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Determining the Prevalence of Upper and Lower Urinary Tract Infections' Pathogens and Their Antibiotic Susceptibility Profile for Adult Patients in Al-Diwaniya, Iraq (Conference Paper)

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Abstract

Until today, one of the leading predominant infections is Urinary tract infection (UTI). It exerts a huge burden on health systems worldwide each year. Treating UTI empirically with antimicrobials improves morbidity rates. This study aims to assess the prevalence of UTI associated bacteria in adult patients and to determine their antibiotic susceptibility profile. A retrospective study was conducted for adult outpatients who visited Al-Diwaniya tertiary hospitals from January 2020 till February 2022 to review their medical and lab records in addition to sociodemographic data. A total of 256 patients' records included of which 204 (79.7%) belong to females and 52 (20.3%) were males with average age of 39.22±17.10 years. The predominant organisms' isolates were Staphylococcus spp. found in 100 records (39.1%), Escherichia coli (E. coli) demonstrated in 90 records (35.2%), and Klebsiella spp. revealed in 23 records (9%). Staphylococcus spp. showed full resistance to cefepime and high resistance to ampicillin (92.9%) followed by ceftazidime (87.5%), and were highly sensitive to vancomycin. The higher resistance profile of E. coli was to ampicillin (97.9%) and ceftriaxone (81.3%) while was highly susceptible to meropenem (97.9%) and amikacin (97.6%). Additionally, Klebsiella spp. was highly susceptible to nitrofurantoin (78.6%), while was completely resistant to ampicillin. This study presents Staphylococcus spp. as the most prevalent gram-positive uropathogen and E. coli as the most prevalent gram-negative bacteria with multidrug resistance profile to commonly used antimicrobials which is an alarming situation to implement an immediate effective stewardship program.

Keywords: Urinary tract, UTI, uropathogen, antimicrobial susceptibility, Iraq.

تحديد انتشار مسببات عدوى المسالك البولية العليا والسفلى وشكل تحسسها للمضادات الحيوية لدى المرضى البالغين في مدينة الديوانية، العراق(بحث مؤتمر)#

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الخلاصة

تعد عدوى المجاري البولية من أحد من الأمراض البكتيرية الواسعة الانتشار حتى يومنا هذا. تسلط هذه العدوى كل سنة عبئ كبير جدا على الأنظمة الصحية حول العالم. ان علاج عدوى المجاري البولي بالمضادات البكتيرية تجريبيا يقلل معدلات المراضة. تهدف هذه الدراسة الى تحديد هذه الممرضات في المرضى البالغين ومدى تحسسها للمضادات البكتيرية. تم تنفيذ هذه الدراسة التراجعية على ملفات المرضى البالغين الذين زاروا العيادات الخارجية في مستشفيات مدينة الديوانية الثالثية للفترة من يناير ٢٠٢٠ وحتى شباط ٢٠٢٢ لجمع بيانات المرضى الديموغرافية والطبية والمختبرية. تم جمع ٢٥٦ سجل طبي للمرضى منه ٢٠٤ (٧٩,٧٪) تعود للاناث و٥٢ (٢٠,٣٪) تعود للذكور وكان معدل العمر ٣٩,٢٢ ± ١٧,١٠ سنوات. كانت أكثر الممرضات المعزولة انتشارا هي المكورات العنقودية والاشريكية القولونية والكلبسيلا (٣٩,١٪، ٣٥,٢٪، ٩٪) على التوالي. كانت بكتريا المكورات العنقودية ذات مقاومة تامة لمضاد السيفيبيم ومقاومة عالية لمضاد الامبسلين، السفتازيديم (٩٢,٩٪، ٨٧,٥٪) على التوالي ولكنها حساسة جدا لمضاد الفنكمايسين. وكانت اعلى مقاومة لبكتيريا الاشريكية القولونية ضد مضاد الامبسلين (٩٧,٩٪)، السفترايكزون (٨١,٣٪)، بينما كانت مضادات الميروبنيم والاميكاسين ذات فعالية عالية ضدها بمقدار (٩٧٪) تقريبا. كانت بكتيريا الكلبسيلا مقاومة تماما لمضاد الامبسلين لكن مضاد النايتروفيورانتوين كان فعالا ضدها (٧٨,٦٪). بينت هذه الدراسة بان المسبب الأكثر انتشارا لعدوى المجاري البولية هي المكورات العنقودية ضمن البكتريا الموجبة لصبغة غرام والاشريكية القولونية ضمن البكتريا السالبة لصبغة غرام وأنها مقاومة لأغلب المضادات البكتيرية شائعة الاستعمال وهي حالة تستوجب وقفة جدية للتطبيق الفوري لبرامج الاشراف على وصف المضادات الحياتية.

الكلمات المفتاحية: المجاري البولية، عدوى المجاري البولية، الممرض البولي، الحساسية للمضادات البكتيرية، العراق.

Introduction

One of the most prevalent bacterial infections is urinary tract infection (UTI) [(1)]. A UTI diagnosis costs more than $6 billion USD yearly and affects 150 million people worldwide [(2)]. Uncomplicated cystitis to severe infections like pyelonephritis and other consequences make up the spectrum of UTI disorders [(3)]. Since the female urethra is structurally less effective in blocking bacterial entry, UTI is often more common in women than in men [(4)].

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In addition, a number of variables, including age, past antibiotic treatment, hospitalization, and catheterization, affect the frequency rate of UTI. It is well known that a single bacterial species is responsible for more than 95% of urinary tract infections. The organism that causes acute infections most frequently is E. coli [5,6]. Some Iraqi studies revealed that the most prevalent pathogenic organisms causing UTI were Staphylococcus spp., E. coli, and Klebsiella pneumonia, all of which were resistant to the most popular medicines [7–10].

Early UTI therapy with first-line antibiotics lowers the rate of morbidity [11]. It is essential to understand the principal bacteria producing urinary tract infections and their respective antibiotic susceptibility patterns in order to deliver an effective empirical therapy [12]. Determining bacteria and their patterns of antibiotic susceptibility permits effective treatment outcomes, regulates the rise in antimicrobial prescription, and aids in the management of antimicrobial resistance, a global public health issue.

This study aims to assess the prevalence of UTI associated bacteria in adult patients and to determine their antibiotic susceptibility profile.

Patients and Methods

This study was a descriptive quantitative retrospective study. Records for 256 adult outpatients who visited Al-Diwaniya tertiary hospitals (Diwaniya Teaching Hospital and Gynecology Teaching Hospital) starting from Jan 2020 till Feb 2022 were reviewed and patients' sociodemographic (age, gender) and laboratory data (urine sample culture and antibiotic susceptibility test) were collected. The inclusion criteria for the current study are records of patients aged ≥ 18 years old presented with upper or lower UTIs and had a urine culture and susceptibility profile, while exclusion criteria are records of patients < 18 years old or ≥ 18 years but with missing data or culture with no growth.

Ethical approval

This study got approval from the scientific and ethical committee at College of Pharmacy, University of Baghdad and the scientific and ethical committee at Iraqi Ministry of Health.

Statistical analysis

Microsoft Office Excel 2016 (Microsoft Corporation, Redmond, Washington, United States) was used to code, enter, and analyze the data. Mean and standard deviation (SD) were used to express age of patients, while numbers, frequencies and percentages were used to express the rest of data.

Results

Two hundred and fifty-six patients' records that match the inclusion criteria were collected in this study, with majority of female patients (204, 79.7%). The average age of them was 39.22±17.10 years. The predominant age group was (18-30) years old (108, 42.2%). More than three quarters of the patients' records (82.0%) were from Al Diwaniyah Teaching Hospital while the rest were from Gynecology Teaching Hospital (Table 1).

Table 1. Characteristics of patients

Characteristic	**Value n (%)**
Age	
Mean ±SD (years)	39.22±17.10
(Minimum-Maximum) (years)	(18 - 85)
Age groups	
18 – 30	108 (42.2)
31 – 40	54 (21.1)
41 – 50	26 (10.2)
51 – 65	45 (17.6)
> 65	23 (9.0)
Gender	
Male	52 (20.3)
Female	204 (79.7)
Hospital	
Al Diwaniyah Teaching Hospital	210 (82.0)
Gynecology Teaching Hospital	46 (18.0)
Total valid record No. = 256, n: number, %: percentage.	

From the collected patients' records, 142 (55.5%) isolates revealed Gram-negative bacteria, and 114 (44.5%) revealed Gram-positive bacteria (Table 2). The predominant isolated organisms were Staphylococcus spp. 100 (39.1%), E. coli 90 (35.2%), Klebsiella spp. 23 (9%), and both Enterococcus spp. and Pseudomonas spp. 10 (3.9%) (Table 2).

Table 2. Prevalence of uropathogens detected in the isolates (n= 256)

Uropathogen	Value n (%)
Gram-negative bacteria	**142 (55.5)**
Escherichia coli	90 (35.2)
Klebsiella spp.	23 (9.0)
Pseudomonas spp.	10 (3.9)
Proteus mirabilis	5 (2.0)
Serratia fonticola	5 (2.0)
Enterobacter spp.	4 (1.6)
Acinetobacter Baum.	1 (0.4)
Aeromonas hydrophilia	1 (0.4)
Burkholderia cepacia	1 (0.4)
Cronobacter sakazakii	1 (0.4)
Raoultella ornithinolytica	1 (0.4)
Gram-positive bacteria	**114 (44.5)**
Staphylococcus spp.	100 (39.1)
Enterococcus spp.	10 (3.9)
Aerococcus viridans	1 (0.4)
Diphtheroid spp.	1 (0.4)
Micrococcus spp.	1 (0.4)
Streptococcus agalactiae	1 (0.4)
Total	256 (100)

n: number, %: percentage

The evaluation of the Antibiotic resistance profile of common Uropathogens to various antimicrobial agents is summarized in Tables 3. Staphylococcus spp. were the prevalent gram-positive uropathogens with full resistance to cefepime and high resistance to ampicillin (92.9%) followed by ceftazidime (87.5%), and norfloxacin (83.3%). Furthermore, around 97% of the isolated Staphylococcus spp. were sensitive to vancomycin. The higher resistance profile of E. coli, the most prevalent Gram-negative uropathogen, was to ampicillin (97.9%), ceftriaxone (81.3%), ceftazidime (79.5%) and ciprofloxacin (64.5%). E. coli was highly susceptible to meropenem (97.9%), imipenem (97.3%) and amikacin (97.6%). K. spp. were highly susceptible to nitrofurantoin (78.6%), imipenem (72.2%), and amikacin (69.6%), while were completely resistant to ampicillin. Additionally, Pseudomonas spp. were highly resistant to norfloxacin (100%), nitrofurantoin (85.7%) and levofloxacin (83.3%), while they were highly sensitive to meropenem (87.5%). Enterococcus spp. was fully resistant to norfloxacin, amikacin, piperacillin-tazobactam, ceftazidime, and cefepime while was sensitive to vancomycin (87.5%). Other uropathogens' resistance rates to commonly used antibiotics are showed in Table 3.

Table 3. Antibiotic resistance profile of common uropathogens.

Antibiotics	Number of resistance isolates n (%)							
	Gram-negative						Gram-positive	
	E. coli	K. spp.	P. spp.	Proteus mirabilis	S. fonticola	E. spp.	Staph. spp.	Enterococcus spp.
Ampicillin	47 (97.9)	10 (100)	0	1 (50)	1 (100)	0	13 (92.9)	3 (75)
TMP/SMX	48 (61.5)	10 (47.6)	0	0	1 (20)	0	29 (51.8)	0
Nitrofurantoin	7 (11.7)	3 (21.4)	6 (85.7)	3 (100)	0	2 (66.7)	19 (28.4)	3 (50)
Ciprofloxacin	49 (64.5)	8 (42.1)	5 (62.5)	2 (66.7)	3 (60)	3 (100)	52 (63.4)	6 (85.7)
Levofloxacin	46 (66.7)	5 (33.3)	5 (83.3)	1 (33.3)	1 (50)	1 (50)	28 (45.2)	4 (57.1)
Norfloxacin	28 (70)	9 (75)	8 (100)	1 (100)	0	1 (50)	35 (83.3)	5 (100)
Vancomycin	0	0	0	0	0	0	2 (3.4)	1 (12.5)
Amikacin	2 (2.4)	7 (30.4)	7 (77.8)	1 (20)	0	1 (25)	20 (30.8)	5 (100)
Gentamycin	38 (54.3)	8 (44.4)	7 (70)	0 (0)	1 (20)	1 (25)	30 (44.8)	5 (71.4)
Imipenem	2 (2.7)	5 (27.8)	4 (50)	3 (100)	0	1 (33.3)	2 (18.2)	1 (50)
Meropenem	1 (2.1)	5 (41.7)	1 (12.5)	0	0	0	1 (33.3)	1 (50)
Piperacillin-Tazobactam	14 (23)	6 (35.3)	0	1 (25)	1 (20)	1 (33.3)	0	1 (100)
Ceftriaxone	52 (81.3)	14 (70)	0	3 (75)	2 (50)	1 (100)	12 (75)	1 (50)
Ceftazidime	58 (79.5)	11 (64.7)	3 (37.5)	2 (50)	2 (40)	2 (66.7)	7 (87.5)	1 (100)
Cefepime	48 (70.6)	10 (55.6)	4 (44.4)	3 (75)	2 (40)	2 (66.7)	4 (100)	1 (100)

n: number, %: percentage.

Discussion

E. coli is regarded as the most frequent uropathogen involved in community-acquired UTI (being implicated in more than half of all UTI cases), which is one of the most common diseases in the world [1,13]. Regional variation in uropathogens' antibiotic resistance profiles is likely due to different prevention and treatment strategies against UTIs or

misuse of drugs and self-medication by the population in different geographic regions [14,15]. This variation urges the need for continuous monitoring to provide updated information to optimize the therapeutic selections.

Data analysis, in this study, revealed that females still the majority among UTIs cases compared to males which is supported predominantly by previous studies [10,16–19]. The finding supports that female continue to be more vulnerable to contracting UTI due to their basic anatomy, whereby their urethra is closer to the anal opening and shorter than men's urethra [20,21]. Again, women's hormonal fluctuations across the menstrual cycle and the possible genetic factor that tends to run in families may also be fueling their vulnerability [14,17,20]. The majority of studies found that gram-negative bacteria [10,16,17] were a common cause of UTI cases rather than gram-positive [8,9,22–24], which are in line with the present study. Possible reason for that is the presence of special virulence factor in gram-negative bacteria like the presence of unique structure and adhesion proteins in gram-negative bacteria, which facilitates attachment to the uroepithelial cell, resulting in high prevalence in UTIs [25]. Analyzing the data of detected uropathogens, our results revealed that E. coli was the most frequent isolate among the isolated gram-negative pathogens. High prevalence of E. coli could be due to the fact that it belongs to the normal flora of the human intestine, and therefore, it easily colonizes the urinary tract and can exhibit multidrug resistance [10]. Furthermore, several literatures from different regions concluded that E. coli was the predominant gram-negative bacteria causing UTIs [8–10,17,23,26–29].

However, the resistance pattern of E. coli to antibiotics has been very different in various studies. In a study conducted in Iran 2006, Sharifian et al. found the highest susceptibility rate of E. coli to ceftriaxone (97.8%) and cefotaxime (95.2%) [14], while in Iraq another pattern found. Other studies carried out in Iraq reported that E. coli was highly sensitive to imipenem and meropenem while has a high resistance profile toward cephalosporines including the third generation [9,10,30]. The Iraqi reports go parallel with this study results in addition to high sensitivity to amikacin. These results also supported by national antimicrobial resistance surveillance done by ministry of health in 2020 [31]. The preserved effectiveness of these agents may be explained by the fact that they are usually used only under medical supervision and not used in community without prescription only seldomly. However, the high resistance of E. coli to ampicillin, quinolones, cefepime, ceftriaxone, and ceftazidime can be explained partially by the high rate of antibiotics abuse and overuse in the region.

In the current study, Klebsiella. spp. also found among uropathogens cause UTI and was susceptible to nitrofurantoin, imipenem, while was fully resistant to ampicillin. Other studies found that Klebsiella. spp. was among the causes of UTI [9,10,31].

In the case of gram-positive bacteria, Staphylococcus spp. were the predominant gram-positive uropathogens that cause UTI. In line with this finding, other studies stated that Staphylococcus spp. as the most common gram-positive uropathogens causing UTIs [10,12,17,32,33]. They showed a high sensitivity toward vancomycin followed by imipenem, while presented a high resistance profile which exceeding 50% toward third and fourth generation cephalosporin and ampicillin. These results supported by other researches globally [8,10,34–37]. Other study yielded different results that showed full resistance to vancomycin [34].

The rising in resistance rate to previously effective antibiotics may be due to uncontrolled usage of prescription only medication including antibiotics and steroids in private settings [15,38,39], and even due to irrational antibiotics prescribing practice [40–44].

One of the limitations of the current study is being retrospective which will limit the flexibility to control study variables and data collected. Other limitation is the inclusion of only public settings data without private settings which causes a loss of vast amount of data. This is because private laboratories in Al Diwaniyah city have no archived patients' records for long periods of time which limits retrospective data collection needed for our research. Carrying out the study in only one city also may be considered as a limitation because it does not reflect a national outcome about UTIs prevalent pathogens and their susceptibility profile. So that, further studies needed to overcome these limitations.

Conclusion

This study presents Staphylococcus spp. as the most prevalent Gram-positive uropathogens and E. coli as the most prevalent gram-negative uropathogen. It also spots the light on the emerging multidrug resistance profile for those pathogens to commonly used antimicrobials such as ampicillin, cephalosporines, and even quinolones. This requires a serious effort to implement the stewardship

programs at public and private settings and to encourage the healthcare providers for rational use of antibiotics.

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