

## Clinical Study

# Antibiotic resistance patterns of microorganisms isolated from nephrology and kidney transplant wards of a referral academic hospital

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## ABSTRACT

**Objective:** Antibiotic use pattern and emergence of resistant bacteria are major concerns in clinical settings. This study aimed to detect common bacteria and their antibiotic sensitivity patterns in nephrology and kidney transplant wards.

**Methods:** This 1-year, observational study was performed in the nephrology and kidney transplant wards of Imam Khomeini Hospital Complex, Tehran, Iran. All patients treated with antimicrobial agents for confirmed or suspected infections were included. Their demographic, clinical, and laboratory data (including biological media used for microbial culture, growth organisms, and antibiograms) were collected. Adherence of antimicrobial regimen to standard guidelines was also assessed.

**Findings:** About half of the patients received antibiotic. The most common infecting bacteria were *Escherichia coli* followed by *Enterococcus* sp. and *Staphylococcus aureus*. *E. coli* showed high rate of sensitivity to carbapenems and nitrofurantoin and high rate of resistance to co-trimoxazole and ciprofloxacin. *Enterococcus* sp. in both wards had high rate of resistance to ampicillin and were all sensitive to linezolid. Unlike to the nephrology ward, more than 50% of *Enterococcus* sp. from kidney transplant ward was resistant to vancomycin. The most common type of *S. aureus* in this nephrology ward was methicillin-resistant *S. aureus* (MRSA). Most commonly-prescribed antibiotics were carbapenems followed by vancomycin, ciprofloxacin, and ceftriaxone. Antibiotic regimens were 75% and 83%, 85% and 91%, and 80% and 87% compatible with international guidelines in antibiotic types, dosages, and treatment durations, respectively, in nephrology and kidney transplant wards, respectively.

**Conclusion:** MRSA, fluoroquinolone-resistant *E. coli*, and vancomycin resistant *Enterococcus* species are major threats in nephrology and kidney transplant wards. Most commonly-prescribed antibiotics were carbapenems that necessitate providing internal guidelines by the teamwork of clinical pharmacist, infectious disease specialists, and nephrologists to avoid the widespread use of broad-spectrum antibiotics.

**Keywords:** Antibiotic resistance; *Escherichia coli*; hemodialysis catheter-related infection; kidney transplant; nephrology

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## INTRODUCTION

Due to the common and sometimes incorrect use of antibiotics, resistant microorganisms have been increasingly emerged. More than 70% of bacterial organisms are resistant to at least one of the commonly used antibiotics.<sup>[1]</sup> Incorrect or insufficient empiric therapy and long-term antibiotic administration are the two most important reasons for increasing antibiotic resistance.<sup>[2]</sup> Antibiotic stewardship programs include not only preventing unnecessary use of antibiotics but also selecting the correct antibiotics' type, dose, treatment duration, and route/mode of administration. Preventing antibiotic resistance, adverse drug reactions, and treatment costs are other aims of antibiotic stewardship programs.<sup>[3]</sup> More than 80% of hospital-acquired infections include urinary tract infections (usually due to urinary catheters), surgical site infections, bloodstream infections (mainly following the use of intravascular catheters), and pneumonia (usually ventilator-associated pneumonia);<sup>[4]</sup> among these, urinary, respiratory, and hemodialysis catheter-related bloodstream infections are common among renal disease patients. Infectious diseases are common cause of morbidity and the second cause of mortality among chronic kidney disease (CKD) patients.<sup>[5-7]</sup> Widespread use of intravascular hemodialysis catheters increases the risk of infection.<sup>[8]</sup> Sepsis-related death among hemodialysis patients is 100 times more than the general population.<sup>[9]</sup>

Gram-positive organisms, mainly *Staphylococcus aureus* and *Staphylococcus epidermidis*, cause about 70% of catheter-related infections.<sup>[10]</sup> *S. aureus* is leading cause of bloodstream infections and subsequent morbidity and mortality among hemodialysis patients.<sup>[6]</sup> *Enterococcus* species are other common organisms inducing hemodialysis catheter-related infections. Increasing rate of vancomycin-resistant *Enterococcus* (VRE), especially among hemodialysis patients is a major concern in nephrology wards worldwide.<sup>[11,12]</sup>

This study was designed to detect common bacterial organisms and their antibiotic sensitivity patterns in the nephrology and kidney transplant wards of a referral academic hospital. This study also compared antibiotic therapy regimens in these two wards with approved clinical guidelines.

## METHODS

This 1-year cross-sectional, observational study was performed from June 22, 2013, to June 22, 2014, in the nephrology and kidney transplant wards of Imam

Khomeini Hospital Complex affiliated to Tehran University of Medical Sciences, Tehran, Iran.

All patients admitted to these wards and treated with antimicrobial agents (antibiotics, antiviral or antifungal agents) for confirmed or suspected nosocomial or community-acquired infectious diseases were included in this study.<sup>[13]</sup> Patients who were administered antimicrobial agents for prophylaxis purposes according to this center protocol were excluded from the study. These excluded patients all were kidney transplant recipients who received intravenous ceftriaxone, intravenous ganciclovir/oral valganciclovir, oral cotrimoxazole, and oral clotrimazole/nystatin for prophylaxis of infection-related to kidney transplant surgery, cytomegalovirus, *Pneumocystis jirovecii* pneumonia, and oral candidiasis, respectively.

Demographic (sex, age, weight, height), clinical, and paraclinical data of the patients were gathered in prepared forms. Patients' clinical data that were collected consisted of chief complaint at admission, diagnosis, and risk factors for infectious diseases including history of chronic organ diseases, hospitalization during last month, taking antibiotic within last month, receiving immunosuppressive drugs, or having urinary or intravascular catheters.<sup>[4-7]</sup>

Paraclinical data including biological media that were used for microbial culture, growth organisms, and results of antibiogram were also collected in these forms. Only data of microbial cultures that were clinically valuable were included in analysis. Those cultures that seem to be contamination according to the standards of Center for Disease Control and Prevention of United States/National Healthcare System Network were excluded.<sup>[13]</sup> Antibiotic susceptibilities of microorganisms were assessed by disc diffusion method. Antibiotic concentrations in applied discs (Padtan Teb, Tehran, Iran) were as follows: Oxacillin 1.5 mcg/disc, cefoxitin 30 mcg/disc, vancomycin 30 mcg/disc, linezolid 30 mcg/disc, nitrofurantoin 10 mcg/disc, ampicillin 10 mcg/disc, penicillin 10 mcg/disc, ceftazidime 30 mcg/disc, ceftriaxone 30 mcg/disc, cefixime 5 mcg/disc, ciprofloxacin 5 mcg/disc, trimethoprim-sulfamethoxazole 1.25/23.75 mcg/disc, gentamicin 10 mcg/disc, amikacin 30 mcg/disc, colistin 10 mcg/disc, ampicillin-sulbactam 10/10 mcg/disc, piperacillin-tazobactam 100/10 mcg/disc, imipenem 10 mcg/disc, erythromycin 5 mcg/disc, chloramphenicol 30 mcg/disc, clindamycin 2 mcg/disc, and rifampicin 5 mcg/disc.

Adherence of antimicrobial therapy in these wards to standard antibiotic regimens (antibiotic type, dose, and treatment duration) with international guidelines and references<sup>[14-17]</sup> were also assessed.

Descriptive analysis of data was done using the Statistical Package for the Social Sciences software (SPSS, version 19.0; SPSS Inc., Chicago, Illinois, USA).

The study protocol was approved by the Local Ethics Committee of Tehran University of Medical Sciences. All patients were provided written informed consent form for using their demographic, clinical, and paraclinical data anonymously in this study.

## RESULTS

### Demographic and clinical data

#### *Nephrology ward*

Of 546 patients who were admitted to the nephrology ward during the study period, 263 patients (134 males and 129 females) (48.1% of the patients) with the mean age of  $54.8 \pm 17.5$ -year-old (ranges from 16 to 91-year-old) received antimicrobial drugs.

The three most common risk factors for infectious susceptibility in antimicrobial-treated patients in this ward were CKD in 245 patients (93% of antibiotic-treated patients), using immunosuppressive drugs in 145 patients (55.13%) and the presence of the urinary catheter in 95 patients (36.12%). Some patients had more than one risk factor.

Of 263 antibiotic-treated patients, 245 were CKD patients; of them, 172 patients (70.2%) were treated with hemodialysis and 22 patients (9%) with peritoneal dialysis. Among the hemodialysis patients, 71 patients (41.2%) were dialyzed using femoral nontunneled double-lumen catheter, 69 (40.1%) through jugular nontunneled, double-lumen catheter, 30 patients (17.4%) by tunneled double-lumen catheter, and 28 patients (16.2%) through arteriovenous fistula. It has to be noted that newly diagnosed end-stage renal disease patients were dialyzed using femoral transient catheters at the first and later converted to permanent dialysis catheters. Therefore, some patients had more than one route for hemodialysis.

#### *Kidney transplant ward*

Of 116 kidney transplant recipients who were admitted in this center during the study period, 70 patients (40 males and 30 females) with the mean age of  $41.3 \pm 13.3$ -year-old (ranges from 15 to 65 years) received antimicrobial agents. All patients in this ward were administered a calcineurin inhibitor (mainly tacrolimus) and mycophenolate mofetil and prednisolone as maintenance immunosuppressive regimen with or without thymoglobulin induction. Other susceptibility factors for infections in these patients were the presence of urinary catheter (60% of antibiotic-treated patients), history of diabetes mellitus (21.4% of the patients), and using antibiotic

during last month (21.4% of patients). Of these 70 antibiotic-treated kidney transplant recipients, 12 patients were treated with hemodialysis during hospitalization via tunneled double-lumen catheter (5 patients), nontunneled, double-lumen catheter (5 patients) or arteriovenous fistula (2 patients).

### Infectious diseases, organisms, and their antibiotic sensitivity pattern

#### *Nephrology ward*

About 82.9% of antibiotic-treated patients had community-acquired and the remaining, hospital-acquired infections. The most common causes of antibiotic administration were urinary tract infections (49.8%) followed by hemodialysis catheter-related (14.1%) and respiratory tract (13.7%) infections.

Four hundred and eighty-three biologic media were sent from 248 out of 263 antibiotic-treated patients for microbial culture; of them, 109 (22.6%) were positive for bacterial growth.

The most common biologic media with positive cultures were urine (79 samples, 72.5%) and blood (17 samples, 15.6%). Of 109 isolated microorganisms from these microbial cultures, the most common organism was *Escherichia coli* (42 samples, 38.5%) followed by *S. aureus* and *Enterococcus* sp. (each 13 samples, 11.9%) [Table 1].

The most common organism isolated from 79 urine cultures were *E. coli* (38 samples, 48.1%) and *Enterococcus* sp. (12 samples, 15.19%). The most prevalent organism isolated from 17 blood samples was *S. aureus* (7 samples, 41.18%).

Isolated *E. coli* species were more sensitive to amikacin (100%), imipenem (97.6%), and nitrofurantoin (97.1%) and more incidences of resistance to cotrimoxazole (75.7%), ciprofloxacin (54%), and ceftazidim (57.1%) [Table 1].

*S. aureus* samples were more sensitive to vancomycin (100%) and cotrimoxazole (90.9%) and more resistant to cefoxitin (i.e., methicillin-resistant *S. aureus* [MRSA]) (58.3%) and erythromycin (41.6%) [Table 1].

*Enterococcus* sp. showed most sensitivity to vancomycin (100%) and linezolid (100%) and most resistance to ampicillin (72.7%) [Table 1].

In this study, *Klebsiella* sp. was sensitive to common applied antibiotics such as gentamicin, cotrimoxazole, and ciprofloxacin. Although low in number (only five positive cultures), isolated *Citrobacter* sp. were all sensitive to imipenem and resistant to ciprofloxacin. Limited numbers of *Pseudomonas aeruginosa* that were isolated in this survey were all sensitive

**Table 1: Antibiotic susceptibility pattern of isolated microorganisms from nephrology ward**

Antibiotics	Community-acquired infections (%)			Nosocomial infections (%)		
	Sensitive	Intermediate	Resistant	Sensitive	Intermediate	Resistant
<i>Escherichia coli</i>						
Ceftriaxone	1 (50)	0	1 (50)	0	0	1 (100)
Ciprofloxacin	9 (31)	3 (10.3)	17 (58.7)	5 (62.5)	0	3 (37.5)
Imipenem	33 (97.1)	0	1 (2.9)	8 (100)	0	0
Co-trimoxazole	7 (24.1)	0	22 (75.9)	1 (12.5)	1 (12.5)	6 (75)
Ceftazidime	9 (32.1)	3 (10.7)	16 (57.2)	2 (28.6)	1 (14.3)	4 (57.1)
Gentamicin	10 (50)	3 (15)	7 (35)	4 (80)	0	1 (20)
Nitrofurantoin	27 (96.4)	0	1 (3.6)	7 (100)	0	0
Ampicillin-sulbactam	20 (62.5)	1 (3.1)	11 (34.4)	4 (66.7)	0	2 (33.3)
Piperacillin-tazobactam	16 (94.1)	1 (5.9)	0	4 (100)	0	0
Amikacin	19 (100)	0	0	6 (100)	0	0
Cefepime	0	0	2 (100)	0	0	0
Cefotaxime	0	0	2 (100)	0	0	1 (100)
<i>Staphylococcus aureus</i>						
Vancomycin	6 (100)	0	0	2 (100)	0	0
Co-trimoxazole	5 (83.3)	0	1 (16.7)	5 (100)	0	0
Linezolid	1 (100)	0	0	2 (100)	0	0
Clindamycin	5 (71.4)	0	2 (28.6)	4 (80)	0	1 (20)
Erythromycin	4 (57.1)	0	3 (42.8)	3 (60)	0	2 (40)
Gentamicin	3 (100)	0	0	2 (100)	0	0
Rifampin	4 (80)	0	1 (20)	5 (100)	0	0
Chloramphenicol	2 (100)	0	0	4 (100)	0	0
Cefoxitin	4 (57.1)	0	3 (42.8)	1 (20)	0	4 (80)
<i>Enterococcus sp.</i>						
Vancomycin	9 (100)	0	0	4 (100)	0	0
Linezolid	9 (100)	0	0	3 (100)	0	0
Ampicillin	2 (28.6)	0	5 (71.4)	1 (25)	0	3 (75)
Gentamicin	1 (25)	0	3 (75)	1 (25)	0	3 (75)
Rifampin	6 (85.7)	0	1 (14.3)	2 (66.7)	0	1 (33.3)
Nitrofurantoin	1 (100)	0	0	1 (100)	0	0
<i>Klebsiella sp.</i>						
Ciprofloxacin	3 (100)	0	0	3 (100)	0	0
Imipenem	3 (100)	0	0	3 (100)	0	0
Co-trimoxazole	2 (100)	0	0	2 (40)	0	3 (60)
Ceftazidim	3 (100)	0	0	3 (100)	0	0
Gentamicin	3 (100)	0	0	2 (100)	0	0
Nitrofurantoin	3 (100)	0	0	2 (100)	0	0
Ampicillin	2 (66.7)	0	1 (33.3)	3 (100)	0	0
Piperacillin-tazobactam	2 (100)	0	0	3 (100)	0	0
Amikacin	1 (100)	0	0	1 (100)	0	0
<i>Citrobacter sp.</i>						
Ciprofloxacin	0	0	3 (100)	0	0	0
Imipenem	4 (100)	0	0	0	0	0
Co-trimoxazole	1 (25)	0	3 (75)	0	0	0
Ceftazidim	1 (25)	1 (25)	2 (50)	0	0	0
Ampicillin-sulbactam	2 (50)	1 (25)	1 (25)	0	0	0
Amikacin	3 (100)	0	0	0	0	0
<i>Pseudomonas aeruginosa</i>						
Ciprofloxacin	4 (100)	0	0	0	0	0
Imipenem	4 (100)	0	0	0	0	0
Ampicillin-sulbactam	0	0	3 (100)	0	0	0
<i>Staphylococcus epidermidis</i>						
Vancomycin	4 (100)	0	0	1 (100)	0	0
Co-trimoxazole	0	0	3 (100)	0	0	1 (100)

Contd...

Table 1: Contd...

Antibiotics	Community-acquired infections (%)			Nosocomial infections (%)		
	Sensitive	Intermediate	Resistant	Sensitive	Intermediate	Resistant
Cefoxitin	0	0	3 (100)	0	0	1 (100)
<i>Staphylococcus haemolyticus</i>						
Clindamycin	0	0	3 (100)	0	0	1 (100)
Erythromycin	0	0	3 (100)	0	0	1 (100)
Rifampin	3 (100)	0	0	1 (100)	0	0
Chloramphenicol	3 (100)	0	0	1 (100)	0	0
Cefoxitin	0	0	3 (100)	0	0	1 (100)

Data are presented as *n* (%) of the samples

to imipenem and ciprofloxacin and resistant to ampicillin-sulbactam.

Among isolated Gram-positive bacteria, *S. epidermidis* (five positive cultures) were all sensitive to vancomycin and all resistant to cefoxitin (i.e., were MRSA), and cotrimoxazole. Four positive cultures for *S. haemolyticus* showed the higher rate of sensitivity to chloramphenicol and rifampin and resistance to clindamycin and erythromycin.

#### Kidney transplant ward

Of 70 antimicrobial-treated kidney transplant recipients during this study, 51.4% and 48.6% of the patients had community-acquired and hospital-acquired infections, respectively. The most common infectious diseases in this ward was urinary tract infection in 42 out of 70 patients (60%) followed by fever of unknown origin in 13 patients (18.6%), respiratory tract infection in six patients (8.6%), surgical site infection in four patients (5.7%), cytomegalovirus infection in four patients (5.7%), and diabetic foot in one patient (1.4%). For 68 out of these 70 patients, microbial cultures of different biological media were available. All of these, 68 patients had urinary culture, 38 of them had blood culture, and 9 of them had microbial culture of other biological media such as wound discharge and catheter tips. Of these available 115 microbial cultures of different biological media, 33 (28.7%) samples (29 urine samples and 4 wound discharge samples) were positive for microbial growth.

Of 33 isolated microorganisms, the most common species were *E. coli* (12 cases [36.3%]) followed by *Enterococcus* species (9 cases [27.3%]) and *Klebsiella* species (4 cases [12.1%]) [Table 2].

All isolated *E. coli* were sensitive to imipenem and nitrofurantoin, and all were resistant to cotrimoxazole. About 66.6% of isolated *E. coli* was resistant to ciprofloxacin [Table 2]. All isolated *Enterococcus* species were sensitive to linezolid and resistant to gentamicin. Resistance rates of *Enterococcus* species to ampicillin and vancomycin were 85.7% and 55.5%,

respectively [Table 2]. Other isolated microbial organisms were too limited in number to be judged about their antibiotic resistance patterns.

#### Adherence to antimicrobial treatment guidelines

##### Nephrology ward

Of 263 antibiotic-treated patients in this ward, 237 patients (90.1%) were treated empirically and 26 patients (9.9%) antibiogram-targeted. Selected antibiotic types for 195 patients (74.14%) were compatible with their microbial cultures or intentional guidelines and references<sup>[14-17]</sup> for that source of infection. Antibiotic therapies of remaining 68 patients (25.9%) were not consistent with known sources for antibiotic selection.

For 222 antibiotic-treated patients (84.41%), antibiotic dosages were compatible with international references and guidelines and patients' hepatic and renal functions.<sup>[14,15]</sup>

Duration of antibiotic therapy in 210 patients (79.85%) was compatible with international guidelines/references. Antibiotic therapy courses were longer or shorter than those recommended in 53 (20.15%) patients.<sup>[14,15]</sup>

The most commonly-prescribed antibiotics during this survey in this ward were carbapenems in 57% of antibiotic-treated patients followed by vancomycin (in 51.3% of the patients), ceftriaxone (in 42.2% of the patients), and ciprofloxacin (in 37.6% of the patients).

##### Kidney transplant ward

Of 70 kidney transplant recipients who received antimicrobial therapy during this survey, 55 patients (78.6%) were treated empirically and 15 patients (21.4%) antibiogram-targeted. Antibiotics' type, dosage, and treatment duration were consistent with references and guidelines<sup>[14-17]</sup> in 58 (82.9%), 64 (91.4%), and 61 (87.1%) patients, respectively.

The most common-prescribed antibiotics in this kidney transplant ward were carbapenems in 75.7% of antibiotic-treated patients followed by vancomycin and ciprofloxacin in 58.6% and 31.4% of the patients.

**Table 2: Antibiotic susceptibility pattern of isolated microorganisms from kidney transplant ward**

Antibiotics	Community-acquired infections (%)			Nosocomial infections (%)		
	Sensitive	Intermediate	Resistant	Sensitive	Intermediate	Resistant
<i>Escherichia coli</i>						
Ceftriaxone	0	0	4 (100)	0	0	0
Ciprofloxacin	1 (14.3)	0	6 (85.7)	2 (100)	0	0
Imipenem	7 (100)	0	0	5 (100)	0	0
Co-trimoxazole	0	0	4 (100)	0	0	3 (100)
Ceftazidim	1 (25)	0	3 (75)	1 (33.3)	0	2 (66.7)
Gentamicin	3 (100)	0	0	1 (33.3)	0 (0)	2 (66.7)
Nitrofurantoin	6 (100)	0	0	4 (100)	0	0
Ampicillin-sulbactam	1 (50)	0	1 (50)	0	0	3 (100)
Piperacillin-tazobactam	2 (100)	0	0	1 (100)	0	0
Amikacin	4 (100)	0	0	2 (66.7)	0	1 (33.3)
Cefepime	0	0	3 (100)	0	0	0
<i>Enterococcus sp.</i>						
Vancomycin	3 (100)	0	0	1 (16.7)	0	5 (83.3)
Linezolid	3 (33.3)	0	6 (66.7)	6 (100)	0	0
Ampicillin	1 (50)	0	1 (50)	0 (0)	0	5 (100)
Gentamicin	0	0	3 (100)	0 (0)	0	4 (100)
Rifampin	2 (66.7)	0	1 (33.3)	1 (20)	1 (20)	3 (60)
Nitrofurantoin	1 (100)	0	0	1 (100)	0	0

Data are presented as *n* (%) of the samples

## DISCUSSION

This survey showed that about half of the patients admitted to our nephrology ward received antibiotic for confirmed or clinically suggested infections. The most common types of infections in these patients were urinary tract infection followed by hemodialysis catheter-related and respiratory tract infections. The most common bacteria causing infection in this ward was *E. coli* followed by *S. aureus* and *Enterococcus sp.* *E. coli* showed the higher rate of sensitivity to imipenem and nitrofurantoin and the higher rate of resistance to co-trimoxazole and ciprofloxacin. *S. aureus* showed the higher rate of resistance to cefoxitin and higher rate of sensitivity to vancomycin; i.e., the most common type of *S. aureus* in this nephrology ward is MRSA. *Enterococcus sp.* in the nephrology ward had high rate of resistance to ampicillin and were sensitive to vancomycin and linezolid. As seen, there is no threat of VRE or vancomycin-resistant *S. aureus* in this ward at this time.

In kidney transplant ward, about 60% of admitted patients received antibiotics for treatment of confirmed or suggested infections. The most common infecting microorganisms in this ward were *E. coli* and *Enterococcus* species. As if findings of the nephrology ward, *E. coli* in the kidney transplant ward showed the most sensitivity to carbapenems and resistance to co-trimoxazole and ciprofloxacin. Isolated *Enterococcus* species from the kidney transplant ward were all sensitive to linezolid and

showed high rate of resistance to ampicillin and gentamicin. In contrast to nephrology ward, about 55% of isolated *Enterococcus* species from kidney transplant ward showed vancomycin resistance. This finding may be due to long-time using of hemodialysis catheter before kidney transplantation that results in widespread use of vancomycin for treating the catheter-related infection. In both wards, the most commonly-prescribed antibiotic class was carbapenems that necessitate providing internal guidelines by the teamwork of pharmacotherapists and nephrologists to avoid the widespread, unnecessary use of broad-spectrum antibiotics. Other highly used antibiotics in this ward were vancomycin, ceftriaxone, and ciprofloxacin.

As noted, high rate of ciprofloxacin resistance of *E. coli* has been found in these two wards.

In agreement with other studies in the same hospital and other hospitals from Iran, the most prevalent organism in the present survey was *E. coli*.<sup>[18-21]</sup> *E. coli* showed a high rate of sensitivity to imipenem in both wards that was in concordance with the findings of Khalili *et al.*,<sup>[22]</sup> Vessal *et al.*,<sup>[23]</sup> Japoni *et al.*,<sup>[24]</sup> and Hadadi *et al.*<sup>[25]</sup> from the same hospital in this study or other hospitals of Iran. In agreement with Khalili *et al.* study in the same hospital, *E. coli* isolates were highly sensitive to piperacillin-tazobactam.<sup>[22]</sup> In the present study, all *E. coli* isolates were sensitive to amikacin and 60% of isolates were sensitive to gentamicin. Gentamicin sensitivity of *E. coli* in Khalili

*et al.*<sup>[18,22]</sup> studies were similar to the present study; however, amikacin resistance rates of 14% and 39% for *E. coli* were reported in Khalili *et al.*<sup>[18,22]</sup> studies. High rate of amikacin-resistant *E. coli* in Khalili *et al.* studies may be due to the collected samples from intensive care units (ICUs) in their study while due to the fear of nephrotoxicity and aminoglycoside; administration is limited in nephrology wards. Restricted aminoglycoside prescribing in nephrology wards may justify the high rate of sensitivity of Gram-negative organisms to this class of antibiotics. As reported by Khalili *et al.*<sup>[18,22]</sup> and Hadadi *et al.*,<sup>[25]</sup> more than 50% of *E. coli* isolates from both wards in this study were resistant to ciprofloxacin. This finding may be due to prevalent irrational ciprofloxacin administration in our community and outpatient settings. Ciprofloxacin may be prescribed as the first-choice antibiotic for complicated cystitis and pyelonephritis.<sup>[14]</sup> These indications might result in increased rate of ciprofloxacin resistance in microorganisms isolated from CKD and kidney transplant patients as two groups of patients with prevalent rate of complicated urinary tract infections. In the present study, resistance rate of *E. coli* isolates to cotrimoxazole was 75% in the nephrology ward and 100% in the kidney transplant ward. This result is compatible with the reports of Khalili *et al.*<sup>[22]</sup> The higher rate of *E. coli* resistance to cotrimoxazole in the kidney transplant ward may be due to the routine administration of this antibiotic in prophylaxis dosage against *P. jirovecii* pneumonia. These findings preclude cotrimoxazole as an option to treat urinary tract infections in our community and hospital settings as recommended by the guideline of Infectious Disease Society of America.<sup>[26]</sup> In our study, about all isolated *E. coli* samples from both wards were sensitive to nitrofurantoin. Khalili *et al.*<sup>[18,22]</sup> reported nitrofurantoin sensitivity of *E. coli* in 80% and 57% of isolates in their two studies in the same and another hospital. Higher sensitivity rate of *E. coli* to nitrofurantoin in the present study can be explained by very limited use of nitrofurantoin in treating urinary tract infection in CKD and kidney transplant patients due to the lack of efficacy.<sup>[16]</sup> Therefore, this high rate of *in vitro* antibiotic sensitivity has no clinical benefit. In the present study in both wards, *E. coli* isolates had very high rate of resistance to ceftriaxone that is in agree with Vessal *et al.* findings.<sup>[23]</sup> These results may be the consequence of broad use of ceftriaxone in our community and as empiric therapies in emergency departments.

Fortunately, all *P. aeruginosa* isolates from nephrology ward in the present study were sensitive to ciprofloxacin and imipenem that is compatible with the findings of Khalili *et al.*<sup>[22]</sup> from the same hospital. In Khalili *et al.*<sup>[18]</sup> and Hadadi's studies<sup>[25]</sup> from other

hospitals, sensitivity rate of *P. aeruginosa* isolates to imipenem and ciprofloxacin were lower that might be due to high number of isolates from samples of ICU patients in their studies.

Regarding Gram-positive organisms in the present study, *S. aureus* isolates had high rate of sensitivity to vancomycin, linezolid, and chloramphenicol that is compatible with the findings of Soltani<sup>[27]</sup> and Khalili *et al.*<sup>[28]</sup> from different wards of the same hospital. In the present study, *S. aureus* isolates from nephrology ward showed sensitivity rate of 90% to cotrimoxazole. Soltani<sup>[27]</sup> showed *S. aureus* sensitivity rate of 61.4% and 100% to cotrimoxazole in all wards and nephrology ward of the same hospital, respectively, about 4 years ago. Higher sensitivity rate of *S. aureus* to cotrimoxazole in nephrology ward compared with other wards, especially infectious diseases departments that included in Soltani<sup>[27]</sup> and Khalili *et al.*<sup>[28]</sup> studies may be due to limited use of cotrimoxazole in nephrology wards due to some concerns of its safety in CKD patients and available safer antibiotic options in most infectious situations<sup>[14,15]</sup> for this patient population. In renal disease patients, cotrimoxazole is usually used as the first-antibiotic choice only for nocardiosis and *Pneumocystis jirovesii* pneumonia treatment/prophylaxis more in kidney transplant recipients.<sup>[14,15]</sup> Compatible with the findings of Soltani<sup>[27]</sup> and Khalili *et al.*,<sup>[28]</sup> more than half of the *S. aureus* isolates were MRSA in our ward.

In agree with results of Khalili *et al.*,<sup>[28]</sup> *S. epidermidis* isolates in our study showed 100% sensitivity rate to vancomycin, but in contrast to Khalili *et al.* finding of about 60% resistance rate of *S. epidermidis* to cotrimoxazole, isolates of our study showed high sensitivity rate to cotrimoxazole that may be due to less use of this antibiotic in the patients with renal diseases in nephrology but not in the kidney transplant ward.

In the present study, all *Enterococcus* species from both wards were sensitive to linezolid. Isolated *Enterococcus* species from nephrology ward all were sensitive to vancomycin while, about half of the isolated species from the kidney transplant ward was resistant to vancomycin. In Soltani<sup>[27]</sup> study from the same hospital, all *Enterococcus* sp. were sensitive to linezolid, but about half of the isolates were resistance to vancomycin (VRE). When they assessed different wards of the hospitals separately, all *Enterococcus* sp. from nephrology ward were sensitive to vancomycin and all VRE were isolated from ICU samples.<sup>[27]</sup> High rate of VRE from kidney transplant ward is a warning finding and may be due to high use of vancomycin to treat hemodialysis catheter-related infection before kidney transplantation. In the present study,

*Enterococcus* sp. showed ampicillin resistance rate of about 73% in nephrology ward and 86% in the kidney transplant ward. In Soltani<sup>[27]</sup> study, ampicillin resistance rate from all wards and nephrology ward of the same hospital were 64% and 50%, respectively. Therefore, ampicillin resistance rate of *Enterococcus* sp. has increased during past 4 years in our nephrology ward. In our survey, resistance rate of *Enterococcus* sp. to rifampin was 20% that is lower than the resistance rate of 50% that had been reported by Khalili *et al.*<sup>[28]</sup> from the same hospital. This discrepancy may be due to the higher use of rifampin in infectious diseases ward that had been included in Khalili *et al.*<sup>[28]</sup> study that may result in increased *Enterococcus* sp. resistance rate to rifampin.

Antibiotic regimens in nephrology ward were 75%, 85%, and 80% compatible with international guidelines/references in antibiotic types, dosages, and treatment duration, respectively. These compliance rates in kidney transplant ward were 83%, 91%, and 87%, respectively. Higher rates of adherence of antibiotic therapy to guidelines/references in kidney transplant ward may be due to regular visits of kidney transplant recipients by clinical pharmacist in this ward. In Khalili *et al.*<sup>[29]</sup> study in the same hospital, adherence of antibiotics' type and dosage to international guidelines/references was 86% and 85%, respectively that were similar to our findings.

In Khalili *et al.*<sup>[29]</sup> study, the most common used antibiotic was ceftriaxone. In our study, carbapenems, vancomycin, ceftriaxone, and ciprofloxacin were more widely used antibiotics. The reason for common administration of carbapenem in the present study may be prevalent upper urinary tract infection in renal disease patients that as a complicated pyelonephritis may justify carbapenem administration. The second common infection in our nephrology ward was hemodialysis catheter-related infection. Since *S. aureus* is a common pathogen in this type of infection, prevalent vancomycin prescribing in this ward is predictable. However, according to the sensitivity pattern of microorganisms that have been attained in this study, it would be rational to change antibiotic choices according to these results in future clinical practices.

About half of the patients admitted in these nephrology and kidney transplant wards received antibiotic for confirmed or clinically suggested infections. The most common types of infection in these patients were urinary tract infection, followed by hemodialysis catheter-related and respiratory tract infections. The most common bacteria causing infection in these two wards were *E. coli*, *Enterococcus*

species, and *S. aureus*. *E. coli* showed high rate of sensitivity to imipenem and high rate of resistance to co-trimoxazole and ciprofloxacin. Therefore, fluoroquinolone-resistant *E. coli* is a major threat in these two wards. About 60% of *S. aureus* in this nephrology ward was MRSA. *Enterococcus* sp. in this ward had high rate of resistance to ampicillin and were sensitive to linezolid. Unlike to *Enterococcus* species isolated from the nephrology ward, more than half of the isolates from kidney transplant ward were resistant to vancomycin. Although antibiotic therapy in this nephrology and kidney transplant wards showed good adherence to international guidelines/references; however, the most commonly-prescribed antibiotic class was carbapenems that necessitate providing internal guidelines by teamwork of clinical pharmacist, nephrologists, and infectious disease specialist to avoid the widespread, unnecessary use of broad-spectrum antibiotics.

## AUTHORS' CONTRIBUTION

Atieh Samanipour contributed in data gathering and manuscript drafting. Simin Dashti-Khavidaki contributed in idea, study design, data gathering, and manuscript drafting and finalizing. Mohammad-Reza Abbasi contributed in study design and patient management. Alireza Abdollahi contributed in providing microorganisms cultures and antibiogram.

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## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Muto CA, Jernigan JA, Ostrowsky BE, Richet HM, Jarvis WR, Boyce JM, *et al.* SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and *Enterococcus*. *Infect Control Hosp Epidemiol* 2003;24:362-86.
2. Fish DN, Ohlinger MJ. Antimicrobial resistance: Factors and outcomes. *Crit Care Clin* 2006;22:291-311, vii.
3. Shlaes DM, Gerding DN, John JF Jr, Craig WA, Bornstein DL, Duncan RA, *et al.* Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: Guidelines for the prevention of antimicrobial resistance in hospitals. *Clin Infect Dis* 1997;25:584-99.
4. Burke JP. Infection control – A problem for patient safety. *N Engl J Med* 2003;348:651-6.



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5. Berman SJ. Infections in patients with end-stage renal disease. An overview. *Infect Dis Clin North Am* 2001;15:709-20, vii.
6. Fitzgerald SF, O’Gorman J, Morris-Downes MM, Crowley RK, Donlon S, Bajwa R, *et al.* A 12-year review of *Staphylococcus aureus* bloodstream infections in haemodialysis patients: More work to be done. *J Hosp Infect* 2011;79:218-21.
7. Lok CE. Avoiding trouble down the line: The management and prevention of hemodialysis catheter-related infections. *Adv Chronic Kidney Dis* 2006;13:225-44.
8. Tokars JL, Miller ER, Stein G. New national surveillance system for hemodialysis-associated infections: Initial results. *Am J Infect Control* 2002;30:288-95.
9. Sarnak MJ, Jaber BL. Mortality caused by sepsis in patients with end-stage renal disease compared with the general population. *Kidney Int* 2000;58:1758-64.
10. Fowler VG Jr, Miro JM, Hoen B, Cabell CH, Abrutyn E, Rubinstein E, *et al.* *Staphylococcus aureus* endocarditis: A consequence of medical progress. *JAMA* 2005;293:3012-21.
11. Cetinkaya Y, Falk P, Mayhall CG. Vancomycin-resistant enterococci. *Clin Microbiol Rev* 2000;13:686-707.
12. Servais A, Mercadal L, Brossier F, Venditto M, Issad B, Isnard-Bagnis C, *et al.* Rapid curbing of a vancomycin-resistant *Enterococcus faecium* outbreak in a nephrology department. *Clin J Am Soc Nephrol* 2009;4:1559-64.
13. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;36:309-32.
14. Gilbert DN. The Sanford Guide to Antimicrobial Therapy. 44<sup>th</sup> ed. Sperryville, USA: Abtimicrobial Therapy Inc.; 2014.
15. Golightly LK. Renal Pharmacotherapy. Dosage Adjustment of Medications Eliminated by the Kidney. New York: Springer; 2013.
16. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O’Grady NP, *et al.* Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009;49:1-45.
17. Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, *et al.* Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. *Clin Infect Dis* 2010;50:625-63.
18. Khalili H, Soltani R, Safhami S, Dashti-Khavidaki S, Alijani B. Antimicrobial resistance pattern of gram-negative bacteria of nosocomial origin at a teaching hospital in the Islamic Republic of Iran. *East Mediterr Health J* 2012;18:172-7.
19. Khameneh ZR, Afshar AT. Antimicrobial susceptibility pattern of urinary tract pathogens. *Saudi J Kidney Dis Transpl* 2009;20:251-3.
20. Behroozzi A, Rahbar M, Yousefi JV. A survey on epidemiology of urinary tract infections and resistance pattern of uropathogens in an Iranian 1000-bed tertiary care hospital. *Afr J Microbiol Res* 2010;4:753-6.
21. Haghi-Ashteiiani M, Sadeghifard N, Abedini M, Taheri-Kalani SS. Etiology and antibacterial resistance of bacterial urinary tract infections in children’s medical center, Tehran, Iran. *Acta Med Iran* 2007;45:153-7.
22. Khalili H, Dashti-Khavidaki S, Shahidi MR, Abdollahi A, Jafari S, Jahangard-Rafsanjani Z, *et al.* Changes in gram negative microorganisms’ resistance pattern during 4 years period in a referral teaching hospital; a surveillance study. *Daru* 2012;20:28.
23. Vessal G, Afhami S, Gholami K, Shafaghi B, Hekmat Yazdi S. Evaluation of antimicrobial resistance among gram-negative isolates collected from intensive care units and reliability of routine disc susceptibility tests at a teaching hospital in Tehran. *Iran J Pharm Res* 2006;2:89-100.
24. Japoni A, Gudarzi M, Farshad S, Basiri E, Ziyaeyan M, Alborzi A, *et al.* Assay for integrons and pattern of antibiotic resistance in clinical *Escherichia coli* strains by PCR-RFLP in Southern Iran. *Jpn J Infect Dis* 2008;61:85-8.
25. Hadadi A, Rasoulinejad M, Maleki Z, Mojtahedzadeh M, Younesian M, Ahmadi SA, *et al.* Antimicrobial resistance patterns among gram-negative bacilli isolated from patients with nosocomial infections: Disk diffusion versus E-test. *Tehran Univ Med J* 2007;65:1-10.
26. 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.
27. Soltani R. Evaluation of Antimicrobial Resistance Pattern of Gram-Positive Microorganisms Isolated from Biologic Samples of Patients Hospitalized at Imam Khomeini Hospital Using Disk Diffusion and E-Test Methods. Clinical Pharmacy Residency Thesis. Tehran University of Medical Sciences, Year: 2009-2010.
28. Khalili H, Dashti-Khavidaki S, Karimzadeh I, Jafari S, Abdollahi A, Shahidi MR, *et al.* Changes in 4-year antimicrobial resistance pattern of gram-positive bacteria at the main referral teaching hospital, Tehran, Iran. *Acta Med Iran* 2012;50:493-504.
29. Khalili H, Elyasi S, Hatamkhani S, Dashti-Khavidaki S. Adherence to empiric antibiotic therapy guideline in a referral teaching hospital, Tehran, Iran. *Acta Med Iran* 2012;50:47-52.