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RESEARCH ARTICLE

ANTIBIOTIC RESISTANCE RATES OF BACTERIAL ISOLATES FROM URINARY TRACT INFECTIONS IN DIABETIC PATIENTS IN SANA'A, YEMEN

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Abstract

Background and Aims: Urinary tract infections (UTIs) are among the most common bacterial infections, particularly among diabetic patients. These infections are often complicated by antibiotic resistance and the patients' susceptibility to infection, making empirical treatment difficult. This study was conducted to identify the pattern of antibiotic resistance in UTI pathogens among diabetic patients in the medical ward of Kuwait Hospital in Sana'a, Yemen, with the aim of improving the empirical treatment of UTIs with antibiotics.
Materials and Methods: Total 454 DM patients were sent to the medical ward of the Al-Kwait University Hospital clinics in Sana'a, Yemen, for this cross-sectional study. In order to perform a urine culture, a clean, sterile urine sample (midstream pee) was collected, cultured, and the pathogenic bacteria were isolated and identified.
Results: The mean patient age was 48.2 years, with 73.1% being ≥ 40 years old. *Escherichia coli* caused 41 (42%) of UTIs, *Klebsiella pneumoniae* 33 (34%), *Pseudomonas aeruginosa* 9 (9.3%), and *Enterococcus faecalis* 6 (6.2%).Resistance rates in *E. coli* are high, reaching 95% for amoxicillin and 70.7% for ampicillin, with varying levels of resistance for other antibiotics, ranging from 36.6% to 92.7% for agents like ceftazidime and ciprofloxacin. Low resistance rates were noted for amikacin (4.9%) and other select antibiotics. *Klebsiella pneumoniae* displayed 100% resistance to amoxicillin and ampicillin, with lower resistance rates for amikacin (0%) and levofloxacin (18.2%).
Conclusions: The increasing resistance of antibiotics highlights the need for up-to-date local data to guide empirical treatment for urinary tract infections (UTIs). Amikacin, cefotaxime, levofloxacin, lomefloxacin , clarithromycin, ciprofloxacin, piperacillin-tazobactam, and tobramycinhave demonstrated low resistance rates and could be an effective first-line treatment for UTIs at Al-Kuwait Hospital.
Keywords: Antimicrobial resistance, diabetes mellitus, empirical treatment, *Escherichia coli*, *Klebsiella*, *Pseudomonas aeruginosa*, uropathogens.

INTRODUCTION

One of the most common bacterial illnesses in the world, urinary tract infections (UTIs) cause considerable morbidity and expensive medical expenses. Recent systematic reviews and meta-analyses indicate that 150 million UTIs happen worldwide each year. Acute uncomplicated cystitis and urethritis are examples of lower urinary tract UTIs, while pyelonephritis, which involves a risk of sepsis, is an example of upper urinary tract UTIs. A few number of *Enterobacteriaceae*, most frequently *E. coli*, which causes 75%–95% of cases of uncomplicated cystitis, are responsible for the great majority of community-acquired UTIs[1]. *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus faecalis*, and *Staphylococcus saprophyticus* are further significant uropathogens[2].
The most significant factor contributing to the rise in antimicrobial resistance worldwide is the rise in prescriptions, indiscriminate usage, and dispensing in poorer nations. Between 700,000 to several million deaths are thought to occur each year, and they continue to pose a serious threat to global public health[3]. Billions of dollars are spent in medical expenses and lost productivity, millions of people have antibiotic resistant germs, and many more pass away[4,5].

Antimicrobial resistance-related mortality may rise over time, according to estimates from the World Health Organisation (WHO) and a United Nations report[6,7]. These days, antimicrobial resistance (AMR) is a serious concern to public health[8,9]. Antimicrobial resistance bacteria are rapidly growing in many hospital departments worldwide, and in Yemen, the issue is more widespread and complicated[10-15]. Antimicrobial resistance is expected to rank among the top causes of death for both hospitalised and non-hospitalized individuals in both developed and developing nations if proper control and preventative measures are not implemented. To cure bacterial infections, antibiotics must be used and administered properly[16]. Antibiotic-resistant pathogenic bacteria can therefore arise as a result of improper antibiotic prescribing and abuse, which can therefore limit treat-ment options, lengthen hospital stays, raise treatment expenses, and ultimately increase mortality[17].

Empiric antibiotic treatment is severely hampered by the high frequency of UTIs and the rising rates of antibiotic resistance among uropathogens. Standard empirical antibiotic regimens for common illnesses, including UTIs, are in danger of being undermined by the global rise in antibiotic resistance. In order to optimise antibiotic selection and inform clinical practice guidelines, surveillance studies that provide current local and regional resistance profiles are crucial. Geographical location, patient demographics, healthcare environments, and even outpatient versus inpatient cohorts can all have a significant impact on resistance patterns. Given the high frequency of UTIs, the possibility of acute morbidity (such as urosepsis and the risk of ascending kidney infection), and the growing problems with multidrug resistant Gram-negative pathogens like carbapenem resistant *Entero-bacteriaceae*, it is imperative to continuously monitor local resistance trends in UTIs[13].

An illustration of the significance of this subject in Sana'a and the circumstances in which this knowledge is also helpful in Sana'a. Doctors rely on administering antibiotics experimentally without bacterial isolation and antibiotic sensitivity testing due to the high rates of antibiotic resistance[11,13,14,21]. An experiment is frequently the first step in treating UTIs. The anti-microbial resistance pattern of urine bacteria provides particular information for treatment. However, because antibiotic resistance is a growing and enduring problem, it is crucial to regularly evaluate resistance patterns in order to enhance the recommendations for empirical antibiotic therapy[22-24]. However, there is a dearth of information regarding the kinds of isolated bacteria from DM UTIs and their profiles of anti-bacterial susceptibility in Sana'a, Yemen.

SUBJECTS AND METHODS

The methodology employed was an active prospective follow-up study. All patients who consented to participate and were seen in the medical ward at Al-Kwait University Hospital in Sana'a, Yemen between January 1, 2024, and December 31, 2024, were the target audience for the study (Time allowed by the hospital's authority). Over the course of the study, 454 individuals with a diagnosis of diabetes mellitus were included. There are 255 females and 199 males between the ages of 10 and 75, with a mean age of 48.2±16.2 years. Clinical, demographic, and UTI-influencing factors were collected for each DM. After that, a midstream urine sample was taken. Following aerobic cultivation of the samples in blood agar and MacConkey agar, the cultures were examined for significant potential UTI bacterial pathogens. Standard laboratory techniques were used to isolate and identify potential bacterial pathogens, and the Clinical and Laboratory Standards Institute (CLSI)[25] described the disc diffusion method for microbial sensitivity testing.

Susceptibility testing

Using Muller-Hinton medium, the isolates were examined for antimicrobial susceptibility using the disc diffusion method in accordance with National Committee for Clinical Laboratory Standards (NCCLS) approvals[25]. Amoxicillin, ampicillin, ampicillin-sulba-ctam, augmentin, cefaclor, cefadroxil, cefepime, cefi-xime, cefoxitin, ceftazidime, ceftriaxone, cefuro-xime, ciprofloxacin, clindamycin, co-trimoxazole, nalidixic acid, and nitrofurantoin were the antimicro-bial drugs that were tested. Levofloxacin, lomeflo-xacin, amik-acin, cefotaxime, and clarithro-mycin (BD-BBL-TM-Sensi-Disc-TM).

Ethical consideration: The Ethics Committee of Sana'a University's Faculty of Medicine and Health Sciences approved the study, and patients gave their informed consent (document number: 2023-35, dated January 25, 2023).

Data analysis: Standard descriptive statistics were applied when the findings were tallied. Numerical variables are summarised using mean values, whilst categorical variables are displayed as counts and percentages.

RESULTS

The age and gender distribution of 454 diabetic individuals who had urinary tract infections tested in Sana'a is displayed in Table 1. The patients' ages ranged from 10 to 75 years, with a mean age ± standard deviation of 48.2 ± 16.2 years. 73.1% of patients were over 40, while 12.3% were in the 30- to 39-year-old age range. With 42.3% of all samples, *E. coli* was the most frequent isolate, followed by *K. pneumoniae* at 34%. *E. faecalis* and *P. aeruginosa* were less prevalent, accounting for 6.2% and 9.3%, respectively. Total 96.04% of patients with urinary tract infections had monocotyledonous pathogen development, whereas 3.96% had mixed pathogen growth. Resistance rates in *E. coli* reached 95% for amoxicillin, 70.7% for ampicillin, 53.3% for ampicillin-sulbactam, 65.8% for augmentin, 60.9% for cefaclor, 65.8% for cefadroxil, 36.6% for cefepime, and 56.1% for cefixime. Resistance rates in *E. coli* ranged from 36.6% to 92.7% for cefoxitin, ceftazidime, ceftriaxone, cefuroxime, ciprofloxacin, clindamycin, co-trimoxazole, nalidixic acid, and nitrofurantoin. While low rates of resistance to *E. coli* bacteria were recorded with amikacin (4.9%), cefotaxime (17.1%), levofloxacin (4.9%), lomefloxacin

(4.9%), and clarithromycin (19.5%), resistance rates of *K. pneumoniae* reached 100% for amoxicillin, ampicillin, cotrimoxazole, and nalidixic acid.
Resistance rates ranged from 39.4% to 87.8% for augmentin, ampicillin-sulbactam, cefaclor, cefadroxil, cefepime, cefixime, cefoxitin, ceftazidime, ceftriaxone, ciprofloxacin, clindamycin, and nitrofurantoin. Low resistance rates of less than 25% were recorded for *K. pneumoniae* with amikacin (0%), levofloxacin (18.2%), lomefloxacin (21.2%), and cefotaxime (21.2%).

Table 1: Sex and age distribution of 454 diabetic patients tested for UTI.

Characters	n (%)
Sex	
Male	199 (43.8)
Female	255 (56.2)
Total	454 (100)
Age in Years	
Less than 20 years	47 (10.4)
20 -29 years	19 (4.2)
30 – 39 years	56 (12.3)
≥ 40 years	332 (73.1)
Mean	48.2 years
SD	16.2 years
Median	53 years
Mode	50 years
Min to Max	10- 75 years

Resistance rates for *P. aeruginosa* ranged from 44.4% to 66.7% for cefaclor, cefadroxil, cefepime, cefixime, and cefoxitin, while resistance was low for ciprofloxacin (22.2%), piperacillin-tazobactam (11.1%), tobramycin (0.0%), amikacin (11.1%), levofloxacin (22.2%), and lomefloxacin (22.2%). *E. faecalis* showed 100% resistance to amoxicillin, ampicillin and nail-dixic acid, while it did not show resistance to most of the antibiotics tested.

Table 2: Bacterial pathogens isolated from urine samples of DM patients with urinary tract infections.

Name of pathogens	n (%)
E. coli	41 (42.3)
K. pneumoniae	33 (34)
P. aeruginosa	9 (9.3)
E. faecalis	6 (6.2)
Mono-growth of pathogens	97 (96.04)
Mixed-growth of pathogens	4 (3.96)

DISCUSSION

In this investigation, resistance rates in *P.aeruginosa*, *K. pneumoniae*, and *E. coli* were more prevalent than in the previous 20 years. Antibiotics boost the selective pressure in bacterial populations, which kills susceptible bacteria and speeds up the growth of resistant bacteria. Resistant bacteria have the benefit of multiplying more quickly than weak germs, even at very low antibiotic concentrations. Alternative treatments are becoming increasingly necessary as antibiotic resistance increases. Although there have been requests for novel antibiotic therapies, there is a dearth of new medication development[26,27].
The rate of antibiotic resistance among the main pathogenic microorganisms isolated from DM patients in one tertiary hospital in Sana'a, Yemen, was examined in the current study. Clinicians are particularly concerned about the occurrence and dissemination of these agents since it is certain that these antibiotic resistance to GNB can cause significant infections, especially in immunocompromised patients such as DM, the elderly, newborns, and infants[25,28]. *E. coli* resistance rates in the current study were 95% for amoxicillin, 70.7% for ampicillin, 53.3% for ampicillin -sulbactam, 65.8% for augmentin, 60.9% for cefaclor, 65.8% for cefadroxil, 36.6% for cefepime, and 56.1% for cefixime. This result is in line with worldwide forecasts that show *E. coli* resistance to conventional antibiotics including ampicillin (up to 88%), trimeth-oprim/sulfamethoxazole, and cipro-floxacin will continue to pose a serious threat to the world in 2024–2026. There is widespread resistance to both ESBL-producing bacteria and third-generation cephalo-sporins; in certain clinical settings, ESBL production rates surpass 40–50%[29]. Additionally, *E. coli*, one of the most commonly isolated Gram-negative pathogens in clinical settings, exhibits persistently high resistance to penicillin (83.92%), cephalosporins (63.05%), and fluoroquinolones (62.21%), which is concerning when treating blood-stream and urinary tract infections[29]. The present study's conclusions also align with the surveillance data from 2024 to 2026. Yemen's *E. coli* has remarkably high, even concerning, levels of resistance to common first-line antibiotics. With 78% of people self-medicating, this condition is linked to the overuse and uncontrolled use of antibiotics. In Yemen, *E. coli* is a prominent source of wound infections and urinary tract infections, and a large percentage of these illnesses have extensively drug-resistant (XDR) or multidrug-resistant (MDR) patterns[30-34].
In the current study, resistance rates of *K. pneumoniae* reached 100% for amoxicillin, ampicillin, cotrim-oxazole, and nalidixic acid. Resistance rates ranged from 39.4% to 87.8% for augmentin, ampicillin -sulbactam, cefaclor, cefadroxil, cefepime, cefixime, cefoxitin, ceftazidime, ceftriaxone, ciprofloxacin, clindamycin, and nitrofurantoin. This result is in line with estimates that *K. pneumoniae* is a high-priority, multidrug-resistant organism worldwide, with over 55% of isolates worldwide currently resistant to third-generation cephalosporins, and in certain areas, resis-tance surpasses 70%. The prevalence of carbap-enem resistant *K. pneumoniae* has increased to 15.1% worldwide, with some studies showing sharp rises from 0% to nearly 40% in some areas, significantly restricting treatment choices[35]. Additionally, obtained results are consistent with recent research showing exceptionally high rates of resistance in *K. pneumoniae* in Yemen, especially among carbapenem-resistant strains (CRKp), which have been extensively documented in clinical specimens.

Table 3: Bacterial antibiotic resistances pattern of DM UTI.

Antibiotics	*E. coli* n=41 n (%)	*K. pneumoniae* n=33 n (%)	*P. aeruginosa* n=9 N (%)	*E. faecalis* n=6 n (%)
Amikacin	2 (4.9)	0 (0)	1 (11.1)	0 (0.0)
Amoxicillin	39 (95)	33 (100)	-	6 (100)
Ampicillin	29 (70.7)	33 (100)	-	6 (100)
Ampicillin -sulbactam	22 (53.6)	7 (21.2)	-	1 (16.7)
Augmentin	27 (65.8)	33 (100)	-	1 (16.7)
Cefaclor	25 (60.9)	27 (81.9)	4 (44.4)	3 (50)
Cefadroxil	27 (65.8)	27 (81.9)	4 (44.4)	3 (50)
Cefepime	15 (36.6)	13 (39.4)	5 (55.6)	0 (0.0)
Cefixime	23 (56.1)	20 (60.6)	6 (66.7)	0 (0.0)
Cefotaxime	7 (17.1)	13 (39.4)	4 (44.4)	0 (0.0)
Cefoxitin	13 (31.7)	14 (42.4)	4 (44.4)	0 (0.0)
Ceftazidime	15 (36.6)	13 (39.4)	5 (55.6)	0 (0.0)
Ceftriaxone	19 (46.3)	13 (39.4)	5 (55.6)	1 (16.7)
Cefuroxime	11 (26.8)	7 (21.2)	4 (44.4)	1 (16.7)
Ciprofloxacin	12 (29.3)	13 (39.4)	2 (22.2)	1 (16.7)
Clarithromycin	8 (19.5)	8 (24.2)	-	0 (0.0)
Clindamycin	10 (24.4)	13 (39.4)	-	1 (16.7)
Co-Trimoxazole	38 (92.7)	33 (100)	-	5 (83.3)
Levofloxacin	2 (4.9)	6 (18.2)	2 (22.2)	1 (16.7)
Lomefloxacin	2 (4.9)	7 (21.2)	2 (22.2)	0 (0.0)
Nalidixic Acid	38 (92.7)	33 (100)	-	6 (100)
Nitrofurantoin	29 (70.7)	26 (87.8)	-	-
Piperacillin-tazobactam	-	-	1 (11.1)	-
Tobramycin	-	-	0 (0.0)	-

This bacterium frequently shows significant levels of resistance to antibiotics used as a last line of defence, is a major source of hospital acquired infections, and has high multidrug resistance[36-39]. In the current study resistance rates for *P. aeruginosa* ranged from 44.4% to 66.7% for cefaclor, cefadroxil, cefepime, cefixime, and while resistance was low for ciprofloxacin (22.2%), piperacillin tazobactam (11.1%), tobramycin (0.0%), amikacin (11.1%), levofloxacin (22.2%), and lomefloxacin (22.2%). Our findings are similar to that reported worldwide in which drug resistance in *P. aeruginosa* is a serious global health problem, with multidrug-resistant strains accounting for between 11.5% and 24.7% of clinical cases and causing approximately 559,000 deaths annually. However, no resistant for carbapenem in our study different from that reported globally in which carbapenem-resistant *P. aeruginosa* exhibits widespread global prevalence (34.7%), with the highest rates in Europe (47.6%) and the lowest in Asia (32.8%)[36]. Also, our findings are similar to that reported from Yemen previously in which *P. aeruginosa* in Yemen exhibits alarming resistance rates, often exceeding 70–90% for common antibiotics such as cephalosporins and ciprofloxacin, with high rates of multidrug resistance. Studies indicate high levels of resistance to amoxicillin/clavulanic acid (96.2%), cefuroxime (94.6%), and ampicillin/ sulbactam (94.5%). While carbapenems (meropenem/ imipenem) often remain effective, resistance is increasing[31-34].

In the current study, *E. faecalis* showed 100% resistance to amoxicillin, ampicillin and nalidixic acid, while it did not show resistance to most of the antibiotics tested (Table 3). *E. faecalis* exhibits high and globally varying rates of resistance, often exceeding 60% to multiple antibiotics in both environmental and animal sources. Although generally more susceptible than *E. faecium*, *E. faecalis* shows significant resistance to tetracycline (51.1%), erythromycin (63%), and gentamicin (36.5%), along with emerging, though lesser, resistance to linezolid (0.6–2.8%) and vancomycin (1.6%)[37]. Also, *E. faecalis* isolates in Yemen exhibit high levels of antibiotic resistance, particularly in hospital-acquired infections, with studies indicating high rates of multidrug resistance (MDR) and resistance to commonly used experimental antibiotics. Resistance rates in clinical isolates (in the Yemeni context): vancomycin-resistant *E. faecalis* (VRE): Significant vancomycin resistance has been reported in VRE in Yemeni studies, with one study reporting a resistance rate of 53.8% in surgical wound/blood culture isolates. More than 70% of these VRE isolates carried the vanA gene[38].

It's crucial to remember that these antibiotics are commonly used in Sana'a hospitals to treat a variety of ailments, including sepsis, lung infections, and urinary tract infections. The main cause of this problem is recognised to be the abuse or overuse of antibiotics, together with their incorrect selection, which results in a daily growth in antibiotic resistance[39]. Therefore, given the current circumstances, the following actions ought to be taken: If the primary pathogenic bacteria have a resistance rate more than 40%, use antibiotics with caution. When the primary pathogenic bacteria have a resistance rate more than 50%, drug sensitivity testing should be utilised to choose the right antibiotics. Antibiotic use should be stopped once the primary pathogenic bacteria's resistance to them surpasses 75%. To ascertain if ongoing drug use is clinically viable, it is crucial to research and assess data pertaining to bacterial resistance[39]. In order to prevent unwanted complications and lower the consequent mortality rate,

it is critical to identify and carefully choose effective antibiotics for treating bacterial infections due to the high level of bacterial resistance to antibiotics[39]. Consequently, it is crucial and strongly advised to understand the patterns of antibiotic resistance in common diseases, to conduct workshops to rectify the prescription of empirical treatment, and to modify the usage of antibiotics.

Limitations of the study

One limitation is the cross-sectional design, which makes it impossible to establish definitive causal relationships between certain factors associated with urinary tract infections, the causative bacteria, and their drug resistance. Another limitation is the focus on a single center: the study was limited to one site in Sana'a, which may not accurately represent the entirety of Yemen. There are also sampling limitations (small sample size of isolated bacteria) and potential biases. Furthermore, the timing of sample collection is problematic; in some cases, urine samples are suspected to have been collected after patients had already begun antibiotic treatment, which could affect pathogen isolation and antibiotic susceptibility patterns. Also, antibiotic discs for GPB as vancomycin were not available during the study.

CONCLUSIONS

The increasing resistance of antibiotics highlights the need for up-to-date local data to guide empirical treatment for urinary tract infections (UTIs). Amikacin, cefotaxime, levofloxacin, lomefloxacin, clarithromycin, ciprofloxacin, piperacillin-tazobactam, and tobramycinhave demonstrated low resistance rates and could be an effective first-line treatment for UTIs at Kuwait Hospital. Continuous monitoring of resistance patterns in UTIs is crucial for improving antibiotic selection and preventing disease complications.

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AUTHOR'S CONTRIBUTION

Hassan SMA: writing original draft, methodology, investigation. **Al-Moyed KA:** methodology, investigation. **Abdu SSA:** writing original draft, methodology. **Al-Arashi IA:** data curation, conceptualization. **Khalil EHA:** formal analysis, conceptualization. **Al-Yosaffi EA:** review and editing, methodology. **Al-Shamahy HA:** formal analysis, data curation, conceptualization. **Ajlabri AAS:** review, editing. Final manuscript was checked and approved by all authors.

DATA AVAILABILITY

The empirical data used to support the study's conclusions are available upon request from the corresponding author.

CONFLICT OF INTEREST

Regarding this project, there are no conflicts of interest.

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