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.
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. Ethical 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 patients, 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. Percath 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)
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/m²), mean ± SD (range)  | 28 ± 12 (22.4–30.4) |
| Survival, N (%)                 |                  |
| Alive                           | 89 (31.0%)       |
| Died same year                  | 6 (2.10%)        |
| Died next year                  |                  |
| 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| 59 (20.6%)       |

Table 1: Patients’ demographics.

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

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 + sulfafoxazole 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 + sulfafoxazole 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 cephalaxin 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 anti-staphylococcal activity. Therefore, it can reduce catheter-related
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 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 |
| Cefepine        | 1 (0 + 1)                                   | RTIs                   | Medicine |
| **Carbapenems** |                                             |                        |          |
| Meropenem       | 86 (0 + 86)                                 | RTIs, empiric          | Medicine |
| **Penicillins** |                                             |                        |          |
| Amoxicillin     | 4 (4 + 0)                                   | GITIs (H-pylori)       | Nephrology |
| Ampicillin      | 5 (0 + 5)                                   | Empiric                | Nephrology & Medicine |
| Clavulacillin   | 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)                                   | Catheter lock, empiric | Nephrology |
| **Aminoglycosides** |                                      |                        |          |
| Gentamicin      | 3 (0 + 3)                                   | Empiric, BSIs          | Nephrology |
| Tobramycin      | 2 (nebulized)                               | -                      |          |
| Amikacin        | 40 (40 + 0)                                 | Empiric, BSIs, VAs     | Nephrology |
| **Fluoroquinolones** |                                        |                        |          |
| 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.
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                  |
| Ceftriaxime              | 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             | 0                 | 2                  |
| **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                  |
| **Fluoroquinolones**     |                         |                           |              |               |                   |                    |
| 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).
| Antibiotic                        | Recommended dosage                                      | 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- | 7.5 mg/kg q 24–48 h. 25 mg/kg q 48hr (severe infections /MDR).        |
|                                  | 72hr after HD only (MDR).                                | 250–500 mg q 24hr.                                                   |
| Amoxicillin (PO)                 | 250–500 mg q 24hr.                                       | 2 g q 8-12hr. 2 g q 6hr (severe infections; meningitis).             |
|                                  | 1 g q 12hr. 2 g q 12-24hr (severe infections; meningitis). |                                                                      |
| Ampicillin (IV)                  | 1.2 g q8hr.                                              |                                                                      |
| Azithromycin (PO/IV)             | 500 mg q 24hr.                                           |                                                                      |
| Aztreonam                        | 1 g q 24hr. 1 g q 12 hr (severe infections; meningitis). |                                                                      |
| Cefazolin                        | 1 g q 24hr.                                              |                                                                      |
| Cefuroxime (PO)                  | 250–500 mg q24hr.                                        |                                                                      |
| Cefuroxime (IV)                  | 1.5 g q 8 hr.                                            |                                                                      |
| Ceftriaxone (IV)                 | 1–2 g q 24hr 2 g q 12 hr (E. faecalis, meningitis).     |                                                                      |
| Cefazidime (IV)                  | 1–2 g q 48-72hr post-HD.                                |                                                                      |
| Cefazidime/avibactam             | 0.94 g q 24-48hr.                                        |                                                                      |
| Cefotaxime                       | 1–2 g q 24hr.                                            |                                                                      |
| Cefepime                         | 2 g q 48-72hr.                                           |                                                                      |
| Ciprofloxacin (PO)               | 250–500 mg q 24hr.                                       |                                                                      |
| Ciprofloxacin (IV)               | 200–400 mg q 24hr.                                       |                                                                      |
| Clarithromycin (PO/IV)           | 250–500 mg q 12 hr.                                      |                                                                      |
| Clindamycin (PO)                 | 150–450 mg q 6hr.                                        |                                                                      |
| Clindamycin (IV)                 | 600–900 mg q 8hr.                                        |                                                                      |
| Colistin (IV)                    | 2 MU q 12hr (non HD days), and 2 MU q 12hr (on HD days, | 6.5–7 MU q 12hr.                                                    |
|                                  | administer additional dose of 1.5 MU post-HD).           |                                                                      |
| Ceftriaxone (PO)                 | 500 mg q 6hr (max: 6 g/d).                               |                                                                      |
| Ceftriaxone (IV)                 | 100 mg q 12hr.                                           |                                                                      |
| Ciprofloxacin (IV)               | 2–3 g q 48-72hr post-HD (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).                       |                                                                      |
| Linezolid (PO/IV)                | 250 mg q 48hr post-HD.                                   |                                                                      |
| Meropenem                        | 600 mg q 12hr.                                           |                                                                      |
| Metronidazole (PO/IV)            | 500 mg q 24hr 1 g q 24hr (severe infections /meningitis). |                                                                      |
| Moxifloxacin (PO/IV)             | 500 mg q 8hr.                                            |                                                                      |
| Piperacillin + tazobactam        | 400 mg q 24hr.                                           |                                                                      |
| Pefloxacin (PO/IV)               | 2.25 g q 8 hr.                                           |                                                                      |
| Ticarcillin + tazobactam         | 400–800 mg q 12 hr, then q 72 hr from 4th day.           |                                                                      |
| TMP (560 mg tab)                 | 50 mg q 12 h. 25 mg q 12 hr (in severe hepatic impairment). |                                                                      |
| Vancomycin (PO)                  | 5–20 mg/kg q 48-72hr (post-HD only). 1 SS tab q 48-72hr post dialysis only (for PCP prophylaxis). |                                                                      |
| Vancomycin (IV)                  | 1525 mg q 6hr. 500 mg q 6hr (severe infections /sepsis). |                                                                      |
| Vancomycin (IV)                  | 15–20 mg/kg q 48-96hr                                   |                                                                      |

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 | Antibiotic Name |
|--------------|-----------------|-----------------|
| G1           | ≥90 Normal or high GFR with kidney damage | Amoxicillin + clavulanate (injectable) |
| G2           | 60–89 mild     | Amoxicillin + clavulanate (oral) |
| G3a          | 45–59 Mild-moderate | Amoxicillin |
| G3b          | 30–44 Moderate-severe | Ampicillin |
| G4           | 15–29 Severe    | Clindamycin |
| G5           | <15 Kidney failure | Clotrimazole |

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

| Antibiotic name | Dose size | Frequency |
|-----------------|-----------|-----------|
| **Trimethoprim + sulfamethoxazole** | 1236 mg (680 mg) | Q36 hr (28 hr) |
| **Tobramycin** | 300 mg | Q12 hr |
| **Tigecycline** | 52.8 mg (12 mg) | Q12 hr |
| **Teicoplanin** | 400 mg | Q12 hr |
| **Rifampicin** | 600 mg | Q24 hr |
| **Piperacillin + tazobactam** | 2.5 g (0.8 g) | Q12 hr |
| **Moxifloxacin** | 400 mg | Q24 hr |
| **Metronidazole (injectable)** | 2 g | Q12 hr |
| **Metronidazole (oral)** | 500 mg | Q8 hr (6 hr) |
| **Cefuroxime (injectable)** | 844 mg (279 mg) | Q12 hr (4 hr) |
| **Cefuroxime (oral)** | 450 mg (112 mg) | Q24 hr (7 hr) |
| **Ceftazidine** | 1.7 g (0.5 g) | Q23 hr (20 hr) |
| **Ceftaxime** | 1.8 g | Q24 hr |
| **Cefoxitin** | 500 mg | Q12 hr |
| **Ciprofloxacin (injectable)** | 400 mg | Q21 hr (6 hr) |
| **Ciprofloxacin (oral)** | 500 mg | Q24 hr (5.4 hr) |
| **Cephemycin** | 825 mg (139 mg) | Q8 hr (2 hr) |
| **Claxacillin** | 2 g (0.3 g) | Q6 hr |
| **Colistin** | 4.7 mg (2.6 mg) | Q12 hr (4 hr) |
| **Doxycline** | 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) |
| **Isomiazid** | 300 mg | Q25 hr (41 hr) |
| **Levofloxacin** | 583 mg (144 mg) | Q40 hr (14 hr) |
| **Linezolid** | 600 mg | Q12 hr |
| **Meronem** | 667 mg (274 mg) | Q12 hr (12 hr) |
| **Metronidazole (injectable)** | 500 mg (141 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)** | 125 mg 901 mg | Q6 hr (31 hr) |
| **Vancomycin (injectable)** | (253 mg) | (13 hr) |

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