Overview on urinary tract infection, bacterial agents, and antibiotic resistance pattern in renal transplant recipients

Xiuchun Zhang¹, Hui Gao¹, Juan Fu¹, Feng Lin¹, Azad Khaledi^{2,3}

¹Department of Infectious Disease, Hainan General Hospital, Haikou, Hainan 570311, China, ²Infectious Diseases Research Center, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, Iran, ³Department of Microbiology and Immunology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, Iran

Background: Urinary tract infection (UTI) is a mainly common infection in kidney transplant recipients. This study decided to investigate UTI, bacterial agents, and antibiotic resistance pattern in kidney transplant recipients from Iran. **Materials and Methods:** Search process was conducted for UTI, bacterial agents, and antibiotic resistance pattern in kidney transplant recipients from Iran via electronic databases (Scopus, PubMed, Web of Science, etc.,) with Mesh terms in either Persian and English languages without limited time to May 31, 2020. Data were analyzed by comprehensive meta-analysis software. **Results:** The combined prevalence of UTI in renal transplant recipients was reported by 31.1%. The combined prevalence of Gram-negative bacteria was 69%. The most common pathogens among Gram negatives were *E. coli* followed by *Klebsiella pneumoniae* with frequency 43.4% and 13%, respectively. Subgroup analysis for Gram-positive bacteria showed the combined prevalence of 31%. The most common microorganism among Gram positives belonged to coagulase-negative *Staphylococci* and Enterococci with a prevalence of 10.2% and 9%, respectively. Subgroup meta-analysis of antibiotic resistance for Gram-negative showed the most resistance to cephalexin followed by carbenicillin with a prevalence of 89.1% and 87.3%, respectively. **Conclusion:** Our review showed a noticeable rate of UTI (31.1%) among renal transplant recipients in Iran and a high prevalence of Gram-negative (69%) and Gram-positive (13%) microorganisms. A high resistance rate was seen against almost all antibiotics used for the treatment of UTI. Therefore, empirical prescription of antibiotics should be avoided, and it should be based on data obtained from antibiogram tests.

Key words: Antibiotic resistance, bacteriuria, kidney grafting, renal transplantation, urinary tract infection

How to cite this article: Zhang X, Gao H, Fu J, Lin F, Khaledi A. Overview on urinary tract infection, bacterial agents, and antibiotic resistance pattern in renal transplant recipients. J Res Med Sci 2021;26:26.

INTRODUCTION

As we know kidney transplantation despite the high cost is clinically effective treatment for the end-step renal disorder,^[1] nowadays, it is possible with a profitable kidney transplant increases quality of life in patients and decreases mortality.^[2] Posttransplant complications are produced such as dialysis and the altered anatomy of the urogenital tract.^[2,3]

The main cause of mortality and morbidity in kidney transplant recipients is bacterial infection.^[4] Urinary

Acces	s this article online
Quick Response Code:	Website: www.jmsjournal.net
	DOI: 10.4103/jrms.JRMS_286_18

tract infection (UTI) is mainly a common infection in kidney transplant recipients.^[5,6] In original, bacteriuria categorizes into two types: asymptomatic bacteriuria (ASB) and symptomatic UTI.^[7] ASB is defined as the growth of bacteria with >10⁵ CFU/mL, wherein the patients do not have any symptoms of infection.^[8] Based on recent reports, treatment of ASB might not be required and there was no adverse side effect on transplant outcomes.

UTI is defined by the overgrowth of bacteria >10⁵ CFU/mL from patients' urine samples alongside with symptoms including dysuria, suprapubic, flank or allograft

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

Address for correspondence: Mr. Hui Gao, Department of Infectious Disease, Hainan General Hospital, Haikou, Hainan 570311, China. E-mail: ghiyou@126.com

Submitted: 29-Apr-2018; Revised: 05-May-2020; Accepted: 25-Oct-2020; Published: 31-Mar-

pain, fever, or chills.^[8] There are a lot of risk factors for susceptibility to UTI such as acute rejection, female sex, older age, longer durations with a urinary catheter, episodes, and receiving a kidney from a deceased donor.^[9]

Organisms that cause UTI post renal transplantation are bacterial, fungal, viral, parasitic, or mycoplasmal.^[10] The order of bacterial UTI pathogens in transplant recipients is comparable to that in the nontransplantation population; Gram-negative bacteria are responsible for over 70% of UTI cases.^[11,12] The high frequent bacterial agents causing UTI are *Escherichia coli*, *K. pneumoniae*, *Enterococcus* sp., *Enterobacter*, *Pseudomonas aeruginosa*, and *Proteus mirabilis*.^[13,14]

In some cases, microorganisms that are not problematic in immunocompromised patients have been involved in posttransplantation UTI.^[15] This possibly due to immunosuppressant drugs used in these patients, which accelerates bacterial–urothelial adherence.^[16] Hence, resistant bacterial strains can cause the problem to patients.^[17]

UTI via the inflammatory cytokine response, free-radical production, CMV reactivation, precipitation of rejection, and pyelonephritis-induced renal scarring can impair graft function.^[15] It is debatable that how much UTI can affect transplant function and patient survival. However, many retrospective studies have found no significant association between UTI, transplantation, and patient survival.^[18]

Concerning the importance of bacterial UTI in renal transplant recipients, and increasing their antibiotic resistance, this study decided to evaluate UTI, bacterial agents, and antibiotic resistance pattern in renal transplant recipients from Iran through systematic review and meta-analysis.

MATERIALS AND METHODS

Strategy search

Prisma protocol (PRISMA, http://www.prisma-statement. org) was used for searching UTI, the prevalence of microorganisms, and antibiotic resistance pattern in kidney transplant recipients from Iran in both international and national online electronic databases such as Scopus, PubMed, Cochrane Library, Web of Sciences, Iranmedex (www. iranmedex.com), Magiran (www.magiran.com), and Scientific Information Database (www.sid.ir). Mesh terms and text words were urinary tract infection, UTI, kidney transplant, renal transplant, post kidney transplant, antimicrobial drug resistance, and antibiotic resistance pattern. Published studies were searched without time limitation until May 31, 2020.

Inclusion and exclusion criteria

Cross-sectional, cohort, and case–control studies addressing the prevalence of UTI, bacterial pathogens, and antibiotic resistance pattern in renal transplant recipients were enrolled in the current systematic review and meta-analysis. Different types of review articles (systematic, narrative review, and met-analysis), studies with missed data, conferences, meetings, abstracts, and studies published in languages other than English or Persian were excluded. Studies introduced other than kidney transplants were excluded from the study. Of note, two reviewers conducted searches independently.

Assessment of selection bias and quality of selected studies

To achieve this purpose, the criteria given in Critical Appraisal Skills Programmed checklists (www.casp-UK) were used. Hence, 10 questions were asked and if the answer was yes, one point would be considered, and if the answer was no, or if there was any doubt, the score would be 0. At the end, according to the scoring system, strong studies scored above 8, average studies between 5 and 8, and weak studies obtained scores below 4 (file 1).

Data extraction

By use of extract forms, the following data extracted: the first author's name, time of the study, publication year, settings, sample size, prevalence of UTI, Genus, and mean age.

Statistical analysis

Comprehensive meta-analysis software was used for data analysis. The prevalence of UTI, antibiotic resistance, and bacterial agents was calculated by 95% confidence intervals. Due to the existence of heterogeneity among studies, a random effects model was used. I^2 and the Q-statistic tests were used for the assessment of heterogeneity among studies included in the present review. P < 0.05 of Q-test and I² test >50% was considered statistically significant.

In this study, we evaluated the publication bias visually through the Funnel plot. If the distribution of articles is evenly placed inside the funnel, it indicates that there is no publication bias, and if they placed outside the funnel or there is a heterogeneous and unbalanced distribution inside the funnel, it indicates the presence of bias in the study publication. In addition to the Funnel plot, the statistical Egger's linear regression test was used to further investigate publication bias. According to this test, if the *P* <

RESULTS

Selection study and features

The selection process is shown in Figure 1. Totally, 819 articles potentially were identified, 18 out of which met inclusion criteria for enrollment in the present systematic review and meta-analysis. Most studies were from Tehran (N = 7), followed by Mashhad (N = 4). Patients had mean age of 5–87 years [Table 1]. Most studies had cross-sectional design and 2 studies were case control.

Overall effects

According to the findings obtained from the systematic review and meta-analysis which are shown in Figure 2 and Table 2, the combined prevalence of UTI in renal transplant recipients was reported by 31.1% (95% Cl: 24.1–39.1), Z = 4.4, Q = 538, $I^2 = 96.8$.

Publication bias

Regarding the Funnel plot [Figure 3], because there was a heterogeneous and unbalanced distribution inside the funnel, and studies placed outside the funnel, it indicated the presence of bias in the publication. To further evaluation, the statistical Egger's Linear Regression Test was used; however, the findings showed no publication bias in the studies included, because P = 0.29 [Table 2].

Subgroup analysis for Gram-negative bacteria

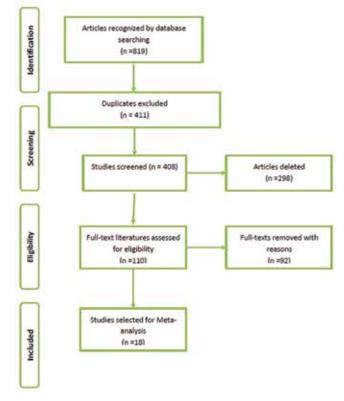
As listed in Table 2, subgroup analysis showed that the combined prevalence of Gram-negative bacteria was 69% (95% CI: 23.6–99.5), Z = 11, Q = 201 and $I^2 = 94$. The most common pathogens among Gram negatives were *E. coli* followed by *K. pneumoniae* with frequency 43.4% (95% CI: 38.4–50.1), and 13% (95% CI: 7–19.9), respectively. Furthermore, the least rate belonged to *Acinetobacter baumannii* with a prevalence of 3% (95% CI: 1.4–5.8).

Subgroup analysis for Gram-positive bacteria

Subgroup analysis for Gram-positive bacteria showed the combined prevalence of 31% (95% Cl: 12.2–48.4), Z = 5.7, Q = 65.1 and $I^2 = 90.8$. The highest predominant microorganism among Gram positives belonged to coagulase-negative *staphylococci* (CoNS) and Enterococci with a prevalence of 10.2% (95% Cl: 5.4–18.2) and 9% (95% Cl: 4-3.9), respectively.

Subgroup analysis for antibiotic resistance

Subgroup meta-analysis of antibiotic resistance for Gram-negative bacteria showed the most resistance to cephalexin followed by carbenicillin and ceftazidime with the prevalence of 89.1% (58.8, 102), 87.3% (58.8, 99.3), and 86.3% (47.4, 88.6), respectively. The least resistance was observed against imipenem with a resistance rate of 13% [Table 3]. Furthermore, based on the data summarized





in Table 4, the highest resistance of Gram-positive bacteria reported against amoxicillin and cephalexin with a resistance rate of 79% (38.1,96) and 74% (33.4,98.91), respectively. The effective antibiotic for treatment of Gram-positive bacteria was reported Polymyxin B (10.6%). Findings of antibiotic resistance for *E. coli* in Table 5 showed the highest resistance against cotrimoxazole and nalidixic acid with a resistance rate of 74.1% and 70%, respectively. As well, the best antibiotics for treatment of UTI caused by *E. coli* were reported imipenem and nitrofurantoin with resistance rates of 13.2% and 19%, respectively.

DISCUSSION

In total, UTI is considered as the most common infection and the most possible site of infection that leads to hospitalization of patients with kidney transplantation.^[20] The prevalence of UTI in kidney transplant recipients is similar in both developed and developing countries.^[5] The prevalence of posttransplant UTI in the kidney transplant recipients varies between 12% and 75%.^[21] Of course, in developing countries, this rate may be higher due to epidemiological exposure and lower standards of hygiene.^[22] A meta-analysis conducted in 2016 showed that the USA had a significantly higher prevalence of UTIs than European countries (41% vs. 33%).^[9]

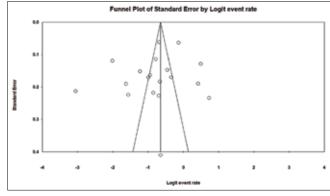
In the present systematic review and meta-analysis, the combined prevalence of UTI in renal transplant recipients was reported by 31.1%. The combined prevalence of Gram-negative bacteria was 69%. The most common pathogens among Gram negatives were *E. coli* followed by *K. pneumoniae* with frequency 43.4% and 13%, respectively. Furthermore, the least rate belonged to *A. baumannii* with prevalence of 3%. Furthermore, subgroup analysis for Gram-positive bacteria showed the combined prevalence of 31%. The highest predominant microorganism among Gram-positives belonged to CoNS and Enterococci with prevalence 10.2% and 9%, respectively.

The prevalence in Iranian studies included in the current review varied from 4.5% to 67.5%. Our result (31.1% UTI's

Study name		Statist	ics for ea	ach study			Eventra	ste an	d 95% CI	
	Event rate	Lower limit	Upper limit	Z-Value	p-Value					
Khosravi	0.336	0.309	0.363	-11.006	0.000	- T	1	1		1
Samanipour	0.603	0.512	0.688	2.212	0.027					
Shirazi	0.333	0.243	0.438	-3.048	0.002				-	
Khosroushahi	0.300	0.218	0.397	-3.883	0.000				-	
Pourmand G	0.415	0.337	0.498	-2.004	0.045					
Zeighami	0.281	0.221	0.350	-5.742	0.000					
Pourmand	0.272	0.211	0.343	-5.770	0.000					
Alimagham	0.621	0.560	0.678	3.836	0.000					
Ghanati	0.165	0.120	0.223	-8.512	0.000					
Shams	0.227	0.179	0.283	-8.074	0.000					
Mansury	0.315	0.268	0.365	-6.822	0.000					
Bahrami	0.389	0.322	0.459	-3.069	0.002					
Akbarzadeh	0.045	0.030	0.067	-14.286	0.000					
Nazemian	0.675	0.567	0.767	3.114	0.002				-	- L
Fallahzadeh	0.174	0.119	0.246	-6.938	0.000			- 11		- L
Pouladfar	0.118	0.096	0.145	-16.866	0.000					
Ghelichi	0.466	0.435	0.497	-2.127	0.033			17		
Esmaeili	0.341	0.265	0.426	-3.590	0.000				H	
	0.311	0.241	0.391	-4.436	0.000				•	
						-1.00	-0.50	0.00	0.50	1.00
							Favours A		Favours B	

prevalence) was in line with our studies conducted in other parts of the world such as Turkey,^[22] Pakistan,^[23] Australia,^[24] and the USA.^[25] Similar findings in other studies support the concept that UTI still is the most predominant infection postrenal transplantation.^[24] The difference in the prevalence of UTI (4.5%–67.5%) in studies included in the present review and other studies from worldwide likely attributed to differences in the definition of UTI, the interval of follow-up, antibiotic prophylaxis used posttransplantation, and inherent differences of the person features among diverse countries.^[9]

Similar to our study, others reported the Gram-negative bacteria as the most common organisms isolated from UTI samples of both the nontransplant and transplant



Figure

Figure 2: Forest plot of the meta-analysis on prevalence of urinary tract infection among kidney transplant recipients in Iran

Table 1: Characteristics of enrolled studies for this systematic and meta-analysis

Study	Time of study	Publication	Location	Sample size	UTI prevalence	Gender (%)		Mean age
						Female	Male	
Khosravi <i>et al</i> . ^[44]	2009-2012	2014	Golestan and Ahvaz	1165	391	34.8	65.2	39.6±2
Samanipour et al. ^[45]	2013-2014	2015	Tehran	116	70	30	70	41.3±13.3
Shirazi <i>et al</i> .[46]	1991-1996	2005	Tehran	87	29	34.4	65.6	-
Mortazavi et al.[47]	1993-2000	2003	Tabriz	100	30	-	-	-
Pourmand et al. [48]	2002-2004	2006	Tehran	142	59	-	-	41±14.47
Zeighami <i>et al</i> . ^[49]	-	2008	Tehran	185	52	-	-	-
Pourmand et al.[50]	2011-2012	2012	Tehran	173	47	39.3	61.7	40.8±14
Alimagham <i>et al.</i> ^[51]	1993-1997	2002	Tehran	256	159	30	70	20-70
Kian Ghanati <i>et al</i> . ^[52]	2009-2010	2012	Tehran	200	33	-	-	10-70
Shams et al.[33]	2012-2014	2016	Mashhad	247	56	40.8	59.2	34.9±13.8
Mansury et al.[53]	2013-2015	2017	Mashhad	356	112	42.1	57.9	-
Bahrami <i>et al</i> . ^[54]	2013-15	2017	Iran	193	75	-	-	34.4±12.2
Sorkhi <i>et al</i> . ^[55]	1999-2008	2016	Iran	508	23	36.3	63.7	43.3±13
Nazemian et al.[56]	1998-2002	2007	Mashhad	83	56	24	76	50-66
Fallahzadeh et al.[57]	1990-2008	2011	Shiraz	138	24	42.7	57.3	13.6±3.5
Pouladfar et al.[58]	2012-2013	2015	Shiraz	676	80	50	50	5-87
Ghelichi et al.[59]	2001-2011	2018	Iran	991	462	39.8	60.2	-
Esmaeili and Mansour ^[60]	2009-2010	2013	Hamadan	132	45	48.5	51.5	-

UTI=Urinary tract infection

Zhang,	et al.:	Bacterial	UTI	in	kidney	transp	lant	recipients
--------	---------	-----------	-----	----	--------	--------	------	------------

Subgroups	Number of study	Random mo	Random model				Egger's test		
		Bacteria prevalence (95% CI) (%)	Ζ	Р	Р	Q	P	t	Р
Overall effects (UTI)	18	31.1 (24.1-39.1)	4.4	0.00	0.00	538	96.8	1	0.29
Gram-negative	17	69 (23.6-99.5)	11	0.01	0.001	201	94	0.32	0.002
Gram-positive	16	31 (12.2-48.4)	5.7	0.00	0.00	65.1	90.8	1.2	0.35
Escherichia coli	18	43.4 (38.4-50.1)	3	0.00	0.001	38.1	90.1	0.2	0.11
Entrobacter spp.	8	5.4 (2.2-12.9)	5.8	0.00	45.2	0.00	84.5	5	0.002
Klebsiella	14	13 (7-19.9)	5.3	0.00	0.00	29	78.2	3.6	0.034
Coagulase negative staph	13	10.2 (5.4-18.2)	8.8	0.001	0.00	111	81	0.00	0.13
Staphylococcus aureus	12	5.8 (2.7-13.1)	8.1	0.000	0.000	12	63	1	0.91
Pseudomonas aeruginosa	13	11.3 (7.9-15.8)	12.1	0.011	0.06	16.5	55.2	4	0.03
Streptococcus	12	6 (2.7-17.7)	6.2	0.23	0.01	44.8	92	1.9	0.19
Acinetobacter	10	3 (1.4-5.8)	13.3	0.00	0.08	11.2	60.4	1.5	0.16
Enterococcus spp.	15	9 (4-3.9)	7.1	0.00	0.001	88	98	1.3	0.002

Table 3: Subgroup meta-analysis of antibiotic resistance pattern for Gram-negative bacteria Subgroups Number of study **Random model** Heterogeneity test Egger's test Ρ ß Р z P Q Resistance rate (95% CI) (%) t Amikacin 11 39 (33.4-40.5) 5.5 0.00 0.32 5.8 92 2.1 0.44 Amoxicillin 11 76 (43.12.-91.7) 2.2 0.01 0.03 5.2 87 11 0.00 Tobramycin 75.1 (34.9-111.2) 0.002 23 0.35 10 1.8 0.11 56 0.43 53 (14.2-61.9) 0.00 72 Kanamycin 10 13 0.07 8.1 1.7 0.46 Erythromycin 10 80.1 (46.8-88.2) 6.1 0.00 0.00 12.1 76 2.4 0.003 Nitrofurantoin 12 41 (28.2-58.2) 1.4 0.00 0.00 72.1 99 0.03 0.5 15 72 (54.3-91.1) 3.3 0.013 0.00 32.1 84 3.7 0.01 Cotrimoxazole 58.2 (52.1-69.6) 4 0.054 0.00 8.3 27.3 0.34 0.33 Cephalotin 13 Gentamicin 13 48 (41-56.8) 0.21 0.00 0.18 17.3 55 0.1 0.26 70.1 (55-95.2) 0.00 0.001 14 72 0.5 Ceftriaxon 10 4.6 0.1 Pipracillin 47.2 (14.9-77.2) 19 10 1.4 0.9 0.00 82.1 0.00 0.0.16 Imipenem 10 13 (4.1-30.2) 1.1 0.00 0.00 32 84 0.3 0.002 0.00 12 77 0.39 Ceftazidime 10 86.3 (47.4-88.6) 0.03 1 1 Nalidixic acid 15 45.3 (9.3,71) 0.7 0.00 0.001 38 85 0.8 0.21 Cefixime 56 (40.3-99) 1.1 0.05 0.001 11.5 81 10 0.3 1 Ciprofloxacin 16 57 (31-72) 0.32 0.6 0.00 43 62 4.2 0.11 Chloramphenicol 13 39.7 (30.4-48.8) 1.7 0.28 0.08 17 47 0.30 0.7 Polymyxin B 10 43.2 (11.2-81.8) 0.00 0.13 0.00 18 82.2 0.00 0.77 Cephalexin 10 89.1 (58.8-102) 8 0.00 0.00 23 80.2 2.5 0.002 Carbenicillin 10 87.3 (58.8-99.3) 8 0.00 0.88 0.33 85.8 1.5 0.004

CI=Confidence interval

patients with the prevalence of 90%.^[10,24] We reported *E. coli* followed by *K. pneumonia* as the most prevalent Gram-negative bacteria, as other reports confirm it.^[26] In line to our study, a study conducted by Senger *et al.* in 2003, *Enterococcus, Staphylococcus,* and *Streptococcus* reported as the highest frequent bacteria.^[26] Similarly, Al Midani *et al.* from the UK,^[27] Camargo *et al.* from Brazil,^[28] Bodro *et al.* from Spain,^[29] reported *E. coli* and *K. pneumonia* as the most frequent Gram-negative bacteria. As well, Ediriweera *et al.* from Sri Lanka reported CoNS as the most Gram+,^[30] Wang *et al.* from Taiwan,^[31] Chuang *et al.* from the USA reported Enterococcus species as the most common Gram-positive bacteria recovered from UTI samples of kidney transplant

recipients.^[32] All studies mentioned are inconsistent with our findings.

Several studies have confirmed that UTI is related to transplant function failure, particularly in the early posttransplant episode,^[6,29,33] but others have not reported such association,^[34-36] Additionally, another one found no profit of antibiotic prophylaxis on transplant function in the first 6 months post transplantation.^[37] Recently, some studies have shown a rising prevalence of infections caused by Multi-drug-resistant (MDR) strains in both immunocompetent and immunocompromised patients. As several reports presented a high rate of infections are

Subgroups	Number of study	Random model			Heteroge	neity test	E	Egger's test		
		Resistance rate (95% CI) (%)	Ζ	Р	Р	Q	P	t	Р	
Amikacin	11	68 (42.9-83.8)	1.1	0.00	0.00	2	67	0.1	0.22	
Nitrofurantoin	11	29.8 (11-78.1)	0.00	0.32	0.2	31	62	0.00	0.4	
Erythromycin	10	69 (41-90)	1.7	0.16	0.9	0.5	25	0.76	0.1	
Kanamycin	10	73 (43.2-87.8)	1.76	0.17	0.4	12	17	0.58	0.11	
Cotrimoxazole	11	44.9 (24.1-65.5)	0.32	0.88	0.4	1.5	0.00	0.66	0.36	
Gentamicin	12	65.9 (38.6-75)	11	0.00	0.11	6	78	1.1	0.31	
Amoxicillin	11	79 (38.1-96)	1.4	1	0.8	2.8	76	1.4	0.21	
Tobramycin	10	62.2 (41.1-80.6)	0.00	0.00	0.01	1	98	0.6	0.5	
Cephalexin	10	78 (50-91.2)	1.4	0.01	0.23	0.1	82	4.1	0.37	
Carbenicillin	10	74 (33.4-98.91)	0.3	0.001	3.12	0.14	72	0.01	0.43	
Chloramphenicol	11	65 (48.6-69.1)	1.2	0.72	0.5	1.6	83	0.01	0.21	
Kanamycin	10	70.6 (41.8-88.4)	0.54	0.10	0.00	0.40	74	0.8	0.15	
Nalidixic acid	11	47.6 (27.1-86)	0.23	0.00	0.00	0.71	59	4.4	0.12	
Tetracycline	11	46.6 (6.17-90.3)	0.03	0.00	0.01	0.2	70.2	3.3	0.01	
Polymyxin B	10	10.6 (4.3-33.6)	2.9	0.01	0.02	0.01	64	5.7	0.001	

 Table 5: Subgroup meta-analysis of antibiotic resistance for Escherichia coli isolates

Subgroups	Number of study	Random mode	Heteroge	neity test	Egger's test				
		Resistance rate (95% CI) (%)	Ζ	Ρ	Р	Q	ľ	t	Р
Nalidixic acid	11	70 (38.4-83.2)	3.2	0.00	0.00	36	85	1	0.6
Amikacin	10	37.4 (29.8.52.3)	3.3	0.05	0.17	11	45	0.73	0.00
Imipenem	12	13.2 (4.1-32.2)	1.1	0.00	30.1	15	63	2.6	0.04
Cephalotin	9	61.6 (58.6-80)	4.5	0.00	0.00	0.01	87	3.5	0.001
Ciprofloxacin	12	59.4 (22.6-85)	0.51	0.59	65.1	0.01	94	7.1	0.39
Tetracycline	11	63 (20-88.3)	0.91	0.73	0.00	32.8	92.1	3	0.22
Gentamicin	13	55 (57.1-57.9)	0.89	0.12	0.00	14	73	0.00	0.01
Nitrofurantoin	11	19 (17.8-60)	14	0.00	0.40	7.1	0.00	2.8	0.00
Cotrimoxazole	13	74.1 (66.3-81.7)	4.2	0.09	0.00	22	59	0.4	0.01
Nalidixic acid	11	68 (33.4-991)	3.2	0.20	0.00	15	83	1	0.23
Chloramphenicol	10	42.4 (22.5-67.1)	0.5	0.10	0.11	173	83	0.03	0.24

CI=Confidence interval

produced by MDR organisms in solid organ recipients, ranging from 6.5% to 56%.^[38-41]

In the present review, subgroup meta-analysis of antibiotic resistance for Gram-negative microorganisms showed the most resistance to cephalexin followed by Carbenicillin and Ceftazidime with the prevalence of 89.1%, 87.3%, and 86.3%, respectively. The least resistance was observed against Imipenem with resistance rate of 13%. Furthermore, the highest resistance of Gram-positive bacteria reported against amoxicillin and cephalexin with resistance rate of 79% and 74%, respectively. The effective antibiotic for the treatment of Gram-positive bacteria was reported Polymyxin B (10.6%). Findings of antibiotic resistance for E. coli showed the highest resistance against Cotrimoxazole and Nalidixic acid with resistance rate of 74.1% and 70%, respectively. As well, the best antibiotic for treatment of UTI caused by E. coli was reported Imipenem and Nitrofurantoin with resistance rate of 13.2% and 19%, respectively.

To our knowledge, ampicillin or amoxicillin were used as the standard treatment for UTI, but various studies from around the world show increased resistance to ampicillin and oxacillin.^[42,43] In agreement with their results, our results showed high resistance against oxacillin in both Gram-negative (76%) and Gram-positive microorganisms (79%), respectively.

Taking into account all these considerations, renal transplant recipients are at high risk for infections caused by MDR strains owing to surgical procedure, long stay in intensive care unit, having underlying diseases, and immunocomponent conditions.^[41] Therefore, infection control measures have a positive impact on the prevention of UTI after renal transplantation.

Finally, findings from this systematic review and meta-analysis showed that the best antibiotics against Gram-negative bacteria were imipenem. Polymyxin B was an effective antibiotic against Gram-positive microorganisms; also, imipenem and nitrofurantoin can be used as the first and second-line treatments of pathogenic *E. coli* isolated from UTI in kidney transplant recipients.

CONCLUSIONS

Our systematic review and meta-analysis by combining data from previously published studies in Iran showed a noticeable rate of UTI (31.1%) among renal transplant recipients. As well as, a high prevalence of Gram-negative (69%) and Gram-positive (13%) microorganisms was observed, where *E. coli* (43.4%) and CoNS (10.2%) were the most among Gram-negative and Gram-positive bacteria, respectively. A high resistance rate was seen against almost all antibiotics used for the treatment of UTI caused by both Gram-negative and Gram-positive bacteria, too. Hence, arbitrary and long-term treatment and empirical prescription should be avoided. Therefore, the antibiotics prescription should be based on data achieved from antibiotic susceptibility tests.

Acknowledgments

We would like to thank our colleagues for their help in this study.

Financial support and sponsorship Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- 1. Pascual M, Theruvath T, Kawai T, Tolkoff-Rubin N, Cosimi AB. Strategies to improve long-term outcomes after renal transplantation. N Engl J Med 2002;346:580-90.
- Hartono C, Dadhania D, Suthanthiran M. Noninvasive diagnosis of acute rejection of solid organ transplants. Front Biosci 2004;9:145-53.
- 3. Hollyer I, Ison MG. The challenge of urinary tract infections in renal transplant recipients. Transpl Infect Dis 2018;20:e12828.
- Kinnunen S, Karhapää P, Juutilainen A, Finne P, Helanterä I. Secular trends in infection-related mortality after kidney transplantation. Clin J Am Soc Nephrol 2018;13:755-62.
- Mihankhah A, Khoshbakht R, Raeisi M, Raeisi V. Prevalence and antibiotic resistance pattern of bacteria isolated from urinary tract infections in Northern Iran. J Res Med Sci 2017;22:108.
- 6. Nickavar A, Sotoudeh K. Treatment and prophylaxis in pediatric urinary tract infection. Int J Prev Med 2011;2:4-9.
- Fernández-Ruiz M, López-Medrano F, Romo EM, Allende LM, Meneu JC, Fundora-Suárez Y, *et al.* Pretransplant lymphocyte count predicts the incidence of infection during the first two years after liver transplantation. Liver Transpl 2009;15:1209-16.
- Parasuraman R, Julian K, AST Infectious Diseases Community of Practice. Urinary tract infections in solid organ transplantation. Am J Transplant 2013;13 Suppl 4:327-36.
- 9. Wu X, Dong Y, Liu Y, Li Y, Sun Y, Wang J, *et al*. The prevalence and predictive factors of urinary tract infection in patients undergoing renal transplantation: A meta-analysis. Am J Infect Control

2016;44:1261-8.

- Valera B, Gentil MA, Cabello V, Fijo J, Cordero E, Cisneros JM. Epidemiology of urinary infections in renal transplant recipients. Transplant Proc 2006;38:2414-5.
- Burgos Revilla FJ, Pascual Santos J, Marcén Letosa R, Gómez Do Santos V, Sánchez-Encinas M, Escudero Barrilero A. [Renal transplantation and urinary infection. Review]. Actas Urol Esp 1999;23:95-104.
- 12. Pelle G, Vimont S, Levy P, Hertig A, Ouali N, Chassin C, *et al.* Acute pyelonephritis represents a risk factor impairing long-term kidney graft function. Am J Trans 2007;4:899-907.
- Gozdowska J, Czerwińska M, Młynarczyk G, Kwiatkowski A, Chmura A, Durlik M, editors. Urinary Tract Infections in Kidney Transplant Recipients Hospitalized at a Transplantation and Nephrology Ward: 1-Year Follow-up. Transplantation Proceedings. Elsevier; 2016.
- 14. de Souza RM, Olsburgh J. Urinary tract infection in the renal transplant patient. Nat Clin Pract Nephrol 2008;4:252-64.
- Goya N, Tanabe K, Iguchi Y, Oshima T, Yagisawa T, Toma H, *et al.* Prevalence of urinary tract infection during outpatient follow-up after renal transplantation. Infection 1997;25:101-5.
- 16. Dadhania D, Muthukumar T, Ding R, Li B, Hartono C, Serur D, *et al.* Molecular signatures of urinary cells distinguish acute rejection of renal allografts from urinary tract infection. Transplantation 2003;75:1752-4.
- 17. John U, Everding AS, Kuwertz-Bröking E, Bulla M, Müller-Wiefel DE, Misselwitz J, *et al.* High prevalence of febrile urinary tract infections after paediatric renal transplantation. Nephrol Dial Transplant 2006;21:3269-74.
- Lyerová L, Lácha J, Skibová J, Teplan V, Vítko S, Schück O. Urinary tract infection in patients with urological complications after renal transplantation with respect to long-term function and allograft survival. Ann Transplant 2001;6:19-20.
- Ahmed I, Sutton AJ, Riley RD. Assessment of publication bias, selection bias, and unavailable data in meta-analyses using individual participant data: A database survey. BMJ 2012;344:d7762.
- 20. Abeysekera N, Graver A, Cooley L, Kirkland G, Jose MD. Infectious complications in the Southern Tasmanian kidney transplant population. Nephrology (Carlton) 2019;24:849-54.
- Aydın S, Patil A, Desai M, Simforoosh N. Five compelling UTI questions after kidney transplant. World J Urol 2020;38:2733–42.
- 22. Yalci A, Celebi Z, Ozbas B, Sengezer O, Unal H, Memikoğlu K, *et al.*, editors. Evaluation of Infectious Complications in the First Year after Kidney Transplantation. Transplantation proceedings: Elsevier; 2015.
- 23. Shohab D, Khawaja A, Atif E, Jamil I, Ali I, Akhter S. Frequency of occurrence of urinary tract infection in double j stented versus non-stented renal transplant recipients. Saudi J Kidney Dis Transpl 2015;26:443-6.
- 24. Olenski S, Scuderi C, Choo A, Bhagat Singh AK, Way M, Jeyaseelan L, *et al*. Urinary tract infections in renal transplant recipients at a quaternary care centre in Australia. BMC Nephrol 2019;20:479.
- 25. Naik AS, Dharnidharka VR, Schnitzler MA, Brennan DC, Segev DL, Axelrod D, *et al.* Clinical and economic consequences of first-year urinary tract infections, sepsis, and pneumonia in contemporary kidney transplantation practice. Trans Int 2016;2:241-52.
- Senger S, Arslan H, Azap Ö, Timurkaynak F, Çağır Ü, Haberal M, editors. Urinary Tract Infections in Renal Transplant Recipients. Transplantation Proceedings: Elsevier; 2007.
- 27. Al Midani A, Elands S, Collier S, Harber M, Shendi A, editors. Impact of Urinary Tract Infections in Kidney Transplant Recipients: A

Proceedings: Elsevier; 2018.

- Camargo LF, Esteves AB, Ulisses LR, Rivelli GG, Mazzali M. Urinary tract infection in renal transplant recipients: Incidence, risk factors, and impact on graft function. Transplant Proc 2014;46:1757-9.
- Bodro M, Sanclemente G, Lipperheide I, Allali M, Marco F, Bosch J, et al. Impact of urinary tract infections on short-term kidney graft outcome. Clin Microbiol Inf 2015;12:1104, e1-8.
- Ediriweera DS, Kasturiratne A, Pathmeswaran A, Gunawardena NK, Wijayawickrama BA, Jayamanne SF, et al. Mapping the risk of snakebite in Sri Lanka A national survey with geospatial analysis. PLoS Negl Trop Dis 2016;10:e0004813.
- 31. Wang KJ, Hong WC. Competitive advantage analysis and strategy formulation of airport city development-the case of Taiwan. Trans Policy 2011;1:276-88.
- 32. Chuang P, Parikh CR, Langone A. Urinary tract infections after renal transplantation: A retrospective review at two US transplant centers. Clin Transplant 2005;19:230-5.
- 33. Shams SF, Eidgahi ES, Lotfi Z, Khaledi A, Shakeri S, Sheikhi M, et al. Urinary tract infections in kidney transplant recipients 1st year after transplantation. J Res Med Sci 2017;22:20.
- 34. Papasotiriou M, Savvidaki E, Kalliakmani P, Papachristou E, Marangos M, Fokaefs E, *et al.* Predisposing factors to the development of urinary tract infections in renal transplant recipients and the impact on the long-term graft function. Ren Fail 2011;33:405-10.
- 35. Origüen J, Fernández-Ruiz M, López-Medrano F, Ruiz-Merlo T, González E, Morales JM, *et al.* Progressive increase of resistance in Enterobacteriaceae urinary isolates from kidney transplant recipients over the past decade: Narrowing of the therapeutic options. Transpl Infect Dis 2016;18:575-84.
- Koch M, Kohnle M, Trapp R, Haastert B, Rump LC, Aker S. Comparable outcome of acute unplanned peritoneal dialysis and haemodialysis. Nephrol Dial Transplant 2012;27:375-80.
- Green H, Rahamimov R, Gafter U, Leibovitci L, Paul M. Antibiotic prophylaxis for urinary tract infections in renal transplant recipients: A systematic review and meta-analysis. Trans Inf Dis 2011;5:441-7.
- Bodro M, Sabé N, Tubau F, Lladó L, Baliellas C, Roca J, *et al.* Risk factors and outcomes of bacteremia caused by drug-resistant ESKAPE pathogens in solid-organ transplant recipients. Transplantation 2013;96:843-9.
- 39. Reddy P, Zembower T, Ison M, Baker T, Stosor V. Carbapenemresistant *Acinetobacter baumannii* infections after organ transplantation. Trans Inf Dis 2010;1:87-93.
- 40. de Gouvêa EF, Martins IS, Halpern M, Ferreira AL, Basto ST, Gonçalves RT, *et al.* The influence of carbapenem resistance on mortality in solid organ transplant recipients with *Acinetobacter baumannii* infection. BMC Infect Dis 2012;12:351.
- 41. Garzoni C, Vergidis P, AST Infectious Diseases Community of Practice. Methicillin-resistant, vancomycin-intermediate and vancomycin-resistant *Staphylococcus aureus* infections in solid organ transplantation. Am J Transplant 2013;13 Suppl 4:50-8.
- Dromigny JA, Nabeth P, Juergens-Behr A, Perrier-Gros-Claude JD. Risk factors for antibiotic-resistant *Escherichia coli* isolated from community-acquired urinary tract infections in Dakar, Senegal. J Antimicrob Chemother 2005;56:236-9.
- 43. Randrianirina F, Soares JL, Carod JF, Ratsima E, Thonnier V, Combe P, *et al*. Antimicrobial resistance among uropathogens that cause community-acquired urinary tract infections

in Antananarivo, Madagascar. J Antimicrob Chemother 2007;59:309-12.

- 44. Khosravi AD, Abasi Montazeri E, Ghorbani A, Parhizgari N. Bacterial urinary tract infection in renal transplant recipients and their antibiotic resistance pattern: A four-year study. Iran J Microbiol 2014;6:74-8.
- 45. Samanipour A, Dashti-Khavidaki S, Abbasi MR, Abdollahi A. Antibiotic resistance patterns of microorganisms isolated from nephrology and kidney transplant wards of a referral academic hospital. J Res Pharm Pract 2016;5:43-51.
- 46. Shirazi M, Ranjbar R, Hemati F, Sadeghifard N. Bacterial infections in renal transplant recipients. Iran J Public Health 2005;3:62-6.
- Mortazavi KM, Koushavar H. Prevalence of Urinary Tract Infections During Outpatient Follow-up after Kidney Transplantation; 2003.
- Pourmand G, Pourmand M, Salem S, Mehrsai A, Taheri Mahmoudi M, Nikoobakht M, et al. Posttransplant infectious complications: A prospective study on 142 kidney allograft recipients. Urol J 2006;3:23-31.
- 49. Zeighami H. Urinary tract infections in renal transplantation patient. Res J Biol Sci 2008;40:1194-6.
- Pourmand M, Keshtvarz M, Talebi M, Mashhadi R. Incidence of Recurrent Urinary Tract Infection after Renal Transplantation. J Med Bacteriol 2015;1-2:27-34.
- 51. Aalimagham M, Pourfarziani V, Hosseini M, Mahfouzi L. Incidence of infections in renal transplant recipients after transplantation. Kowsar Med J 2003;4:309-12.
- 52. Kian Ghanati FF, Hosseini Moghaddam M, Latif Gachkar AK, Adabian S, Sajadini RS. Analysis of genetic determinants involved in antibiotic resistance in clinical strains isolated from urine samples of renal transplantation recipients. Int J Curr Res 2012;4:139-43.
- Mansury D, Khaledi A, Ghazvini K, Sabbagh MG, Zare H, Rokni-Hosseini MH, et al. Study of Bacterial Infections Among Patients Receiving Kidney Transplant in Mashhad, Iran. Exp Clin Transplant 2018;16:282-6.
- Bahrami A, Shams SF, Eidgahi ES, Lotfi Z, Sheikhi M, Shakeri S. Epidemiology of Infectious Complications in Renal Allograft Recipients in the First Year After Transplant. Exp Clin Transplant 2017;15:631-5.
- Sorkhi H, Oliaei F, Rajabpoor MM, Taghavi M. Comparison of urinary tract infection after kidney transplantation between adult and children. Caspian J Pediat 2016;1:96-9.
- Nazemian F, Naghibi M, Farazi E. Kidney transplantation in elderly Iranian patients. Saudi J Kidney Dis Transpl 2007;18:391-6.
- 57. Fallahzadeh MK, Fallahzadeh MH, Derakhshan A, Basiratnia M, Hoseini Al-Hashemi G, Fallahzadeh MA, *et al.* Urinary tract infection after kidney transplantation in children and adolescents. Iran J Kidney Dis 2011;5:416-9.
- Pouladfar G, Jafarpour Z, Hosseini SA, Janghorban P, Roozbeh J. Antibiotic selective pressure and development of bacterial resistance detected in bacteriuria following kidney transplantation. Transplant Proc 2015;47:1131-5.
- 59. Ghojogh MG, Salarilak S, Afshari AT, Khalkhali HR, Mohammadi-Fallah MR, Makhdoomi K. The effect of urinary tract infection on patient and graft survival rate in a group of kidney transplanted patients. J Renal Injury Prevent 2018; 4:292-6.
- 60. Esmaeili RA, Mansour N. Comparison of the frequency of bacterial infections before and after kidney transplantation. Lab Med J 2013;5:252-