What Left for Us for Urinary Tract Infection Treatment? An Experience from the South of Iran

Abstract

Background: The aim of the study is to define the prevalence and antimicrobial susceptibility pattern of bacteria from cases of urinary tract infections (UTIs). Materials and Methods: A retrospective analysis of urinary pathogens and their antimicrobial susceptibility was done on urine cultures at Shiraz University Laboratory from 2015 to 2017. Antimicrobial susceptibility tests have done using the disk-diffusion technique as per the standard of CSLI. Results: During 2 years of study, 3489 samples were culture positive. Escherichia coli was the dominant isolate (84%), followed by Klebsiella spp. (10.7%) and Enterococci spp. (2.2%). The overall resistance rates to trimethoprim-sulfamethoxazole, ceftriaxone, and ciprofloxacin were 56.1%, 47.2%, and 37%, respectively. The most frequently isolated bacteria were E. coli, which had resistance rates of 58.6%, 49.1% to TMP-STX, and cefixime, also sensitivity rates of 95.1% to nitrofurantoin (FM). Conclusions: In the study area, resistance rates to fluoroquinolones and cephalosporins were high. Because most isolates were sensitive to FM and aminoglycoside, they are suggested as appropriate antimicrobials for empirical treatment of UTIs before available urine culture results.

Keywords: Antibiotic resistance, antibiotic therapy, urinary tract infection

Introduction

Urinary tract infections (UTIs) are among the most important human bacterial infections that cause a high burden to the health-care system (approximately 1.6 billion dollars per year in the United States of America).[1] When antibiotics use excessively, unsuitable emergency resistance pathogens are associated with them.[2]

It has been categorized in different methods; one is community-acquired and hospital-acquired and another is iatrogenic. Other categorizations are complicated and uncomplicated, upper UTIs (kidneys and ureters), and lower UTIs (bladder and urethra).[3]

Isberg et al. showed no difference existed in dues incidence within 30 days between men treated with narrow- or broad-spectrum antibiotics.[4]

For proper antibiotic therapy, there are important factors which we should consider as follows: patient acceptance, cost, and insurance supports; duration of treatment; drug side effects; and microorganisms cause infection and their antibiotic resistance.[5,5] Globally, many studies conducted to evaluate the pathogens cause UTI and antibiotic resistance among them because it leads us to empirical proper therapy as it minimizes complications and patient morbidity.[6-10]

Escherichia coli (75%–95% in different societies) and other Enterobacteriaceae such as Klebsiella pneumonia and Proteus mirabilis and some pathogens such as Staphylococcus saprophyticus are the most typical pathogens which cause UTIs in most studies.[7,11-13]

For empirical therapy, according to the latest Infectious Diseases Society of America (IDSA) guideline, the first-line treatment of cystitis is trimethoprim/sulfamethoxazole (STX), nitrofurantoin (FM), and fosfomycin. The second line of antibiotic therapy is considered quinolones such as ciprofloxacin, levofloxacin, and ofloxacin. Other alternative treatments are amoxicillin-clavulanate, cefdinir, cefaclor, cefpodoxime, and cefuroxime. Pyelonephritis ambulatory treatments

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are considered as fluoroquinolones, trimethoprim-STX, aminoglycoside, ceftriaxone, and aztreonam oral beta-lactam (with less efficacy).

Till this time, studies revealed increasing resistance among antibiotics such as STX-trimethoprim that previously, in guidelines suggested as the first line of empirical therapy for both cystitis and pyelonephritis in outpatient settings, so only in community with a low level of resistance can be used as empirical therapy. For example, in the study conducted in Spain and published in 2017, STX-trimethoprim has come to the second line of empirical therapy of cystitis.

These findings emerge us to restudy UTI bacterial patterns and their resistance patterns in different countries and communities. Among these studies, some of them focused on community-acquired UTIs that are most UTIs to suggest proper empirical therapy and reveal the bacterial and resistance patterns in community-acquired UTI.

In Iran, many studies are performed but have not focused on the community-acquired ones alone. In Shiraz and Fars province, no study has been conducted to evaluate bacterial patterns and antibiotic resistance patterns of community-acquired UTI alone. The only research was about seasonal patterns and bacterial resistance of E. coli in three neighbor city Shiraz, Marvdasht and Saadat Shahr with about 300 samples.

Hence, in this study, we have tried to find bacterial and antibiotic resistance patterns among community-acquired UTI of ambulatory patients referred to OPD diagnostic center with high referral population from southern Iran, Shahid Motahari Diagnostic Center in Shiraz, Fars, which means community-acquired UTI that includes upper UTIs (pyelonephritis) and lower UTIs (cystitis).

Materials and Methods

Study design

A retrospective analysis of urine culture results was performed at the primary Shiraz University of Medical sciences affiliated clinic (Motahari) during the 2 years, from March 2015 to March 2017. The age and sex of patients, the microorganism isolated, and the antimicrobial susceptibility profiles were collected from the records using a standard data collection form.

Culture and identification

A midstream urine sample had taken from all referral patients who suspicious of UTI. Samples were cultured before 2 h after obtaining, at 36°C for 18–24 h on MacConkey and Blood agars. When bacterial growth of a uropathogen happened, disk-diffusion tests were performed using the Kirby–Bauer method and the Clinical and Laboratory Standards Institute (CLSI) criteria. A significant bacterial infection had defined as the growth of more than 10^5 colony-forming units/ml of a single species cultured from urine. Samples with mixed results were excluded from the study.

Antimicrobial susceptibility tests

According to the standard operational procedures, antimicrobial susceptibility tests were performed with the disk-diffusion method, taken out from standard CLSI method, for checking the resistance pattern of uropathogen. Resistance rates to the following antibiotics were examined as follows: nalidixic acid (NA)(30 micg), trimethoprim/STX (25 micg), cephalexin (30 micg), cefixime (CFM) (5 micg), norfloxacin (NOR) (10 micg), ceftriaxone (CRO) (30 micg), cefotaxime (CTX) (30 micg), ciprofloxacin (CP) (5 micg), cefotaxime (CT) (30 micg), gentamycin (GEN) (10 mg), imipenem (IMP) (10 micg), amikacin (AN) (30 micg), and FM (30 micg).

Non-susceptibility to the third-generation cephalosporin, ceftriaxone, was considered an indicator of extended-spectrum beta-lactamase (ESBL) production.

Statistical analysis

In this study, analysis of data was performed by IBM SPSS Statistics Version 22.0 (IBM Corp., Armonk, NY, USA) 21. A descriptive study of data such as bacterial patterns, bacterial resistance patterns, sex and age of patients, frequencies, and its percentage, age of patients performed by mean ± standard deviation (SD).

Pearson’s Chi-squared test is used for comparing qualitative variables and analysis of variance test is used for average age expression in bacterial pattern and antibiotic resistance pattern. In all tests, the percentage error of 5% has considered.

Results

In total, we captured valid urine culture results for 3489 patients during 2 years of the study. The majority of the positive samples (89.3%) had collected from female patients. The age of the patients ranged from 1 year to 93 years, with a mean age of 39.17 (SD = 20.45) years [Table 1].

The most common pathogen was E. coli that responsible for about 2932 (84%) of all positive samples, and other pathogens were grown in about 10.3% of samples with the least role for Citrobacter by 0.1 positive rates [Table 2]. Gram-negative and Gram-positive bacteria were responsible for 97.8% and 2.2% of the isolates, respectively [Table 2]. The distribution of uropathogen among the sexes, on the other hand, was mainly the same. E. coli and Klebsiella were the most responsible bacteria in both sexes [Table 3].

The specific susceptibility profiles of each bacterial isolate are shown in Table 4. E. coli (n = 2932)
showed high resistance rates against NA (59.8%), trimethoprim-STX (58.6%), cephalxin (49.1%), cefixime (43.4%), ceftiraxone (39%), ciprofloxacin (35.9%), cefotizoxime (27.7%), and imipenem (20.3%). The only drugs against E. coli to which the resistance rate was detected under 20% were gentamicin (17.8%), amikacin (5.3%), and FM (4.9%). For other bacteria that were responsible for UTI in ambulatory patients, some similar resistance patterns can be found.

The overall susceptibility profiles of bacterial isolates are shown in Table 5. trimethoprim/STX had the highest total resistance of 56.1%, followed by cephalxin (47.2%) and cefepime (42.8%). FM and amikacin had overall resistance rates of 8.3% and 10.3%, respectively.

In terms of ESBL production, 1,146 (39%) strains of E. coli have been suspected of ESBL production. Furthermore, results show ESBL suspiciousness among 22.5% of Klebsiella and 40% of Citrobacter growths.

In this study, we found no meaningful statistical relation between age and bacterial pattern ($P = 0.1$).

**Discussion**

UTI is one of the most common infectious diseases diagnosed worldwide. New antimicrobials have improved the management of this infection among patients in hospital or ambulatory settings. However, these days, the management of UTI infections has been complicated by increasing the emergence of antimicrobial drug resistance.

For many years ago, multidrug persistence has appeared threat due to misuse of antibiotics. Therefore, it is necessary that we know about the changing in the spectrum of drug resistance to decrease the threats to the failure of treatment or the complexities associated with chronic infection.[25]

Plate et al. showed that two-thirds of women who would not care for an UTI episode are willing to postpone their antibiotics.[21]

Although the prevalence of etiologic microorganism in different parts of the world is slightly similar, antimicrobial resistance patterns described from other regions are notably different, and antimicrobial resistance increases. In our study, E. coli was the most predominant bacterium isolated from urine, followed by Klebsiella spp., Enterobacter spp., Acinetobacter spp., Pseudomonas spp., Proteus spp., and Citrobacter spp. The isolation rates of E. coli and other pathogens in this study were comparable to the rates documented previously in our region and worldwide but a lower role for Citrobacter and Proteus spp.[5–7] In our study, the age and sex distribution of UTI matched with that found in other studies.[26,27]

Statistically, a significant difference was observed between genders as some of the pathogens were isolated, such as *Streptococcus faecalis*, Citrobacter, and Acinetobacter. In our study, we found no meaningful statistical relation between age and bacterial pattern ($P = 0.1$).

### Table 1: The frequency distribution of patients in different age group

| Age group (years) | Male, n (%) | Female, n (%) |
|-------------------|-------------|---------------|
| 1-5              | 17 (4.5)    | 204 (6.4)     |
| 5-18             | 30 (7.8)    | 304 (9.5)     |
| 18-65            | 245 (64.5)  | 2417 (75.5)   |
| 65               | 88 (23.2)   | 274 (8.6)     |

### Table 2: The bacterial patterns of positive culture urinary tract infection during the year 2015-2017

| Isolated bacteria | n (%) |
|-------------------|-------|
| *Escherichia coli* | 2932 (84) |
| *Klebsiella pneumoniae* | 375 (10.7) |
| *Streptococcus faecalis* | 77 (2.2) |
| *Enterobacter* | 55 (1.5) |
| *Acinetobacter* | 17 (0.48) |
| *Pseudomonas* | 16 (0.45) |
| Proteus | 12 (0.34) |
| Citrobacter | 5 (0.14) |
| Total | 3489 (100) |

### Table 3: The bacterial patterns of ambulatory patients with positive urine culture in different patients’ sex

| Microorganism            | Sex | Female, n (%) | Male, n (%) |
|--------------------------|-----|---------------|-------------|
| *Escherichia coli*       |     | 2626 (81.2)   | 306 (81.1)  |
| *Klebsiella pneumoniae*  |     | 337 (10.4)    | 36 (9.3)    |
| *Enterobacter*           |     | 47 (1.5)      | 8 (2.1)     |
| Proteus                  |     | 11 (0.3)      | 1 (0.3)     |
| *Pseudomonas*            |     | 13 (0.4)      | 3 (0.8)     |
| Citrobacter              |     | 5 (0.2)       | 0           |
| *Streptococcus faecalis* |     | 65 (2)        | 12 (3.2)    |
| Acinetobacter            |     | 11 (0.3)      | 6 (1.6)     |

### Table 4: Antibiotic resistance pattern in Gram-positive and negative bacteria in positive cultured urine sample

| Antibiotic resistance pattern | Resistant | Intermediate | Sensitive |
|-------------------------------|-----------|--------------|----------|
| STX                           | 2030 (56.1) | 101 (2.8)    | 1489 (41.1) |
| GM                            | 756 (20.9)  | 172 (4.8)    | 2691 (74.4) |
| AN                            | 370 (10.3)  | 280 (7.7)    | 2970 (82)   |
| IMP                           | 742 (20.5)  | 148 (4.1)    | 2730 (75.4) |
| CP                            | 1205 (33.3) | 131 (3.6)    | 2284 (63.1) |
| CRO                           | 1340 (37)   | 71 (2)       | 2210 (61)   |
| FM                            | 300 (8.3)   | 155 (4.3)    | 3166 (87.4) |
| NOR                           | 1452 (40.1) | 77 (2.1)     | 2092 (57.8) |
| CN                            | 1708 (47.2) | 229 (6.3)    | 1683 (46.5) |
| CFM                           | 1550 (42.8) | 330 (9.1)    | 1741 (48.1) |
| CT                            | 993 (27.4)  | 103 (2.8)    | 2524 (69.7) |
| CTX                           | 1313 (36.3) | 68 (1.8)     | 2239 (61.9) |
| NA                            | 2088 (57.7) | 80 (2.2)     | 1452 (40.1) |

| IMP, CP, Ciprofloxacin, CRO, Cefixime, FM, Nitrofurantoin, NOR, Norfloxacin, CN, Cephalxin, CFM, Cefixime, CT, Cefotaxime, CTX, Cefotaxime, NA, Nalidixic acid, AN, Amikacin, GM, Gentamycin, STX, Sulfamethoxazole |
We observed the growth of the ESBL-producing organisms were resistant to quinolone and trimethoprim-STX. The most effective antibiotic was FM, with 95%, followed by amikacin with an 83% efficacy rate.

In a previous study conducted that the prevalence of E. coli was higher in females than males, 11.5% and 8.3%, respectively,[41] while in our study, this prevalence was approximately equal in both sex (81.1%).

Resistance against FM, the first-choice antibiotic in uncomplicated lower UTIs in Iran, seems to be significant in various studies.[18,42,43] We also found the same pattern with 8.3% overall to FM. This increase demonstrates that frequent use of the antibiotic for an extended period will elevate the resistance.

Chardavoyne et al. survey the usage of suitable different types of antibiotics besides on guideline. They conclude that subordination to the IDSA opinions and narrow-spectrum antibiotics can be effective and lead to decreasing unnecessary antibiotic days.[44]

This retrospective study is based on the results of routine microbiological tests which were done between 2015 and 2017. Due to the nature of the retrospective analysis, we could not follow patients’ clinical settings. Thus, the study did not support clinical data such as underlying disease or specific symptoms of patients.

**Conclusion**

The situation, we face in Iran, is challenging because of the increasing resistance of bacteria to available antibacterial, resulting in a growing lack of acceptable therapeutic options for UTIs. The ever increasing use of third-generation cephalosporin for any probable infectious disease has led to an increasing rate of ESBL among Gram-negatives. The
emergence of ESBL-producing *E. coli* is so alarming and the appearance of resistant *Klebsiella* spp. in the population.

The optimal drug for the therapy of a patient with UTIs depends on many factors. Each agent has pros and cons related to its use or misuse, and the choice of therapy is made on an individual basis. One of the most crucial factors for choosing the first-line agent depends on the local pattern of resistance.

In respect to our finding, in cases of uncomplicated lower UTIs, we suggest a 5–7-day course of FM as the first-choice empirical treatment. Particular attention should be given to patients who have tissue involvement symptoms and developing signs of an upper UTI. For this group, FM should not be a therapeutic consideration because of the reduced tissue penetration of this medicine.

The catastrophe is empirical therapy for outpatient management of upper UTIs. We do not have any oral medication with an acceptable sensitivity profile. Our therapeutic options are running out. Regarding resistance rates, parenteral use of aminoglycoside should be considered as first-choice empirical therapy in all cases of upper UTI and changing based on individual urine culture result and pattern of antibiotic susceptibility.

**Limitation of the study**

Such all retrospective studies, we had limitation in gathering more specific detail of demographic and clinical manifestation data. Furthermore, we had no data about MIC of antibiotics for etiologic agents.

**MeSH terms:** urinary tract infection; urinary anti-infective agents; antibiotic resistance, bacterial.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Foxman B. Epidemiology of urinary tract infections: Incidence, morbidity, and economic costs. Dis Mon 2003;49:53-70.
2. Plate A, Kronenberg A, Risch M, Mueller Y, Di Gangi S, Rosemann T, et al. Treatment of urinary tract infections in Swiss primary care: Quality and determinants of antibiotic prescribing. BMC Fam Pract 2020;21:125.
3. Grigoryan L, Trautner BW, Gupta K. Diagnosis and management of urinary tract infections in the outpatient setting: A review. JAMA 2014;312:1677-84.
4. Kromfält Isberg H, Hedin K, Melander E, Mölstad S, Cronberg O, Engström S, et al. Different antibiotic regimes in men diagnosed with lower urinary tract infection – A retrospective register-based study. Scand J Prim Health Care 2020;38:291-9.
5. Sedighi I, Solgi A, Amanati A, Alikhani MY. Choosing the correct empirical antibiotic for urinary tract infection in pediatric: Surveillance of antimicrobial susceptibility pattern of *Escherichia coli* by E-test method. Iran J Microbiol 2014;6:387-91.
6. Sanchez GV, Master RN, Karlowsky JA, Bordon JM. *In vitro* antimicrobial resistance of urinary *Escherichia coli* isolates among U.S. outpatients from 2000 to 2010. Antimicrob Agents Chemother 2012;56:2181-3.
7. Linhares I, Raposo T, Rodrigues A, Almeida A. Frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections: A ten-year surveillance study (2000-2009). BMC Infect Dis 2013;13:19.
8. Kahlmeter G. Prevalence and antimicrobial susceptibility of pathogens in uncomplicated cystitis in Europe. The ECO.SENS study. Int J Antimicrob Agents 2003;22 Suppl 2:99-52.
9. Prakash D, Saxena RS. Distribution and antimicrobial susceptibility pattern of bacterial pathogens causing urinary tract infection in urban community of Meerut city, India. ISRN Microbiol 2013.
10. Naber KG, Schito G, Botto H, Palou J, Mazzei T. Surveillance study in Europe and Brazil on clinical aspects and Antimicrobial Resistance Epidemiology in Females with Cystitis (ARESC): Implications for empiric therapy. Eur Urol 2008;54:1164-75.
11. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 2011;52:e103-20.
12. Czaja CA, Scholes D, Hooton TM, Stamm WE. Population-based epidemiologic analysis of acute pyelonephritis. Clin Infect Dis 2007;45:273-80.
13. Chochlakis E, Tosiello RL, Haverstock DC, Tice AD. Demographic, clinical, and treatment parameters influencing the outcome of acute cystitis. Clin Infect Dis 1999;29:113-9.
14. Aliaga L, Moreno M, Aomar I, Moya S, Ceballos A, Giner P. Treatment of acute uncomplicated cystitis: A clinical review. Clin Med Investigations 2017;2:9.
15. Mirsoleymani SR, Salimi M, Shareghi Brojeni M, Ranjarb M, Mehtarpoor M. Bacterial pathogens and antimicrobial resistance patterns in pediatric urinary tract infections: A four-year surveillance study (2009-2012). Int J Pediatr 2014;2014:155-160.
16. Khoshbakht R, Salimi A, Shirzad Aski H, Keshavarzi H. Antibiotic susceptibility of bacterial strains isolated from urinary tract infections in Karaj, Iran. Journal of the Hellenic Veterinary Medical Society 2012;6:86-90.
17. Mirzarazi M, Rezatofighi SE, Pourmahdi M, Mohajeri MR. Antibiotic resistance of isolated gram negative bacteria from urinary tract infections (UTIs) in Isfahan. Jundishapur J Microbiol. 2013;6 (1): 86-90.
18. Piranfar V, Mirnejad R, Erfani M. Incidence and antibiotic susceptibility pattern of most common bacterial pathogen causing urinary tract infection (UTI) in Tehran, Iran, 2012-2013. Int J Enteric Pathog 2014;2: Int J Enteric Pathog AA-SS.
19. Nozarian Z, Abdollahi A. Microbial etiology and antimicrobial susceptibility pattern of most common bacterial pathogen implicated in urinary tract infection in Tehran, Iran. Int J Pathol 2013;10:54-60.
20. Saffar MJ, Enayti AA, Abbola 1A, Razai MS, Saffar H. Antibacterial susceptibility of uropathogens in 3 hospitals, Sari, Islamic Republic of Iran, 2002-2003. East Mediterr Health J 2008;14:556-63.
21. 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 (Baltimore) 2015;94:e1606.
Farvardin M. Effect of seasonal changes on the prevalence of uropathogens in 2010-2011 and determination of antibiotic resistance pattern of *Escherichia coli* in three neighbor cities Shiraz, Marvdasht and Saadat-Shahr. Iran J Med Microb 2014;7:47-50.

23. European Confederation of Laboratory Medicine. European urinalysis guidelines. Scand J Clin Lab Invest Suppl 2000;231:1-86.

24. Wayne P. Performance Standards for Antimicrobial Susceptibility Testing; 20th Informational Supplement. CLSI Document M100-S20: Clinical and Laboratory Standard Institute (CLSI); 2010.

25. Khan MI, Xu S, Ali MM, Ali R, Kazmi A, Akhtar N, et al. Assessment of multidrug resistance in bacterial isolates from urinary tract-infected patients. J Radiat Res Appl Sci 2020;13:267-75.

26. Ganesh R, Shrestha D, Bhattachan B, Rai G. Epidemiology of urinary tract infection and antimicrobial resistance in a pediatric hospital in Nepal. BMC Infect Dis 2019;19:420.

27. Pezzani M, Antinori S. Introduction to urinary tract infections: An overview on epidemiology, risk factors, microbiology and treatment options. In: Imaging and Intervention in Urinary Tract Infections and Urosepsis. Springer, Cham ?; 2018. p. 7-16.

28. Abelson B, Sun D, Que L, Nebel RA, Baker D, Popiel P, et al. Sex differences in lower urinary tract biology and physiology. Biol Sex Differ 2018;9:45.

29. McLellan LK, Hunstad DA. Urinary tract infection: Pathogenesis and outlook. Trend Mol Med 2016;22:946-57.

30. Kolawole AS, Kolawole OM, Kandaki-Olukenyi Y, Babatunde SK, Durovade KA, Kolawole CF. Prevalence of urinary tract infections (UTI) among patients attending Dalhatu Araf Specialist Hospital, Lafia, Nasarawa state, Nigeria. Int J Med Med Sci 2009;1:163-7.

31. Tavakol M, Momtaz H. Determination of antibiotic resistance profile in *Klebsiella pneumonia* strains isolated from urinary tract infections of patients hospitalized in Peyambaran hospital (Tehran-Iran). Feyz J Kashan Univ Med Sci 2017;21:74-82.

32. Bours PH, Polak R, Hoepelman AI, Delgado E, Jarquin A, Matute AJ. Increasing resistance in community-acquired urinary tract infections in Latin America, five years after the implementation of national therapeutic guidelines. Int J Infect Dis 2010;14:e770-4.

33. Tandogdu Z, Wagenlehner FM. Global epidemiology of urinary tract infections. Curr Opin Infect Dis 2016;29:73-9.

34. Farajinia S, Alikhani MY, Ghotaslou R, Naghili B, Nakhilband A. Causative agents and antimicrobial susceptibilities of urinary tract infections in the northwest of Iran. Int J Infect Dis 2009;13:140-4.

35. Tabar MM, Mirkalantari S, Amoli RI. Detection of ctx-M gene in ESBL-producing *E. coli* strains isolated from urinary tract infection in Semnan, Iran. Electron Physician 2016;8:2686-90.

36. Ghanavati R, Ohadi E, Kazemian H, Yazdani F, Torki A, Kalani BS, et al. Evaluation of fosfomycin activity against extended spectrum beta lactamase (ESBL) producing *Enterobacteriaceae* isolated from three centers of Tehran, Iran. Recent Pat Anti infect Drug Discov 2018;13:180-6.

37. Molsenbour P, Abasazade A, Afsiasiabian S, Hajibagheri K, Barari M, Roshani D, et al. Risk factors, and antibiotic resistance pattern of *Escherichia coli* with extended-spectrum β-lactamase enzyme in west of Iran. J Med Physiol 2019;4:7.

38. Lob SH, Nicolle LE, Hohan DJ, Kazmierczak KM, Badal RE, Sahm DF. Susceptibility patterns and ESBL rates of *Escherichia coli* from urinary tract infections in Canada and the United States, SMART 2010-2014. Diagn Microbiol Infect Dis 2016;85:459-65.

39. Pietsch M, Eller C, Wendt C, Holfelder M, Falgenhauer L, Fruth A, et al. Molecular characterisation of extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* isolates from hospital and ambulatory patients in Germany. Vet Microbiol 2017;200:130-7.

40. Treviño M, Losada I, Fernández-Pérez B, Coira A, Peña-Rodríguez MF, Hervada X, et al. Surveillance of antimicrobial susceptibility of *Escherichia coli* producing urinary tract infections in Galicia (Spain). Rev Esp Quimioter 2016;29:86-90.

41. Odongo I, Ssemambo R, Kungu JM. Prevalence of *Escherichia coli* and its antimicrobial susceptibility profiles among patients with UTI at Mulago Hospital, Kampala, Uganda. Interdiscip Perspect Infect Dis 2020;2020:8042540.

42. Ghanbari F, Khademi F, Saberianpour S, Shahin M, Ghanbari N, Naderi K, et al. An epidemiological study on the prevalence and antibiotic resistance patterns of bacteria isolated from urinary tract infections in central Iran. Avicenna J Clin Microbiol Infect 2017;4:42214-42214.

43. Habibi Asl B, Asghari R, Ahangarzadeh Rezaee M, Mohammad Zadeh A, Abiri R. Evaluation of etiologic agents and antimicrobial resistance pattern of urinary tract infections in the northwest of Iran. Journal of Research in Clinical Medicine, 2018;6:7-12.

44. Chardavoyne PC, Kasmire KE. Appropriateness of antibiotic prescriptions for urinary tract infections. West J Emerg Med 2020;21:633-9.