http://www.cjmb.org

Open Access Original Article

Crescent Journal of Medical and Biological Sciences
Vol. 6, No. 4, October 2019, 498–504
eISSN 2148-9696

Antibiotic Resistance Pattern and Risk Factors Associated With Urinary Tract Infections With *Pseudomonas aeruginosa* Among Women in North West of Iran

Samaneh Rouhi[1,2], Rashid Ramazanzadeh[2,3*]

Abstract

Objectives: Urinary tract infections (UTIs) are related to female anatomy, sexual activity, and menopause. The present study aimed to survey the antibiotic resistance pattern and some risk factors that are associated with UTIs with *Pseudomonas aeruginosa*.

Materials and Methods: In this case-control study, 26 and 21 women patients with and without *P. aeruginosa* UTIs in case and control groups were considered, respectively, in North West of Iran from December 2015 to August 2017. *P. aeruginosa* was detected in urine samples using phonotypic test and polymerase chain reaction (PCR). Then, several risk factors were highlighted, including diabetes, kidney failure, pregnancy, residence, hospitalized, ICU stay, ventilator support, nosocomial infection, antibiotic use in the past 14 days, and age. Finally, the disk diffusion method was used to investigate the antimicrobial resistance pattern, followed by analyzing the data by Fisher's exact test and SPSS 16 (95% CI, $P \leq 0.05$).

Results: Based on the results, 26 *P. aeruginosa* strains were detected in both phenotypic test and PCR. In addition, a significant relationship was observed between diabetes, hospitalization, pregnancy, kidney failure, residence, and nosocomial infections with UTIs ($P \leq 0.005$). The highest and lowest rate of antibiotic resistance belonged to cefpodoxime and trimethoprim/sulfamethoxazole (each one with 92.30%) and imipenem (19.23%).

Conclusions: Overall, UTIs and antibiotic resistance related to *P. aeruginosa* was observed among women and diabetes and hospitalization were detected as the potential risk factors. Considering the geographic location of Kurdistan province, evaluating the risk factors and periodic reports on antibiotic resistance for UTIs can be more effective in its control and treatment in this area.

Keywords: Antibiotic Resistance Pattern, Risk Factors, Urinary Tract Infections, *Pseudomonas aeruginosa*, Women

Introduction

Urinary tract infections (UTIs) are considered as one of the most common bacterial infections (1) which are more prevalent in women than men. Some risk factors and reasons specific to women for UTIs include female anatomy (e.g., short urethra because it shortens the distance through which bacteria reach to the bladder) and certain types of birth control (e.g., spermicide-based contraception, menopause, pregnancy, and the contamination of the urinary tract with faecal flora) (2-4). Other UTI-related factors are diabetes, catheter use, sexual activity (2,3), age, education level, nosocomial infection (1,5,6), resident, hygiene, and antibiotic therapy (7,8). Previous research showed that UTIs cause preterm labor, low birth weight, congenital heart abnormalities, mental retardation, along with the infections of amniotic fluid and endometritis (9). In addition, it is the third most common bacterium associated with hospital-acquired catheter-associated UTIs which causes diseases, especially among immune-compromised patients (10,11). Further, this bacterium has several pathogen factors such as protease and elastase. Evidence indicated that elastase and protease production (which damages the tissues) in *Pseudomonas aeruginosa* strains isolated from UTIs are higher in comparison with other diseases related to this bacterium (11). Iron-limiting conditions are reported in the urinary tract as well. The formation of biofilms and adherence to human uroepithelial cells by *P. aeruginosa* that causes decreasing phagocytosis of *P. aeruginosa* are also found in conditions of iron deficiency (12). On the other hand, natural anti-microbial peptides such as defensin, elafin, cathelicidin, secretory, and lysozyme are mainly produced by epithelial cell genital, urinary tract, and neutrophils and the productions of these materials are regulated by bacterial production and inflammation. When the host immune system is disrupted, these substances are not produced and thus bacteria such as *P. aeruginosa* in this place produce an infection (13). Antibiotic resistance in this bacterium is increasing and it is common as multi-drug resistant bacteria. Furthermore, the emergence of the high prevalence of resistance to different categories of antibiotics among *P. aeruginosa* is common (10,14,15).

Received 9 May 2018, **Accepted** 11 September 2018, **Available online** 10 October 2018

[1]Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran. [2]Cellular and Molecular Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran. [3]Microbiology Department, Kurdistan University of Medical Sciences, Sanandaj, Iran.
*Corresponding Author: Rashid Ramazanzadeh, Tel: +98 9143104424, Email: atrop_t51@yahoo.com

Different studies showed UTIs with *P. aeruginosa* and its antibiotic resistance in humans. For example, Alijahan et al demonstrated the risk factors in a patient with UTIs such as age, resident, and pregnancy (16). In another study, Jiménez-Guerra et al concluded that 555 (84.2%) out of 659 *P. aeruginosa* isolates were related to patients with UTIs (17). Similarly, Rezai et al reported that beta-lactam resistant *P. aeruginosa* was separated from 14.63% of patients from among 205 cases with nosocomial infections in intensive care unit (18). UTIs are the second prominent type of infection in the human. Although many studies are conducted on *Escherichia coli*, which is the main cause of UTIs, there is little information about other bacterial pathogens causing UTIs including *P. aeruginosa*. The existence of such information about UTI pathogenesis and the associated risk factors are regarded as important bottlenecks regarding the creation of effective preventive approaches for this disease. *P. aeruginosa* is resistant to many antibiotics and this resistance is a major problem in the treatment (11). Given the important explanations about this type of infection, finding preventive actions for UTIs and the possible complications is affordable. On the other hand, the prevention of the occurrence of any disorder requires the recognition of their risk factors. Therefore, evaluating UTI in women and its influential risk factors is necessary for its control and prevention. Additionally, prescribing appropriate antibiotics for the treatment of UTIs among the female population is of great importance for maintaining health in such a population. Thus, this study sought to investigate the antibiotic resistance pattern and identify and highlight some risk factors related to UTIs with *P. aeruginosa* among women in Kurdistan province tertiary hospitals in Iran.

Materials and Methods

Study Population

A total of 47 women patients were included in this case-control analytic-observational study, who were within the age range of 5-81 years (mean ± standard deviation: 47.32±19.99). More precisely, twenty-six 5-80-year-old (49.15±20.30) patients with *P. aeruginosa* UTIs and twenty-one 6-81- year-old (45.05±19.87) cases without UTIs in the case and control groups, respectively, were considered, who attended Kurdistan tertiary hospitals from December 2015 to August 2017. Then, the patients were referred to the physician and questioned about the UTI symptoms (e.g., dysuria, urgency, frequency, suprapubic pain, or hematuria) during the patient visit. Next, the UTI suspected patients were referred to the laboratory for urine testing and final confirmation based on the symptoms, laboratory results, and having $>10^3$ CFU/mL of related uropathogen in the midstream urine culture. Census sampling was performed based on the aim of this study. Women were considered as a case if they had the symptoms of UTIs, and *P. aeruginosa* was separated from their urine sample in the laboratory. However, if women had UTI symptoms but had no bacteria or other microorganisms in their urine were considered as the control. The questionnaire containing demographic information and risk factors were filled by women after obtaining informed consent (The ethics code of MUK. REC. 1394/337).

Risk Factor Detection

For each woman patient with and without UTIs, demographic information and clinical data were collected encompassing the risk factors such as diabetes, kidney failure, pregnancy, residence, hospitalized, ICU stay, ventilator support, nosocomial infection, antibiotic use in the past 14 days, and age (3,9,16,19). The results of laboratory tests were compared and matched with the checklists.

Pseudomonas aeruginosa Isolated From Patients With Phenotypic Test

Pseudomonas aeruginosa was detected in 26 urine samples that were taken from 26 women as the case group. Phenotypic test for *P. aeruginosa* detection included the routine cultured on blood agar, MacConkey, eosin-methylene blue agar, and Müller-Hinton agar (MHA, Merck, Germany) and the samples were finally incubated at 37°C for 24 hours. In addition, growth in an aerobic environment, gram-stain, oxidase and catalase test (PattanTeb, Iran), movement test in sulfur-indole-motility agar, indole, methyl red, Voges-Proskauer, and Simmons citrate tests were performed on the collected samples. Eventually, urease, oxidative/fermentative, arginine dehydrogenase, lysine decarboxylase, and ornithine decarboxylase tests were applied on the strains (Merck, Germany) as well (20).

Pseudomonas aeruginosa Detection Using Polymerase Chain Reaction

The pure colonies of the overnight culture of *P. aeruginosa* on MHA were dissolved in 500 µL sterile deionized water in 1.5 mL tube, followed by adding the powdered glass and 500 µL Tris-EDTA (ethylene diamine tetraacetic acid, 10mM Tris, 1mM EDTA, pH 8.0) to the tubes. After the centrifugation (7000 rpm for 5 minutes), 20 µL of supernatant was used as DNA and stored in the refrigerator at -20°C. Then, 3 µL of DNA in the concentration of <50 ng/uL was utilized as the DNA template in PCR. Next, gyrase B was applied as the housekeeping gene to identify the specific *P. aeruginosa* strain. PCR in the volume of 25 µL with forward (F-5´-CCTGACCATCCGTCGCCACAAC-3´) and reverse (R-5´-CGCAGCAGGATGCCGACGCC-3´) primers (222 bp, SinaClon, Iran) was performed (7.5 µL deionized water, 3 µL DNA template in the concentration of around <50 ng/uL, 1 µL forward and 1 µL reverse primers in the concentrations of 0.5 µM, and 12.5 µL 2X Master mix) as well. PCR condition was as follows:

- Initial denaturation at 95°C for 5 minutes at 1 cycle, followed by 35 cycles;
- Denaturation at 94°C for 45 seconds;
- Annealing at 66°C for 45 seconds;
- Extension at 72°C for 1 minute;
- Final extension at 72°C for 10 minutes at 1 cycle.

Further, *P. aeruginosa* strain ATCC 25922 (Pasteur Institute, Iran) and deionized water were applied as positive and negative controls, respectively. Finally, 8 µL of the amplification product was loaded on 2% agarose gel with a ladder 1500 bp (SinaClon, Iran) (21).

Antibiotic Resistance Pattern of *Pseudomonas aeruginosa* Isolated From Urine Samples

Several antibiotic disks were applied for this step (Rosco, Denmark) as follows: Trimethoprim-sulfametoxazol (25 µg); colistin (10 µg), nalidixic acid (30 µg), tobramycin (10 µg), gentamicin (10 µg), tetracycline (30 µg), amikacin (30 µg), imipenem (10 µg), ceftriaxone (30 µg), ciprofloxacin (5 µg), amoxicillin (10 µg), ceftazidime (30 µg), cefotaxime (30 µg), cefpodoxime (10 µg), and cefepime (30 µg).

Pseudomonas aeruginosa isolates were cultured on blood agar at 37°C for 24 hours, followed by preparing a 0.5 McFarland 1.5×10^8 CFU/mL standard of such isolates. Then, they were cultured on MHA, and the antibiotic disks were placed on MHA plates with a 2-2.5 cm distance. After incubation in 37°C for 24 hours, the inhibition zone diameter was measured and compared with the Clinical and Laboratory Standards Institute Standard (22).

Statistical Analysis

Data and variables in this study were analyzed using univariate and logistic regression analyses. In addition, Fisher exact test was utilized to compare dichotomous variables using SPSS 16 (SPSS Inc., Chicago, IL, USA) with the odds ratio, 95% confidence intervals, and $P \leq 0.05$.

Results

A number of 47 women patients were considered in the current study, including 26 (55.31%) and 21 (44.68%) women patients with positive *P. aeruginosa* UTIs and without UTIs as the case and control, respectively. Based on phenotypic test and polymerase chain reaction, 26 (55.31%) *P. aeruginosa* strains were taken from 47 urine samples (Figure 1).

The majority of *P. aeruginosa* strains were taken from the samples of patients within the age range of 5-40 years. Further, a significant relationship was observed between diabetes (P = 0.000), hospitalization (P = 0.000), pregnancy (P = 0.003), kidney failure (P = 0.05), residence (P = 0.007), and nosocomial infections (P = 0.008) with *P. aeruginosa* UTIs. Similarly, diabetes and hospitalization were detected as the potential risk factors for *P. aeruginosa* UTIs with a confidence interval of 95%, and 288.71 (46.64, 1786.90) and P= 0.000 for each one. However, no significant relationship was found between ICU stay (P = 0.553), ventilator support (P = 0.553), age (P = 0.316), and antibiotic use in the past 14 days (P = 0.237) and *P. aeruginosa* UTIs (Table 1).

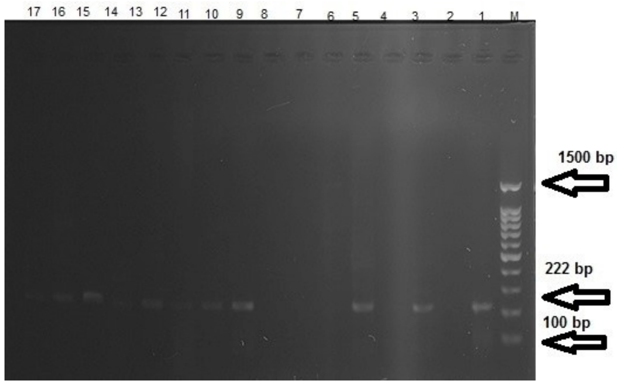

Figure 1. Polymerase Chain Reaction Products From Gyrase B (*gyr*B) for *P. aeruginosa* Strain Detection.
Note. Line M (Marker): Molecular weight (100–1500 bp); Line 1: Positive control; Line 2: Negative control; Lines 4, 6, 7, and 8: Negative examples of *gyr*B; Lines 3, 5, 9 to 17: Positive examples of *gyr*B (bond length = 222 bp).

The results obtained from antibiotic resistance pattern showed that from 26 P. aeruginosa isolates (obtained 26 urine samples of women with UTIs), higher rate of antibiotic resistance was belonged to trimetoprim-sulfametoxazol and cefpodoxime each one with 92.30%. Also lower rate of antibiotic resistance was related to imipenem with 19.23% (Table 2).

Discussion

Pseudomonas aeruginosa has a wide distribution in the environment, but their colonization in the human is rare. In some cases, *P. aeruginosa* is the first agent of respiratory infection and UTIs (23). Furthermore, UTIs are the most common nosocomial infections, but they are associated with less morbidity when compared to the other nosocomial infections. Moreover, UTIs occasionally lead to bacteraemia and death (23,24). In our study, *P. aeruginosa* UTI was found in 26 women patients during the period of study. Additionally, Lamas Ferreiro et al reported that *P. aeruginosa* UTIs are related to high mortality in hospitalized patients with chronic renal failure, advanced liver disease, and diabetes mellitus (15), which is in line with the findings of the present study. In our study, a significant relationship was observed between diabetes and hospitalization with *P. aeruginosa* UTIs. Diabetes and related complications can damage various organ systems such as kidney and causes nephropathy. Therefore, diabetic patients easily suffer from UTIs (25). Likewise, UTIs are one of the most prevalent infections in hospitalized patients and 7%–10% of UTIs in these patients due to *P. aeruginosa*. In addition, hospitalized patients have a weaker immune system and antibiotic resistance is high in most of these patients thus they are easily infected with antibiotic resistant *P. aeruginosa* (14). Singh et al

Table 1. The Frequency and Relationship of Risk Factors and UTIs Caused by *Pseudomonas aeruginosa*

Risk Factors	Positive -UTIs	Negative -UTIs	Total	*P* Value	OR (95% CI)
Diabetes					
Yes	23 (88.46%)	0	23		
No	3 (11.54%)	21 (100%)	24	0.000	288.71(46.64, 1786.90)
Kidney failure					
Yes	15 (57.69%)	0	15		
No	11 (42.30%)	21 (100%)	32	0.05	277.69 (50.36, 1721.80)
Pregnancy					
Yes	16 (61.35%)	0	16		
No	10 (38.46%)	21 (100%)	31	0.003	263.68(35.69, 1700.90)
Residence					
Rural	7 (26.92%)	14 (66.66%)	21		
Urban	19 (73.07%)	7 (33.33%)	26	0.007	256.00 (22.60, 1688.10)
Hospitalized					
Yes	23 (88.46%)	0	23		
No	3 (11.54%)	21 (100%)	24	0.000	288.71 (46.64, 1786.90)
ICU stay					
Yes	1 (3.85%)	0	1		
No	25 (96.15%)	21 (100%)	46	0.553	2.52 (0.35, 18.17)
Ventilator support					
Yes	1 (3.85%)	0	1		
No	25 (96.15%)	21 (100%)	46	0.553	2.52 (0.35, 18.17)
Nosocomial infection					
Yes	4 (15.39%)	11 (52.39%)	15		
No	22 (84.61%)	10 (47.61%)	32	0.008	0.165 (0.042, 0.648)
Antibiotic use in the past 14 days					
Yes	15 (57.69%)	9 (42.86%)	24		
No	11 (42.30%)	12 (57.14%)	23	0.237	1.81 (0.56, 5.81)
Age					
5-40years	9 (36.62%)	5 (23.81%)	14	0.316	1.69 (0.46, 6.14)
41-81years	17 (65.38%)	16 (76.19%)	33		

Note. UTIs: Urinary tract infections; OR: Odds ratio; CI: Confidence interval; ICU: Intensive care unit**;** $^{*}P \leq 0.05$.

Table 2. The Antibiotic Resistance Pattern of *P. aeruginosa* Isolated From 26 Urine Samples of Women With UTIs

Antimicrobial Agents	Resistant No. (%)	Intermediate No. (%)	Susceptible No. (%)
SXT	24 (92.30)	-	2 (7.69)
CO	10 (38.46)	-	16 (61.53)
NAL	21 (80.76)	1 (3.84)	4 (15.38)
TOB	13 (50)	-	13 (50)
GEN	12 (46.15)	3 (11.53)	11 (42.30)
TET	23 (88.46)	-	3 (11.53)
AMI	13 (50)	-	13 (50)
IMP	5 (19.23)	-	21 (80.76)
CTR	19 (73.07)	5 (19.23)	2 (7.69)
CIPR	17 (65.38)	3 (11.53)	6 (23.07)
AMOXY	23 (88.46)	1 (3.84)	2 (7.69)
CAZ	17 (65.38)	-	9 (34.61)
CTX	22 (84.61)	-	4 (15.38)
CPD	24 (92.30)	-	2 (7.69)
FEP	19 (73.07)	3 (11.53)	4 (15.38)

Note. UTIs: Urinary tract infections; SXT: Trimethoprime/Sulfamethoxazole; CO: Colistin; NAL: Nalidixic acid; TOB: Tobramycin; GEN: Gentamicin; TET: Tetracycline; AMI: Amikacin; IMP: Imipenem; CTR: Ceftriaxone; CIPR: Ciprofloxacin; AMOXY: Amoxicillin; CAZ: Ceftazidime; CTX: Cefotaxime; CPD: Cefpodoxime; FEC: Cefepime.

found that pregnancy, sexual activity, antibiotic resistance, socioeconomic status, as well as underlying diseases such as complication in pregnant women, anemia, and diabetes are regarded as prominent risk factors in women with UTIs (26). In our study, pregnancy was a significant risk factor in UTIs. According to previous evidence, hormones and changes in the urinary tract in pregnancy make women more likely to develop UTIs (27). Further, Djordjevic et al reported that stay in the hospital and the previous use of penicillins and their combinations with the inhibitors of β-lactamases were the most prominent risk factors among 79 case (11.9%) and 586 (88.1%) control patients with nosocomial UTIs caused by *P. aeruginosa* and *Acinetobacter* species (28). In our study, a significant relationship existed between nosocomial infections and *P. aeruginosa* UTIs while no significant relationship was detected between antibiotic use in the past 14 days and *P. aeruginosa* UTIs. Antibiogram test before its prescription can be a good guide for treating the patients who suffer from UTIs since they are one of the most nosocomial infections and the patients are easily infected due to their low immunity and antibiotic resistance. Other factors such as age and the length of hospitalization can be as the risk factors for increasing these infections and thus should be considered as well (29). In a study conducted by Castle et al, resident and facility factors were associated with the incidence of UTIs, which are in conformity with the results of our study. Increasing the level of the resident of lifestyle and health may reduce the risk of UTIs (30). Similarly, Hsiao et al concluded that UTIs in patients had a direct relationship with chronic kidney disease (31). These results corroborate with the findings of the current study. In our study, kidney disease was also identified as a contributing factor disease in UTIs associated with *P. aeruginosa*. The clinical features and different risk factors of UTIs are significantly different, but some studies showed that an underlying disease such as kidney failure plays an important role in UTIs (32,33). Furthermore, Iwuafor et al reported that between 71 patients, bloodstream infections (49.0%) and UTIs (35.6%) were the most common infections in ICU. Moreover, Iwuafor et al found that the use of antibiotics, surgery in ICU, urethral catheterization, and endotracheal intubation were among the risk factors for UTIs and BSI infection in ICU (29). Likewise, Borgatta et al indicated that the rate of different infections such as UTIs in ICU had a significant relationship with a long ICU stay. Contrarily, no significant relationship was observed between ICU stay and UTIs in our study. According to previous research, *P. aeruginosa* was one of the most common bacteria which was isolated from UTIs (34). Based on the findings of another study, the genetic diversity of the bacterial strains, the rate of bacterial virulence, and host epithelial cell characteristics were identified as the determinants of the rate of infections in patients, leading to contradictory findings in different studies (13). Kalra and Raizada showed that patients with immune deficiency or a weaker immune system, as well as those using ventilator were more likely to be exposed to UTIs. However, ventilator support had no significant role in UTIs with *P. aeruginosa* in the present study. *P. aeruginosa* is the most common bacterial pathogen with widespread distribution in health care settings and a higher prevalence of *P. aeruginosa* isolates among catheterized and patients with ventilator support (35). The prevalence of UTIs is related to the duration of the use of the catheter, age, along with the duration of hospitalization, and previous UTI (36). All these factors can affect the patients and cause contradictory results in different studies. Shah et al, investigating 245 *P. aeruginosa* isolates separated from the urine samples of UTIs in patients, found that these bacteria were more resistant to ceclor and cefizox (each one 100%) while less resistant to augmentin (97.6%) (3). Additionally, Hashemi et al reported that from 243 *P. aeruginosa* isolates, the highest levels of resistance was against streptomycin (100%), nalidixic acid (100%), and aztreonam (100%) whereas the lowest level was to gentamycin (83.95%) (1). In our study, *P. aeruginosa* isolates demonstrated high resistance to the used antibiotics cefpodoxime and trimethoprim/sulfamethoxazole (each one 92.30) and the lowest antibiotic resistance was related to imipenem (19.23%). Antibiotic resistance levels in different samples differentiate according to geographical conditions, compliance with sanitary and antibiotic prescriptions in each hospital, the distribution of bacterial resistance genes, and patient conditions. This result suggests that antibiotic testing should be performed before the administration of the antibiotic in order to use the best antibiotic to treat UTIs (37,38). In the present study, women patients with *P. aeruginosa* UTIs were considered in two case and control groups. Nowadays, the treatment of UTIs is a challenge in clinical sciences due to antibiotic resistance in bacteria. Similarly, the UTIs pose a risk to women in various aspects of health. Therefore, studying, preventing, controlling, and treating UTIs can be easier by knowing its risk factors. Eventually, traveling to the border countries of the area from Iran is common given the strategic location of the northwest province of Iran, the border areas, and geographic location. Thus, evaluating the risk factors of the antibiotic survey in the treatment of UTIs can be more effective in controlling, preventing, and treating UTIs in women in this area and the surrounding areas. It makes a major effort in the health of a large number of women as well.

Conclusions

The results revealed that UTIs were related to *P. aeruginosa* strains. Most of the risk factors of *P. aeruginosa*-related UTIs were statistically significantly associated with diabetes, kidney failure, pregnancy, residence, hospitalization, and nosocomial infections. However, there was no relationship between UTIs in this study and ICU stay, ventilator support, age, and antibiotic use. Regarding the strategic location of the cities in the northwest of Iran, controlling, preventing, and treating UTI in women in this area and the surrounding areas can be more effective by evaluating its risk factors.

Acknowledgments

This is part of a PhD thesis submitted by Samaneh Rouhi, a PhD student of molecular epidemiology of bacteria. The authors wish to extend their gratitude to the Research Deputy of Kurdistan University of Medical Sciences for their financial support.

Conflict of Interests

None to be declared.

Ethical Issues

All the stages of the current research were in accordance with the standards and regulations of the Ethical Committee of Kurdistan University of Medical Sciences.

Financial Support

The authors would like to thank the Research Deputy of Kurdistan University of Medical Sciences for their

financial support.

References

1. Hashemi NS, Mojiri M, Yazdani Kachouyi P, Eskandari S, Mohammadian M, Alavi I. Prevalence of antibiotic resistance and blaIMP-1 gene among Pseudomonas aeruginosa strains isolated from burn and urinary tract infections in Isfahan, central Iran. Microbiol Res. 2017;8(2):59-63. doi:10.4081/mr.2017.7295
2. Najar MS, Saldanha CL, Banday KA. Approach to urinary tract infections. Indian J Nephrol. 2009;19(4):129-139. doi:10.4103/0971-4065.59333
3. Shah DA, Wasim S, Essa Abdullah F. Antibiotic resistance pattern of Pseudomonas aeruginosa isolated from urine samples of Urinary Tract Infections patients in Karachi, Pakistan. Pak J Med Sci. 2015;31(2):341-345. doi:10.12669/pjms.312.6839
4. Su C. Female lower urinary tract infection. JTUA. 2008;19(1):12-20.
5. Hu KK, Boyko EJ, Scholes D, et al. Risk factors for urinary tract infections in postmenopausal women. Arch Intern Med. 2004;164(9):989-993. doi:10.1001/archinte.164.9.989
6. Krieger JN, Kaiser DL, Wenzel RP. Nosocomial urinary tract infections: secular trends, treatment and economics in a university hospital. J Urol. 1983;130(1):102-106. doi:10.1016/s0022-5347(17)50980-5
7. Matuszkiewicz-Rowińska J, Małyszko J, Wieliczko M. Urinary tract infections in pregnancy: old and new unresolved diagnostic and therapeutic problems. Arch Med Sci. 2015;11(1):67-77. doi:10.5114/aoms.2013.39202
8. Ahmed H, Davies F, Francis N, Farewell D, Butler C, Paranjothy S. Long-term antibiotics for prevention of recurrent urinary tract infection in older adults: systematic review and meta-analysis of randomised trials. BMJ Open. 2017;7(5):e015233. doi:10.1136/bmjopen-2016-015233
9. Wilson CB. Remington and Klein's infectious diseases of the fetus and newborn infant. Elsevier Health Sciences; 2015.
10. Rezai MS, Bagheri-Nesami M, Hajalibeig A, Ahangarkani F. Multidrug and Cross-resistance Pattern of ESBL-producing Enterobacteriaceae Agents of Nosocomial Infections in Intensive Care Units. Journal of Mazandaran University of Medical Sciences. 2017;26(144):39-49. [Persian].
11. Mittal R, Aggarwal S, Sharma S, Chhibber S, Harjai K. Urinary tract infections caused by Pseudomonas aeruginosa: a minireview. J Infect Public Health. 2009;2(3):101-111. doi:10.1016/j.jiph.2009.08.003
12. Mittal R, Sharma S, Chhibber S, Harjai K. Iron dictates the virulence of Pseudomonas aeruginosa in urinary tract infections. J Biomed Sci. 2008;15(6):731-741. doi:10.1007/s11373-008-9274-7
13. Amjadi F, Salehi E, Mehdizadeh M, Aflatoonian R. Role of the innate immunity in female reproductive tract. Adv Biomed Res. 2014;3:1. doi:10.4103/2277-9175.124626
14. Hoang S, Georget A, Asselineau J, et al. Risk factors for colonization and infection by Pseudomonas aeruginosa in patients hospitalized in intensive care units in France. PLoS One. 2018;13(3):e0193300. doi:10.1371/journal.pone.0193300
15. Lamas Ferreiro JL, Álvarez Otero J, González González L, et al. Pseudomonas aeruginosa urinary tract infections in hospitalized patients: Mortality and prognostic factors. PLoS One. 2017;12(5):e0178178. doi:10.1371/journal.pone.0178178
16. Alijahan R, Pourfarzi F, Salimi S, Tahmasebi P, Moradi S, Hazrati S. Prevalence of urinary tract infection and associated risk factors in pregnant women. Iran South Med J. 2014;17(4):676-686. [Persian].
17. Jiménez-Guerra G, Heras-Cañas V, Gutiérrez-Soto M, et al. Urinary tract infection by Acinetobacter baumannii and Pseudomonas aeruginosa: evolution of antimicrobial resistance and therapeutic alternatives. J Med Microbiol. 2018. doi:10.1099/jmm.0.000742
18. Rezai MS, Ahangarkani F, Rafiei A, Hajalibeig A, Bagheri-Nesami M. Extended-Spectrum Beta-Lactamases Producing Pseudomonas aeruginosa Isolated From Patients With Ventilator Associated Nosocomial Infection. Arch Clin Infect Dis. 2018;13(4):e13974. doi:10.5812/archcid.13974
19. Minardi D, d'Anzeo G, Cantoro D, Conti A, Muzzonigro G. Urinary tract infections in women: etiology and treatment options. Int J Gen Med. 2011;4:333-343. doi:10.2147/ijgm.s11767
20. Ramazanzadeh R, Rouhi S, Hosainzadegan H, Shakib P, Nouri B. Co-occurrence of Extended-Spectrum Beta-Lactamases in Isolated Enterobacter spp. From Patients Specimens. Arch Clin Infect Dis. 2016;11(3):e26837. doi:10.5812/archcid.26837
21. Mulamattathil SG, Bezuidenhout C, Mbewe M, Ateba CN. Isolation of environmental bacteria from surface and drinking water in mafikeng, South Africa, and characterization using their antibiotic resistance profiles. J Pathog. 2014;2014:371208. doi:10.1155/2014/371208
22. Clinical and Laboratory Standards Institute (CLSI) MS. Performance Standards for Antimicrobial Susceptibility Testing. 26th ed. CLSI; 2016.
23. Tuon FF, Gortz LW, Rocha JL. Risk factors for pan-resistant Pseudomonas aeruginosa bacteremia and the adequacy of antibiotic therapy. Braz J Infect Dis. 2012;16(4):351-356. doi:10.1016/j.bjid.2012.06.009
24. Peleg AY, Hooper DC. Hospital-acquired infections due to gram-negative bacteria. N Engl J Med. 2010;362(19):1804-1813. doi:10.1056/NEJMra0904124
25. Chawla A, Chawla R, Jaggi S. Microvasular and macrovascular complications in diabetes mellitus: Distinct or continuum? Indian J Endocrinol Metab. 2016;20(4):546-551. doi:10.4103/2230-8210.183480
26. Singh B, Tilak R, Srivastava R, Katiyar D. Urinary Tract infection and its risk factors in Women: an Appraisal. J Pure Appl Microbiol. 2014;8(5):4155-62.
27. Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. Cardiovasc J Afr. 2016;27(2):89-94. doi:10.5830/cvja-2016-021
28. Djordjevic Z, Folic MM, Zivic Z, Markovic V, Jankovic SM. Nosocomial urinary tract infections caused by Pseudomonas aeruginosa and Acinetobacter species: sensitivity to antibiotics and risk factors. Am J Infect Control. 2013;41(12):1182-1187. doi:10.1016/j.ajic.2013.02.018
29. Iwuafor AA, Ogunsola FT, Oladele RO, et al. Incidence, Clinical Outcome and Risk Factors of Intensive Care Unit Infections in the Lagos University Teaching Hospital (LUTH), Lagos, Nigeria. PLoS One. 2016;11(10):e0165242.

doi:10.1371/journal.pone.0165242
30. Castle N, Engberg JB, Wagner LM, Handler S. Resident and Facility Factors Associated With the Incidence of Urinary Tract Infections Identified in the Nursing Home Minimum Data Set. J Appl Gerontol. 2017;36(2):173-194. doi:10.1177/0733464815584666
31. Hsiao CY, Lin HL, Lin YK, et al. Urinary tract infection in patients with chronic kidney disease. Turk J Med Sci. 2014;44(1):145-149.
32. Pourmand M, Keshtvarz M, Soltan Dallal M, Talebi M, Bakhtiari R, Pourmand G. Urinary tract infection in renal transplant patients in Sina University Hospital. Tehran University Medical Journal. 2013;71(2):114-121. [Persian].
33. Ghalandari Shamami M, Mirzaei M, Najar Peerayeh S. Frequency of papaA, papC genes and antimicrobial resistance pattern in uropathogenic Escherichia coli. Journal of Microbial World. 2016;9(1):44-52. [Persian].
34. Borgatta B, Lagunes L, Imbiscuso AT, Larrosa MN, Lujan M, Rello J. Infections in intensive care unit adult patients harboring multidrug-resistant Pseudomonas aeruginosa: implications for prevention and therapy. Eur J Clin Microbiol Infect Dis. 2017;36(7):1097-1104. doi:10.1007/s10096-016-2894-3
35. Kalra OP, Raizada A. Approach to a patient with urosepsis. J Glob Infect Dis. 2009;1(1):57-63. doi:10.4103/0974-777x.52984
36. Al-Hazmi H. Role of duration of catheterization and length of hospital stay on the rate of catheter-related hospital-acquired urinary tract infections. Res Rep Urol. 2015;7:41-47. doi:10.2147/rru.s75419
37. Bagheri-Nesami M, Rafiei A, Eslami G, et al. Assessment of extended-spectrum beta-lactamases and integrons among Enterobacteriaceae in device-associated infections: multicenter study in north of Iran. Antimicrob Resist Infect Control. 2016;5:52. doi:10.1186/s13756-016-0143-2
38. Behzadnia S, Davoudi A, Rezai MS, Ahangarkani F. Nosocomial infections in pediatric population and antibiotic resistance of the causative organisms in north of iran. Iran Red Crescent Med J. 2014;16(2):e14562. doi:10.5812/ircmj.14562