Overview of Polypharmacy and Drug Interactions in Chronic Kidney Disease Patients at Siloam Hospitals Lippo Village

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Abstract

Patients diagnosed with CKD in Indonesia have increased from 2% in 2013 to 3.8% in 2018. Polypharmacy is commonly found in CKD patients, especially in CKD patients with comorbidities. CKD with comorbidities will make the treatment more complex and expensive. This study was conducted to assess the relationship between polypharmacy and drug interactions in CKD patients. Data analysis was carried out descriptively on CKD patients at "X" Hospital in the period October to December 2022 and data were displayed in the form of tables and graphs. The results showed that the majority of patients with chronic kidney disease (CKD) were aged 46-65 years with 42 patients (50.0%). Chronic kidney disease (CKD) patients who get prescriptions for more than 5 drugs are 80 (95.2%) patients. Comorbidities that often occur in chronic kidney disease (CKD) patients are hypertension with 62 (19.62%) patients, diabetes mellitus with 29 (9.18%) patients, and coronary heart disease with 27 (8.54%) patients. From 84 patients, there were 626 potential drug interactions including 152 (24.28%) drug interactions with minor severity, 434 (69.33%) drug interactions with moderate severity, and 40 (6.39%) drug interactions with major severity. CKD patients who have one or more comorbidities will increase the risk of polypharmacy and an increased risk of drug interactions.

Keywords: Polypharmacy, Drug Interactions, Chronic Renal Failure

1. INTRODUCTION

Chronic renal failure, also known as chronic kidney disease (CKD), is a disease that affects more than 10% of the world's population, more than 800 million in 2022. Chronic kidney disease (CKD) is one of the non-communicable diseases that shows an increase in mortality rates (Kovesdy, 2022). Based on the evaluation of Riskesdas in 2018, the prevalence of CKD patients diagnosed by doctors in patients aged more than 15 years has increased from 2013 at 2% to 3.8% in 2018 (2018 Riskesdas, 2018).

CKD accompanied by comorbidities increases the complexity and cost of care due to the many therapies that must be undertaken for life. Common comorbidities are hypertension and diabetes. Comorbidities and polypharmacy are common in chronic kidney disease (CKD) patients, leading to an increased potential for drug interactions (MacRae et al., 2021). According to research conducted by Shahzadi et al (2022), 67 patients out of 96 chronic kidney disease (CKD) patients used more than five kinds of drugs simultaneously (polypharmacy).

Polypharmacy is mostly found in chronic kidney disease (CKD) patients with comorbidities, namely 80.2% of the patient population has hypertension, 25.0% of patients have diabetes mellitus, 17.7% of patients have hypertension and diabetes mellitus, and the remaining 12.5% with other complications (Shahzadi et al., 2022). According to a previous study, out of 209 patients, 46 (22.0%) patients were prescribed <5 drugs and 163 (78.0%) patients were prescribed >5 drugs (Sleem A., Masood I., 2017).

Polypharmacy can have adverse effects on patients such as decreased quality of life, increased risk of death, increased occurrence of adverse drug effects, increased inaccuracy in drug selection, and increased drug incompatibility (Cepeda & Morley, 2012). Factors such as errors in drug selection, taking into account renal function, dosing, selection of route of administration, and how to use the drug can lead to potential unwanted drug interactions. Therefore, drug interactions in chronic kidney disease (CKD) patients are a serious problem and need to be monitored in drug prescribing (Cascorbi, 2012). This study aims to determine This study aims to determine the overview of polypharmacy and drug interactions that occur due to polypharmacy in chronic kidney disease (CKD) patients at "X" Hospital, Tangerang.

2. METHODS

This study has met the ethical requirements on the date of The Mochtar Riady Institute for Nanotechnology Ethics Committee (MRIN EC) with number 002/MRIN-EC/ECL/II/2023. This study was analysed using descriptive methods on outpatients suffering from chronic kidney disease at Hospital "X" Tangerang retrospectively by analysing prescription data and laboratory results in medical records in the time span of October 1 to December 31, 2022.

The inclusion criteria in this study include patients suffering from chronic kidney disease in the period 1 October to 31 December 2022, chronic kidney disease patients aged> 18 years, patients suffering from chronic kidney disease with category G3a-G5, and having a history of control at least once a month in 3 consecutive months. While the exclusion criteria are patients who have incomplete and illegible medical record data.

Collection of patient demographic data such as gender, age, glomerular filtration rate (GFR) value, number of prescribed drugs, comorbidities, and prescribed drugs will be recorded based on existing data in medical records. Drug interactions will be analysed based on the prescribed drugs using the interaction checker available at www.drugs.com and medscape. Drug interactions that have been analysed using the interaction checker will be checked whether the drug interaction occurred in the patient by adjusting laboratory data such as blood pressure, triglyceride values, and uric acid. The data from the analysis will be displayed in a table.

3. RESULTS AND DISCUSSION

Based on table 1, there were 84 chronic kidney disease (CKD) patients studied with the majority being male patients with 49 patients (58.3%). The majority of patients with chronic kidney disease (CKD) are aged 46-65 years with 42 patients (50.0%). About 29 (35.4%) chronic kidney disease (CKD) patients were included in category 5. Almost all chronic kidney disease (CKD) patients

were prescribed ≥5 drugs, totalling 80 (95.2%) patients. Comorbidities that often occur in chronic kidney disease (CKD) patients are hypertension with 62 (19.62%) patients, diabetes mellitus with 29 (9.18%) patients, and coronary heart disease with 27 (8.54%) patients.

Table 1. Patient Demographic Characteristics

Characteristics	Frequency	Percentage (%)
Gender		
Male	49	58,3
Women	35	41,7
Age		
17-25 years (teenager)	0	0
26-45 yaers (adult)	6	7,1
46-65 years (eldery)	42	50,0
>65 years (seniors)	36	42,9
Classification of CKD according to GFR values		
3a	14	16,7
3b	20	23,8
4	21	25,0
5	29	35,4
Number of drugs prescribed		
<5 drugs	4	4,8
≥5 drugs	80	95,2
Comorbidities		
Hypertension	62	19,62
Diabetes mellitus	29	9,18
Coronary heart disease	27	8,54

Table 2 shows that antihypertensive and diuretic drugs are the most commonly used drugs by CKD patients, namely 197 drugs (29.67%). This is in line with previous research where deuretic drugs (furosemide) were 88 drugs (71.6%) and antihypertensive drugs (lisinopril) were 65 drugs (52.9%) and calcium carbonat (supplements) were 63 drugs (51.22%) (Okunade, 2018).

Table 2. Prescribed drug classes

No.	Drug Group	Frequency	Percentage
1.	Antihypertensives and diuretics	197	29,67
2.	Vitamins and supplements	162	24,40
3.	Lipid-lowering drugs	58	8,73
4.	Antiplatelets	40	6,02
5.	Antidiabetes	39	5,87
6.	Antigout	34	5,12
7.	Analgesics	26	3,92

Table 2. Prescribed drug classes (continued)

No.	Drug Group	Frequency	Percentage
8.	Antitussive, expectorant and mucolytic	13	1,96
9.	Anticonvulsant	13	1,96
10.	Antacids, Proton Pump Inhibitors (ppi) and H2 receptor antagonists	13	1,96

According to the number of potential drug interactions that occurred, out of 84 patients there were 626 potential drug interactions including 152 (24.28%) drug interactions with minor severity, 434 (69.33%) drug interactions with moderate severity, and 40 (6.39%) drug interactions with major severity which can be seen in table 3. According to research conducted by Sleem (2017), 30 (5.5%) were classified as contraindications, 75 (13.9%) as major, 306 (56.6%) as moderate, and 130 (24.0%) as minor. Drug interactions with minor severity generally do not cause serious effects on patients.

Table 3. Number of Potential Drug Interactions in CKD Patients

No.	Interaction	Frequency	Percentage
1.	*Minor*	152	24,28
2.	*Moderate*	434	69,33
3.	*Major*	40	6,39

One of the potential drug interactions with moderate severity that often appears is sodium bicarbonate with allopurinol, which was found in 34 (19.21%) cases which can be seen in table 4. The interaction that arises is a decrease in the therapeutic effect of allopurinol as an

antigout. This can occur because sodium bicarbonate can increase the pH of the stomach so that it inhibits the absorption of allopurinol which causes blood drug levels to decrease. This can be overcome by taking allopurinol 2 hours before or after consuming sodium bicarbonate.

Table 4. Potential Drug Interactions in Frequently Occurring CKD Patients

No.	Drug Interactions	Severity	Mechanism	Resulting Effects	Frequency	Percentage
1.	Sodium bicarbonate + allopurinol	*Moderate*	Absorption pharmacokinetics	Decreased therapeutic effect of allopurinol	34	19,21
2.	Calcium carbonate + amlodipine	*Moderate*	Absorption pharmacokinetics	Decreased therapeutic effect of amlodipine	21	11,86
3.	Sodium bicarbonate + acetylsalicylic acid	*Minor*	Excretion pharmacokinetics	Decreased/increased therapeutic effect of acetylsalicylic acid	19	10,73
4.	Sodium bicarbonate + bisoprolol	*Moderate*	Absorption pharmacokinetics	Decreased therapeutic effect of bisoprolol	17	9,60
5.	Amlodipine + simvastatin	*Major*	Pharmacodynamics	Increased risk of myopathy and rhabdomyolysis	15	8,47

In this study, drug interactions that occurred in many patients were interactions between antihypertensive drugs and other drugs such as calcium carbonate which is included in supplements which can be seen in table 5. This is in line with the data in table 2, namely the number of classes of antihypertensive drugs, diuretics, and supplements that are widely prescribed Antihypertensive and antigout drugs are drugs that are often prescribed simultaneously with other drugs in CKD patients. Drug interactions that occur in patients are blood pressure, triglyceride values, and uric acid that do not reach their therapeutic targets. CKD is pathophysiologically related to hypertension so uncontrolled blood pressure is not always due to drug interactions. However, management of drug interactions can help improve blood pressure control. The same applies to triglyceride and uric acid values, diet and physical activity may also affect triglyceride and uric acid values, but this study did not examine these specifically. Drug interaction management can help improve blood pressure, triglyceride and uric acid control in patients. If the potential drug interactions that occur are absorption pharmacokinetics, it can be overcome by giving a 2-hour interval before or after taking other drugs. However, there are also potential drug interactions that cannot be overcome by giving a break in taking the drug, so it is necessary to monitor the side effects and effectiveness of the drug such as the administration of antihypertensive drugs and hydrochlorothiazide recommended in the JNC 8 guideline to achieve therapeutic targets.

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Table 5. Manifestations of drug interactions between hypertension drugs and other drugs in CKD Patients

No.	Drug Interactions	Drug Interaction Effects	Mechanism	Assessment Indicator	Frequency	Percentage
1.	Calcium carbonate	Decreased antihypertensive effect	Absorption pharmacokinetics	Uncontrolled systolic and diastolic blood pressure (>140/90mmHg)	14	36,84
2.	Acetylsalicylic acid	Decreased antihypertensive effect	Pharmacodynamics	Uncontrolled systolic and diastolic blood pressure (140/90mmHg)	11	28,95
3.	Sodium Bicarbonate	Decreasing antihypertensive effect	Pharmacokinetics (absorbs)	Uncontrolled systolic and diastolic blood pressure (140/90mmHg)	7	18,46
4.	Hydrochlorothiazide	Increased risk of hyperglycaemia and hypertriglyceridemia	Pharmacodynamics	Uncontrolled triglyceride values (>150 mg/dL)	1	2,63
5.	Calcium Lactate	Lowering effect of hypertension	Pharmacodynamics	Uncontrolled systolic and diastolic blood pressure (140/90mmHg)	1	2,63
6.	Methylprednisolone	Lowering effect of hypertension	Pharmacodynamics	Uncontrolled systolic and diastolic blood pressure (140/90mmHg)	1	2,63
7.	Spironolactone	Increased risk of Hyperglycaemia and hypertriglycerides	Pharmacodynamics	Uncontrolled triglyceride values (>150 mg/dL)	1	2,63

Table 6. Relationship between comorbidities and drug interactions

No.	Number of Comorbidities	Number of Patients	Average amount of medicine	Average drug interaction
1.	0	1	6	2
2.	1	10	5,6	2,9
3.	2	12	6,75	4,58
4.	3	18	7,27	5,55
5.	4	13	7,69	6,69
6.	5	12	9,91	10
7.	6	9	9,77	12,88
8.	7	7	12,28	14,85
9.	8	2	8,5	7

Table 6 shows that the more comorbidities a CKD patient has, the more drugs are prescribed, thus increasing the risk of drug interactions. CKD patients without co-morbidities received an average number of drugs of 6 and an average drug interaction of 2. Meanwhile, CKD patients with seven co-morbidities were prescribed an average number of drugs and an average drug

interaction of 2. Patients with eight comorbidities had an average number of drugs of 12.28 and an average drug interaction of 14.85. CKD patients with eight co-morbidities had a smaller average number of drugs and drug interactions than those with seven co-morbidities because the number of patients with eight co-morbidities was only two patients.

4. CONCLUSIONS

CKD patients who have one or more comorbidities will increase the risk of polypharmacy because patients are not only given drugs to treat CKD but also to treat comorbidities, especially comorbidities that are directly related to the development of severity in CKD. Polypharmacy also plays a role in increasing the risk of drug interactions because the more drugs administered, the more pharmacokinetic and pharmacodynamic interactions of the prescribed drugs.

5. ACKNOWLEDGEMENTS

hank you to Hospital "X" Tangerang for allowing the research.

6. LITERATURE

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