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Original Research

Evaluation of Drug-Related Problems in the Chronic Kidney Disease Clinic at the University Hospital in Thailand

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Abstract

Background: The chronic kidney disease (CKD) clinic plays a vital role in providing comprehensive ambulatory care for patients with CKD. Pharmacists contribute to ensuring proper drug use and identifying potential drug-related problems (DRPs). However, the evaluation of DRPs in the early phase of CKD clinic, particularly in resource-limited countries, remains limited. **Objective:** This study aimed to assess the prevalence of DRPs in CKD patients attending a CKD clinic, investigate the associated drug categories, and identify factors contributing to DRPs in CKD patients. **Methods:** A cross-sectional study was conducted from January 2020 to June 2021 among CKD patients attending a CKD clinic. Patient information records were used to collect demographic and relevant CKD data. A checklist for DRPs related to CKD progression and complications was utilized. Eight categories of unmet DRPs were examined. Multiple linear regression was used to investigate the relationship between pre-defined factors and the number of DRPs per patients. **Results:** The study included 80 patients with a total of 1,073 prescribed medications. The mean age was 73.1 ± 10.0 years, and the mean estimated glomerular filtration rate (eGFR) was 43.4± 12.9 mL/min/1.73 m². A total of 269 DRPs (25.1% of prescriptions) were identified, primarily involving the need for additional drug therapy (14.9%), dosage too high (6.3%), and inappropriate drug therapy (1.5%). Notably, renin-angiotensin-aldosterone system (RAAS) blockers were frequently omitted when indicated. NSAID use, non-compliance, and drug interactions were notable issues. The significant predictor of DRPs was the number of medications more than 7 items (ß = 0.258, P = 0.02). **Conclusions:** Implementing medication optimization in CKD care involving multidisciplinary teams and pharmacists is essential. Our study highlights the importance of ACEIs/ARBs, dosage adjustments, avoiding nephrotoxic agents, addressing non-compliance, and managing drug interactions for improved CKD care. The study identifies polypharmacy as a significant predictor of DRPs among CKD patients, facilitating targeted interventions for at-risk patients.

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INTRODUCTION

Chronic kidney disease (CKD) has been recognized as a significant public health problem worldwide. The estimated global prevalence of CKD is 13.4% and is predicted to become the fifth leading cause of death by 2040.[1-2] Individuals with kidney diseases are among the most vulnerable in the population, requiring consistent patient care. CKD is typically a lifelong disease, beginning with asymptomatic stages and progressing to end-stage kidney disease, necessitating kidney replacement therapy. The consequences of CKD not only impact patient quality of life but also entail significant involvement from healthcare providers at every stage of CKD management. Additionally, the projected increase in CKD patients in the future will impose a substantial economic burden at both global and national levels.[2]

The main goal of managing CKD patients is to prevent the progression of CKD to complete loss of kidney function, treat CKD complications, and prevent heart disease.[3] To achieve these goals, early detection of abnormalities and the use of several medications are necessary. Medications used in CKD patients are indicated for the treatment of both co-morbidities and specific kidney complications. As a result, polypharmacy is common in CKD across all stages of kidney disease, leading to drug-related problems (DRPs).[4-5] Several studies conducted in kidney patients have identified DRPs across various clinical spectrums, including patients with acute kidney injury, CKD, or those receiving kidney replacement therapy.[4–8] A

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multidisciplinary team, consisting of specialists highly skilled and trained in their respective fields, collaborates to provide comprehensive patient care for many chronic diseases, including CKD. Such team collaboration has shown a positive impact on patient outcomes and the cost of care.[9] In the setting of kidney patients, pharmacists play a pivotal role in identifying medication problems and increasing patient knowledge about CKD and associated diseases.[6-7,10] A recent systematic review demonstrated the positive impact of clinical pharmacy services on CKD patients in various aspects and settings.[11] While studies have showcased the effectiveness of multidisciplinary teams in the care of CKD patients as part of national policies in certain regions, there remains a scarcity of research focused on evaluating DRPs specifically in CKD clinics in resource-limited countries. Therefore, caution should be exercised when attempting to generalize findings from other studies to this particular context. The study primarily focused on DRPs in CKD patients attending a CKD clinic, including the prevalence of DRPs, the most common medications associated with DRPs, and factors contributing to DRPs in CKD patients.

METHODS

Study setting and CKD clinic

At Golden Jubilee Medical Center, a hospital operated by the Faculty of Medicine Siriraj Hospital, Mahidol University, a CKD clinic was established and has been implemented in the ambulatory care department since 2017 as part of the national CKD service plan. The CKD clinic is served by a multidisciplinary team consisting of nephrologists, pharmacists, nurses, nutritionists, and social workers. Initially, patients with stage 3-5 CKD (pre-dialysis) were selected to attend the CKD clinic, where they receive multidisciplinary care. The pharmacists responsible for patient care in the CKD clinic review all medications and the latest laboratory results from the hospital records approximately one week before the patient's appointment. On the clinic day, the pharmacists primarily perform medication reconciliation, identify nephrotoxic medications such as non-steroidal anti-inflammatory drugs (NSAIDs), assess patient compliance, and provide patient education. These activities are documented in the pharmacy note within the medical record. If the pharmacists identify any DRPs, they consult with physicians or provide education to the patients. The CKD service follows up with patients every 3–12 months for stage 3 CKD and conducts closer monitoring of patients with stage 4–5 CKD (every 1-3 months). The flowchart depicting the services provided to patients attending the CKD clinic is presented in Figure 1.

CKD = chronic kidney disease, CKD-MBD = chronic kidney disease-mineral and bone disorder, eGFR = estimated glomerular filtration rate, ESKD = end stage kidney disease, ND = non-dialysis

Study design

The cross-sectional study included CKD patients attending CKD clinics at Golden Jubilee Medical Center between January 2020

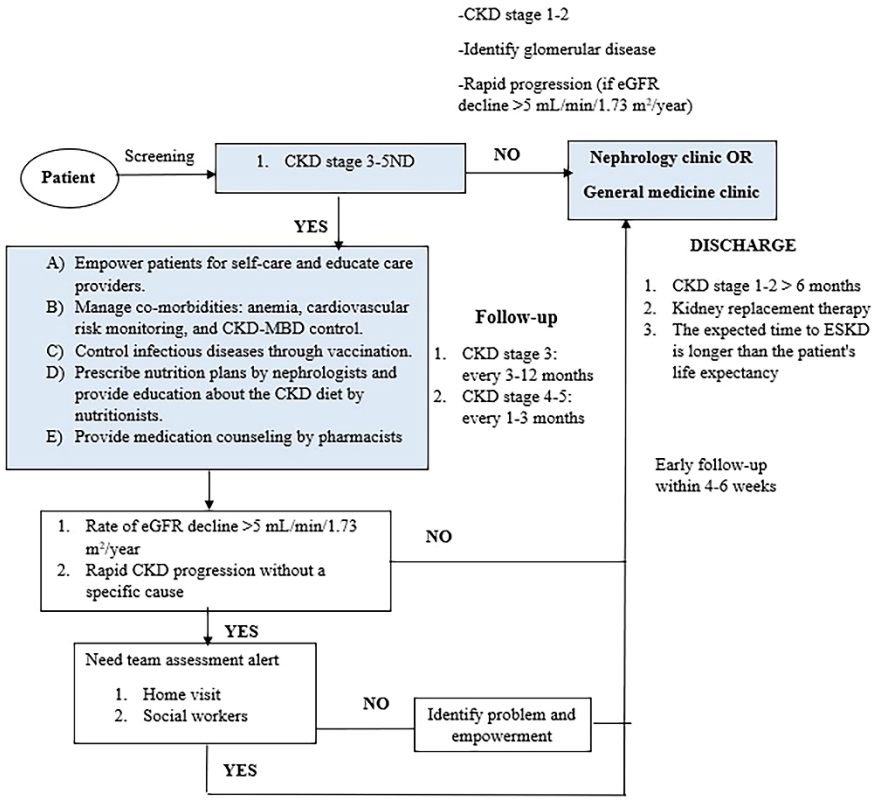

Figure 1. Process flow chart of CKD clinic

and June 2021. As each patient could attend the CKD clinic multiple times during the study period, we used the number of medications prescribed to gauge the quality and detect DRPs, which determined the sample size calculation. The formula used for sample size calculation was $N = [Z^2_{\alpha/2} \times P (1-P)]/M^2$, where Z represents the Z statistic for a 95% confidence level, P is the proportion of DRPs found in CKD patients (0.13 based on a study by Jones SA[12]), and M is the margin of error (0.05). Consequently, a minimum sample size of 174 prescriptions was deemed appropriate for our study.

Ethics Approval

This study protocol was approved by the Institutional Review Board of Siriraj Hospital, Mahidol University, Thailand (IRB Number: 733/2564 (IRB4)). The study was also registered and approved by the Thai Clinical Trials Registry (TCTR20220503003). This study was solely a retrospective review of the data gathered from the electronic medical record based on routine service. Therefore, formal consent from individual patients was not required.

Participant selection

Adult patients (age ≥18 years) with stages 3-5 CKD (non-dialysis) or diagnosed with CKD, receiving care at the CKD clinic at the study site, were eligible for inclusion in the study. We identified potential study participants by reviewing the pharmacist records of patients attending CKD clinics during the study period. Patients with insufficient information to evaluate kidney function or drug information were excluded from the study.

Data collection and DRP detection

We administered a structured patient information record to each study participant to collect demographic data and relevant clinical history related to CKD progression and medication review. The interview was followed by a retrospective chart review of the participant's clinical and medication records to gather additional information, such as physical examination findings and laboratory results. The investigators also collected information on the participant's history of NSAID use and non-compliance, based on the pharmacist's records in the CKD clinic.

Each participant's data were reviewed alongside a list of all prescribed medications to identify and classify potential DRPs using the Hepler and Strand classifications.[13] Eight categories of unmet DRPs, including unnecessary drug therapy, need for additional drug therapy, inappropriate drug use, dosage too low, adverse drug reactions, dosage too high, non-adherence or non-compliance, and drug interactions, were assessed. A checklist of criteria for evaluating DRPs in slowing CKD progression and managing CKD complications was developed and finalized by our investigators, who are board-certified pharmacotherapy specialists with experience in pharmacotherapy for kidney disease. The DRP checklist in our study adhered to standard clinical practice guidelines, including the Kidney Disease Improving Global Outcomes (KDIGO) guidelines.[14-19] Additionally, we referred to Micromedex®[20-21] for prescribing information, determining the clinical significance of drug-drug interactions, and evidence-based recommendations for CKD care.[3,22–26] (Appendix 1).

Data analyses

Baseline patient characteristics, information regarding kidney function, information on drug therapies, and DRP findings were analyzed using descriptive analysis. Continuous data were presented as mean ± standard deviation (SD) or median ± interquartile range (IQR), depending on the normality of the data distribution. Dichotomous data were presented as rates and percentages. The primary outcome was the total number of DRPs observed from the list of all medications prescribed to patients attending the CKD clinic at each visit. The relative frequencies of individual categories of DRPs were calculated as proportions of the total number of DRPs observed across all drug prescriptions. The percentages of drug items that caused each type of DRP were investigated.

Multiple linear regression was utilized to investigate the relationship between pre-defined factors and the number of DRPs per patient. To ensure adequate statistical power, given the relatively small sample size of 80 patients, two covariates were selected: estimated glomerular filtration rate (eGFR) and the number of medications; these covariates were chosen based on the rule of thumb proposed by Wilson Vanvoorhis CR,[27] as well as a study by Holm H[4], which demonstrated their significant association with DRPs in CKD patients. A significance level of $p \leq 0.05$ was used to determine statistical significance. Additionally, sensitivity analyses were conducted to identify the threshold number of medications that could lead to significant DRPs, which could be valuable for workflow and workload planning. The data analyses were performed using IBM SPSS Statistics Version 18.

RESULTS

During the study period, 475 patients were admitted to the CKD clinic. Among them, 395 patients were excluded due to insufficient information for evaluating kidney function or drug-related details. Consequently, 80 patients were included, and a total of 1,073 prescribed drugs provided sufficient statistical power for the study. The patients had a mean age of 73.1 ± 10.0 years, with a mean eGFR of 43.4 ± 12.9 mL/min/1.73 m², as shown in Table 1. The majority of the patients (52.5%) had stage

Table 1. Baseline characteristics (N= 80)

Baseline characteristics	Number of patients, n (%)
Male (%)	46 (57.5%)
Age, year ± SD	73.1 ± 10.0
-Age ≤ 60 years (%)	9 (11.2%)
-Age > 60 years (%)	71 (88.8%)
Weight, kg ± SD	64.7 ± 10.8
Height, cm ± SD	162.4 ± 9.1
Body mass index, kg/m² ± SD	24.6 ± 9.1
eGFR, mL/min/1.73 m² ± SD	43.4 ± 12.9

-Stage 1 (%)	1 (1.3%)
-Stage 2 (%)	3 (3.8%)
-Stage 3a (%)	42 (52.5%)
-Stage 3b (%)	28 (35.0%)
-Stage 4 (%)	6 (7.5%)
Total protein to creatinine ratio, mg/mg ± SD	0.4 ± 0.6
Underlying disease (%)	
-Dyslipidemia	64 (80.0%)
-Hypertension	57 (71.0%)
-Type 2 diabetes mellitus	32 (40.0%)
CKD complications* (%)	
-Anemia	30 (37.5%)
-Hyperkalemia	30 (37.5%)
-Hyperuricemia	23 (28.8%)
-Vitamin D deficiency	15 (18.8%)
-Metabolic acidosis	7 (8.8%)
Current use of NSAIDs at CKD clinic visit	8 (10.0%)
Number of prescription drugs per patient, item ± SD	13.4 ± 12.9
- ≤ 5 items (%)	30 (37.5%)
- > 5 items (%)	50 (62.5%)

CKD = chronic kidney disease, eGFR = estimated glomerular filtration rate, NSAIDs = non-steroidal anti-inflammatory drugs
* Complications were considered when patients did not achieve the goal of each condition in more than 50% of their visits.

3a CKD, followed by stage 3b, 4, 2, and 1 CKD, respectively. The mean urinary protein to creatinine ratio was 0.4 ± 0.6 mg/g, categorized as stage A1. More than 70% of the patients had hypertension and dyslipidemia, and 40% had type 2 diabetes mellitus. Approximately 40% of the patients had anemia and hyperkalemia as CKD complications. Eight patients (10%) received NSAIDs, which were considered DRPs (inappropriate therapy). The mean number of prescription drugs was 13.4 ± 12.9 items per patient, and the majority of patients received more than 5 items.

Frequency of DRPs and medications related to each DRP category

We identified a total of 269 DRPs, accounting for 25.1% of all prescriptions in the study. Among these, the three most prevalent DRP categories were the need for additional drug therapy (14.9%), dosage too high (6.3%), and inappropriate drug therapy (1.5%), respectively. Interestingly, no DRPs were found in the dosage too low and adverse drug reaction categories (Figure 2).

Among CKD patients with hypertension, the most frequently absent medications were angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) (n=46, 28.8%). In cases where ACEI/ARB therapy was necessary, patients exhibited uncontrolled hypertension (blood pressure >130/80 mmHg), albuminuria (stage A1), or had diabetes mellitus, indicating the appropriateness of using medications that target the renin-angiotensin-aldosterone system (RAAS).

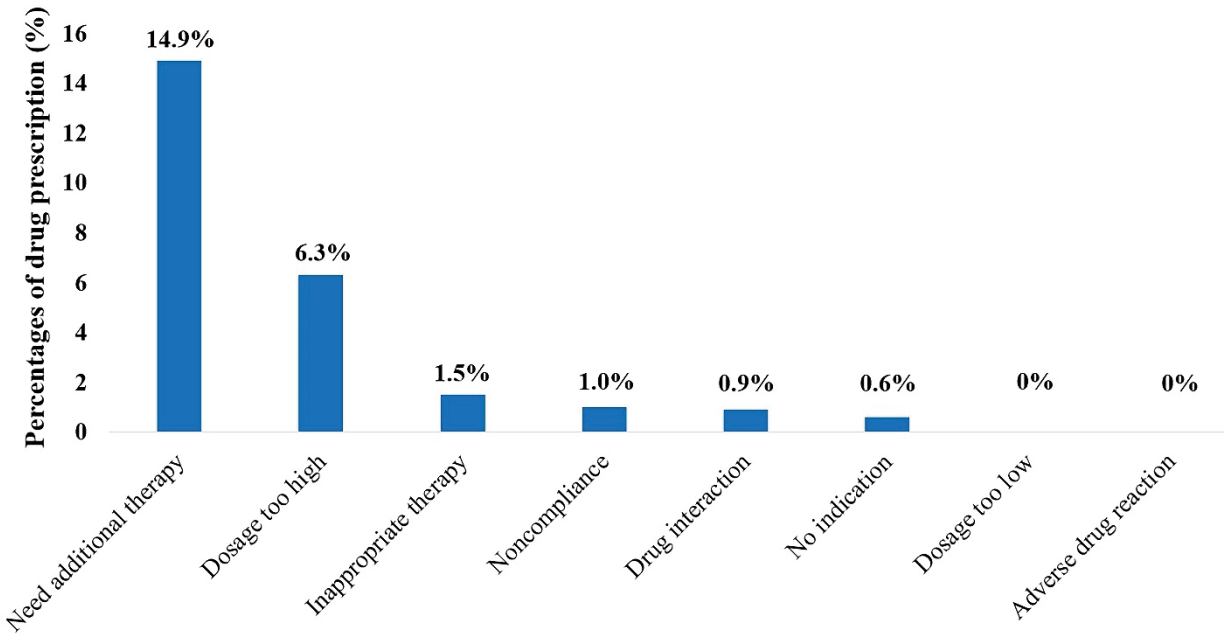

Figure 2. The percentage of each drug-related problem (DRP) category

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Among the drug groups requiring additional therapy for the treatment of anemia in CKD, vitamin B12, ferrous salt, and folic acid were identified. The primary cause of dosage too high was found to be a natural vitamin D supplement, followed by darbepoetin for erythropoietin stimulation, and other medications that were not appropriately adjusted based on the patient's eGFR in accordance with reference guidelines. The most common inappropriate therapy problem identified in this DRP category was the prescription of non-steroidal anti-inflammatory drugs (NSAIDs) by non-nephrologists. These prescriptions were screened by pharmacists, as patients attending CKD clinics were specifically targeted for evaluation in this regard. Nephrologists acknowledged and acted upon the information provided by pharmacists to discontinue the use of NSAIDs due to their potential kidney toxicity. Sodium-glucose cotransporter-2 (SGLT2) inhibitors were prescribed for 4 patients with eGFR below the recommended range, and the combination of drugs in the same mechanism, calcium channel blockers or RAAS inhibitors, fell into the DRP category of inappropriate therapy. Non-compliance was identified in 11 instances, accounting for 1% of drug prescriptions. A comprehensive list of drugs associated with each DRP category is shown in Table 2.

The relationship between covariates and the occurrence of DRPs

Multiple linear regression revealed a correlation between the number of medications and the incidence of DRPs (ß = 0.436, P = 0.01). Our sensitivity analyses indicated no relationship between the occurrence of DRPs and the number of medications exceeding 5 items. However, a significant association was observed for the number of medications exceeding 7 items (ß = 0.258, P = 0.02). Regarding kidney impairment, there was no significant correlation found between the decrease in kidney function (as measured by eGFR) and the occurrence of a high number of DRPs (ß = -0.141, P = 0.21). The majority of patients in the study had stage 3a or 3b CKD (87% of patients), and they had a higher percentage of prescriptions causing DRPs

Table 2. The proportion of drug causing drug-related problems (DRPs)

Drugs		**The proportion of drug-related problems (%)**
Need additional therapy		**160 (100.0%)**
ACEIs/ARBs		46 (28.8%)
Vitamin B12		36 (22.5%)
Ferrous salt tablet		28 (17.5%)
Folic acid		25 (15.6%)
Others		25 (15.6%)
Dosage too high		**68 (100.0%)**
Calciferol		51 (75.0%)
Darbepoetin alfa		6 (8.8%)
Silodosin		4 (5.9%)
Cefdinir		2 (2.9%)
Others		5 (7.4%)
Inappropriate therapy		**16 (100.0%)**
NSAIDs		10 (62.5%)
Empagliflozin/linagliptin		4 (25.0%)
Amlodipine with manidipine		1 (6.3%)
Captopril with losartan		1 (6.3%)
No indication		**6 (100.0%)**
Silodosin		4 (66.7%)
Tamsulosin		1 (16.7%)
Sildenafil		1 (16.7%)
Drug interaction	***Severity of interaction****	**10 (100.0%)**
Calcium carbonate with ferrous fumarate	Minor	6 (60.0%)
Furosemide with pioglitazone	Moderate	2 (20.0%)
Azithromycin with simvastatin	Major	1 (10.0%)
Simvastatin with fenofibrate	Major	1 (10.0%)

ACEIs = angiotensin converting enzyme inhibitors, ARBs = angiotensin receptor blockers, DRPs = drug-related problems, NSAIDs = non-steroidal anti-inflammatory drugs
*Severity of interaction was classified by Micromedex®

compared to those with stage 1, 2, and 4 CKD (approximately 10% of prescription for stage 3a, 3b CKD and 4% of prescriptions for stage 1, 2, and 4 CKD).

DISCUSSION

A multidisciplinary team involves a range of health professionals to deliver comprehensive patient care. Many studies in resource-limited settings have shown that engaging with specialists can effectively enhance health outcomes and delay the progression of CKD.[28–30] Our study findings revealed that even with a multidisciplinary approach, 25% of drug prescriptions in patients with CKD still require medication therapy optimization. The primary focus should be on adding drugs that assist in delaying the progression of kidney disease, as well as adjusting dosages based on kidney function, which were identified as the two most prevalent DRP categories, accounting for approximately 80% of overall DRPs identified. These interventions are crucial for maximizing therapeutic effectiveness, enhancing the quality of life, and minimizing adverse drug reactions among CKD patients.

Pharmacists play a crucial role in identifying, addressing, and preventing DRPs in the multidisciplinary team for kidney patients.[6-7,10] The prevalence of DRPs among kidney patients varies across several studies, influenced by factors such as the composition and working procedures of the healthcare team, drug utilization patterns dictated by hospital policies and patient insurance, as well as the availability and accessibility of evidence databases and patient information. In a prospective study conducted by Mongaret C,[31] the role of community pharmacists (CPs) in detecting DRPs based on kidney function was investigated. Due to limited access to laboratory data, including eGFR, patients in the study provided their test information (including eGFR) during subsequent visits to the CPs. The results demonstrated that considering eGFR enabled CPs to detect a higher number of DRPs, with 70% of the DRPs attributed to the dosage being too high. While most studies have primarily examined high-income countries[4,8,10,32-33], our study aligns with the work of Njeri LW[5] who explored DRPs among adult CKD patients in an upper-middle-income country. They reported a high prevalence of DRPs (4.5 ± 1.4 DRPs per patient) among both ambulatory renal clinic and inpatient care settings employing a multidisciplinary team approach. Given the limited literature on the frequency and specific predictors of DRPs in CKD patients residing in resource-limited countries, our study holds value in shedding light on the actual state of medication problems and can contribute to improving CKD care within specific settings.

Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are first-line antihypertensive agents in CKD as they have a kidney-protective effect to slow CKD progression and reduce albuminuria.[14-15] ACEIs and ARBs are strongly recommended in patients with type 2 diabetes mellitus (DM) and a high level of albuminuria.[14-15,34] Our study found that ACEIs/ARBs was missing in CKD patients who have uncontrolled hypertension, DM, and any level of albuminuria. The previous study found that pharmacist-driven intervention can support the use of ACEIs/ARBs for CKD patients.[32] For pre-dialysis CKD with anemia, the patients should receive oral iron salt, folic acid, vitamin B12 based on clinical signs and symptoms of insufficiency.[35] Laboratory screening for CKD complications, such as hemoglobin levels, iron indices, and other potential causes of anemia, is crucial for assessing the necessity of those medications for anemia treatment. These medications address prevalent issues identified in our study and should be prescribed to patients as needed.

Several drugs need to be adjusted depending on the level of kidney impairment. Previous studies have found that not adjusting the dose according to patients' kidney function is a common DRP in CKD patients.[4,7,32] The reference for dose adjustment varies; therefore, pharmacists need to evaluate reliable sources and consider other factors. For example, we determined the criteria for the dose and duration of calciferol depending on the level of vitamin D insufficiency according to the KDOQI guideline 2003.[36] We had limited information regarding other indications for using oral vitamin D analogs, such as osteoporosis, which may allow for a higher dose than indicated in CKD. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors have the potential to exert kidney-protective properties besides being glucose-lowering agents.[37-38] In patients with impaired kidney function, SGLT-2 inhibitors are less effective in reducing blood glucose because they cannot fully excrete and act in the kidney site of action.[39] Empagliflozin is not recommended in patients with eGFR <30 mL/min/1.73 m^2 according to the prescribing information during the time of the study investigation.[40] However, the KDIGO guideline 2022 now recommends empagliflozin in patients with eGFR >20 mL/min/1.73 m^2 based on the positive kidney outcomes observed in patients with declining kidney function in the landmark study.[41-42] For dose suggestions in CKD, pharmacists should regularly update evidence-based information to determine the dose appropriately.

In our practice, we screened NSAIDs use and patient non-compliance in all CKD patients who attended the CKD clinic. NSAIDs, including COX-2 inhibitors, have been associated with acute kidney injury in the general population and disease progression in patients with CKD.[43-44] In some countries, including Thailand, NSAIDs can be dispensed by pharmacists in drug stores, making it easy for CKD patients to unintentionally administer them.[45] A recent systematic review found that patient awareness of NSAID risks was low, and information regarding the kidney risks associated with NSAID prescriptions was provided less frequently to patients in the Asia-Pacific Region.[46] Non-compliance can significantly impact treatment outcomes in various diseases, including CKD.[47] The results of our study identified these problems in our CKD patients, and interventions to address the relevant DRPs (informing physicians and patients) were performed in the clinic. Screening for drug and herbal-induced kidney toxicity and evaluating patients' compliance should continue as part of pharmacists' responsibilities in CKD services.

When exploring factors associated with DRPs, our results differed from those of other studies[4-5] in that we did not find an

association between kidney function and DRPs. The proposed explanation may lie in the different eGFR values of the studied patients. Although the majority of patients were in stage 3 CKD, which was similar to other studies, the proportions were approximately 90% in our study and 70% in the studies by Holm and Njeri. The different distributions of patients in each study may influence the factors associated with DRPs. Nevertheless, our findings support the results of prior investigations indicating that patients receiving polypharmacy are at an elevated risk of experiencing DRPs.[4-5] Given that our study found an association between patients who received more than seven medications and an increased risk of DRPs. We can utilize these key findings to select subsets of patients who are prescribed more than seven medications for effective pharmacy management and workflow planning in our practice. Additionally, the risk of drug interactions increases when patients take multiple medications concurrently. Our study revealed that certain drug interactions encountered by patients were necessary for the management of CKD complications. For example, calcium carbonate can reduce the absorption of ferrous fumarate when taken at the same time.[21] Therefore, pharmacists can educate patients on how to properly manage this interaction. It is important to note that while many drug interactions may be permissible in real-world practice, pharmacists must be aware of the severity of the interaction and how to manage it if the patient still requires the medications.

This study serves as an example of implementing a teamwork policy for the care of patients with CKD in the clinic. We developed a checklist for potential DRPs in CKD patients based on current evidence-based information to facilitate effective DRP screening. Since the CKD clinic in our center is in its early stages, the information regarding the prevalence and magnitude of DRPs addresses various practical problems and local issues, which can guide us in finding solutions to these problems. As each practice center may have different contexts, our findings can be applied to other ambulatory settings by considering factors such as the predominant CKD staging, common patient complications, and patient behavior. We acknowledge the limitations of retrospective analysis based on the hospital database, which prevented us from exploring complete epidemiological data or determining the actual reasons for the observed DRPs. Further analysis of the impact of CKD clinics, including the role of pharmacists, on CKD outcomes or the financial implications of reducing the cost of care would be valuable for future studies.

CONCLUSION

Even with the involvement of a multidisciplinary team, including pharmacists, efforts to implement medication optimization services remain important, as our study identified 25.1% of DRPs. Our findings emphasize the significance of suggesting ACEIs/ARBs for preventing CKD progression, considering dosage adjustments, staying updated with current information, avoiding nephrotoxic agents, addressing non-compliance, and managing drug interactions in the CKD clinic. Patients receiving polypharmacy are at an increased risk of DRPs and should be targeted in the ambulatory CKD setting.

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CREDIT AUTHOR STATEMENT

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CONFLICTS OF INTEREST

All authors have no conflict of interest to declare.

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APPENDIX 1

Checklist for drug-related problem screening

Definition: A = dosage too high, B = dosage too low, C = inappropriate therapy, D = no indication, E = need additional drug therapy, F = adverse drug reaction, G = non-compliance, H = drug interaction

DRP category	Criteria
Delay CKD progression	
Hypertension	
E	Not receiving ACEIs/ARBs when the patient has hypertension (blood pressure > 130/80 mmHg)
	Albuminuria (urine albumin to creatinine ratio > 3.4 mg/mmol or 30 mg/g)
	No albuminuria
F	Receiving ACEIs/ARBs and experiencing adverse drug reactions
	Hyperkalemia (potassium level > 4.5 mmol/L)
	Acute kidney injury (serum creatinine > 30% from baseline within 2 weeks after starting/increasing dose)
	Others ….
C	Receiving a combination of RAAS blockers (ACEIs + ARBs)
C	Receiving hydrochlorothiazide when the patient has a CrCL < 30 mL/min
G	Unable to control water restriction/salt intake (>2 g/day) as recorded in medical notes
A	Receiving a dosage that is too high for anti-hypertensive medications
Diabetes mellitus	
C	Receiving the first dose of metformin and having eGFR ≤ 45 mL/min/1.73 m²
C	Receiving metformin and having eGFR ≤ 30 mL/min/1.73 m² (patient has previously received it)
C	Receiving anti-diabetic medication that is contraindicated when patient's eGFR is < 30 mL/min/1.73 m²
A	Receiving a dosage that is too high of anti-diabetic medications
Lipid abnormalities	
E	Not receiving a statin in a patient with LDL-C ≥ 110 mg/dL
F	Receiving a statin and having elevated ALT > 3 times the upper limit of normal (ULN) without any dose reduction or discontinuation
F	Receiving a statin and having creatine kinase > 10 times the ULN
F	Receiving a statin and having creatine kinase < 10 times the ULN with statin toxicity symptoms (e.g., myalgia, dark or cola-colored urine)
E	Not receiving triglyceride-reducing agents when triglycerides > 200 mg/dL
A	Receiving a dosage that is too high of anti-lipid medications
Treatment of CKD complications	
Anemia	
E	Not receiving oral iron agents when the patient has not received ESA and has hemoglobin (Hb) < 12 g/dL (female) or < 13 g/dL (male)
C	ESA discontinuation/reduction was not performed when the Hb level was > 13 g/dL
A	Receiving a dosage that is too high of oral iron (> 200 mg of elemental iron/day)
B	Receiving a dosage that is too low of oral iron (< 200 mg of elemental iron/day)
E	Not receiving folic acid and vitamin B12 when the Hb level is < 12 g/dL (female) or < 13 g/dL (male)
F	Having an adverse drug reaction (ADR) from oral iron (e.g., vomiting, constipation, abdominal pain)
F	Having an ADR from intravenous iron (e.g., allergic reaction, hypotension, dizziness, dyspnea, headache, back pain, myalgia, arthralgia)
Hyperphosphatemia	
C	Receiving calcium-containing phosphate binder in a patient having hypercalcemia (correct calcium level > 10.5 mg/dL)
A	Receiving a calcium-containing phosphate binder of more than 1,500 mg/day
H	Receiving a calcium-containing phosphate binder at the same time as an oral iron agent
C	Receiving an aluminum-containing phosphate binder for more than 4 weeks

A	Receiving lanthanum in excess of the maximum dose (3,000 mg/day)
A	Receiving sevelamer in excess of the maximum dose (1,600 mg three times a day)
G	Non-compliance with phosphate binder medication (calcium and lanthanum should be chewed, sevelamer should not be chewed when administered)
Secondary hyperparathyroidism	
E	Not receiving any medications to reduce iPTH levels (when the patient can control calcium and phosphate levels)
F	Receiving vitamin D analogs (alfa-calcidol, calcitriol) and experiencing adverse drug reactions
	Hypercalcemia (serum calcium > 10.5 mg/dL)
	Hyperphosphatemia (serum phosphate > 5.5 mg/dL)
F	Receiving cinacalcet and experiencing hypocalcemia (serum calcium < 7.5 mg/dL)
H	Receiving cinacalcet in combination with CYP3A4 inhibitor medication (e.g., ketoconazole) or CYP3A4 inducer (e.g., phenytoin, carbamazepine) or CYP2D6 inhibitor/inducer
Metabolic acidosis	
E	Not receiving sodium bicarbonate when the patient has a serum bicarbonate level < 22 mEq/L
Hyperkalemia	
E	Not receiving potassium exchange resins (calcium polystyrene sulfonate, sodium polystyrene sulfonate) when the serum potassium is ≥ 5.5 mEq/L
C	Patient having serum potassium > 6 mEq/L and receiving a drug that causes hyperkalemia (e.g., potassium-sparing diuretic, potassium supplementation)
Vitamin D deficiency	
E	Not receiving vitamin D analogs (cholecalciferol/ergocalciferol) and having a 25(OH)D level < 30 ng/mL
A	Receiving a dosage that is too high for vitamin D analogs

ACEI = angiotensin converting enzyme inhibitor, ALT = alanine aminotransferase

ARB = angiotensin receptor blocker, CrCL = creatinine clearance, eGFR = estimated glomerular filtration rate, LDL-C = low density lipoprotein cholesterol, RAAS = renin angiotensin aldosterone system

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