Original Article

Anti-microbial Resistance Pattern of Uropathogens Isolated from Hospitalized Patients in Imam Khomeini hospital, Tehran, Iran

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Received: 14 August, 2017; Accepted: 12 October, 2017

Abstract

Background: Urinary tract infection (UTI) is one of the most common type of bacterial infectious diseases which occurs in all age groups. The aim of this study was to determine anti-microbial resistance pattern of bacterial pathogens causing UTIs in hospitalized patients at the Imam Khomeini Hospital, Tehran, Iran. **Materials and Methods:** Urine samples were collected from 11157 hospitalized patients at different wards of Imam Khomeini Hospital in Tehran, between January 2015 and December 2015.The cultured plates were assessed for significant bacterial growth. Anti-microbial susceptibility test was performed using standard disk diffusion method. **Results:** Out of the 11157 collected urine samples, significant bacterial growth of 25.38% was observed. The most common cause of UTI was gram-negative bacteria (82.2%). More than 50% of the gram-negative bacteria were resistant to ceftriaxone, ceftazidime and trimethoprim-sulfamethoxazole. Enterococcus spp. (10.1%) was found as the third causative agent of UTIs and the most common gram-positive bacteria. **Conclusion:** We conclude that the examination of the most common etiological agent of UTIs and their antimicrobial resistance patterns is advantageous and necessary in order to design a guideline for empirical therapy.
Keywords: Urine Tract Infection (UTIs), Antibiotic resistance, Uropathogens.

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Please cite this article as: Jasemi SS, Rahdar HA, Karami-Zarandi M, Mahfouzi S, Abdollahi A, Feizabadi MM. Anti-microbial Resistance Pattern of Uropathogens Isolated from Hospitalized Patients in Imam Khomeini hospital, Tehran, Iran. Arch Med Lab Sci. 2017; 3(4): 1-5.

Introduction

Urinary tract infection (UTI) is one of the most common type of bacterial infectious diseases which occurs in all age groups(1, 2). It is estimated that 150 million UTIs happens yearly word-wide. In general, the primary causing agent of UTIs is Escherichia coli, followed by Klebsiella pneumoniae, Staphylococcus saprophyticus, Enterococcus faecalis, group B Streptococcus, Proteus mirabilis, Pseudomonas aeruginosa and Staphylococcus aureus(3).

Empirical therapy is often started before laboratory report results. In other hands, the rapid emergence of antibiotic resistance is currently considered as a serious problem in choosing the suitable treatment for infectious disease such as UTIs (4, 5).

If UTIs is not timely diagnosed and treated, it can cause undesirable effects such as recurrent infection, pyelonephritis with sepsis, premature birth in pregnant women, chronic renal failure, renal dialysis and finally renal transplantations (3, 6, 7).

In order to achieve a successful outcome with empirical antibiotics, knowledge about the anti-microbial resistance patterns of common uropathogens in each region is essential (8). The aim of this study was to investigate the anti-microbial resistance pattern of uropathogenic bacteria isolated from hospitalized patients in the Imam Khomeini Hospital, Tehran, Iran.

Methods

Isolation and Identification of Bacteria. In this cross sectional study, 11157 urine samples of hospitalized patients were received as part of routine clinical practice by the laboratory of the Imam Khomeini Hospitals during 2015. This hospital is a one of the oldest and largest referral hospital with about 1400 active beds and patients were admitted with various illnesses from different parts of Iran.

According to standard urine culture method, one calibrated wire loop (1µl) of fresh urine samples was cultured on 5% blood agar and MacConkey agar (Merck, Germany) plates and incubated aerobically overnight at 37°C.

The cultured plates were assessed for bacterial growth. Then the colony count was performed on the cultured plates. The samples with the number of colonies more than ≥105 colony-forming units per ml (CFU/mL), having one or up to 2 types of colony, were considered positive for UTIs and processed further for identification and susceptibility testing. All bacterial isolates were identified and confirmed by conventional biochemical test.

Anti-microbial Susceptibility Testing. Antibiotic resistance evaluation was performed on Mueller-Hinton agar, using disk diffusion method according to the guidelines recommended by Clinical and Laboratory Standards Institute (CLSI 2014). Results were determined after incubation for 16 to 18 h at 37°C and interpreted according to CLSI. E.coli ATCC 25922 and P. aeruginosa ATCC 27853 strains, S. aureus (ATCC 25923), and E. faecalis (ATCC 29212) were used for the quality control of the susceptibility test.

Statistical Analysis. Data analysis was performed using SPSS software version 18 (SPSS Inc., USA). Descriptive results were shown as frequencies (counts) and percentage of frequencies also p values of less than 0.05 were considered as statistically significant.

Results

Of the 11157 cultured urine samples, 2832 samples (25.38%) showed significant bacterial growth. Among the positive cases, 1782 (63 %) were women and 1050 (37 %) were men. The most common cause of urinary tract infection was gram-negative bacteria (82.2%) followed by gram- positive bacteria (17.8%). E. coli (47.7%) was the most predominant isolated bacteria, followed by Klebsiella spp. (20.4%), Enterococcus spp. (10.1%), P. aeruginosa (5.2%), coagulase negative Staphylococcus (3.9%), Citrobacter spp. (2.7%), Acinetobacter baumannii (2.6%), Enterobacter spp (2.6%), Streptococcus spp. (2.3%), S. aureus (1.4%), Proteus spp. (0.7%) and Providensia spp. (0.2%), (Figure 1). The most common isolated uropathogens in gram-negative and gram- positive bacteria were E. coli (47.7%) and Enterococcus spp. (10.1%), respectively.

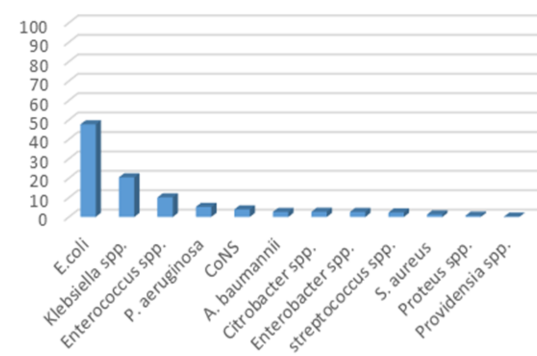

Figure 1. Distribution of positive isolated bacteria from UTIs.

Table 1 shows the resistance rate to anti-microbial drugs among gram negative bacteria. In this study, more than 50 percent of the gram-negative bacteria were resistance to ceftriaxone, ceftazidime and trimethoprim-sulfamethoxazole. The rates of resistance to other antibiotics were as follows: ciprofloxacin (47.55%) ampicillin-sulbactam (37.1%), gentamycin (23.9%), nitrofurantoin (17.9%), imipenem (13.6%) and amikacin (11.1%).

In our study, E. coli was the most frequent causing agent of UTIs. It showed the highest rate of resistance to trimethoprim-sulfamethoxazole and

Table1. Antibiotic resistance pattern of gram negative bacteria

Antibiotic	CIP	CRO	GN	AK	SAM	CAZ	SXT	IMI	NIT
Bacteria					N (%)				
E.coli	610 (45.18)	729 (54)	135 (10)	27 (2)	324 (24)	918 (68)	918 (68)	27 (2)	27 (2)
Klebsiella spp.	283 (49)	318 (55)	214 (37)	127 (22)	278 (48)	278 (48)	301 (52)	145 (25)	174 (30)
Providencia spp.	3 (50)	0 (0)	2 (33)	3 (50)	0 (0)	6 (100)	6 (100)	3 (50)	3 (50)
Proteus spp.	0 (0)	0 (0)	0 (0)	0 (0)	6 (28)	0 (0)	15 (72)	0 (0)	10 (47)
P. aeruginosa	48 (32)	99 (66)	60 (40)	24 (16)	132 (88)	126 (84)	135 (90)	48 (32)	120 (80)
Citrobacter spp.	49 (66)	52 (70)	28 (37)	9 (12)	40 (53)	30 (40)	47 (63)	15 (20)	16 (22)
Enterobacter spp.	50 (70)	36 (50)	43 (60)	13 (18)	39 (54)	37 (50)	52 (72)	7 (10)	7 (10)
A. baumannii	64 (85)	68 (91)	75 (100)	57 (76)	45 (60)	69 (92)	66 (88)	72 (96)	60 (80)
Total	1107 (47.55)	1302 (55.92)	557 (23.92)	260 (11.16)	864 (37.11)	1464 (62.88)	1540 (66.15)	317 (13.61)	417 (17.91)

Abbreviations: AK, Amikacin; CAZ, Ceftazidime; CIP, Ciprofloxacin; CRO, Ceftriaxone; Gn, Gentamycin; IMP, Imipenem; Nit, Nitrofurantoin; SAM, Ampicillin sulbactam; SXT, Trimethoprim-sulfamethoxazole

Table2. Antibiotic resistance pattern of gram positive bacteria

Antibiotic	CAZ	SXT	NIT	AMP	E	LNZ	VA	RIF	C	CTX
bacteria					N (%)					
S. aureus	-	8 (20)	4 (10)	-	19 (50)	-	6 (16)	15 (40)	4 (10)	29 (75)
CoNS	-	40 (36)	0 (0)	-	80 (72)	-	0 (0)	11 (10)	0 (0)	100 (90)
Enterococcus spp.	-	-	8 (23)	187 (65)	256 (89)	3 (1)	34 (12)	-	-	-
Streptococcus spp.	30 (45)	-	0 (0)	26 (40)	38 (57)	0 (0)	10 (16)	-	-	-

Abbreviations: AMP, Ampicillin; C, Chloramphenicol; ; CAZ, Ceftazidime; CoNS, coagulase negative streptococcus; CXT, Cefotaxime; E, Erythromycin; LNZ, Linezolid; Nit, Nitrofurantoin; RIF, Rifampicin; SXT, Trimethoprim-sulfamethoxazole; V, Vancomycin

ceftazidime (68%), followed by ceftriaxone (54%) and ciprofloxacin (45.18%). Klebsiella spp. as a second causative agent of UTIs had moderate resistance to ceftriaxone (55%), trimethoprim-sulfamethoxazole (52%), ciprofloxacin (49%), ceftazidime (48%) and ampicillin-sulbactam (48%). Rate of resistance to other antibiotics were as follows: gentamycin (37%), amikacin (22%), imipenem (25%) and nitrofurantoin (30%).

Enterococcus spp. was the third causative agent and the most common gram-positive bacteria (Table 2). The most frequent resistances were observed in erythromycin (89%), and ampicillin (65%). Rates of resistances to nitrofurantoin, linezolid and vancomycin were 23%, 1 % and 12%, respectively.

P. aeruginosaas as a fourth causative agent of UTIs had highest resistance rates to trimethoprim-sulfamethoxazole (90%), ampicillin-sulbactam (88%), ceftazidime (84%) and nitrofurantoin (80%), respectively. Rate of resistance to other antibiotics were as follows: ceftriaxone (66%), gentamycin (40%), imipenem (32%), ciprofloxacin (32%) and amikacin (16%).

As it was shown in table 1, an alarming anti-microbial resistance was seen in A. baumannii isolates (>60%), against almost all antibiotics tested. Results of antibiotic resistance for other isolated bacteria are presented in Table 1.

Discussion

Treatment of UTI is challenging due to appearance of pathogens with growing resistance to anti-microbial agents (3, 9, 10). The prevalence of etiological agents of UTIs and their antibiotic resistance profile vary at different times and geographical locations, and therefore examining the local etiology of UTI is advantageous and necessary in order to design a guideline for empirical therapy (1).

In this study, we evaluated the isolated bacterial agents and antibiotic resistance profile of UTIs in a tertiary referral hospital in Tehran, Iran, for a period of 12 months. In this study, UTI distribution was significantly more common in women (63% of the positive cultures) compared to men ($P < 0.05$). This result is consistent with previous studies, both in Iran and in other countries (1, 2, 11, 12). women are more disposed to UTIs which is probably due to differences between the men and women genitourinary structures and physiology(9).

E. coli was the most predominant isolated bacteria in our study, followed by Klebsiella spp., Enterococcus spp. and P. aeruginosa, confirming the previous reports (6, 8, 13). However, there were controversial data from other studies, reporting different results (11, 14-16). There are various reasons which can cause this difference such as, variation in sample size, geographical region or patient population.

The most common causing agent of UTIs in this study was gram-negative bacteria, resistant to numerous antibiotics available at our setting. Moreover, over 50% of gram-negative bacteria showed resistance to ceftriaxone, ceftazidime and trimethoprim-sulfamethoxazole. Usually, arbitrary consumption of antibiotic during the treatment of various infections led to antibiotic resistance. This is consistent with previous studies in Iran (13, 17, 18).

The most effective anti-microbial agents in our study were amikacin, imipenem and nitrofurantoin for gram-negative bacilli (83%-89%) which is consistent with the study of Nozarian et al., performed in this center in 2013 with high susceptibility isolates to amikacin (94.1%), imipenem (98.9%) and nitrofurantoin (96%), respectively. However, rate of resistance to these antibiotics are rising (12). It is possible that routine consumption of these antibiotics has caused this resistance.

A. baumannii has high resistance to all tested antibiotics, thus the therapy with available antibiotic may fail. Our data shows significant increase in rate of antibiotic resistance comparing to the previous studies (19, 20). It has been suggested that lack of timely treatment and excessive use of antibiotics is the reason for increased resistance (21). Due to increasing rate of antibiotic resistance and limited choice for appropriate antibiotic for resistant strain, having information about susceptibility of other antibiotics, as well as synergism between the rests of antibiotics is essential.

In conclusion, our results revealed increased resistance to multiple antibiotics among the urinary isolates. Hence, judicious use of antibiotics and implementation of antibiotic stewardship program is highly essential to prevent the emergence and spread antimicrobial resistance. Pattern of antibiotic resistance varies in different regions and times, therefore a periodic check for antibiotic resistance profile are required.

Conflicts of Interest

All authors declare that they have no conflict of interest.

Acknowledgment

The authors would like to thank personnel of medical microbiology laboratory of Imam Khomeini Hospital for their assistance in this project.

References

1. Saima Mollick1 TD, Md. Jabir Hasnain, Mushtaque Ahmed. Isolation and Characterization of Pathogens Responsible for Urinary Tract Infection in Bangladesh and Determination of their Antibiotic Susceptibility Pattern. J App Pharm Sci 2016; 6: 72-76.

2. T Shilpi MA, SMA Huq, SK Baul , et al. Isolation of Bacteria Causing Urinary Tract Infections and their Antibiotic Susceptibility Profile at Anwer Khan Modern Medical College Hospital. AKMMC 2013; 4: 23-27.

3. Flores-Mireles AL, Walker JN, Caparon M, et al. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat rev Microbiol 2015;13: 269-284.

4. Stultz JS, Doern CD, Godbout E. Antibiotic Resistance in Pediatric Urinary Tract Infections.Curr Infect Dis Rep 2016;18: 40.

5. Zilberberg MD, Nathanson BH, Sulham K, et al. Carbapenem resistance, inappropriate empiric treatment and outcomes among patients hospitalized with Enterobacteriaceae urinary tract infection, pneumonia and sepsis. BMC infectious diseases 2017;17: 279.
6. Kalal BS, Nagaraj S. Urinary tract infections: a retrospective, descriptive study of causative organisms and antimicrobial pattern of samples received for culture, from a tertiary care setting. Germs 2016; 6: 132-138.
7. Nielubowicz GR, Mobley HL. Host-pathogen interactions in urinary tract infection. Nat Rev Urol 2010; 7: 430-441.
8. Chiu CC, Lin TC, Wu RX, et al. Etiologies of community-onset urinary tract infections requiring hospitalization and antimicrobial susceptibilities of causative microorganisms. J Micobiol Immunol infect 2016; 50: 879-885.
9. Foxman B. Urinary tract infection syndromes: occurrence, recurrence, bacteriology, risk factors, and disease burden. Infect Dis Clin North Am 2014; 28:1-13.
10. Yilmaz Y, Tekkanat Tazegun Z, Aydin E, Dulger M. Bacterial Uropathogens Causing Urinary Tract Infection and Their Resistance Patterns Among Children in Turkey. Iran Red Crescent Med J 2016;18(6):e26610.
11. Goli Angoti HG, Maryam Hajizadeh, Zahra Tabatabaii. Bacteria Isolated from Urinary Tract Infection among Patients and Determination of the Antibiotic Susceptibility Patterns of the Gram Negative Bacteria in Iran. Novelty in Biomedicine 2015; 4:1-4.
12. Nozarian Z, Abdollahi A. Microbial Etiology and Antimicrobial Susceptibility of Bactria Implicated in Urinary Tract Infection in Tehran, Iran. Iran J Pathol 2015;10: 54-60.
13. Rezaee MA, Abdinia B. Etiology and Antimicrobial Susceptibility Pattern of Pathogenic Bacteria in Children Subjected to UTI: A Referral Hospital-Based Study in Northwest of Iran. Medicine 2015;94:e1606.
14. Arslan B KZ, Ergin ÖY, Bozkurt İH, et al. Pathogen Bacteria of the Urinary Tract Isolated from Urine Cultures and Their Susceptibility. Erciyes Med J 2014;1: 29-34.
15. Karimian M, Kermani R, Khaleghi M, et al. Antibiotic susceptibility patterns of isolates from children with urinary tract infection in Isfahan, Iran: Impact on empirical treatment. J Glob Antimicrob Resist 2017;9: 3-7.
16. Jean SS, Coombs G, Ling T, et al. Epidemiology and antimicrobial susceptibility profiles of pathogens causing urinary tract infections in the Asia-Pacific region: Results from the Study for Monitoring Antimicrobial Resistance Trends (SMART), 2010-2013. Int J Antimicrob Agents. 2016;47: 328-234.
17. Naderi A, Kasra-Kermanshahi R, Gharavi S, et al. Study of antagonistic effects of Lactobacillus strains as probiotics on multi drug resistant (MDR) bacteria isolated from urinary tract infections (UTIs). Iran J basic Med Sciences 2014;17:201-208.
18. Khosravi AD, Abasi Montazeri E, Ghorbani A, et al. Bacterial urinary tract infection in renal transplant recipients and their antibiotic resistance pattern: A four-year study. Iran J Microbiol 2014;6:74-78.
19. Mashouf RY, Babalhavaeji H, Yousef J. Urinary tract infections: bacteriology and antibiotic resistance patterns. Indian J pediatr 2009;46: 617-620.
20. Mansour A, Manijeh M, Zohreh P. Study of bacteria isolated from urinary tract infections and determination of their susceptibility to antibiotics. Jundishapur J Microbiol 2009; 3:118-123.
21. Arason VA, Sigurdsson JA. The problems of antibiotic overuse. Scan J Prim Health Care 2010;28:65-66.