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Drug-related problems identified by clinical pharmacists in an academic medical centre in Thailand

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ABSTRACT

Background: Drug-related problems (DRPs) are important issues that interfere with therapeutic outcomes and can cause adverse events. Pharmacists play a vital role in identifying and resolving DRPs. This study aimed to determine the characteristics, and severity of DPRs, including clinical pharmacists' interventions.

Method: A retrospective study was conducted at Ramathibodi Hospital, a tertiary university hospital in Thailand. We collected data from the drug-related problem system and the electronic medical record. Descriptive statistics were performed with Statistical Package for Social Sciences (SPSS) software version 18.0.

Results: There were 580 patients (20.44%) who had at least one DRP. We classified 1255 DRPs based on Cipolle-Strand-Morley Criteria 2012. The most common DRPs were the need for additional drug therapy (27.09%), followed by dosage too low (26.93%) and dosage too high (22.31%). Anti-infective agents (23.71%) and omeprazole (2.70%) were the most common drug groups and drugs causing DRPs, respectively. The severity of DRPs was mostly categorised to be 'no harm' (95.46%). Almost all of the interventions were completely accepted by physicians (99.12%).

Conclusion: The most common DRPs were the need for additional drug therapy and dosage adjustment of antimicrobial agents. The clinical pharmacists on wards are effective in preventing and resolving DRPs.

KEYWORDS Drug-related problems; inpatients; clinical pharmacists; Thailand

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Introduction

A drug-related problem (DRP) is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes (Hepler & Strand, 1990). DRPs are important problems in healthcare systems worldwide, associated with patient harm and increased economic burden. DRPs can occur at all steps of the treatment process, mainly during prescribing, transcribing, and dispensing. Most of them can be preventable by pharmaceutical care services (Krähenbühl-Melcher et al., 2007; van den Bemt et al., 2000). DRPs more frequently occur in hospitalised patients who have multiple changes in medication regimens, and they are commonly found in internal medicine wards, especially in university hospitals due to the complexity of patient care (Blix et al., 2004; Krähenbühl-Melcher et al., 2007; Sarfaraz et al., 2017). The high prevalence of DRPs has been associated with an advanced age, a higher number of medications used, multiple comorbidities, and prolonged hospitalisation (Bekele et al., 2021; Blix et al., 2004; Garin et al., 2021; Lea et al., 2019; Sarfaraz et al., 2017; Urbina et al., 2014). Studies investigating DRPs among hospitalised patients have been conducted worldwide. In Thailand, DRPs identified from patients admitted to a general medical ward or a medical intensive care unit ranged from 23 to 74% (Chanatepaporn, 2013; Deawjaroen et al., 2022; Kitpaiboontawee, 2017; Tharanon et al., 2022; Wanishayakorn et al., 2022).

Pharmaceutical care is a key strategy to identify and resolve DRPs. Clinical pharmacists have an important role in healthcare teams to improve patient care by supporting drug therapy management. There are no credentials in Thailand for working as a clinical pharmacist. The practice of clinical pharmacists in Thailand typically focuses on patient-oriented service that requires specialised therapeutic knowledge and experience to evaluate the appropriateness of patients' medications on various units. Several studies have shown that clinical pharmacists play an essential role in acute care for resolving DRPs, including cost-saving (Abunahlah et al., 2018; Albayrak et al., 2022; Al-Maqbali et al., 2022; Blix et al., 2006; Guignard et al., 2015; Lampert et al., 2008; Reinau et al., 2019). Understanding the characteristics of DRPs may provide implementation to improve clinical pharmacy services. Although their contributions to patient care have been shown in various countries, the role of clinical pharmacists in Thailand remains to be clearly elucidated. Therefore, the aim of this study was to describe the characteristics of DRPs in hospitalised patients, including characteristics and results of clinical pharmacists' interventions at a tertiary university hospital in Thailand.

Methods

Study design and participants

This study was a retrospective descriptive study at Ramathibodi Hospital, a tertiary university hospital in Thailand. Patients who were admitted to the medical wards or the intermediate care unit from July 2019 to June 2020, who were prescribed at least one medication were included. Patients were excluded if they were not prescribed any medication. The study period was 6 months from August 2021 to February 2022 for data collection and analysis. DRPs were categorised into seven major classes according to the Cipolle-Strand-Morley (2012) criteria; unnecessary drug therapy, need additional drug therapy, ineffective drug therapy, dosage too low, dosage too high, adverse drug reaction (ADR) and non-compliance (Cipolle et al., 2012). The study was approved by Human Research Ethics Committee, Faculty of Medicine Ramathibodi Hospital, Mahidol University (COA.MURA2021/685). Institutional Review Boards in Mahidol University are in full compliance with International Guidelines for Human Research Protection involved Declaration of Helsinki, The Belmont Report, CIOMS Guidelines and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP). In view of the retrospective nature of the study informed consent was not required.

Clinical pharmacy practice in this setting

The clinical pharmacists routinely worked on the wards from Monday to Friday (average 6 h per day) for rounds with the healthcare team and remained on wards to provide pharmaceutical care. However, working on weekend support for some cases may be need to closely monitored. The junior clinical pharmacists were trained by the senior clinical pharmacists with board-certified pharmacotherapy specialist or Master of Science in clinical pharmacy. They also have working experiences on wards with healthcare teams. The training includes advanced skills and knowledge for a specific population depending on the characteristics of patients admitted in each unit. Appropriate training was provided prior to commencing the work on ward (at least 3 months) and qualified by a senior pharmacist. There have been 1–2 clinical pharmacists on each ward.

Data collection

Data were collected from the drug-related problem system which was filled in the database by the clinical pharmacists and electronic medical record (EMR). Clinical pharmacists on wards performed daily medication reviews to identify DRPs on the basis of pharmaceutical care. An intervention was verbal direct communication with physicians. In addition, the severity of these DRPs was

assessed using the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP). The results of the intervention were categorised as accepted, partially accepted, or not accepted interventions.

Data analysis

Data were analysed using SPSS software version 18.0. Characteristics of DRPs, drug-causing DRPs, the severity of DRPs, and the clinical pharmacists' interventions were analysed using descriptive statistics; frequency and percentage for categorical variables and mean ± standard deviation (SD) or median (interquartile range) for quantitative variables.

Results

During the one-year study period, 2837 patients were included in the study. Among these patients, DRPs were found by clinical pharmacists in 580 patients (20.44%). Most of the patients were the elderly (≥65 years). The median age was 65 (29) years. Females were predominant (54.31%). Most of the DRPs were found in patients who were admitted to the female medical ward (47.93%). Characteristics of patients are shown in Table 1.

Characteristics of drug-related problems

A total of 1255 DRPs were identified among 580 patients, giving an average of 2.16 DRPs per patient. The three majority of DRPs were the need for additional drug therapy (27.09%), dosage too low (26.93%) and dosage too high (22.31%), respectively. The identified DRPs based on Cipolle-Strand-Morley criteria 2012 are shown in Table 2. Regarding the stage of care, the problems were mostly found during hospital stay (51.55%) with dosage too low and dosage too high (52.70%; 341/647) being the most commonly identified. The need for additional therapy was mainly found at discharge when compared with other stages (52.65%; 179/340). The summarised DRPs at each stage of care are presented in Table 2.

Table 1. Characteristics of patients with DRPs ($n = 580$).

Characteristics	Value
Male (%)	265 (45.69)
Female (%)	315 (54.31)
Age, years	
<65	283 (48.79)
≥65	297 (51.21)
Medical wards	
Male-medical ward	200 (34.48%)
Female-medical ward	278 (47.93%)
Intermediate care unit	102 (17.59%)

Table 2. DRPs were categorised into different types and the stage of care.

Drug-related problems ($n = 1255$)	Frequency (%)	Admission ($n = 139$)	During hospital ($n = 647$)	Discharge ($n = 469$)
1. Need additional drug therapy	340 (27.09)	74	87	179
2. Dosage too low	338 (26.93)	18	170	150
3. Dosage too high	280 (22.31)	18	171	91
4. Unnecessary drug therapy	155 (12.35)	4	133	18
5. Ineffective drug	101 (8.05)	4	72	25
6. Non-adherence	27 (2.15)	20	5	2
7. Adverse drug reaction	14 (1.12)	1	9	4

Drug classes involved in drug-related problems

A total of 1295 drugs were involved in DRPs, which were categorised as AHFS Pharmacologic Therapeutic Classification. The drug classes mostly involved in causing DRPs were found to be anti-infective agents 307 items (23.71%), Electrolytic Caloric and Water balance agents 179 items (13.82%), and Cardiovascular drugs 171 items (13.20%), respectively. The frequency of drug groups causing DRPs is shown in Table 3. Omeprazole was the most common drug causing DRPs (2.7%; 35/1295), and mostly required for additional therapy. Ganciclovir and cefepime were commonly related to dose selection as dosage too low and dosage too high. The top 10 drugs causing DRPs are presented in Table 4.

The classification of severity of DRPs

The severity of DRPs was mostly categorised to be 'no harm' as severity B and C (95.46%). The severity with potential harm (Category D) and with harm (Category E) accounted for 3.75% and 0.80%, respectively. Most of the DRPs with potential harm resulted from dosage too high of drug therapy (34.04%; 16/47). In addition, almost all of the DRPs with harm (Category E) were related

Table 3. Classification of drug groups causing DRPs.

Drug classes	Frequency (%)
Anti-infective agents	307 (23.71)
Electrolytic, Caloric and Water balance	179 (13.82)
Cardiovascular drugs	171 (13.20)
Hormones and Synthetic Substitutes	103 (7.95)
Gastrointestinal drugs	92 (7.10)
Blood formation, Coagulation and Thrombosis	85 (6.56)
Central Nervous System agents	83 (6.41)
Miscellaneous Therapeutic agents	82 (6.33)
Vitamins	61 (4.71)
Respiratory tract agents	35 (2.70)
Autonomic drugs	30 (2.32)
Eye, Ear Nose and Throat (EENT) preparations	23 (1.78)
Skin and Mucous Membrane agents	21 (1.62)
Antineoplastic agents	8 (0.62)
Total	1295 (100)

Table 4. Top 10 drugs causing DRPs ($n = 1295$).

No.	Drugs	Frequency (%)
1	Omeprazole	35 (2.70)
2	Co-trimoxazole	34 (2.63)
3	Ganciclovir Atorvastatin	29 (2.24)
4	Acyclovir	28 (2.16)
5	Tacrolimus Prednisolone	27 (2.08)
6	Calcium carbonate	25 (1.93)
7	Lamivudine Potassium chloride	24 (1.85)
8	Cefepime Furosemide Vitamin D	22 (1.70)
9	Sodium bicarbonate	21 (1.62)
10	Vitamin B	19 (1.47)

Table 5. The severity of DRPs classified according to severity by The National Coordinating Council for Medication Error Reporting and Prevention.

Category	Frequency (%)
B (The DRP occurred but did not reach the patient)	952 (75.86)
C (The DRP occurred and reached the patient, but did not cause patient harm)	246 (19.60)
D (The DRP occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm)	47 (3.75)
E (The DRP occurred that may have contributed to or resulted in temporary harm to the patient and required intervention)	10 (0.80)
Total	1255

to non-adherence to medications before hospitalisation (9 problems). The type of severity is presented in Table 5, and the details of DRPs with Category E are shown in Table 6.

Clinical pharmacists' interventions to resolve the DRPs

Clinical pharmacists' interventions were provided according to DRPs identification (Table 7). All DRPs were verbally and directly discussed with physicians

Table 6. The details of DRPs that may have contributed to temporary harm to the patient and required intervention.

Category	Drugs	Details
E	Aspirin, doxazosin, enalapril, hydralazine, lercanidipine, doxofylline, tiotropium	Patient stop taking their medications for months, and may relate to admission with dyspnea and high blood pressure.
	Cefepime	Patient received high dose (did not adjust according to renal function), and then found neurotoxicity.
	Valproic acid	Patient has misunderstanding how to use medication.
	Insulin	Patient has fear about self-injection, and then found hyperglycemia.

Table 7. Characteristics and results of the clinical pharmacists' interventions.

		The number of interventions		
Category	Frequency (%)	Accepted	Partially accepted	Not accepted
Drug recommendation	340 (27.09)	337	2	1
Dose adjustment	618 (49.24)	614	1	3
Drug discontinuation	156 (12.43)	155	1	0
Drug change	103 (8.21)	101	1	1
Administration change	11 (0.88)	11	0	0
Provision of information	27 (2.15)	26	1	0
Total	1255 (100)	1244	6	5

to resolve the problems. The acceptance of the interventions was 99.12%, whereas 0.48% was partially accepted. It can be concluded that the clinical pharmacists' participation in medicine wards is effective in resolving DRPs.

Discussion

This study analysed DRPs identified by clinical pharmacists in hospitalised patients at a tertiary teaching hospital in Thailand. We found that 580 patients (20.44%) had at least one DRP. This number is lower than that found in critically ill patients. The two studies by Tharanon et al. (2022) and Albayrak et al. (2022) reported that around 70% of patients admitted to the medical intensive care unit (ICU) had at least one DRP. Patients hospitalised in the ICU are prone to polypharmacy from their multiple comorbidities and organ dysfunction, which are potentially inappropriate dosage adjustment, adverse drug reactions, and drug–drug interactions (Abunahlah et al., 2018; Ni et al., 2021; Peterson & Gustafsson, 2017). In addition, the average DRP per patient with an identified case was 2.2. This in line with several studies where an average 1–2 DRPs per patient were found (Albayrak et al., 2022; Bekele et al., 2021; Blix et al., 2004; Garin et al., 2021; Sefera et al., 2022; Semcharoen et al., 2019; Liu et al., 2021; Tharanon et al., 2022). This average number is slightly higher than that found by Semcharoen et al. (1.04) (2019) and Liu et al. (1.2) (2021), which studied DRPs in specific settings at the neurology unit and stroke unit, respectively. This may be explained by more specialised services and medical experts than one in general medical wards. However, the prevalence and average number of DRPs per patient could vary among healthcare settings, study populations, and DRPs classification.

The Pharmaceutical Care Network Europe (PCNE) system used in other studies is different from the one used in our study. The PCNE is a much more details classification that consists of primary domains and subdomains to identify problems, including causes and interventions. Therefore, more DRPs may be identified and classified into different groups. In this study, DRPs were categorised according to Cipolle et al. (2012). The majority of problems were classified as need for additional drug therapy and dosage

too low (approximately equal to 27%), followed by dosage too high (22.31%). Although the type of DRPs may be differently classified among studies, drug and dose selection were frequently identified in causing problems aligned with several studies (Blix et al., 2004; Garin et al., 2021; Wincent et al., 2017). Our finding is also similar to studies conducted in Thailand. Chanatepaporn et al. reported that DRPs was commonly found as improper dose regimen (32.94%) and untreated indication (10%) (Chanatepaporn, 2013). Semcharoen et al. found that the most of DRPs were untreated indications (22.6%) among inpatients admitted to the stroke unit (Semcharoen et al., 2019). In a study by Deawjaroen et al., the most frequent problems leading to DRPs among hospitalised patients at general medical wards were untreated symptoms/indications (30.7%) (Deawjaroen et al., 2022). In contrast with a study conducted in Thailand, a dosage too high was found to be the most DRPs (27.7%) in critically ill patients at a tertiary university hospital (Tharanon et al., 2022). This difference may be resulted from disease severity in renal impairment, and several medications used in ICU that affect drug-drug interaction. In another study at medical wards of southwestern Ethiopian hospitals, DRPs were mainly found as unnecessary drug therapy (27.79%) (Bekele et al., 2021). Characteristics of DRPs among studies could be varied from classification system, different populations, disease severity, and health care services in each setting.

Considering the stage of care, the most frequent DRPs commonly occur during hospital stay (52%), classified as inappropriate dosing (overdose or under-dose). Additionally, no drug treatment with existing diseases or conditions was commonly found on hospital discharge (52.65%) when compared with other stages. These problems were identified by the clinical pharmacists as prescribing errors (82.12%) in the medication reconciliation process. Consistent with the study of Deawjaroen et al., the omission of medications was commonly found on hospital discharge (Deawjaroen et al., 2022). In another study, the main problems were dosage too low and the need for additional drug therapy in patients followed up by pharmacists after hospital discharge (Westberg et al., 2017). Therefore, comprehensively reviewed discharge medication is an important process to resolve DRPs and reduce the risk of hospital readmissions.

The severity of DRPs was mostly considered as 'no harm' with NCC-MERP classifications of B–C (95.46%) in line with findings from several studies. The severity of DRPs with no harm was commonly assessed in a tertiary academic hospital in Thailand (Tharanon et al., 2022) and in China (Li et al., 2020) as 78.2% and 86.9%, respectively. Similar to other studies in a tertiary teaching hospital in China, most DRPs classified as no harm and potential harm (B-D) varied from 75% to 89% (H. Liu et al., 2022; Meng et al., 2021; P. Liu et al., 2021). This result also implied that clinical pharmacists could detect and manage DRPs prior to being harmed. However, one of the problems that

caused harm to the patient and required intervention (Category E) in our study was no dosage adjustment according to renal function (adverse event from dosage too high) during the hospital stay. Other medications were frequently found as cardiovascular drugs from non-adherence that may be related to hospital admission. As the result, mainly DRPs with harm were non-adherence caused by misunderstanding the use of medicine, no concern about taking medication, and inability to self-administer the drug product appropriately. Therefore, clinical pharmacist counselling is an essential role to improve patient medication adherence before discharge.

The drug groups causing most DRPs were anti-infective agents (23.71%), which is in accordance with several studies (Deawjaroen et al., 2022; Garin et al., 2021; Hohmann et al., 2012; Li et al., 2020; Lombardi et al., 2018; Sarfaraz et al., 2017; Tharanon et al., 2022; Wanishayakorn et al., 2022). Most of the anti-infective agents were dose-related problems. Furthermore, antimicrobials were the most frequently involved drug group of clinical pharmacists' interventions at a tertiary care hospital in Oman (30%) (Al-Maqbali et al., 2022), and in Abu Dhabi (31%) (Al-Quteimat et al., 2023). In contrast to findings from other studies where proton pump inhibitors (Tharanon et al., 2022) and analgesics (Francisco et al., 2021) were the most common drug classes involved in pharmacists' interventions. Additionally, warfarin and prednisolone were mostly found to be involved in DRPs reported by Blix et al. (2004). However, the drug that most frequently caused DRPs in this study was omeprazole, similar to a study conducted at the University of Gondar showed that omeprazole (17.6%) was commonly found (Bhagavathula et al., 2017).

The acceptance rate of the clinical pharmacists' interventions was high at 99.12%. Almost all of the clinical pharmacist's interventions were accepted by physicians which led to changes in drug therapy. This seems to be consistent with other studies on the internal medicine ward of teaching hospitals, where a high acceptance rate was reported to be more than 90%; Swiss university hospital (96.8%) (Reinau et al., 2019), Brazilian teaching hospital (97.8%) (Francisco et al., 2021), Italy hospital (93.2%) (Lombardi et al., 2018). This result indicates that ward-based clinical pharmacy services in this setting were recognised with positive collaboration between physicians and clinical pharmacists. In this study, dose adjustment was the most common intervention (49.24%), followed by recommending the addition of a drug therapy (27.09%). Consistent with the findings by Al-Maqbali et al. (2022), their results showed that adjusting doses was the most common intervention, followed by recommending the addition of a drug therapy at a tertiary care university hospital in Oman. Similar to Albayrak et al., dose changes (56.79%) were reported in most of the interventions at the ICU of a university hospital in Turkey (Albayrak et al., 2022).

The strengths of this study indicate that clinical pharmacists have an important role in identifying DRPs and preventing harm to hospitalised

patients, and the results provide information to implement ward-based pharmacy services, especially in a similar setting. This study has some limitations as follows. First, this study is a retrospective descriptive study in which analysis using data collected from the clinical pharmacist record of routine pharmacy service. A prospective study may be more complete data to elucidate the results. Second, this study was conducted in a single academic centre. The results might not be generalised to others. Thus, future studies can be performed with multiple settings, and a factor associated with DRPs in Thailand should be clarified to implement an optimal pharmacy service.

Conclusion

The most common DRPs identified were the need for additional drug therapy and dosage adjustment of antimicrobial agents. Most of the clinical pharmacists' interventions could prevent harm to patients. Clinical pharmacy practices should focus on medication discharge counselling, medication reconciliation at discharge, and antimicrobial stewardship. Further prospective studies are needed to elucidate the impact of ward-based pharmacy services.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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