# Effectiveness of Clinical Pharmacist Collaborative Care in Resolution of Antibiotic Drug-Related Problems in an Intensive Care Unit

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**Citation**

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**Abstract**

**Introduction**: Antibiotic drug-related problems (DRPs) are relatively complex in intensive care units. The effectiveness of clinical pharmacists' collaborative practice on identification and resolution of antibiotic DRPs in the intensive care unit (ICU) had to be studied.

**Methods**: A quasi-experimental study was conducted in an ICU of a tertiary-level care hospital in the UAE. On-duty clinical pharmacists performed medication reviews of antibiotics and interventions in collaboration with other healthcare professionals. The PCNE classification system V 9.0 was used to categorize antibiotic DRPs. An experienced clinical pharmacist verified the documented DRPs. Interventions were implemented primarily in collaboration with physicians.

**Results**: A total of 103 patients on antibiotic prescriptions were reviewed; 28 (27.2%) patients had antibiotic DRPs. A total of 40 DRPs were identified in the 28 patients (1.43 DRPs per patient); 33 (82.5%) DRPs were associated with the restricted antibiotics. The majority of DRPs were related to treatment safety 24 (60%), followed by treatment effectiveness 13 (32.5%). The most common causes of DRPs were related to dose selection 21 (51.2%). A total of 80 interventions were proposed by clinical pharmacists, an average of 2 interventions per DRP. Out of 40 DRPs, 31 (77.5%) DRPs were fully resolved, 2 (5%) were partially resolved due to complexity of disease, and 5 (12.5%) were unresolved but monitored closely if any harm is happening for the patients. Outcome of 2 (5%) interventions were not known as data were inconclusive to categorize.

**Conclusion**: DRPs are common with antibiotics, especially with restricted antibiotics. This study suggests that collaborative practice interventions of clinical pharmacists were effective in the identification and resolution of antibiotic DRPs.

## INTRODUCTION

Antibiotic drug-related problems (DRPs) pose challenges in pharmacotherapeutic management in infectious diseases [1]. Around 1 in 10 hospitalized patients experience DRPs, and 50% of these problems are preventable [2, 3]. A DRP is defined by the Pharmaceutical Care Network Europe (PCNE V 9.0) as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes [4]. Previous studies have been identified antibiotics as one of the most common therapeutic classes associated with DRPs [5, 6]. Action is needed to ensure DRPs due to antibiotics are prevented when possible. Appropriate antibiotic usage is also warranted to prevent the development of antimicrobial resistance and the preservation of effective antibiograms. Increasing microbial resistance to existing antibiotics and the slow pace of development of new antibiotics requires restricting and optimizing the use of antibiotics, particularly broad-spectrum agents. Antimicrobial stewardship (ASP) programs to optimize the use of these drugs are of critical importance to ensure that the best possible care is provided to patients [7].

When high usage of antibiotics is commonly observed in critically ill patients, in clinical practice, a wide range of antibiotic-related DRPs may arise [8]. Ineffective treatments, adverse drug reactions, interactions, and contraindications are examples of DRPs. These DRPs may be caused by Inappropriate choice of drugs, medication errors, compliance

problems, and untreated conditions are among others. Finally, the presence of polypharmacy, comorbidities, increased age, and impaired hepatic or renal function, lack of coordination among health care professionals, may increase the risk of DRPs [4, 9].

Optimization of drug therapy and preventing DRPs has been consistently shown to reduce health care expenditure, reduce mortality, and produce other humanistic outcomes [10, 11]. Patients admitted to an intensive care setting are at higher risk for antibiotic-related DRPs that are often associated with increased morbidity and mortality [12, 13]. The reasons for the DRPs to occur more often in the critical care setting could be due to the severity of the patient's illness and the complexity of the drug regimen hence making a significant association with the prolonged duration of ICU stay [14]. Consequently, DRPs increase treatment costs due to this increased length of stay [15].

The clinical pharmacist is a core member of the ASP team with drug expertise [16]. Pharmacist activities in the ICUs are associated with beneficial clinical and financial outcomes [17, 18, 19]. Identifying antibiotic-related DRPs is to improve patient safety and simultaneously balance the treatment with directives from the ASP.

## METHODS

A quasi-experimental single-site study was conducted to identify and resolve antibiotic-related DRPs in the intensive care setting. It was a population-based study, including all patients treated with antibiotics for infections in the ICU over the study period. Patients in the ICU with no antibiotic orders were excluded from the study. Chi square test was performed to find if any statistically significant (p-value 0.5) different exist among gender groups and age groups in the occurrence of antibiotic DRPs.

The study was conducted at a 9-bed ICU of a Joint Commission International (JCI) accredited hospital in the UAE, offering clinical pharmacy services around the clock and establishing ASP. The data collection was during the study period from December 2019 to April 2020.

Direct patient care services offered by the department of clinical pharmacy at the hospital include medication history interview and reconciliation, medication order review, evaluating appropriateness and effectiveness of medications, recognizing untreated health conditions, drug information consultation, and pharmacokinetic and pharmacodynamics (PK-PD) consideration. As a part of the patient care process, clinical pharmacists identify and resolve DRPs in collaboration with other healthcare professionals. Interventions made to manage DRPs were discussed with the treating clinicians and were recorded in the patient's medication order sheets.

All the clinical pharmacists on duty are involved in identifying and resolving DRPs. As part of the study, the DRPs were documented using the Pharmaceutical Care Network Europe (PCNE) classification for Drug-Related Problems (DRPs), Version 9.0 [4]. The DRPs were verified by a clinical pharmacist with more practice experience in infectious diseases. As per the hospital's policy, antibiotics are classified into Non-restricted, Semi-restricted, and Restricted antibiotics to promote their prudent use. A specialist can prescribe restricted antibiotics, but for more than 72 hours, they need approval from the ASP team filling a due form. Antibiotic classification on their restricted status at the study site is shown in Table 1. The study process is shown in Figure 1. Institutional Review Board of Gulf Medical University approved this research.

## RESULTS

A total of 40 DRPs were identified among 103 patients admitted to the ICU on antibiotic orders during the study period. These 40 DRPs occurred in 28 patients of the 103 total patients. The range of DRPs per patient was 1-4. The mean age of patients with DRPs was 43.5±19.2 years, ranging from 1 - 81 years old as shown in Table 2. No significant difference was observed among gender or age groups in occurrences of antibiotic DRPs.

Meropenem and vancomycin were the most common antibiotics involved in the DRPs. However, antibiotics belonging to other subclasses were also identified to be related to DRPs. Antibiotics were classified as restricted, semi-restricted and non-restricted at the study site. Most numbers of DRPs were found with restricted antibiotics, as shown in Table 3.

Analysis of DRPs using the PCNE (V 9.0) classification system showed that 24 (60%) of all DRPs were related to treatment safety, 13 (32.5%) treatment effectiveness, and 3 (7.5%) related to others.

According to PCNE, each problem can have more than one cause and a maximum of three causes can be assigned to one problem [4]. The analysis of 40 DRPs revealed a total of 41

causes; 21 (51.2%) were related to dose selection, 6 (14.6%) to drug selection, 2 (4.9%) to dispensing, 12 (29.3%) to others, like inappropriate monitoring, no apparent cause and reasons not specified.

A total of 80 interventions were made for 40 DRPs, as sometimes one problem leads to multiple interventions (range 1-3 interventions for one problem). For example, a 56-year-old patient with Diabetes being treated with injection vancomycin for MRSA cellulitis developed rashes due to a faster infusion rate. The intervention made was to decrease the rate of infusion. Based on PCNE standards, the intervention was at the prescriber level as this was discussed with the prescriber at drug level intervention as the nurse was instructed to administer the drug at a slower rate, and thirdly side effect was reported to authorities. Based on PCNE classification, 42 (52.5%) interventions were at the prescriber level, 34 (42.5%) at the drug level and the remaining 4 (5%) were other intervention or activity.

The prescribing physicians were directly contacted either in person or by telephone for all interventions and the process was documented in the patient medical record. A total of 73 (91.6%) interventions were accepted and prescribers did not accept 7 (8.8%) interventions. The analysis of outcomes of 40 identified DRPs revealed that 31 (77.5%) DRPs were totally solved, 2 (5%) was partially resolved due to complexity of disease, 5 (12.5%) were unresolved but monitored closely if any harm is happening for the patients. Outcome of 2 (5%) interventions were not known as data was missing.

**Figure 1**

Study flow diagram

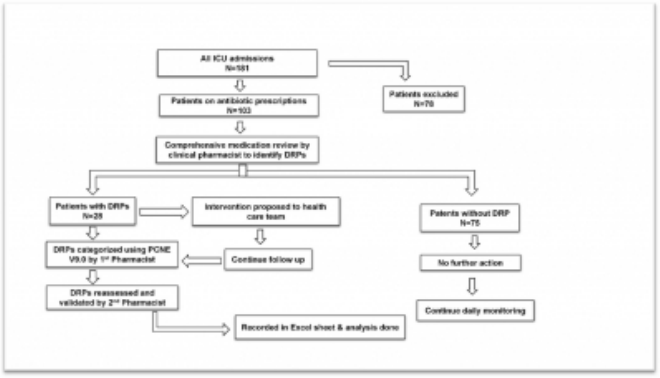


**Table 1**

Antibiotic Classification as per the Hospital Antibiotic Policy

| Non-restricted antibiotics | Semi-restricted antibiotics | Restricted antibiotics |
|---|---|---|
| Cephalosporins (1st and 2nd generation) | Cephalosporins (3rd and 4th generation) | Carbapenems (Meropenem, Imipenem, Ertapenem) |
| Erythromycin | Ciprofloxacin | Glycopeptide (Vancomycin, Teicoplanin) |
| Azithromycin | Levofloxacin | Aminoglycosides (Amikacin) |
| Clarithromycin | Ofloxacin | Piperacillin, Tazobactam |
| Clindamycin | Moxifloxacin | Colistin |
| Amoxicillin | Gentamicin | Polymyxin-B |
| Amoxicillin/clavulanic acid | | Tigecycline |
| Benzyl penicillin | | Linezolid |
| Benzathine penicillin | | Tedizolid |
| Doxycycline | | |
| Nitrofurantoin | | |
| Sulfamethoxazole/trimethoprim | | |
| Metronidazole | | |

**Table 2**

Demographic of the study population receiving antibiotics in intensive care unit

| **Total no of patients on antibiotic orders = 103** | | | |
|---|---|---|---|
| **Total no of patients with DRPs = 28** | | | |
| **Characteristics** | **Patients with DRPs = 28** | **Patients with no DRPs = 75** | **P-value*** |
| **Gender** | Numbers | Numbers | 0.73 |
| Male | 20 | 51 | |
| Female | 8 | 24 | |
| **Age (years)** | | | 0.83 |
| <1 | 1 | 2 | |
| 1-20 | 3 | 4 | |
| 21-40 | 10 | 28 | |
| 41-60 | 10 | 22 | |
| >60 | 5 | 18 | |
| **Mean age** | **43.5 (SD±19.2)** | **45 (SD±20.5)** | |

*Test of significance was calculated using Chi square test

**Table 3**

Drug-related problems related to restricted, semi-restricted and non-restricted antibiotics

| Total number of DRPs = 40 | |
|---|---|
| **Restricted antibiotics** | Numbers (%) |
| Meropenem | 17 (42.5) |
| vancomycin | 6 (15) |
| Teicoplanin | 4 (10) |
| Piperacillin/Tazobactam | 3 (7.5) |
| Colistin | 2 (5) |
| Amikacin | 1 (2.5) |
| **Total** | **33 (82.5%)** |
| **Semi-restricted antibiotics** | |
| Levofloxacin | 1 (2.5) |
| Cefepime | 1 (2.5) |
| **Total** | **2 (5%)** |
| **Non-restricted antibiotics** | |
| Clarithromycin | 3 (7.5) |
| Amoxicillin/clavulanic acid | 1 (2.5) |
| Metronidazole | 1 (2.5) |
| **Total** | **5 (12.5%)** |

## DISCUSSIONS

We could not find any published study specifically on antibiotic DRPs in ICU patients for direct comparison. When compared with one Chinese study conducted by Zhu et al. in the respiratory unit, which also used PCNE classification, the average number of DRPs per patient was 2.5, which was almost double as compared to our study. This reduced rate of DRPs in our study maybe because we have included only those DRPs that are specific to antibiotics while the study by Zhu et al. included all the drug classes patient is receiving [20].

In our study, we did not find any association between age and number of DRPs, but from published studies, data about the association between age and DRPs is conflicting. Some studies in geriatric patients have found that higher age is associated with more DRPs [21, 22]. Whereas studies by Koh Y et al. and Blix HS et al. did not find any association between age and number of DRPs [23, 24].

Among the various classes of antibiotics included in DRPs, a higher percentage of DRPs were observed in restricted antibiotics (82.5%) as compared to semi-restricted (5%) and non-restricted antibiotics (12.5%). In our study, among restricted antibiotics, meropenem caused highest number of DRPs, followed by vancomycin and teicoplanin. This higher percentage of DRPs with restricted antibiotics is probably because patients admitted to ICU have a more complicated situation with their infection leading to empirical usage of restricted antibiotics to cover resistant organisms [25].

In our study, more drug-related problems are related to treatment safety (60%) as compared to treatment effectiveness (32.5%). This was similar to one study evaluating DRPs among hospitalized patients with chronic obstructive pulmonary disease, using PCNE classification, but was inconsistent with previous studies where the most common identified DRPs type was treatment effectiveness [20, 26, 27]. This discrepancy with other studies might be because of differences in the study setting and different patient populations as our study is performed in ICU where patients are critically ill, and treatment safety is a major concern.

In our study, the most common causes of DRPs were related to dose selection. Among dose selection sub-domains, overdose was the most frequent cause (26.8%), which is comparable to one Kuwaiti study (30.8%) [28]. This high dosing problem was observed in patients with renal impairment where higher than recommended doses were prescribed. Many patients were receiving supra-therapeutic doses of meropenem. Also, there were sub-therapeutic dosages observed with teicoplanin, where the patient was prescribed 200 mg, while the correct dose was 400 mg. Thus, patients in ICU with an impaired kidney function must be considered for comprehensive therapeutic review by pharmacists [29].

In our study, an average of 2 interventions per DRPs was made, similar to a Chinese study by Zhu et al. (1.9) [20]. Interventions suggested to resolve DRPs were accepted to a larger degree (91.25%), which is comparable to findings in a Turkish study (93%) [30]. Chinese (96.2%) [20]. and another Cyprus study (93.1%) [27]. In our study, out of 91.25% accepted interventions, 87.5% were fully implemented; this was similar to the Swiss university hospital study (83%) [31] but lower than the study conducted in Italy (93.2%) [6]. This high acceptance illustrates the interprofessional collaboration of clinical pharmacists with other healthcare professionals in providing the best patient care. Appropriate medication reviews and interventions significantly reduce DRPs in patients admitted to ICU as these patients are at high risk for developing drug therapy problems due to complex treatment regimens [32].

The average number of DRPs found in our study per patient was less as compared to other studies. This might be because

of our focus on antibiotic-related DRPs, while other drugs were also associated with DRPs and the presence of clinical pharmacists in the hospital for many years might have a reduced number of potential DRPs that could be seen in hospitals expanding clinical pharmacy services. Due to differences in pharmacy team models in other institutions and our focus on antibiotics, our findings may not be generalizable to other settings and drugs.

## CONCLUSION

Chances of DRPs are high with restricted antibiotics. A comprehensive medication review is recommended for early identification and resolution of DRPs. Collaborative practice of clinical pharmacists resulted in the identification and resolution of antibiotic DRPs. High rates of resolution of DRPs were achieved. Further research on effectiveness of collaborative practice in more clinical areas are recommended.

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