Alqalam Journal of Medical and Applied Sciences. 2025;8(1):352-358
https://doi.org/10.54361/ajmas.258151

Original article

Drug Susceptibility Patterns of Uropathogens Isolates from Suspected UTI Patients Attending Zawia Medical Center, Libya

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Abstract
Urinary tract infections (UTIs) are among the common reasons for seeking medical attention in the community. Understanding the characteristics of uropathogens and their antimicrobial susceptibility pattern in a particular setting can provide evidence for the appropriate management of cases. Therefore, the aim of current study is to determine the prevalence of uropathogens associated with UTIs, and estimated their sensitivity profile among different age groups in Zawia Teaching hospital. A retrospective study was conducted from 1st January, 2022 to December 31th 2022 in Zawia Teaching hospital. Patients of all ages and both sexes were included in the study. Laboratory reports of patients with a positive urine culture (≥10^5 CFU/mL) and antibiotic susceptibility testing were included in the study. Out of 1966 samples, 506 cases were a positive culture. Of whom, 378(74.70%) were female and 128(25.30%) were male. The majority of positive cultures was recorded in the adolescent age group of 11–20 years (38.14%). Regarding the isolated uropathogens, the *E. coli* was the dominant bacterial isolate with 261 (51.58%) of the total samples. On the other hand, the gram-positive bacteria (*Staphylococcus* spp) recorded the lowest abundant uropathogen with 15 (2.96%) of the total examined samples. The *Pseudomonas spp* was the most resistant bacterium. For all Gram-negative bacteria were highly resistant to Augmentin, whereas Gram-positive bacteria were highly resistant to Penicillin. The obtained results emphasized the emergence of highly resistant bacteria to most of the tested antimicrobials and propose the need for physicians to change their treatment pattern depending on antimicrobial susceptibility results.
Keywords: UTI, Uropathogens, Antimicrobial Resistance, Libya.

Introduction

Urinary tract infections (UTIs) are the second most frequent cause of hospitalization [1, 2]. Every year, approximately 150 million people worldwide are diagnosed with UTIs [3], resulting in medical costs from treatments and lost productivity of more than US$6 billion [4]. Regardless of the location of the urinary tract infection, the presence of significant actively-multiplying bacteria in urine are referred to as urinary tract infection [5]. Its clinical manifestations range from asymptomatic infection to serious conditions such pyelonephritis, cystitis, ureteritis, urethritis, and urine sepsis [6,7].

Even though UTIs are more common in both sexes, studies suggest that women are more likely to suffer from this infection than men. Anatomical position, physiological changes around the menstrual cycle, vaginal intercourse, using contraceptive approaches like spermicide and diaphragm, and lack of prostatic fluid that has antimicrobial characteristics are some of the causes [5, 8, 9]. Other risk factors include a history of recurrent UTIs, poor fluid intake, and having a catheter or drain in the bladder [10,11]. Although men are less likely to get urinary tract infections than women, the infection is more severe in men when it occurs [12, 13].

UTIs can be either asymptomatic or symptomatic, and are characterized by a wide range of symptoms ranging from mild irritable urination to sepsis. Major symptoms may include: Urgency (a strong need to urinate frequently), dysuria (a burning sensation in the bladder while urinating), and discomfort or pressure in the lower abdomen with pelvic or back pain. There can also be hematuria [cloudy or bloody urine] with a possible foul odor, nocturia (excessive urination at night) and polyuria [14]. The majority of patients seek treatment for the most prevalent symptoms, which are frequency and dysuria. The presence of dysuria and urinary frequency increase the chances of possessing UTI to more than 90%, and deciding the diagnosis can be based mainly on medical history [15].

The cause of UTI is associated with the large variety of microbial organisms— such as: bacteria, viruses and fungi. According to Ramesh *et al* [16], the major causative organism in UTI are bacteria and account for more than 95 % of cases. Several studies report on the prevalence of pathogens from microbiological examination of urine from patients suspected of UTI suggested that *Escherichia, Staphylococcus, Klebsiella, Pseudomonas and Proteus* species were the most common isolated pathogens among other pathogens [17,18]. *Escherichia coli* [*E. coli*] is the most common causative bacteria in acute UTI acquired in the community, accounting for approximately 80 percent of infections [17, 19, and 20]. *Klebsiella* and *Proteus* species, and gram-positive cocci account for the last 20% [17].

Received: *26-12-2024* - ***Accepted***: *16-02-2025* - ***Published***: *24-02-2025*

Laboratory testing and the analysis of the patient's clinical symptoms are the primary methods used to diagnose UTIs [21]. Regular laboratory tests include testing for antibiotic susceptibility and cultural evaluation are routine laboratory procedures. A quick recovery and the avoidance of certain consequences, including sepsis, kidney failure, or pyelonephritis, can be facilitated by an early and precise diagnosis [22]. Antibiotics usually are the first line treatment for urinary tract infections. Nonetheless, therapy is frequently initiated empirically, and therapy is based on information determined from the antimicrobial resistance pattern of the urinary pathogens [23]. The most often prescribed ones are Nalidixic acid, Levofloxacin, Ciprofloxacin, Cephalexin, Trimethoprim/sulfamethoxazole, and Nitrofurantoin [24, 25, and 26].
Unfortunately, the extensive use of these antimicrobial agents has invariably resulted in the development of antibiotic resistance, which, has now become a major problem worldwide [27]. The increase in multidrug resistance in bacterial uropathogens is a significant health problem [28].
Around the world, antimicrobial resistance is rising, and incorrect antibiotic use is a major contributing reason. The other involves prescribing antibiotics in an irrational and wrong manner. When prescribing drugs rationally, the most crucial factors are time, dosage, and mode of delivery. Several studies indicated that between 30 and 60 percent of antibiotic prescriptions and usage have been inappropriate [29]. Furthermore, uropathogen distribution and antimicrobial sensitivity patterns can vary from region to region, it is vital to investigate them and gather data in our community [30). Therefore, we have planned the study to analyze data of the organisms causing UTI and their antibiotic sensitivity patterns, from our hospital in Zawia city.

Methods

Study design

A descriptive retrospective analysis was performed on the laboratory records of all patients who submit urine sample to laboratory of Zawia teaching hospital from 1stJan, 2022 to Dec 31th 2022.

Samples

This study included single (pure culture) bacterial species identified from positive urine cultures. Positive urine cultures were those that contained ≥ 10^5 colony-forming units (CFU) of a single recognized bacterial species per milliliter. Midstream urine specimens were collected from adult patients using sterile containers, while suprapubic aspiration specimens were collected from infants by pediatricians. 1µl of the specimen were inoculated through an incinerated wire loop on CLED-agar, and then incubated for 24–48 hours at 37°C. After 24 hours of incubation, if more than one type of organism was isolated, results were recorded as "mixed culture," and are excluded from this study. For midstream urine samples, equal to 10^5 CFU/ml of a single potential microorganism or above is interpreted as positive. Patients with positive urine cultures were categorized into different groups based on their age.
A gram stain was performed to confirm and identify the pathogen and classified as Gram-positive cocci (GPC) or Gram- negative rods (GNR), followed by full identification and antibiotic sensitivity testing using the VITEK system (bioMerieux, UK).

Data analysis

Obtained data were analyzed and interpreted according to the guidelines of the Clinical Laboratory Standards Institute (CLSI). Susceptibility of recovered Gram-negative and Gram-positive UTI-related bacteria was evaluated against a panel of antibiotics. Data were provided as the numbers of instances (or resistant cases) for each isolated species and the percentages to the total. Patient demographics, urine culture reports, and profiles of antibiotic resistance were electronically downloaded from the hospitals' medical records. This study was approved by the ethics committee of the faculty of Medicine, Zawia University and Zawia Teaching Hospital (2022).

Results

A total of 1966 samples of urine tested in the study. Table 1 summarizes the descriptive statistics of the study variables. Approximately one quarter of urine samples were positive of bacterial pathogens. Of whom, 378 (74.70%) were female and 128 (25.30%) were male. The prevalence of UTI was highest in the adolescent age group of 11–20 years (38.14%) followed by the children age group of 0-10 years (30.8%). Regarding the isolated uropathogens, the *E. coli* was the dominant bacterial isolate with 261 (51.58%) of the total samples, followed by *Klebsiella* spp (19.56%). other Gram-negative uropathogens reported include *Bacillus* ssp (9.7%), *Pseudomonas* spp (6.32%), and *Proteus* spp (4.94%). On the other hand, the gram-positive bacteria (*Staphylococcus* spp) recorded the lowest abundant uropathogen with 15 (2.96%) of the total examined samples.

Received*: 26-12-2024 -* ***Accepted****: 16-02-2025 -* ***Published****: 24-02-2025*

Table 1. Characteristics of the study variables. (n=1966)

Variables	Number	Frequency (%)
Examined samples		
Non-infected	1460	74.3%
Infected	506	25.7%
Gender		
Male	128	25.30%
Female	378	74.70%
Age groups		
0- 10	156	30.8%
11- 20	193	38.14%
21 – 30	31	6.12%
31 - 40	37	7.31%
41 - 60	49	9.68%
>61	40	7.90%
Isolated uropathogens		
Bacillus	49	9.7%
Candida	25	4.94%
E. coli	261	51.58%
Klebsiella	99	19.56%
Proteus	25	4.94%
Pseudomonas	32	6.32%
Staphylococcus spp	15	2.96%

The table 2 represent the distribution of isolated uropathogens in relation to patients' gender and age. For all age groups, Urinary tract infection was highest in females as compared to in men. Furthermore, the age groups of children and adolescents coincided with the highest occurrences of E. coli.

Table 2. Distribution of isolated uropathogens by age group and sex

Isolated organism	**Age groups**											
	0—10		11—20		21—30		31—40		41—60		≥ 61	
	F	M	F	M	F	M	F	M	F	M	F	M
E. coli	84 32.18 %	12 4.60%	71 27.20 %	24 9.19%	13 4.98%	0 0%	12 4.59 %	2 0.76 %	24 9.19 %	1 0.38 %	11 4.21 %	7 2.68 %
Klebsiella	16 16.16 %	8 8.08%	23 23.23 %	15 15.15 %	4 4.04%	2 2.02 %	9 9.09 %	2 2.02 %	8 8.08 %	2 2.02 %	7 7.07 %	3 3.03 %
Bacillus	11 22.44 %	1 2.04%	14 28.57 %	4 8.16%	8 16.32 %	0 0.0%	4 8.16 %	1 2.04 %	4 8.16 %	1 2.04 %	1 2.04 %	0 0.0%
Pseudomonas	3 9.37%	4 12.5%	8 25%	7 21.87 %	0 0.0%	0 0.0%	0 0.0%	0 0.0%	2 6.25 %	1 3,12 %	3 9.37 %	4 12.5 %
Proteus	4 16%	3 12%	8 32%	3 12%	0 0.0%	0 0.0%	3 12%	1 4%	0 0.0%	1 4%	1 4%	1 4%
Candida	5 20%	3 12%	6 24%	3 12%	2 8%	0 0.0%	1 4%	0 0.0%	1 4%	1 4%	0 0.0%	2 8%
Staphylococcus spp	1 6.66%	2 13.33 %	2 13.33 %	5 33.33 %	1 6.66%	1 6.66 %	1 6.66 %	1 6.66 %	0 0.0%	0 0.0%	1 6.66 %	0 0.0%

In the present study, the antimicrobial resistance patterns of tested organisms were identified. As displayed in table 3, among the Gram-negative bacteria, *E. coli* was the most frequent strain, but *Pseudomonas sp* was the most resistant bacterium. The latter showed 84.37% resistance to ceftriaxone followed by cefotaxime (78.12%), (68.75%) to Augmentin and doxycycline, and (62.5%) to each Bactrim, Nalidixic acid, and nitrofurantoin. Sensitivity to *E. coli* was the highest for amikacin (98.45%) and imipenem (98.06%), whereas the highest level of resistance was observed for Augmentin (63.03%). All other Gram-negative isolates were resistant to different level. Gram-positive bacteria Staphylococcus species showed 100% sensitivity to cefixime, doxycycline, and imipenem, whereas a high level of resistance was observed to penicillin (46.66%).

Received*: 26-12-2024 -* ***Accepted****: 16-02-2025 -* ***Published****: 24-02-2025*

Table 3. Antimicrobial resistance patterns of isolated organisms from Patients with UTIs in Zawia Teaching hospital (n=506)

Antimicrobial agent	Bacilli (n=49)	E.Coli (n=261)	Klebsiella (n=99)	Proteus (n=25)	Pseudo-monas sp (n=32)	Staphylo-coccus (n=15)
Amikacin	0 (0.0%)	4 (1.55%)	3 (3.03%)	0 [0.00%)	0 (0.0%)	1 (6.66%)
Augmantin	24 (48.97%)	162 (63.03%)	69 (69.69%)	5 (20.0%)	22 (68.75%)	5 (33.33%)
Bactrim	16 (32.65%)	82 (31.90%)	42 (42.42%)	8 (32%)	20 (62.5%)	2 (13.33%)
Cefixime	14 (28.57%)	22 (8.56%)	18 (18.18%)	11 (44%)	19 (59.37%)	0 (0.00%)
Cefotaxime	19 (38.77%)	76 (29.57%)	43 (43.43%)	10 (40%)	25 (78.12%)	4 (26.66%)
Ceftazidime	14 (28.57%)	47 (18.28%)	29 (29.29%)	14 (56%)	11 (34.37%)	4 (26.66%)
Ceftriaxone	20(40.81%)	65 (25.29%)	33 (33.33%)	3 (12%)	27 (84.37%)	6 (40%)
Ciprofloxacin	13 (26.53%)	54 (21.01%)	20 (20.20%)	7 (28%)	2 (8%)	4 (26.66%)
Doxycycline	20 (40.81%)	107 (41.63%)	46 (46.46%)	14 (56%)	22 (68.75%)	0 (0.00%)
Gentamycin	11 (22.44%)	49 (19.06%)	24 (24.24%)	5 (20%)	3 (9.37%)	2 (13.33%)
Imipenem	3 (6.12%)	5 (1.94%)	1 (1.01%)	12 (48%)	3 (9.37%)	0 (0.00%)
Nalidixicacin	28 (57.14%)	79 (30.73%)	36 (36.36%)	11 (44%)	20 (62.5%)	1 (6.66%)
Nitrofurantoin	27 (55.10%)	49 (19.06%)	69 (69.69%)	21 (84%)	20 (62.5%)	2 (13.33%)
Penicilillin	0 (0.00%)	0 (0.00%)	1 (1.01%)	0 (0.0%)	0 (0.0%)	7 (46.66%)
Tetracycline	9 (18.36%)	51 (19.84%)	27 (27.27%)	7 (28%)	13 (40.62%)	1 (6.66%)

Discussion

The evaluation and practical assessment of antibiotic resistance patterns through regional surveillance programs is the first step towards obtaining proper management and good control policy for reducing the development of antibiotic resistance [31]. Therefore, result of this study evaluated the susceptibility profile of urinary pathogens across various age groups in 2022 at Zawia Hospital, and estimated the prevalence of these pathogens associated with UTIs.

Our data showed that, 2.96% of the 506 pathogenic isolates were Gram-positive, 92.10% were Gram-negative, and 4.94 % were Candida species. According to the bacterial identification, E. coli made up roughly 50.79% of the Gram-negative bacteria, followed by Klebsiella species 19.56% and pseudomonas species 6.32%. This predominance could be due to their distinctive features such as flagella and pili, which help for their adhesion to the urinary epithelium and raise risks for infection [32].

This study detected the dominance of Escherichia coli and Klebsiella pneumonia which was almost identical compared with other researches in Libya and other neighbor countries. In Northwest Libya, Abujnah et al have found a predominance of Escherichia coli (56%) and Klebsiella pneumonia (19%) [33]. In another study in Messalata, Libya, Mahammed et al have reported the predominance of Escherichia coli (56%) and Klebsiella pneumonia (17%) [34]. In Southern Tunisia, the authors have found Escherichia coli (68%) and Klebsiella pneumonia (13%) as predominance uropathogens among patients of UTIs [35]. Moreover, this finding is comparable with other studies elsewhere in Africa indicating E. coli was the most prevalent bacterial isolated uropathogen [36, 37].

Staphylococcus aureus was the most dominant Gram positive uropathogen isolated in our study. This is consistent with the results of studies which revealed a high frequency of *S.aureus* in patients with UTI [38]. On the other hand, this result is contrast to what other previous studies were reported. For instance, Ayoyi et al [39] and Okonko et al [40] reported that isolated coagulase-negative Staphylococcus and Enterococcus were the most dominant Gram-positive uropathogen. The fact that most isolates were from female patients suggests that women are more likely than men to get UTIs [38, 41]. The close proximity of the anus to the vagina and the presence of a short, warm, and moist urethra may be contributing factors to the higher

Received*: 26-12-2024 -* ***Accepted****: 16-02-2025 -* ***Published****: 24-02-2025*

incidence of UTIs in women. Furthermore, the highest prevalence of E. coli was found in the age groups of children and adolescents. This finding may indicate that these age groups continue to practice inadequate personal hygiene [1].

In this study, the isolates from UTI patients showed a significant level of resistance to several medicines. The majority of bacteria exhibited resistance to three or more antibiotics. A greater level of resistance was found to the routinely used empirical treatments for the majority of UTIs, including, nitrofurantoin, Augmentin, trimethoprim–sulfamethoxazole, doxycycline, Nalidixic acid, ceftriaxone, and cefotaxime. On the other hand, tetracycline, cefixime, and ceftazidime, have varying degrees of effectiveness. Our antimicrobial resistance profile results are constant to what other previous studies were reported [42]. Antibiotic abuse and the use of antibiotics prior to laboratory testing for antimicrobial susceptibility are two potential causes of this condition. Furthermore, in developing countries like Libya, where medications are widely accessible without a prescription, antibiotic resistance is a prevalent occurrence. In order to address the issue of antibiotic resistance, numerous research emphasize the necessity of using antibiotics appropriately [43]. Our findings were differed significantly from what Ashur et al. 2021 [31]. Ashur and colleagues conducted a cross sectional survey on 200 outpatients who had symptoms of UTI from Tripoli Medical Center aged 30 years, which revealed that the majority of urine pathogens exhibited great sensitivity to doxycycline and high resistance to amoxicillin [31]. The susceptibility patterns of microorganisms may vary in different communities [44]. This finding emphasizes the importance of regular local surveillance programs to assess antimicrobial resistance in our city.

Conclusion

In the current study, the prevalence of UTI in adolescents and children were high, and the *E. coli* was the leading uropathogen. This study also showed increased levels of resistance to common antimicrobials, observed multi-drug resistance is becoming a major issue in the treatment of uropathogens in Libya. This demonstrates the need for conducting national and local antimicrobial surveillance and strict adherence to antibiotic policy to prevent the spread of drug-resistant microbes in our country.

Conflict of interest. Nil

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Received: *26-12-2024* - ***Accepted***: *16-02-2025* - ***Published***: *24-02-2025*

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Received*: 26-12-2024 -* ***Accepted****: 16-02-2025 -* ***Published****: 24-02-2025*

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المستخلص

تعد التهابات المسالك البولية من الأسباب الشائعة لطلب الرعاية الطبية في المجتمع. إن فهم خصائص مسببات الأمراض البولية ونمط حساسيتها للمضادات الحيوية في بيئة معينة يمكن أن يوفر دليلاً على الإدارة المناسبة للحالات. لذلك، فإن الهدف من الدراسة الحالية هو تحديد انتشار مسببات الأمراض البولية المرتبطة بالتهابات المسالك البولية، وتقدير ملف حساسيتها بين الفئات العمرية المختلفة في مستشفى الزاوية التعليمي. أجريت دراسة بأثر رجعي من 1 يناير 2022 إلى 31 ديسمبر 2022 في مستشفى الزاوية التعليمي. تم تضمين المرضى من جميع الأعمار وكلا الجنسين في الدراسة. تم تضمين التقارير المعملية للمرضى الذين لديهم مزرعة بول إيجابية (≥105 CFU / mL) واختبار حساسية المضادات الحيوية في الدراسة. من بين 1966 عينة، كانت 506 حالة مزرعة إيجابية. من بينهم 378 (74.70٪) من الإناث و 128 (25.30٪) من الذكور. تم تسجيل غالبية الثقافات الإيجابية في الفئة العمرية للمراهقين من 11 إلى 20 عامًا (38.14٪). فيما يتعلق بمسببات الأمراض البولية المعزولة، كانت الإشريكية القولونية هي العزلة البكتيرية السائدة بنسبة 261 (51.58٪) من إجمالي العينات. من ناحية أخرى، سجلت البكتيريا إيجابية الجرام (Staphylococcus spp) أقل مسببات الأمراض البولية وفرة بنسبة 15 (2.96٪) من إجمالي العينات المفحوصة. كانت Pseudomonas spp هي البكتيريا الأكثر مقاومة. بالنسبة لجميع البكتيريا سلبية الجرام كانت شديدة المقاومة لأوجمنتين، في حين كانت البكتيريا إيجابية الجرام شديدة المقاومة للبنسلين. أكدت النتائج التي تم الحصول عليها على ظهور بكتيريا شديدة المقاومة لمعظم مضادات الميكروبات المختبرة وتقترح الحاجة إلى قيام الأطباء بتغيير نمط علاجهم اعتمادًا على نتائج حساسية مضادات الميكروبات.

Received*: 26-12-2024 -* ***Accepted****: 16-02-2025 -* ***Published****: 24-02-2025*