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Original article

Antibiotics utilization patterns and dosage appropriateness among patients receiving hemodialysis

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ABSTRACT

Chronic kidney disease (CKD) is a global health challenge, with a reported prevalence of around 10%. Prescribing for patients receiving hemodialysis (HD) is challenging and complicated by polypharmacy, comorbidities, and changes in clearance of medications. The aim of this study was to evaluate antibiotics utilization patterns and dosage appropriateness in patients receiving HD at a tertiary hospital. A retrospective study was carried on 287 adult inpatients, who received HD and at least one antibiotic in a tertiary hospital in Oman. Data were extracted using the hospital's electronic patient information system. Dosage appropriateness was assessed by identifying the dosage and frequency of prescribed antibiotics and comparing them with international guidelines. The main outcome measures were antibiotics utilization patterns and dosing inappropriateness. The most commonly prescribed parenteral antibiotic was piperacillin + tazobactam (20%), while the most common prescribed oral antibiotic was azithromycin (41.7%). For prophylaxis, cefazolin (54.6%) was the main antibiotic prescribed. The most commonly used antibiotic for external use was mupirocin ointment (38.5%). The overall dosing inappropriateness was 29.5%. Vancomycin was the most common parenteral antibiotic subjected to dosing inappropriateness (19.8%). However, trimethoprim + sulfamethoxazole was more inappropriately prescribed among the oral route (28.6%).

In conclusion, the most utilized antibiotic was piperacillin + tazobactam followed by vancomycin. The study reported some inappropriate dosing of antibiotics. Such a study opens the door for the establishment of local guidelines for the improved practice of antibiotics use in HD patients.

1. Introduction

CKD is a global health challenge, with a prevalence of around 10% (Al Alawi et al., 2017; Vilay 2019). A rapid rise in both the incidence and prevalence of CKD has been reported in the past decades and the prevalence had doubled in the last couple of years (Lederer and Ouseph., 2007). According to the World Health Organization (WHO) rank, Oman comes as 51st top country where CKD is a significant cause of death, and it is the 6th major cause of death in the Sultanate (Al Alawi et al., 2017).

Prescribing for patients receiving hemodialysis (HD) is challenging and complicated by polypharmacy, comorbidities, and changes in the clearance of medications (Smyth et al., 2016). Usually, a complex regimen is required, accompanied by continuous therapeutic monitoring and adjustment through a reduction in dose, increase in dosing interval, or a combination of both (Al-Ramahi 2012; Smyth et al., 2016).

Patients on HD are prone to infections, especially those caused by multi-drug resistant (MDR) organisms (Hui et al., 2017). Infections are a major cause of morbidity and mortality in this population, and it is the second important cause of death (Suzuki et al., 2016; Worth et al., 2017; Vilay 2019). Exposure to antibiotics is the major risk factor for the progress of antimicrobial resistance and infections by antibiotic-resistant pathogens. There is currently only limited research on the topic, not only in Oman, but also the region at large.

The aim of the study was to evaluate the utilization patterns of antibiotic use, in patients receiving HD and to assess dosage appropriateness of the prescribed antibiotics.

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2. Patients and methods

2.1. Study design

This was a retrospective study on a sample of patients who received HD in a tertiary hospital in Oman and who were selected randomly from the register of the dialysis unit.

The inclusion criteria were adult inpatients (≥18 years) who received intermittent HD or continuous venovenous HD who were admitted under any medical specialty, and received at least one antibiotic from January 2018 to December 2019.

2.2. Data collection

A record of patients who received HD at the dialysis unit was obtained. Data of 287 patients, who met the inclusion criteria, were extracted by reviewing their medical records using the hospital's information system (TrakCare), including:

1. Patients' data (age, weight, height, gender, smoking, and survival).
2. Medical history (comorbidities including hypertension (HTN), dyslipidemia, diabetes mellitus (DM), cardiovascular disease (CVD), respiratory disease, previous or current cancer, hepatic impairment, previous kidney transplant, and anuria).
3. HD primary indication, type, frequency, vascular type at enrolment, and dates of HD sessions.
4. Details of the prescribed antibiotics (name, indication, strength, route of administration, duration, location of admission, microscopy, culture's date & result, and allergy to antibiotics).

Different comorbidities were defined as the following:

- Hypertension: measured blood pressure is ≥ 140/90 mmHg.
- Diabetes mellitus: fasting plasma glucose level of more than 7.0 mm/L (126 mg/dL), or 2-hour oral glucose tolerance test of more than 11.1 mm/L (200 mg/dL).
- Cardiovascular diseases: any disorder related to heart and blood vessels and confirmed by specialized doctor based on signs and symptoms, and after the investigational test, including coronary heart disease, cerebrovascular disease, peripheral arterial disease, deep vein thrombosis or pulmonary embolism, rheumatic heart disease and congenital heart disease.
- Hepatic impairment: any significant elevations in liver enzymes including alanine aminotransferase, alkaline phosphatase and aspartate aminotransferase, or any abnormalities in albumin, prothrombin time/international normalized ratio and serum bilirubin level. This observation is supported by history and physical examination to confirm it is liver-related.

Indications of antibiotics were classified as prophylaxis, respiratory tract infections (RTIs), skin and soft tissue infections (SSTIs), vascular access infections (VAIs), bloodstream infections (BSIs), urinary tract infections (UTIs), gastrointestinal tract infections, other infections (eyes, nose, ears infections, bones & joints infections, infections of the reproductive system), and unknown source of infection.

2.3. Dosage inappropriateness

Dosage inappropriateness was assessed by identifying the dosage and frequency of prescribed antibiotics and comparing them with international guidelines. Other factors including patient's weight, infection type, HD type, and dates of HD sessions were taken into consideration during the assessment of dosage inappropriateness. Dosing inappropriateness was classified into small doses, larger doses, too long interval, and too short interval. Stanford Health Care Antimicrobial Dosing Reference Guide (2020) and The Renal Drug Handbook (5th edition) were referred for this purpose. Appendix table A shows the appropriate dosing of antibiotics among hemodialysis patients as set on the international guidelines. To the best of our knowledge, there are no local guidelines followed for prescribing antibiotics in HD patients.

2.4. Sample size estimation

Based on a study conducted by Hui et al. (2017) in Australia and performed on HD patients, it was documented that inappropriate prescribing of antibiotics reached 24.6%. Based on this study, a sample size of 285 or more was needed to detect inappropriateness of antibiotic use of at least 25%, with a confidence level of 95% and a 5% margin of error. The study eventually sampled 287 patients.

2.5. Statistical analysis

Descriptive statistics were used to describe the data. Categorical variables were presented as percentages, and differences analyzed using Chi-square test and Fisher's exact test for expected cells of < 5. Continuous variables were presented as mean, standard deviation and range. An a priori two-tailed level of significance was set at 0.05. Data was performed using Stata software version 13.1 (STATA Corporation, College Station, TX, USA).

2.6. Eethical approval

Ethical approval of this study from the Medical Research and Ethics Committee (MREC). The study was also performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Since personal identification information was marked prior to the analysis, informed consent was not sought.

3. Results

3.1. Patients' demographics

Table 1 illustrates the patients' demographics and clinical characteristics. The mean age of the patients was 58 ± 17 years old, and 63% (180/287) of the patients were males. Thirty-one percent (89/287) of the patients died within the same year of admission. HTN, DM, and CVD were the most common comorbidities found in the patients with a prevalence of 80% (230/287), 60% (172/287) and 49% (140/287), respectively. Out of the 287 inpatients, 11% (n = 31) had a hepatic impairment, and 4 (1.4%) of them had allergies to antibiotics. The documented allergies were toward ceftriaxone, vancomycin, and amoxicillin. One of the patients had allergies against two antibiotics, gentamicin and tazocin. The indication for HD was classified as acute kidney injury (AKI) (30%; 86/287) and CKD G5 (70%; 201/287). The major cause of the CKD G5 in the patients was diabetic nephropathy. Permcath and arteriovenous fistula (AVF) were the most common vascular access for HD (45%; 128/287 and 39%, respectively). Anuria was reported in 21% (59/287) of the patients.

3.2. Antibiotics utilization patterns

The total number of prescribed antibiotics was 717 courses, with 37 different antibiotics. They were administered parenterally (86%; 614/717), orally (10%; 72/717), as nebulization (0.7%; 5/717)

Table 1
Patients' demographics.

Variable	N = 287 patients
Age (years), mean ± SD (range)	58 ± 17 (18–95)
Gender, N (%)	
Males	180 (62.7%)
Females	107 (37.3%)
BMI (kg/m^2), mean ± SD (range)	28 ± 12 (22.4–30.4)
Survival, N (%)	
Alive	
Died same year	89 (31.0%)
Died next year	6 (2.10%)
Smokers, N (%)	22 (7.7%)
Comorbidities, N (%)	
HTN	230 (80.1%)
Dyslipidemia	50 (17.4%)
DM	172 (59.9%)
CVD	140 (48.8%)
Respiratory disease	33 (11.5%)
Previous or current cancer	25 (8.7%)
Hepatic impairment at enrollment (%)	31 (10.8%)
Allergy to antibiotics, N (%)	4 (1.4%)
Primary indication of HD, N (%)	
AKI	86 (30.0%)
CKD G5	201 (70.0%)
DM	63 (22.0%)
HTN	48 (16.7%)
SLE	12 (4.2%)
FSGS	5 (1.7%)
Others	21 (7.3%)
unknown	52 (18.1%)
Vascular access at enrollment, N (%)	
AVF	112 (39.0%)
AV graft	8 (2.8%)
Permcath	128 (44.6%)
Quinton	90 (31.8%)
HD frequency, N (%)	
Twice weekly	36 (12.5%)
Thrice weekly	165 (57.5%)
Not fixed (AKI)	86 (30.0%)
Previous kidney transplant, N (%)	30 (7.3%)
Presence of anuria at enrollment, N (%)	59 (20.6%)

Abbreviations: BMI body mass index, HTN hypertension, DM diabetes mellitus, CVD cardiovascular disease, HD hemodialysis, AKI acute kidney injury, CKD G5 chronic kidney disease cateogry 5, SLE systemic lupus erythmatous, FSG focal segemental glomerularosclerosis, AVF arteriovenous fistula, N total sample analysed

or topically (3.6%; 26/717). A total of 173 (24%) courses were given as a single dose versus 544 (76%) courses as multiple doses.

Out of the 287 patients, only 44 (15%) of them received antibiotics for prophylaxis, 101 patients (35%; 101/287) were prescribed antibiotics empirically and had no infections. The empiric use reached 244 courses (34%; 244/717), and 429 courses were for therapeutic use (60%; 429/717). The remaining 6% (44/717) of the courses were administered as prophylaxis.

The most utilized antibiotic was piperacillin + tazobactam (17%; 123/717). The same antibiotic was the commonest among the parenteral antibiotics (20%; 123/614). However, azithromycin was the commonly prescribed antibiotic via the oral route (42%; 30/72).

For prophylaxis, cefazolin was the main antibiotic (55%; 24/44) prescribed, followed by amoxicillin + clavulanate (16%; 7/44). Cefazolin was used in AVF creation and repair, and permcath insertion. In addition, it was the option for orthopedic and cardiothoracic procedures. Amoxicillin + clavulanate was also common for vascular access-related procedures. Moreover, it was the option for debridement and amputation procedures apart from its role in treating SSTIs (cellulitis), (Table 2).

A total of 5 courses of antibiotics were administered as nebulization, particularly, colistin (3/5) and tobramycin (2/5). Vancomycin and aminoglycosides (amikacin & gentamicin) were prescribed as catheter lock in catheter-related BSIs in four courses.

Out of the 717 courses, a total of 26 courses of the antibiotics were prescribed for external use. The most commonly used antibiotic was mupirocin ointment (39%;10/26), mostly in renal and surgical inpatients, either as therapeutic for treating SSTIs and VAIs or as empiric therapy for suspected methicillin-resistant *Staphylococcus aureus* (*MRSA)* infections. Other prescribed antibiotics were moxifloxacin (9/26), fusidic acid (3/26), ofloxacin (1/26), cefuroxime eye drops (1/26), sulfadiazine cream (1/26), and fusidic acid ointment (1/26).

3.3. Antibiotics dosing inappropriateness

Table 3 shows dosing inappropriateness of all prescribed antibiotics. The overall dosing inappropriateness was 30% (204/691). Dosing inappropriateness was classified into small doses, larger doses, too long interval, and too short interval. Too short interval (39%; 79/204) followed by larger doses (35%; 71/204) were the major causes of inappropriateness, and both resulting in overdosing. Other types of dosing inappropriateness accounting for 27%, small doses (26/204) and a long dosing interval (28/204) (Table 4).

Vancomycin was the most common parenteral antibiotic subjected to dosing inappropriateness (38/102). This was due mainly to the intervals between doses being short. However, trimethoprim + sulfamethoxazole was the most common inappropriately prescribed among the oral route (2/3). Among the nebulized antibiotics, colistin was the most inappropriately prescribed antibiotic (3/3). The main cause of inappropriateness for trimethoprim + sulfamethoxazole and colistin was large doses.

4. Discussion

A total of 717 courses of antibiotics were prescribed. The extensively used route of antibiotics administration was the parenteral route (86%). Therapeutic use was the commonest purpose of antibiotics, like in previous studies (Snyder et al., 2013; Hui et al., 2017).

The commonly utilized antibiotics parenterally were piperacillin + tazobactam and vancomycin. Unlike previous studies, the use of piperacillin + tazobactam exceeded the use of vancomycin (Hui et al., 2017) and cefazolin (Berman et al., 2004). It was commonly prescribed as empiric therapy or to treat RTIs caused by either gram-negative or gram-positive bacteria.

Azithromycin was the commonly prescribed antibiotic via the oral route for the same indication as piperacillin + tazobactam. Only one study evaluated the oral antibiotics among HD (Hui et al., 2017) and showed that amoxicillin + clavulanate and cephalexin were more commonly used, particularly to treat RTIs, SSTIs, and UTIs.

Cefazolin was amongst the commonly utilized antibiotic as prophylaxis, mostly in inpatients admitted under Nephrology or Surgery specialties. In a previous study, it was more prescribed to treat SSTIs (Snyder et al., 2013). A study included 3,162 consecutive, percutaneous access- related procedures reported a 0.06% rate of infectious complications, claiming the reduced need for antibiotics use as prophylaxis except for procedures of peritoneal dialysis and HD-tunnelled catheters, accidentally extruded (Salman and Asif, 2009). The presence of a single study in such a complicated area indicates data insufficiency to drive a conclusion, and further studies are needed.

The topical antibiotics administered reached 26 courses. Mupirocin was the most used antibiotic, mainly in SSTIs & VAIs. A randomized prospective trial (Sesso et al., 1998) showed increased benefits with the use of mupirocin in HD patients. It has an antistaphylococcal activity. Therefore, it can reduce catheter-related

Table 2
Utilization patterns of antibiotics among hemodialysis patients.

Antibiotic name	Total number prescribed (oral + parenteral)	Most common indication	Location
Glycopeptides			
Vancomycin	104 (2 + 102)	VAI, BSI	Medicine
Teicoplanin	3 (0 + 3)	Empiric	-
Cephalosporins			
Cefazolin	38 (0 + 38)	Prophylaxis	Nephrology & Surgery
Cefuroxime	8 (1 + 7)	Empiric, prophylaxis	Nephrology
Ceftriaxone	78 (0 + 78)	Empiric	Medicine & Emergency
Ceftazidime	14 (0 + 14)	BSIs	Medicine
Cefotaxime	1 (0 + 1)	Empiric	Medicine
Cefepime	1 (0 + 1)	RTIs	Medicine
Carbapenems			
Meropenem	86 (0 + 86)	RTIs, empiric	Medicine
Penicillin			
Amoxicillin	4 (4 + 0)	GITIs (*H-pylori*)	Nephrology
Ampicillin	5 (0 + 5)	Empiric	Nephrology & Medicine
Cloxacillin	8 (0 + 8)	Empiric, BSIs	Nephrology
Tetracyclines			
Tigecycline	14 (0 + 14)	Empiric, RTIs	Medicine
Doxycycline	4 (4 + 0)	Empiric, SSTIs	Medicine
Macrolides			
Erythromycin	1 (1 + 0)	SSTIs	Nephrology
Azithromycin	36 (30 + 6)	RTI, empiric	Medicine
Clarithromycin	6 (6 + 0)	GITIs (*H-pylori*)	Nephrology & Medicine
Lincosamide			
Clindamycin	7 (0 + 7)	Empiric	Medicine
Oxazolidinones			
Linezolid	2 (0 + 2)	–	Medicine
Aminoglycosides			
Gentamicin	3 (0 + 3)	Catheter lock, empiric	Nephrology
Tobramycin	2 (nebulized)	-	-
Amikacin	40 (0 + 40)	Empiric, BSIs, VAIs	Nephrology
Fluroquinolones			
Ciprofloxacin	14 (4 + 10)	RTIs, BSIs	Medicine
Levofloxacin	3 (2 + 1)	Empiric	-
Moxifloxacin	2 (2 + 0)	Empiric	Nephrology
Combination			
Trimethoprim + sulfamethoxazole	8 (3 + 5)	Empiric	Nephrology
Piperacillin + tazobactam	123 (0 + 123)	Empiric, RTIs	Medicine
Amoxicillin + clavulanate	20 (7 + 13)	Prophylaxis, empiric	Surgery
Lipopeptide			
Fosfomycin	3 (0 + 3)	SSTIs	Medicine & Nephrology
Antimycobacterial			
Rifampicin	1 (1 + 0)	RTI (TB)	Medicine
Isoniazid	2 (2 + 0)	RTI (TB)	-
Polymyxin			
Colistin	37 (0 + 34), 3 (nebulized)	RTIs	Medicine
Nitroimidazole			
Metronidazole	15 (4 + 11)	Empiric, BSIs	Medicine

Abbreviations: VAI vascular access infection, BSI blood stream infection, RTI respiratory tract infection, GITI gastrointestinal tract infection, SSTI skin & soft tissue infection, TB tuberculosis

infections and bacteremia through its application at the insertion site of vascular access.

Vancomycin and aminoglycosides (amikacin & gentamicin) were prescribed as catheter lock in catheter-related BSIs. According to a study that assessed the pathogenesis and prevention of bacterial infections in HD patients (Jaber, 2005), the use of gentamicin-citrate catheter lock can reduce the incidence of infections (mainly bacteremia & pneumonia) compared to using heparin without any significant difference in the occurrence of catheter malfunctions.

This study reported an overall inappropriate dosing of 30% among HD population in the hospital. The same percentage was observed in a study in the outpatient HD unit (Snyder et al., 2013). A similar study included patients from the hospital settings (Hui et al., 2017) reported an overall of 25% inappropriate dosing and indications. This previous study included intravenous and oral antibiotics only.

A too-short interval followed by larger doses were the major causes of inappropriateness in the current and previous studies (Hui et al., 2017). In the current study, vancomycin was the most common parenteral antibiotic subjected to dosing inappropriateness, and usually administered within short intervals between doses. Similarly, vancomycin was commonly inappropriately prescribed in the outpatients, followed by third and fourth generation cephalosporins (Snyder et al., 2013). However, cefazolin and meropenem were the most inappropriately prescribed antibiotics based on a previous study included patients from the hospital settings (Hui et al., 2017). Trimethoprim + sulfamethoxazole was more inappropriately prescribed among the oral route due to large size doses. This combination used to treat a number of infections in HD, such as *Pneumocystis jirovecii* pneumonia (also as prophylaxis), acute exacerbation of chronic bronchitis, and UTIs. There is limited data available regarding drug dosing in renal replacement therapy (RRT) despite its use for a half-century. Observation of clinical parameters is the only way to guide its proper dosing in the absence of therapeutic drug monitoring. Studies recommended the need for further pharmacokinetics studies, especially in the presence of a modern variety of RRT (Clajus et al., 2013).

Table 3
Dosing inappropriateness of the prescribed antibiotics.

Antibiotic name	Total number prescribed	Total inappropriate dosing	% of inappropriateness
Glycopeptides			
Vancomycin	104	38	36.50%
Teicoplanin	3	1	33.30%
Cephalosporins			
Cefazolin	38	16	42%
Cefuroxime	8	4	50%
Ceftriaxone	78	2	2.6%
Ceftazidime	14	6	43%
Cefotaxime	1	0	0%
Cefepime	1	1	100%
Carbapenems			
Meropenem	86	29	33.7%
Penicillin			
Amoxicillin	4	1	25%
Ampicillin	5	2	40%
Cloxacillin	8	2	25%
Tetracyclines			
Tigecycline	14	1	7%
Doxycycline	4	0	0%
Macrolides			
Erythromycin	1	0	0%
Azithromycin	36	0	0%
Clarithromycin	6	0	0%
Lincosamide			
Clindamycin	7	2	28.6%
Oxazolidinones			
Linezolid	2	0	0%
Aminoglycosides			
Gentamicin	3	2	66.70%
Tobramycin	2	2	100%
Amikacin	40	18	45%
Fluroquinolones			
Ciprofloxacin	14	2	14.3%
Levofloxacin	3	0	0%
Moxifloxacin	2	1	50%
Combination			
Trimethoprim + sulfamethoxazole	8	5	62.5%
Piperacillin + tazobactam	123	23	18.70%
Amoxicillin + clavulanate	20	10	50%
Lipopeptide			
Fosfomycin	3	0	0%
Antimycobacterial			
Rifampicin	1	1	100%
Isoniazid	2	1	50%
Polymyxin			
Colistin	37	31	83.8%
Nitroimidazole			
Metronidazole	15	3	20%

Nebulized colistin was usually administered with doses larger than the recommended. This antibiotic displays concentration-dependent killing of gram-negative organisms and some data suggest that the administration of a high dose of colistin over an extended interval in the critical care settings might be more efficacious. However, many studies showed no advantage of using a high dose over the lower doses. But there will be an increased risk for toxicity and development of resistance (Kalin et al., 2012; Ghazaeian et al., 2017).

In conclusion, the current study provides a useful summary of commonly prescribed antibiotics (parenteral, oral, nebulized, and topical), and their inappropriate use in patients receiving HD in Oman. Such a study opens the door for the improved practice of antibiotics use in HD patients and effective prescribing.

Table 4
Reasons for dosage inappropriateness of the prescribed antibiotics.

Antibiotic name	Total number prescribed	Total inappropriate dosing	Dose too low	Dose too high	Interval too long	Interval too short
Glycopeptides						
Vancomycin	104	38	12	6	1	19
Teicoplanin	3	1	0	1	0	0
Cephalosporins						
Cefazolin	38	16	0	6	0	10
Cefuroxime	8	4	0	1	0	3
Ceftriaxone	78	2	0	0	1	1
Ceftazidime	14	6	1	4	0	1
Cefotaxime	1	0	0	0	0	0
Cefepime	1	1	0	0	0	1
Carbapenems						
Meropenem	86	29	1	2	2	24
Penicillin						
Amoxicillin	4	1	0	0	0	1
Ampicillin	5	2	0	0	0	2
Cloxacillin	8	2	1	0	1	0
Tetracyclines						
Tigecycline	14	1	0	1	0	0
Doxycycline	4	0	0	0	0	0
Macrolides						
Erythromycin	1	0	0	0	0	0
Azithromycin	36	0	0	0	0	0
Clarithromycin	6	0	0	0	0	0
Lincosamide						
Clindamycin	7	2	0	0	2	0
Oxazolidinones						
Linezolid	2	0	0	0	0	0
Aminoglycosides						
Gentamicin	3	2	1	1	0	0
Tobramycin	2	2	0	2	0	0
Amikacin	40	18	5	11	0	2
Fluroquinolones						
Ciprofloxacin	14	2	0	0	0	2
Levofloxacin	3	0	0	0	0	0
Moxifloxacin	*2*	1	0	1	0	0
Combination						
Trimethoprim + sulfamethoxazole	8	5	0	4	1	0
Piperacillin + tazobactam	123	23	3	0	14	6
Amoxicillin + clavulanate	20	10	0	0	3	7
Lipopeptide						
Fosfomycin	3	0	0	0	0	0
Antimycobacterial						
Rifampicin	1	1	1	0	0	0
Isoniazid	2	1	0	0	1	0
Polymyxin						
Colistin	37	31	1	30	0	0
Nitroimidazole						
Metronidazole	15	3	0	1	2	0

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix

(See Table A1, B1, C1).

Table A1
Appropriate dosing of antibiotics among hemodialysis patients as set on the international guidelines.

Antibiotic	Recommended dosage	
	IHD	CRRT
Amoxicillin + clavulanate (PO)	875/125 mg q12hr.	875/125 mg q12hr.
Amoxicillin + clavulanate (IV)	1.2 g q12hr or 600 mg q 8hr.	1.2 g q8hr.
Amikacin (IV)	5–7.5 mg/kg q 48-72hr after HD only. 15–25 mg/kg q 48-72hr after HD only (MDR).	7.5 mg/kg q 24–48 h. 25 mg/kg q 48hr (severe infections /MDR).
Amoxicillin (PO)	250–500 mg q 24hr.	250–500 mg q 24hr.
Ampicillin (IV)	1 g q 12hr. 2 g q 12-24hr (severe infections; meningitis).	2 g q 8-12hr. 2 g q 6hr (severe infections; meningitis).
Azithromycin (PO/IV)	500 mg q 24hr.	500 mg q 24hr.
Aztreonam	1 g q 24hr. 1 g q 12hr (severe infections; meningitis).	1 g q 8hr or 2 g q 12hr.
Cefazolin	1 g q 24hr.	2 g q 12hr.
Cefuroxime (PO)	250–500 mg q24hr.	250–500 mg q24hr.
Cefuroxime (IV)	1.5 g q 24hr.	1.5 g q 12hr.
Ceftriaxone (IV)	1–2 g q 24hr 2 g q 12hr (*E.faecalis*, meningitis).	2 g q 12-24hr.
Ceftazidime (IV)	1–2 g q 48-72hr post-HD.	2 g q 12hr.
Ceftazidime/avibactam	0.94 g q 24-48hr.	1.25–2.5 g q 8hr.
Cefotaxime	1–2 g q 24hr.	2 g q 12hr.
Cefepime	2 g q 48-72hr.	1 g q 8hr.
Ciprofloxacin (PO)	250–500 mg q 24hr.	500 mg q 12hr.
Ciprofloxacin (IV)	200–400 mg q 24hr.	400 mg q 12hr.
Clarithromycin (PO/IV)	250–500 mg q 12 hr.	250–500 mg q 12 hr.
Clindamycin (PO)	150–450 mg q 6hr.	150–450 mg q 6hr.
Clindamycin (IV)	600–900 mg q 8hr.	600–900 mg q 8hr.
Colistin (IV)	2 MU q 12hr (non HD days), and 2 MU q 12hr (on HD days, administer additional dose of 1.5 MU post-HD).	6.5–7 MU q 12hr.
Colistin (Nebulized)	2 MU q 12hr. 4–4.5 MU q 8hr (VAP).	2 MU q 12hr. 4–4.5 MU q 8hr (VAP).
Cloxacillin	250–500 mg q 6hr (max: 6 g/d).	250–500 mg q 6hr (max: 6 g/d).
Doxycycline	100 mg q 12hr.	100 mg q 12hr.
Erythromycin (PO)	250–500 mg q 6hr.	250–500 mg q 6hr.
Fosfomycin	2–3 g q 48-72hr post-HD (max 3 doses).	2–3 g q 48-72hr (max 3 doses).
Gentamicin	1 mg/kg q 48-72hr post-HD (gram positive) or 1.5 mg/kg q 48-72hr post-HD (gram negative).	1 mg/kg q 24 h, then per level (gram positive) or 1.5–2.5 mg/kg q 24–48 h (gram negative).
Isoniazed (PO)	300 mg q 24hr	300 mg q 24hr.
Levofloxacin (PO/IV)	250 mg q 48hr post-HD. 500 mg q 48hr/post HD (*stenotrphomonas*, *Pseudomonas*).	500 mg q 24hr.
Linezolid (PO/IV)	600 mg q 12hr	600 mg q 12hr.
Meropenem	500 mg q 24hr 1 g q 24hr (severe infections / meningitis).	1 g q 8hr. 2 g q 12hr (severe infections / meningitis).
Metronidazole (PO/IV)	500 mg q 8hr.	500 mg q 6-8hr.
Moxifloxacin (PO/IV)	400 mg q 24hr.	400 mg q 24hr.
Piperacillin + tazobactam	2.25 g q 8hr.	4.5 g q 8hr.
Rifampicin (PO/IV) (many potential drug interactions)	600 mg q 24hr.	600 mg q 24hr.
Teicoplanin	400–800 mg q 12hr, then q 72hr from 4th day.	400–800 mg q 12hr, then q 72hr from 4th day.
Tigecycline	50 mg q 12 h. 25 mg q 12hr (in severe hepatic impairment).	50 mg q 12 h 25 mg q 12hr (in severe hepatic impairment).
Tobramycin (Nebulized)	1 mg/kg q 24hr	1.5–2 mg/kg q 24hr
Trimethoprim + sulfamethoxazole (PO/IV) DS: 160 mg TMP (960 mg tab) SS: 80 mg TMP (480 mg tab)	5–20 mg/kg TMP q 48-72hr (post-HD only). 1 SS tab q 48-72hr post dialysis only (for PCP prophylaxis).	2.5–5 mg/kg TMP q 12hr. 5–10 mg/kg TMP q 8-12hr (PCP/ *stenotrphomonas)*
Vancomycin (PO)	125 mg q 6hr. 500 mg q 6hr (severe infections / sepsis).	125 mg q 6hr. 500 mg q 6hr (severe infections / sepsis).
Vancomycin (IV)	15–20 mg/kg q 48-96hr	15–20 mg /kg q 24hr

PO, per oral, IV intravenous, IHD intermittent haemodialysis, CRRT continuous renal replacement therapy, MDR multi-drug resistant, MU million unit, VAP ventilator acquired pneumonia, TMP trimethoprim, PCP Pneumocystis pneumonia, SS single strength.
*Severe hepatic impairment: liver cirrhosis.

Table B1
Basis for classifying CKD at SQUH.

Stage of CKD	GFR	Description
G1	≥90	Normal or high GFR with kidney damage
G2	60–89	mild
G3a	45–59	Mild-moderate
G3b	30–44	Moderate-severe
G4	15–29	Severe
G5	<15	Kidney failure

Table C1
Antibiotics dose sizes and dosing intervals among the population.

Antibiotic name	Dose size	Frequency
	Mean +/- standard deviation	
Amoxicillin + clavulanate (injectable)	1.2 g (875/125) mg	Q12 hr (7 hr)
Amoxicillin + clavulanate (oral)		Q12 hr
Amikacin	583 mg (267 mg)	Q30 hr (15 hr)
Amoxicillin	667 mg (258 mg)	Q18 hr (9 hr)
Ampicillin	1.6 g (0.5 g)	Q18 hr (3 hr)
Azithromycin	494 mg (38 mg)	Q2 hr
Cefazolin	1.4 g (0.5 g)	Q23 hr (12 hr)
Cefuroxime (injectable) Cefuroxime	844 mg (279 mg)	Q12 hr (4 hr)
(oral)	450 mg (112 mg)	Q24 hr (7 hr)
Ceftriaxone	1.8 g	Q24 hr
Ceftazidime	1.7 g (0.5 g)	Q33 hr (20 hr)
Cefotaxime	2 g	Q12 hr
Cefepime	500 mg	Q12 hr
Ciprofloxacin (injectable)	400 mg	Q21 hr (6 hr)
Ciprofloxacin (oral)	500 mg	Q24 hr (5.4 hr)
Clarithromycin	416 mg (129 mg)	Q12 hr (7 hr)
Clindamycin	825 mg (139 mg)	Q8 hr (2 hr)
Cloxacillin	2 g (0.3 g)	Q6 hr
Colistin	4.7 m (2.6 m)	Q12 hr (4 hr)
Doxycycline	100 mg	Q12 hr
Erythromycin	250 mg	Q6 hr
Fosfomycin	2 g	Q54 hr (12 hr)
Gentamicin	131 mg (55 mg)	Q24 hr (15 hr)
Isoniazed	300 mg	Q25 hr (41 hr)
Levofloxacin	583 mg (144 mg)	Q40 hr (14 hr)
Linezolid	600 mg	Q12 hr
Meropenem	667 mg (274 mg)	Q12 hr (12 hr)
Metronidazole (injectable)	500 mg 414 mg	Q8 hr (6 hr)
Metronidazole (oral)	(38 mg)	Q8 hr (6 hr)
Moxifloxacin	400 mg	Q24 hr
Piperacillin + tazobactam	2.5 g (0.8 g)	Q8 hr (6 hr)
Rifampicin	600 mg	Q72 hr
Teicoplanin	400 mg	Q12 hr
Tigecycline	52.8 mg (12 mg)	Q12 hr
Tobramycin	300 mg	Q12 hr
Trimethoprim + sulfamethoxazole	1236 mg (680 mg)	Q36 hr (28 hr)
Vancomycin (oral) Vancomycin	125 mg 901 mg	Q6 hr Q31 hr
(injectable)	(253 mg)	(13 hr)

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