, MDR-urinary tract infections (MDR-UTIs) are regarded as a prevalent cause of morbidity and mortality, particularly among critically ill patients in intensive care units. The development, amplification, and spread of MDR infections are commonly associated with intensive care units due to the compromised protective mechanisms caused by invasive procedures and the impaired immune response resulting from trauma, surgery, comorbidities, and sepsis. Frequent occurrences of MDR development and spread in the ICU are attributable to the use of broad-spectrum antibiotics. The prevalence and distribution patterns of microorganism species vary across countries and healthcare centers. Therefore, we aimed to evaluate the prevalence and risk factors of MDR-UTI among Egyptian critically ill patients and determine the potential risk factors in different intensive care units of Ain Shams University hospitals.

of kidney function tests, pyelonephritis, sepsis, septic shock, morbidity, and mortality. Managing UTIs in chronic kidney disease (CKD) patients poses difficulties due to the variability in glomerular filtration rate (GFR) and antibiotic dosages. Antibiotic abuse is a significant cause of MDR-UTI (5).

CKD patients experience higher rates of infection, resulting in more frequent antibiotic use and hospitalization, increasing their exposure to microbes and, thereby, MDR-UTIs (6).

The definition of MDR refers to isolates that demonstrate resistance or intermediate susceptibility to ≥3 of the following antimicrobial categories: (a) penicillin with or without beta-lactamase inhibitors; (b) cephalosporins either ceftriaxone or cefepime; (c) carbapenems; (d) fluoroquinolones; (e) gentamicin or amikacin; (f) trimethoprim sulfamethoxazole (TMP-SMX); and (g) nitrofurantoin (7). The primary mechanism of resistance is the production of enzymes that degrade β-lactam antibiotics. Extended-spectrum β-lactamases (ESBLs) enzymes can hydrolyze and cause resistance to newer types of β-lactam antibiotics, such as expanded spectrum 3^{rd} generation cephalosporins and monobactams. However, they do not affect the cephamycin (e.g., cefoxitin and cefotetan) and carbapenems. A significant cause of bacteremia in hospitalized and non-hospitalized patients is the dissemination of ESBL-producing Enterobacteriaceae, leading to increased rates of treatment failure and mortality (8).

Insertion of an indwelling urinary catheter is a common practice in ICUs to accurately measure urinary output in critically ill patients, post-operative patients, patients with prolonged immobilization, and other appropriate indications. Urinary catheters pose a significant risk for healthcare-associated infections, contributing to 20% to 30% of such infections. Consequently, there are significant financial implications associated with the excessive use of antimicrobials, as well as prolonged duration of ICU stays, hospitalization, morbidity, and mortality (9). The second leading cause of bloodstream infection next to central line insertion is catheter-associated UTI. Prolonged catheterization with each day of catheter in situ increases the incidence of bacteriuria by 3% to 7%. Other risk factors of UTI include female gender, older age, immune-compromised, diabetes mellitus, orthopedic, neurological conditions, and critically ill patients (10).

Objectives

Our study aimed to determine the prevalence, potential risk factors, and outcomes in critically ill patients with MDR-UTIs admitted to ICU at Ain Shams University hospitals.

Patients and Methods

Study design

This cross-sectional study included 383 critically ill patients in tertiary hospitals at Ain Shams University in different ICUs (general medical ICU, geriatric ICU, and surgery ICU) over a 6-month duration. Inclusion criteria were patients who a) aged ≥18 years, b) had urine cultures with significant bacterial growth (defined as >10^5 CFU/mL). Informed consent was obtained from all eligible patients. Clinical data included demographic data, hospitalization duration, medical comorbidities, relevant surgical history before UTI, prior antibiotic use within three months, and empiric treatment. Patients were classified according to MDR organisms into MDR and non-MDR UTI groups.

Clinical data was collected including (a) Demographic data, duration of hospitalization, medical comorbidities, relevant surgical history before UTI, prior antibiotic use within three months, empiric treatment, (b) The clinical diagnosis of UTI (lower or upper UTI) or asymptomatic bacteriuria, (c) Presence of chronic indwelling urinary catheters, hospitalization for at least 48 hours, regular hemodialysis or undergoing urological procedures within the past three months as a risk for healthcare-associated infections.

Concerning urine cultures, patients with positive urine culture first episode diagnosed by significant bacterial growth (defined as >10^5 CFU/mL) were only included in the study analysis. Isolates that are resistant or have intermediate susceptibility to ≥3 of the antimicrobial defined MDR isolates, whereas isolates that did not satisfy this criterion are not classified as MDR isolates. The disc diffusion method and automated antimicrobial susceptibility testing by Vitek 2 were used to identify rates and patterns of antibiotic resistance. Biochemical parameters, such as serum hemoglobin, albumin, creatinine, and C-reactive protein (CRP), were used to estimate the GFR using the Modification of Diet in Renal Disease (MDRD) equation.

The collection of midstream urine samples by clean catch technique was done in the morning. For patients with an indwelling catheter, disinfection of the urinary catheter collection port with 70% alcohol was done. The catheter was clamped 5cm distal to the port for 15 minutes before collecting 10-15 mL of urine using a syringe under aseptic conditions. The urine was collected in a sterile urine container in case of a urinary catheter without a sample port. The container was labeled with patients' full names and IDs, and then the urine sample was transferred within two hours for analysis, culture, and sensitivity testing in the microbiology laboratory of the same institution using disc diffusion according to the Clinical & Laboratory Standards Institute (CLSI 2021).

Antibiotic susceptibility was determined for the following antibiotics: penicillin, cephalosporins, carbapenems, fluoroquinolones, amikacin, TMP-SMX, and nitrofurantoin.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp). Qualitative data were described using numbers and percentages. The Kolmogorov-Smirnov test was used to determine the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). The significance of the obtained results was judged at the 5% level. The tests used were 1) The chi-square test for categorical variables to compare different groups, 2) the student t-test for normally distributed quantitative variables, to compare two studied groups, and 3) the Whitney test for abnormally distributed quantitative variables and compare between two studied groups.

Results

Out of the 395 critically ill patients diagnosed with UTI (Figure 1), 383 patients had positive urine cultures, patients with contaminated samples were excluded, 210 patients had non-MDR UTIs, and 173 had MDR UTIs. In all studied cases, the mean age was 63.07-year (±17.82 SD) with (53.3%) female prevalence, and the mean duration of hospitalization was 3.32 days (±3.08 SD). The most common medical comorbidities, among all the studied cases, were 193 (68.2%) with hypertension and 196 (69.3%) with diabetes mellitus.88 (31.1%) patients were with CKD. The demographic data in the MDR uropathogen group versus patients with non-MDR uropathogen are shown in (Table 1). The majority of the patients were symptomatic UTIs. Only 20 (5.2%) of the total studied patients were asymptomatic. The most common presentation is dysuria in 322 (84.1%) and 184 (48%) with fever. In addition, 102 (26.6%) patients had supra-pubic pain, hematuria in 17 (4.4%), and nocturia in 59 (15.4%). There were 109 patients with lower UTI (28.5%), 116 with upper UTI (30.3%), and 138 with upper and lower UTI (36.0%).

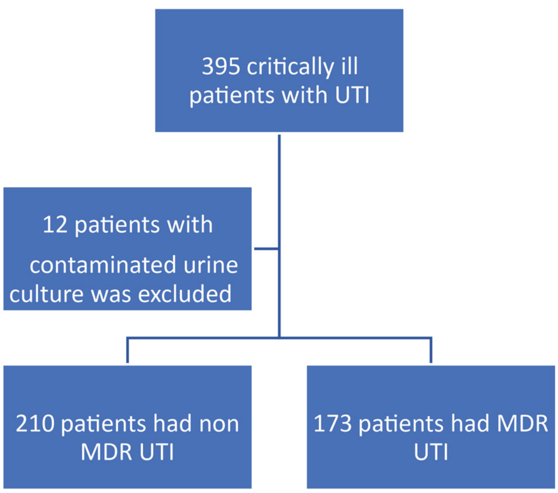

Figure 1. Flowchart of inclusion of critically ill patients diagnosed with UTI.

In the MDR UTI group, males were more prevalent at 61.3%, and hospitalization duration was longer compared to non-MDR (mean was five days and one day, respectively) with *P* value <0.001. Diagnoses of the patients at the time of ICU admission (Figure 2).

As regards the cause of ICU admission, 102 MDR patients presented with septic shock versus 58 non-MDR patients (χ^2 = 0.789, P<0.001). Additionally, 32 MDR patients presented with acute kidney injury (AKI) versus 19 non-MDR patients (χ^2 = 0.789, P<0.001), with a statistically significant difference between MDR and non-MDR UTI.

Furthermore, 78% of the patients under study were found to have chronic indwelling urinary catheters, which served as a risk factor for UTI. Concerning hospitalization for at least 48 hours, regular hemodialysis, and undergoing urological procedures within the past three months (P<0.001), there was a high statistically significant correlation between both groups (Table 2).

As regards laboratory data, MDR UTI patients have higher mean serum creatinine with P<0.005 and lower eGFR with mean 26.7 ± 5.60 mL/min/1.73 m^2 in comparison to non-MDR 31.1 ± 6.30 mL/min/1.73 m^2 with P<0.002. Lower serum albumin levels in the MDR group compared to the non-MDR group with the mean of 2.2 ± 0.6 g/dL and 2.9 ± 0.5 g/dL, respectively, with P<0.02. CRP was higher in the MDR group than non-MDR with P<0.001 (Table 3).

Regarding uropathogens, *E. coli* was the most common (29.2%) (Figure 3). *Klebsiella* and *Enterococcus* were the most common uropathogenic among MDR cases compared to patients with non-MDR UTI P<0.001, while *E. coli* was the most common uropathogen among non-MDR UTI cases (Table 4). Penicillin has the most common antimicrobial resistance. *Enterococcus* species is naturally resistant to cephalosporins, amikacin, and TMP-SMX (Table 5).

Discussion

Antibiotic resistance is a significant healthcare problem worldwide. Frequent utilization of antibiotics at higher rates secondary to UTI treatment failure results in

Table 1. Demographic data distribution and duration of hospital stay among studied cases

	All cases (N=383)		Cases				Test of sig.	*P* value
			Non-MDR (n=210)		MDR (n=173)			
Age (years)								
Range	21–86		23–84		21–86		t= 2.824	0.005*
Mean ± SD	63.07 ± 17.82		60.76 ± 17.18		65.88 ± 18.23			
Gender	No.	%		%	No.	%		
Female	204	53.3	137	65.2	67	38.7	χ^2= 26.779	<0.001*
Male	179	46.7	73	34.8	106	61.3		
Residence								
Rural	183	47.8	86	41.0	97	56.1	χ^2= 8.688	0.002*
Urban	200	52.2	124	59.0	76	43.9		
Duration of hospital stay (days)								
Range	0–10		0–6		0–10		U= 8491.0	<0.001*
Mean ± SD	3.32 ± 3.08		1 (0 – 3)		5 (2 – 8)			

SD, Standard deviation; IQR, Interquartile range; t; Student t-test, U; Mann-Whitney U test.
* Statistically significant at $P \le 0.05$.

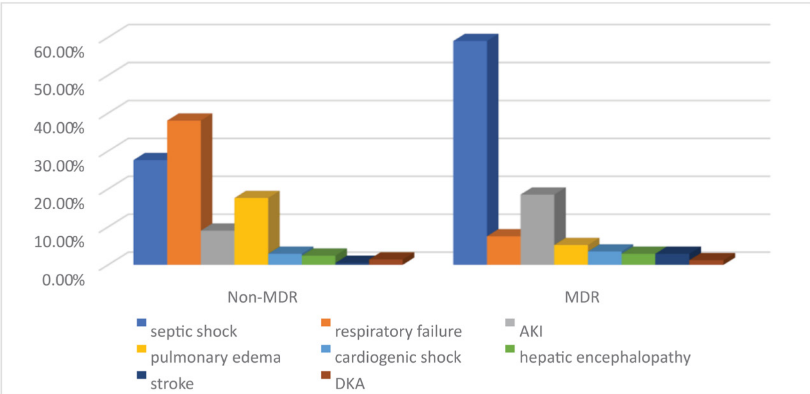

Figure 2. Causes of ICU admission among patients with MDR UTI versus patients with MDR UTI.

multidrug resistance. Some virulent bacteria, such as Escherichia coli, are multidrug-resistant to antibiotics. Escherichia coli is a gram-negative bacterium with beta-lactam enzyme generation in a large spectrum, resulting in most beta-lactam antibiotic resistance (11).

Multiple invasive procedures in ICU patients result in defects of the anatomical barriers' defensive mechanisms and immune response impairment induced by trauma, surgery, and sepsis. In addition, critically ill ICU patients are more prone to infections with frequent use of broad-spectrum antibiotics that lead to multidrug-resistant microorganisms. Compared to other departments, ICUs have a higher rate of nosocomial infections caused by MDR microorganisms (1).

MDR was defined as an acquired nonsusceptibility organism to at least one agent in three or more antimicrobial categories. Extensively drug-resistant organisms were susceptible to only one or two antimicrobial categories (i.e., nonsusceptibility to at least one agent in all but two or fewer antimicrobial categories). Pan drug resistance organisms exhibited resistance to all agents across all antimicrobial categories (12).

Furthermore, it was found that 75% to 90% of UTI bacterial uropathogens were *E. coli*. MDR *E. coli* produces ESBL that hydrolyze penicillin rings, resulting in a significant obstacle in managing UTIs. MDR UTI leads to ineffective, delayed management and severe clinical outcomes, such as sepsis, renal impairment, and prolonged hospitalization (13).

ESBL MDR *E. coli*'s resistance to penicillin, first-, second, and third-generation cephalosporins, and monobactams (aztreonam) increased due to β-lactam antibiotics abuse. 300 ESBL gene variants have been found in diverse Enterobacteriaceae and non-enteric organisms. Antibiotic resistance genes in these MDR uropathogens often code for resistance to cotrimoxazole, quinolones, and aminoglycosides (14).

Among the 383 critically ill patients diagnosed with UTI, the study revealed that 45.2% had MDR-UTI, while 54.8% had non-MDR UTI. The mean age in all cases was

Table 2. Relation between MDR and healthcare-associated risks

	All cases (N=383)		Cases				Test of sig.	*P* value
			Non-MDR (n=210)		MDR (n=173)			
	No.	%	No.	%	No.	%		
Presence of chronic indwelling urinary catheters	301	78.6	180	85.7	121	69.9	χ^2= 0.789	0.374
Hospital stays for at least 48 hours	221	57.7	86	41	135	78	χ^2= 0.789	<0.001*
Regular hemodialysis	88	23.0	33	15.7	55	31.8	χ^2= 13.855	<0.001*
Undergoing urological procedures within the past 3 months	95	24.8	17	8	78	45	χ^2= 69.591	<0.001*

* Statistically significant at $P \leq 0.05$.

Table 3. Laboratory investigations in MDR UTI patients

	All cases (N=383)	Cases		Test of sig.	*P* value
		Non-MDR (n=210)	MDR (n=173)		
Serum creatinine (mg/dL)					
Range	0.7-18	0.7-12	1.0-18	t= 3.333	0.005*
Mean ± SD	3.07 ± 2.02	1.9 ± 0.9	3.15 ± 1.01		
eGFR (mL/min/1.73 m^2)					
Range	2.0-115	4.3-115.0	2.0-80.2	t= 1.490	0.002*
Mean ± SD	28.7 ± 7.5	31.1 ± 6.30	26.7 ± 5.60		
Hemoglobin (g/dL)					
Range	6.4-12	6.4-12	7.2-11	t= 2.262	0.01*
Mean ± SD	9.4 ± 1.7	9.20 ± 3.01	8.70 ± 1.24		
Serum albumin (g/dL)					
Range	1.9-4.2	2.1-4.2	1.9-3.5	t= 12.727	0.02*
Mean ± SD	2.4 ± 0.8	2.9 ± 0.5	2.2 ± 0.6		
CRP (mg/L)					
Range	22 – 410	22-301	56-410	t= 5.412	<0.001*
Mean ± SD	133 ± 17	76 ± 26	98 ± 21		

SD, Standard deviation; IQR, Interquartile range; CRP, C-reactive protein; GFR, Glomerular filtration rate.
* Statistically significant at $P \leq 0.05$.

63.07-year (±17.82 SD) with (53.3%) female prevalence. Regarding age, one possible explanation is that older individuals are more likely to have compromised immune systems, a higher risk for comorbidities, including neurological diseases, diabetes, and cardiovascular diseases, and undergo invasive mechanical procedures with long-term uncontrolled antibiotic use, making them frequently hospitalized. The higher incidence among females can be attributed to anatomical disparities in the urethra between males and females. Specifically, the female urethra is relatively shorter and wider, and it directly connects to the bladder, facilitating easier bacterial entry compared to the male urethra. However, the prevalence of male gender was higher in cases of MDR-UTI. This can be explained by the fact that male patients tend to experience more complications, necessitating more extensive therapy and invasive interventions.

The mean duration of hospitalization was 3.32 days (±3.08 SD) with a range (0-10). The predominant medical comorbidities observed in the studied cases are diabetes mellitus and hypertension (68.2% and 69.3%, respectively). This finding can be explained by patients with comorbidities who had prolonged hospitalizations, invasive device insertion, and broad-spectrum antibiotics use, increasing MDR organism rate.

The most common presentation is dysuria 84.1%, followed by fever 48%. There 28.5% of patients with lower UTI, 30.3% with upper UTI, 36.0% with upper and lower UTI, and 5.2% were asymptomatic.

Regarding healthcare-associated infections, 78% of the patients studied had chronic indwelling urinary catheters, which increased their risk of UTIs. However, there was a significant difference between patients with MDR infections and those without MDR infections in terms of hospitalization for at least 48 hours, regular hemodialysis, and recent urological procedures within the past three months. This difference was statistically significant with a $P < 0.001$.

As regards laboratory data, MDR UTI patients exhibit elevated mean serum creatinine ($P < 0.005$) and reduced

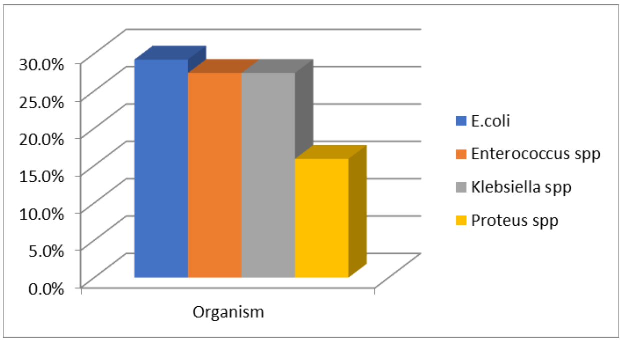

Figure 3. Uropathogenic prevalence among critically ill patients in ICUs (n=383 patients).

eGFR (26.7 ± 5.60 mL/min/1.73 m^2) compared to non-MDR (31.1 ± 6.30 mL/min/1.73 m^2) patients ($P<0.002$). The MDR group exhibited a significantly reduced serum albumin level in comparison to the non-MDR group (mean: 2.2 ± 0.6 g/dL versus 2.9 ± 0.5 g/dL, respectively), with a $P<0.02$. The MDR group had a significantly higher CRP than the non-MDR group ($P<0.001$). *E. coli* was the most prevalent uropathogen among all cases examined in the study (29.2%). Among MDR cases with a p-value less than 0.001 (46.8% and 41.6%, respectively), *Klebsiella* and *Enterococcus* were the most prevalent uropathogens. However, *E. coli* was the most prevalent uropathogen among non-MDR UTI cases. The most prevalent form of antimicrobial resistance was penicillin, whereas *Enterococcus* species were naturally resistant to cephalosporins, amikacin, and TMP-SMX.

Consistent with the current study's findings, Su et al (6) examined the relationship between impaired kidney function and MDR infections in 42 863 patients. They found that individuals with lower estimated GFR (eGFR) had higher odds of MDR pathogens, with a statistically significant ($P = 0.004$), which aligns with the results of the present study. This finding can be explained by patients with impairment of kidney function having a functional impairment of the immune systems, increased release of reactive oxygen species, uremic toxins, and exposure to healthcare staff, increasing their susceptibility to MDR uropathogenic infection.

Concerning the cause of ICU admission, MDR patients presented with septic shock and AKI more than non-MDR patients, with a statistically significant difference between MDR and non-MDR UTI. This finding can be explained by MDR patients having older age, distinct clinical features in the male gender, comorbidities, prolonged hospitalization, and previous urological procedures in comparison to non-MDR patients, and these resulted in bacteremia and sepsis. Sepsis can lead to AKI, as well as the increased virulence of multidrug-resistant uropathogens. The use of combined antibiotics to treat AKI is an additional contributing factor.

In agreement with the current study's findings regarding risk factors for UTI, Tenney et al (15) conducted a systemic review study that identified the possible MDR-UTI risk factors. Elderly patients (50–65 years) had MDR-UTI, indicating that advanced age is a significant risk factor. Based on 10 studies involving a total of 26 501 participants, it has been found that being female does not

Table 4. The pattern of uropathogenic microorganisms among patients with MDR and non-MDR UTI

	All cases (N=383)		Cases				Test of sig.	*P* value
			Non-MDR (n=210)		MDR (n=173)			
	No.	%	No.	%	No.	%		
E. coli	112	29.2	103	49.0	9	5.2	χ^2= 69.591	0.002
Enterococcus	105	27.4	32	15.2	73	42.1	χ^2= 0.691	<0.001*
Klebsiella	105	27.4	24	11.4	81	46.8	χ^2= 12.655	<0.001*
Proteus	61	15.9	51	24.2	10	5.78	χ^2= 0.691	<0.001*

* Statistically significant at $P \leq 0.05$.

Table 5. Antimicrobial resistance profile of the common uropathogens among critically ill patients in ICUs

	Organisms							
	E. coli (n=105)		*Enterococcus* spp (n=61)		*Klebsiella* spp (n=105)		*Proteus* spp (n=112)	
	No.	%	No.	%	No.	%	No.	%
Penicillin	47	44.8	36	59.0	47	44.8	52	46.4
Cephalosporins	32	30.5	-	-	26	24.8	40	35.7
Carbapenems	38	36.2	20	32.8	29	27.6	43	38.4
Fluoroquinolones	33	31.4	22	36.1	28	26.7	38	33.9
Amikacin	41	39.0	-	-	27	25.7	32	28.6
TMP-SMX	31	29.5	-	-	37	35.2	29	25.9
Nitrofurantoin	32	30.5	22	36.1	27	25.7	-	-

increase the risk of developing MDR-UTI. This finding is consistent with the present study's findings, which showed that males were more commonly affected by MDR UTI. Urinary catheters are associated with an increased risk of developing UTIs in 11 out of 14 studies. Additionally, they are a risk factor for MDR UTIs.

In contrast to Mohamed et al study, which studied 779 urine cultures retrospectively for three years and showed the prevalence of urinary catheter associated urinary tract infections (CA-UTIs) 12.7% with a mean age of 41.2 years, the highest MDR UTI and the most predominant pathogen in ICUs was *Acinetobacter baumannii*, followed by *Pseudomonas aeruginosa*. However, in agreement with our study, MDR uropathogens had prolonged hospitalizations, and penicillin and cephalosporins were the highest antimicrobial resistance against uropathogens. The difference can be explained by the study population selected from both ICU and non-ICU stays, younger mean age groups, local antimicrobial resistance rates, surveillance differences, and lack of data about previous antimicrobial use (16).

In contrast to the present study, Li and colleagues' study was an observational study that included a meta-analysis and systematic review of 8785 patients admitted to the hospital. A total of 615 patients were diagnosed with catheter-associated UTI. Nevertheless, participants with diabetes exhibited a higher prevalence of catheter-associated UTI. Risk factors for catheter-associated UTI showed that age, diabetes, catheterization duration, previous antibiotic usage, and length of ICU stay exhibited varying degrees of statistically significant heterogeneity (I^2 > 50%, $P < 0.05$). These results agree with the present study's findings (17).

Conversely, the study conducted by Haque Sumon et al examined MDR UTI in 326 CKD patients at a tertiary hospital. The study found a higher prevalence of MDR gram-negative isolates among female patients. The predominant clinical presentations mostly were dysuria, fever, and loin pain. The most prevalent bacterial isolate was *E. coli*. However, the prevalence of MDR UTI is higher than in the present study. This disparity can be attributed to the fact that the previous studies focused exclusively on patients with CKD, whereas only 31.1% of our patients had this condition. Uremic toxins in patients with CKD have a detrimental impact on both humoral and cellular immunity, thereby elevating the risk of infections, including UTIs (18).

Furthermore, *E. coli* was the most common pathogen in all studied cases in this study. It was resistant to penicillin, followed by aminoglycosides, carbapenems, quinolones, nitrofurantoin, and cephalosporins. This can be suggested by the significant relationship between the extensive use of antimicrobials and antimicrobial resistance. In agreement with the study, Alanazi et al (19) retrospectively conducted patients diagnosed with UTIs in the emergency department. 91.98% were gram-negative organisms, and 6.79% were gram-positive organisms. *E. coli* was the most common UTIs pathogen isolated from pediatric, adult, and elderly urine cultures, respectively, so it was the most prevalent pathogen. There was also a high rate of resistance to cotrimoxazole and ampicillin.

In contrast, a comprehensive analysis of 25 studies involving 31 284 patients with positive urine cultures has been conducted to identify MDR-UTI risk factors. These studies demonstrated that *E. coli* was the causative pathogen. Previous antibiotic usage was the most common risk factor. In at least two different studies, eleven other risk factors were identified, including age, both male and female gender, minority ethnicity, recent travel, previous hospitalization, nursing home residence, urinary catheterization, previous hospitalization, previous UTIs, diabetes, and immunocompromised patients (15). There was a disagreement with the present study where *Klebsiella* and *Enterococcus* were the most common uropathogenic among MDR cases (46.8%, 41.6% respectively) ($P < 0.001$), while *E. coli* was the most common uropathogen among non-MDR UTI cases. The variation in patient types hospitalized, antibiotic policies with improper hospital hygiene, and infection control policies among geographical regions. Consequently, uropathogenic organisms develop resistance to numerous antibiotics, and genes containing resistance determinants are transmitted among Gram-negative organisms.

The study demonstrated that *Klebsiella* exhibited resistance to penicillin, followed by TMP-SMX, carbapenems, aminoglycosides, and nitrofurantoin. A potential explanation is that these antibiotics are the most commonly prescribed drugs in clinical settings in this area. In agreement with this study, Miftode et al (20) analyzed 75 cases retrospectively with a *K. pneumoniae* UTI confirmed diagnosis at discharge for six months. Regarding age, the occurrence of ESBL+ *K. pneumoniae* UTIs was observed in elderly patients. An additional risk factor is that 58.2% of patients with ESBL+ infections had previously been admitted to the hospital. In addition, patients with urinary catheters presented more with ESBL+ infections ($P = 0.0012$). The ESBL+ KP patients had extremely low susceptibility rates to ciprofloxacin, gentamicin, amikacin, imipenem, meropenem, and colistin, with 0%, 8.9%, 58.9%, 67.7%, 67.7%, and 67.7%, respectively.

In agreement with the present study, Ibrahim and Al Bshabshe et al (21,22) investigated the prevalence and risk factors of MDR *K. pneumoniae* infection among admitted patients in a referral hospital located in Saudi Arabia. The results revealed increased rates of MDR *K. pneumoniae* and highest antibiotic resistance to penicillin. The risk factors include male gender, older age group, diabetes, invasive medical devices, and ICU admission.

In contrast to the current study, an observational study (23) included 100 septic patients who were hospitalized in a general ICU. A total of 28% of the patients had UTIs, while 6% had urosepsis. The patients who presented with

UTIs were predominantly male, with a mean age of 58.71 ± 19.45 years. The most prevalent organism among the 28 strains identified through urine cultures was *K. pneumoniae* (n = 12). Concerning antibiotic resistance from the 28 isolates, 27 were resistant to ciprofloxacin, meropenem, and ceftriaxone, 23 to amikacin, 28 to cefepime, and 26 to ceftazidime. This result can be explained by the fact that the frequency of UTI pathogens may vary by patient population, previous antibiotic usage, hospital, and type of ICU patient, and these changes over time, emphasizing the need for continuous, timely, local surveillance data.

Klebsiella is a common uropathogenic among MDR cases in our study owing to plasmid-mediated properties, length of hospitalization, and performance of invasive procedures, including urinary catheters, as a risk factor for the acquisition of these resistant strains. As a result, this has become a significant problem in intensive care due to MDR and the potential transfer of plasmids to other uropathogens.

In this study, *Enterococcus* accounts for 41.6% of MDR UTI patients and showed resistance to penicillin, followed by nitrofurantoin, fluoroquinolones carbapenems, nitrofurantoin, and carbapenems. Enterococci possess virulence genes coding for virulence factors. These virulence factors include bacteriocins, serine protease, hemolysin, cytolysin, and gelatinase. Moreover, *Enterococcus* can produce toxic oxygen metabolites, resulting in cell injury, colonization of host tissue, and modulation of host defense mechanisms that facilitate its invasion (24).

In agreement with this study, another cross-sectional laboratory-based study was conducted to examine the isolated species of enterococci and the different virulence markers and gene distribution among these species. The study determined the antibiotic resistance patterns of enterococci. The results indicated that 61% of the samples exhibited resistance to ampicillin (25).

Consistent with our findings, Bhatt et al cross-sectionally studied the prevalence of MDR enterococci and its antimicrobial susceptibility in tertiary centers. In addition, enterococci accounted for 63% of the MDR organisms. Risk factors for MDR enterococci were older patients, prolonged hospitalizations, and previous exposure to antibiotics. Most of the isolates were resistant to penicillin. *E. faecalis* was the most common isolate. This finding indicates the need for various phenotypic tests as well as correct speciation for understanding antibiotic resistance (26).

Inconsistent with our findings, Haghi et al investigated the antimicrobial susceptibility of enterococci in hospitalized patients. Additionally, 36% of enterococci were multidrug-resistant. 86% of enterococci were tetracycline resistant, followed by 73% ciprofloxacin resistant, 53% quinupristin-dalfopristin resistant, 50% gentamicin, and 34% streptomycin resistant. Biofilm formation in UTIs exhibits a vital role in UTI as 74% of enterococci showed biofilm formation phenotype. The E. faecium isolates exhibited greater resistance to aminoglycosides and vancomycin, possibly due to a higher prevalence of virulence genes among *Enterococcus faecalis* isolates compared to *E. faecium* (27). Enterococci inhabit the bowels of healthy populations, and the development of antimicrobial resistance of enterococci is associated with prolonged hospitalization, empirical antibiotic use, and lack of sufficient programs to control the rapid spread of enterococci.

Conclusion

The prevalence of MDR UTI was 45.2% among critically ill ICU patients in Ain Shams University hospitals. *Klebsiella* and *Enterococcus* were the most common uropathogenic among MDR UTIs, with resistance mainly to penicillins and carbapenems. The hospital stay >48 hours, hemodialysis, and urological procedures were the most significant risk factors for MDR UTI. Critically ill patients with septic shock and AKI were significantly associated with the presence of MDR UTI. An updated local antibiogram database in the hospitals is recommended. Appropriate regular surveillance, infection control measures, and evidence-based recommendations for uropathogenic treatment protocols are recommended to avoid emerging resistant uropathogens among critically ill patients.

Limitations of this study

The limitations of this study are that it is a pilot study, and follow-up of the patient could not be done to study the long-term effect of MDRUTI on eGFR and the effect on patient survival as the study is a cross-sectional study.

Authors' contribution

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Conflicts of interest

The authors declare that there is no conflict of interest.

Ethical issues

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Ain Shams University Hospital Research Committee (Ethics Committee reference number: FWA 000017585). Prior to any intervention, all participants provided written informed consent. Accordingly, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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