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DRUG DOSE ADJUSTMENT IN CHRONIC KIDNEY FAILURE PATIENTS AT HOSPITAL X

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ABSTRACT

Chronic Kidney Disease (CKD) is a significant global health issue, with increasing incidence rates, high treatment costs, and poor prognosis. Adjusting drug dosages in patients with CKD is essential to prevent worsening conditions and ensure proper therapy. This study examines the drug adjustment practices at Hospital X. This research method uses a descriptive research uses secondary data from medical records (Jan-Dec 2021) of CKD patients at Hospital X. Data include patient demographics, comorbidities, medications, and dosage adjustments according to the Renal Pharmacotherapy Handbook. Results: Among the 52 patients, the majority were female (60%) and aged 46-65 years (57%). Ranitidine was the most prescribed drug (47.37%) for CKD patients, with 56.76% dosages aligning with renal dosing guidelines. This study concluded that ranitidine was the most common medication, and over half of the prescriptions were aligned with the renal dosing guidelines.

Keywords: drug dose adjustment, chronic kidney failure, renal pharmacotherapy

INTRODUCTION

Chronic Kidney Disease (CKD) is a progressive condition marked by reduced Glomerular Filtration Rates (GFR) that significantly impact health. In general, chronic kidney failure reduces glomerular filtration and/or active secretion, which causes a decrease in drug excretion via the kidneys, resulting in a longer elimination half-life of the drug. According to the 2018 Basic Health Research (Riskesdas), four out of every 1,000 Indonesians suffer from kidney failure. According to data from the Institute for Health Metrics and Evaluation (IHME) in 2017, this non-communicable disease ranks as the 12th leading cause of death globally. Its incidence has continued to rise over the years, with 346,641 cases recorded in 2000, increasing to 440,750 in 2010, and reaching 520,207 in 2017. The prevalence of chronic kidney failure among Indonesians aged ≥ 15 years was 0.38% (approximately 739,208 people), with the highest prevalence in North Kalimantan (0.64%) and the lowest in West Sulawesi (0.18%). Indonesia faces a growing CKD prevalence, underscoring the need for effective drug dosing adjustments in patients with CKD, especially at facilities such as Hospital X, where patients with CKD frequently receive treatment. The results of previous research showed that of the 132 samples, 86 patients received drugs that required dose adjustment. Of the 86 patients, 29 (33.72%) received therapy that met the appropriate dose, and 57 (66.27%) did not comply. This study aimed to examine this phenomenon in a clinical setting.

RESEARCH METHODS

Equipment and Materials

The population in this study were medical records of chronic kidney failure patients at the Hospital X Inpatient Installation for the period January – December 2021. The sample used in this study was medical record data from Failed Patients Chronic Kidney in the Patient Installation at Hospital X, which met the inclusion criteria. The pulation obtained in this study was 96 and the medical records of 52 patients were obtained according to the inclusion criteria. Purposive sampling was used, and the medical records of patients who met the inclusion criteria were taken as sample studies. The data included age, sex, weight, body height, serum creatinine values, comorbidities, names of drugs that need to be adjusted for dosage, method of administering the drug, and dosage.

Inclusion criteria are patient medical record samples with complete medical records including age, gender, weight, height, comorbidities, serum creatinine values, name of drug, method of drug administration and dose used. Exclusion criteria were medical records of patients with chronic kidney failure who did not have laboratory data in the form of serum creatinine values and medical records of patients with chronic kidney failure who were illegible.

Research Procedure

After obtaining the appropriate ethical letter, the researcher immediately collected data using observation techniques by collecting medical records from patients with chronic kidney failure at Hospital X. The data collected in this study were in the form of patient data information in accordance with the research objectives. The data were then written on a data collection sheet.

Data Analysis

Data analysis was carried out to determine whether the dose of medication administered to patients with chronic kidney failure was in accordance with the drug dosage stated in the literature. Determination of the suitability of dose and frequency was calculated based on the filtration rate Filtration Glomerulus (GFR). The method used to calculate creatinine clearance is the Cokroft and Gault formula (Ashley and Dunleavy, 2017).

$$\text{Male} \quad CrCl = \frac{(140 - usi \times BW)}{72 \times Scr}$$

$$\text{Female} \quad \text{Cr}Cl = \frac{0{,}85\ (\ 140 - usia\ ) \times BW)}{72 \times}$$

Information :

CrCl	: Creatinine clearance
BW	: Body weight (kg)
Scr	: Serum creatinine
Value 0.85	: Corrected value for women

After the GFR or creatinine clearance value is obtained, it is carried out adjust the dose that has been given to the drug dose stated in the Hand Book of Renal Pharmacotherapy dosage adjustment of medication eliminated by the kidney in 2013 according to the calculated GFR classification.

RESULTS AND DISCUSSION

Based on research that has been carried out at the Hospital X medical records installation found a population of Chronic Kidney Failure (CKD) patients inpatient installations in 2021 will be 96 patients. Of the population that has obtained, screening is carried out according to the inclusion and exclusion criteria, and 52 samples were obtained that met the inclusion criteria.

Table I. Characteristics of CKD Patients Based On Gender

Gender	Amount	Percentage (%)
Male	21	40%
Female	31	60%
Total	**52**	**100%**

The percentage of kidney failure sufferers who were female was more frequent, namely 31 patients with a percentage of 60% compared to patients. There were only 21 male patients with a percentage of 40%. This is not in line with research that has been conducted previously where the number of female patients with chronic kidney failure was as much as 41 people with a presentation of 77%, while patients were male. There were only 11 men with a percentage of 23% (Pakingki *et al.*, 2019). Patients with chronic kidney failure are more likely to develop chronic kidney failure due to pregnancy. Pregnancy complicated by preeclampsia can lead to chronic kidney disease. Apart from pregnancy, other causes that can trigger chronic kidney disease are UTI or urinary tract infections because women's urinary tract is shorter than that of men, lupus, and cervical cancer, which can only be experienced by women (Yuliasari, Aditya and Susanto, 2021).

Table II. Characteristics of CKD Patients Based on Age

Age	Gander		Amount	Percentage (%)
	Male	Female		
Teenagers 10 – 25	1	0	1	2 %
Adults 26 – 45	7	7	14	27 %
Middle Aged 46 – 65	10	20	30	57 %
Elderly > 65	3	4	7	14 %
Total	**21**	**31**	**52**	**100 %**

Based on age characteristics, the most chronic kidney failure patients were patients aged between 46-65 years with a total of 30 patients, including 10 male patients and 20 female patients and a percentage of 57%. This is in accordance with the previous research conducted by (Yuliasari, Aditya and Susanto, 2021). The age of most CKD patients in their study was approximately 45-64 years. The high number of sufferers of chronic kidney failure aged >26 years, is due to the fact that with increasing age there is a decline in kidney function which can lead to an increase in risk factors for developing diseases that can trigger chronic kidney failure, one of which is hypertension. Hypertension is also caused by several factors, such as obesity, lack of physical exercise, and excessive consumption of salt, which can increase the number of patients with chronic kidney failure (Yuliasari, Aditya and Susanto, 2021).

Table III. Patient Characteristics Based on Comorbidities

Types Comorbid	Frequency	Percentage (%)
Anemia	8	15,4 %
Hemorrhoids	1	2 %
Tuberculosis	1	2 %
Heart Disease	3	5,8 %
Hypertension	5	9,6 %
DM Type 2	4	7,7 %
Strokes	1	2 %
Asthma	1	2 %
Gastritis	7	13,5 %
Post-Op Kidney	2	4 %
Leucemia	1	2 %
Hyperuricemia	1	2 %
Without Comorbidities	17	32 %
Total	**52**	**100 %**

The most common comorbidity experienced by patients with chronic kidney failure was anemia, with a total of 15.4%, while the number of patients without comorbidities was 17 (32 %). This is in accordance with research conducted by (Yuliasari, Aditya, and Susanto (2021), where the most common comorbidity experienced by chronic kidney failure patients was anemia (71 patients, 53.78%). Anemia is the highest complication that occurs in patients with chronic kidney failure and can be caused by erythropoitant deficiency, and erythropoietin (EPO) is recommended. The aim of treating anemia in patients with chronic kidney failure is to achieve a target Hb level >10 g/dL and Ht >30%. This Hb target can be achieved through conservative management or erythropoietin therapy (Lubis *et al.*, 2022).

Table IV. Characteristics of CKD Patients Based on Disease Degree

Degrees GGK	LFG	Amount	Percentage (%)
I	>90	0	0
II	60 – 89	2	3.85 %
III	30 – 59	8	15.38 %
IV	15 – 29	16	30.77 %
V	<15 or dialysis	26	50 %
	Total	52	100 %

Based on previous research, most data were obtained for sufferers with grade 5 chronic kidney failure with GFR values <15 ml/minute with a total of 26 patients with a percentage of 50%, followed by grade 4 with GFR values of 15 – 29 ml/minute with 16 patients (30.77 %). Meanwhile, from the data above, no patients with grade 1 or mild disease were found in the Inpatient Installation at Hospital X. This is in accordance with the research conducted by Yuliasari, Aditya, and Susanto (2021), where patients with disease degree 5 had the highest degree of disease experienced by kidney failure patients.

In his study, there were 58 chronic patients (43.93 %). A high number of patients experiencing grade 5 disease also occurs because the majority of patients refuse to undergo hemodialysis (Andriani, Rahmawati and Andayani, 2021).

Table V. Patients Who Require Drug Dose Adjustments

Criteria	Amount	Percentage (%)
CKD patients who receive medication and require dose adjustments	36	69.2 %
CKD patients who receive medication without requiring dose adjustments	16	30.8 %
Total	**52**	**100 %**

Based on the above data, only 36 patients with chronic kidney failure (69.2 %) received medical therapy and required drug dose adjustments. This is because of several reasons why chronic renal failure patients do not receive drugs that require dose adjustments, such as having a creatinine clearance value of >60 mL/minute or patients who have allergies to several drugs (Andriani, Rahmawati and Andayani, 2021).

Table VI. Classes of Drugs That Require Dose Adjustment in CKD Patients

Drug Class	Drug Name	Frequency	Presentation (%)
H2 Blockers	Ranitidine	19	50 %
Analgesic	Paracetamol	8	21 %
NSAIDs	Ketorolac	2	5.3 %
Antitubercular	Ethambutol	1	2.6 %
Gout	Allopurinol	2	5.3 %
Antihypertensive	Captopril	3	7.9 %
	Bisoprolol	2	5.3 %
Antibacterial	Ceftazidime	2	5.3 %
Total		**38**	**100 %**

Based on the above data, it is known that the histamine H2 receptor antagonist group is the most common class of drugs administered to patients with chronic kidney failure, namely 19 treatment frequencies with a percentage of 50%, and the largest class of drugs administered to patients with CKD after H2 receptor antagonists is the analgesic drug class, with a total of 8 treatment frequencies and a percentage of 21%. This is different from the research conducted by, where the class of drugs frequently administered to patients with chronic kidney failure in their research was the antihypertensive drug class, with a total of 70 treatment frequencies (53.03%). This may be because drugs in the histamine H2 receptor antagonist class are strongly recommended to adjust the drug dose because it is associated with the potential for unwanted side effects (Andriani, Rahmawati and Andayani, 2021).

Table VII. Appropriate Drug Dosage in CKD Patients

Appropriate drug dosage	Frequency of Treatment	Presentation (%)
In accordance	22	57.9 %
Not Accordance	16	42.1 %
Total	**38**	**100 %**

Based on research that has been carried out, of the 38 treatment frequencies that required dose adjustments, 22 frequencies (57.9 %) of the treatment administered to chronic kidney failure patients were in accordance with the Hand Book of Renal Pharmacotherapy dosage adjustment of medication eliminated by the kidney in 2013, while for the other 16 treatment frequencies, the doses given were not in accordance with the literature. The dose discrepancy found in this study could be due to several considerations made by health workers based on the patient's kidney function (Andriani, Rahmawati and Andayani, 2021).

Table VIII. Drug Used by CKD Patients

Drug Name	Frequency	Accordance	%	Not Accordance	%
Ranitidine	19	10	52.63	9	47.37
Captopril	3	3	100	0	0
Paracetamol	8	8	100	0	0
Ketorolac	2	0	0	2	100
Allopurinol	2	0	0	2	100
Ethambutol	1	0	0	1	100
Ceftazidime	2	1	50	1	50
Bisoprolol	1	0	0	1	100
Total	**38**	**22**	**57.9**	**16**	**42.1**

In the research that has been carried out, ranitidine is the most widely used drug, with 19 treatment frequencies, where the dose administered at 10 treatment frequencies is in accordance with the literature, while the other 9 treatment frequencies are not appropriate and require dose adjustment. Based on the Hand Book of Renal Pharmacotherapy dosage adjustment of medication eliminated by the kidney in 2013, the recommended dose of ranitidine for patients with GFR values <10 mL/minute is 50 mg intravenously every 24 hours and for oral use 75-150 mg every 24 hours, while the dose administered was 2 × 50 mg intravenously, which exceeded the recommended dose; therefore, it was necessary to adjust the dose (Edition, 2013).

Ranitidine dose adjustments need to be made in CKD patients because patients with reduced GFR experience a significant increase in the AUC or Area Under Curve, this increase in AUC is the basis for the need to adjust the dose of ranitidine because it is associated with the potential for unwanted side effects (Yuliasari, Aditya, and Susanto, 2021).

Captopril was used 3 times, and for each treatment the dose used was in accordance with the literature. According to the Hand Book of Renal Pharmacotherapy dosage adjustment of

medication eliminated by the kidney, patients with GFR values of 10-50 mL/minute the recommended dose is 18.75 mg orally every 12 hours and the maximum use of captopril is 450 mg per day, whereas according to data. The dose of captopril used was 12.5 mg every 8 hours, meaning that the dose given was in accordance with the literature (Edition, 2013).

Paracetamol is an analgesic that requires dose adjustment for CKD patients. In this study, paracetamol was used 8 times for treatment, all doses given were in accordance with the Hand Book of Renal Pharmacotherapy dosage adjustment of medication eliminated by the kidney, therefore there was no need for paracetamol to adjust the dose (Edition, 2013).

According to Tuloli et al. (2019), the recommended dose of ketorolac for patients with CrCl 20-50 ml/min/1.73 m2 is 15 mg every 6 hours or a maximum of 60 mg/day, while for patients with CrCl < 20 ml/min/ 1.73 m2, it is recommended to avoid the use of ketorolac. Meanwhile, according to the Hand Book of Renal Pharmacotherapy dosage adjustment of medication eliminated by the kidney, ketorolac is not recommended for CKD patients (Edition, 2013) In this study, ketorolac was prescribed 2 times, where the dose given was 3 x 30mg, the dose given was more than the recommended dose, so it was necessary to adjust the dose. Ketorolac use without dose adjustment in CKD patients can increase the risk of undesirable drug effects, including bleeding in the digestive tract, increased urinary frequency, oliguria, acute renal failure, hyponatremia, hyperkalemia, and increased serum urea and creatinine levels (Tuloli *et al.*, 2019).

In this study, allopurinol was used twice, and the doses administered for both treatments were not in accordance with the literature. Based on the Renal Pharmacotherapy Dosage adjustment of medications eliminated by the kidneys, the recommended dose of allopurinol for patients with GFR <10 mL/minute is 100 mg every 24 hours or 150 mg every 48 hours, while the dose given is 300 mg every 24 hours, meaning the dose given exceeds the recommended dose; therefore, a dose adjustment must be made to allopurinol. Dosage adjustments need to be made because allopurinol can slow the progression of kidney disease; however, excessive doses to patients with chronic kidney failure can trigger allopurinol toxicity (Zazuli *et al.*, 2017).

According to the Renal Pharmacotherapy Dosage adjustment of medications eliminated by the kidneys, the recommended dose of ethambutol for chronic kidney failure patients with a GFR <10 mL/minute is 7 mg/kg every 24 hours, while the dose given is 1 × 500 mg with body weight the patient is 50 kg, meaning the dose given is not appropriate in the literature and exceeds the recommended dose; therefore, dose adjustment is necessary. This is because ethambutol is excreted through the kidneys and also prevents eye problems that can occur due to excessive doses of ethambutol (Edition, 2013).

Ceftazidime was prescribed twice in this study was prescribed 2 times, 1 of which the dose given was in accordance with the literature, one of which was not appropriate. Based on Renal Pharmacotherapy Dosage adjustment of medications eliminated by the kidneys, the recommended dose of ceftazidime for patients with GFR <10 mL/minute is 0.5 – 1 gr every 24 hours, while the dose given is 2 × 1 g, meaning the dose given does not correspond to or exceeds the recommended dose; therefore, it is necessary to adjust the dose. Ceftazidime dose adjustments are made to reduce side effects, toxicity, and outcomes and to optimize the therapeutic effect (Rosyid and Thaha, 2013).

In Renal Pharmacotherapy Dosage adjustment of medications eliminated by the kidneys, bisoprolol is included in the drugs that require dose adjustment for CKD patients. As in this study, bisoprolol was administered to patients with GFR values of 8 mL/minute, at a dose of 5 mg bisoprolol 2 times a day. Based on the literature, for GFR 10 - 15 mL/minute a dose of 5 mg bisoprolol was given once a day. As the dose administered to this patient exceeded the prescribed dose, it was necessary to adjust the dose. ß-blockers such as bisoprolol used to treat hypertension can cause decreased kidney function, which can occur due to a reduction

in renal blood flow and a decrease in glomerular filtration rate due to reduced cardiac output and a decrease in blood pressure caused by the use of ß-blocker drugs (Panggabean, Sriwahyuni and Aldi, 2023).

This study had several limitations that should be considered. First, the sample size was relatively small, with data derived solely from the medical records of a single hospital, which may limit the generalizability of our findings to other healthcare settings. Second, the study relied on retrospective data collection, which could introduce biases, such as incomplete or inaccurate medical records. Third, this study did not account for the potential impact of patient adherence to prescribed regimens on treatment outcomes. Lastly, the assessment of dose adjustments was limited to the available guidelines without considering potential innovations or variations in clinical practice. Future studies with larger multicenter cohorts and a prospective design are recommended to validate and expand these findings.

CONCLUSION

Based on research that has been carried out, the characteristics of chronic kidney failure patients in the Inpatient Installation at Hospital X. Gender of patients and women had the highest number (60 %). Age: Chronic Kidney Failure sufferers were mostly 46-56 years old, with a total of 57%, and anemia was the most common history of comorbidities experienced by patients with Chronic Kidney Failure (22.8 %). Regarding the degree of Glomerular Filtration Rate (GFR), 50% of patients with chronic kidney failure experience GFR values <15 mL/meni, and the drug most commonly used in chronic kidney failure patients who need dose adjustments at Hospital X is ranitidine with a quantity of 50%, and 56.76% of the medication doses administered to patients with chronic kidney failure at Hospital X are in accordance with the Renal Pharmacotherapy Handbook Dosage Adjustment of medications eliminated by the kidney. These findings emphasize the urgent need for precise drug dose adjustments in patients Disease (CKD) patients to mitigate the risks associated with incorrect dosing. The significant prevalence of anemia and advanced CKD stages (GFR <15 mL/minute) highlights the necessity for integrated management strategies, including early diagnosis, regular monitoring of renal function, and personalized pharmacotherapy. Optimizing drug regimens, as shown by the frequent use of ranitidine and the underutilization of dose adjustments in specific cases, can minimize adverse drug effects and improve patient outcomes. This research underscores the critical role of adherence to renal dosing guidelines in clinical practice, particularly in facilities managing a high volume of CKD patients, to reduce morbidity and enhance the quality of care.

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