Original Research

EVALUASI KETEPATAN DOSIS PADA PASIEN GAGAL JANTUNG KONGESTIF DENGAN GAGAL GINJAL KRONIS DI RSUD KABUPATEN KEDIRI

Evaluation of Dose Appropriateness in Congestive Heart Failure Patients with Chronic Kidney Disease at RSUD Kabupaten Kediri

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Abstrak

Congestive heart failure (CHF) merupakan penyakit kronis yang memerlukan terapi jangka panjang. Pada pasien dengan komorbid *chronic kidney disease* (CKD), penyesuaian dosis obat diperlukan untuk mencegah toksisitas akibat penurunan fungsi ginjal. Penelitian ini bertujuan untuk mengevaluasi profil terapi dan ketepatan dosis pada pasien CHF dengan CKD di ruang rawat inap RSUD Kabupaten Kediri periode Januari–Desember 2022. Penelitian ini merupakan studi observasional retrospektif menggunakan data rekam medis dengan teknik total sampling, melibatkan 72 pasien. Evaluasi ketepatan dosis dilakukan berdasarkan estimasi laju filtrasi glomerulus (eGFR) menggunakan rumus *Cockcroft–Gault* dan dibandingkan dengan referensi *The Renal Drug Handbook*. Hasil penelitian menunjukkan mayoritas pasien berjenis kelamin perempuan (54,17%) dan berada pada kelompok usia 45–54 tahun (41,67%). Sebagian besar pasien memiliki komorbid tambahan (80,56%), dengan anemia sebagai penyakit penyerta terbanyak. Berdasarkan stadium CKD, mayoritas pasien berada pada stadium 5 (77,78%). Terapi kombinasi dua obat merupakan pola terapi terbanyak (30,57%), dengan kombinasi diuretik dan ARB paling sering digunakan. Evaluasi ketepatan dosis menunjukkan bahwa 69 pasien (95,83%) menerima dosis yang sesuai dengan fungsi ginjal, sedangkan 3 pasien (4,17%) tidak sesuai, terutama spironolakton dan akarbose yang seharusnya dihindari pada nilai eGFR rendah. Dapat disimpulkan bahwa sebagian besar pasien CHF dengan CKD telah menerima terapi dengan dosis yang sesuai berdasarkan fungsi ginjal, meskipun masih ditemukan kasus ketidaktepatan dosis yang berpotensi meningkatkan risiko efek samping.

Kata kunci: *congestive heart failure* (CHF); *chronic kidney disease* (CKD); ketepatan Dosis; eGFR

Abstract

Congestive heart failure (CHF) is a chronic condition requiring long-term therapy. In patients with comorbid chronic kidney disease (CKD), dose adjustment is essential to prevent drug toxicity due to impaired renal function. This study aimed to evaluate the therapy profile and dose appropriateness in patients with CHF and CKD hospitalized at RSUD Kediri during January–December 2022. This was a retrospective observational study using medical record data with

a total sampling technique, involving 72 patients. Dose appropriateness was evaluated based on the estimated glomerular filtration rate (eGFR) calculated using the Cockcroft–Gault equation and compared with *The Renal Drug Handbook* as the reference. The results showed that most patients were female (54.17%) and aged 45–54 years (41.67%). The majority had additional comorbidities (80.56%), with anemia as the most common, and were classified as CKD stage 5 (77.78%). The most common therapy pattern was a two-drug combination (30.57%), primarily diuretics and angiotensin receptor blockers (ARBs). Dose evaluation indicated that 95.83% of patients received appropriate doses, while 4.17% received inappropriate doses, particularly in the use of spironolactone and acarbose, which should be avoided in patients with low eGFR. In conclusion, most patients with CHF and CKD received appropriate dosing based on renal function, although some inappropriate dosing cases were still identified, which may increase the risk of adverse effects.

Keywords: congestive heart failure (CHF); chronic kidney disease (CKD); dosing appropriateness; eGFR

INTRODUCTION

Congestive heart failure (CHF) is a clinical condition in which the heart is unable to pump sufficient blood to meet the body's oxygen demands due to structural and/or functional myocardial abnormalities [1]. According to the Global Burden of Disease study (2017), approximately 64.3 million people worldwide are affected by CHF, with a prevalence of 1.7% in European countries. [2]. In Indonesia, the prevalence is higher, reaching approximately 5%, with the highest CHF-related mortality rate in Southeast Asia at 21.4% [3].

CHF is a chronic condition requiring long-term pharmacological therapy and careful dose adjustment based on the patient's clinical status. The primary goals of therapy include improving quality of life, prolonging survival, and reducing rehospitalization rates [1]. However, rehospitalization remains a major concern, with a global 30-day rate of 13.2% and a higher rate of up to 29% reported in Indonesia [4,5].

Chronic kidney disease (CKD) is one of the most common comorbidities in patients with CHF. CKD is characterized by a decline in the estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m^2, which significantly affects drug pharmacokinetics and pharmacodynamics [6]. In patients with CHF and CKD, impaired renal function alters drug clearance, increasing the risk of drug accumulation, toxicity, and adverse drug reactions. Therefore, dose adjustment based on renal function is essential to ensure both the safety and effectiveness of therapy.

Polypharmacy is frequently encountered in patients with CHF and CKD, further increasing the risk of inappropriate dosing [7]. Previous studies have reported a considerable proportion of dosing inappropriateness, with 55% of patients receiving incorrect doses, particularly for beta-blockers and digoxin [8], and 19% involving drugs such as angiotensin-converting enzyme (ACE) inhibitors and digoxin [9]. However, most of these studies were conducted in different healthcare settings and populations, and limited data are available regarding dose appropriateness in hospitalized CHF patients with CKD in Indonesian regional hospitals. This indicates a gap in evidence, particularly in evaluating real-world prescribing practices in local clinical settings.

Therefore, this study aimed to evaluate the therapeutic profile and dose appropriateness of medications in hospitalized patients with CHF and comorbid CKD at RSUD Kabupaten Kediri, based on renal function. This study is expected to provide evidence on the appropriateness of drug dosing in clinical practice and contribute to improving the safety and effectiveness of pharmacotherapy in this patient population.

This study received ethical approval as stated in the ethical clearance certificate issued by the Ethics Committee of Institut Ilmu Kesehatan Bhakti Wiyata Kediri, with approval number 405/FF/EP/II/2023.

METHODS

Study Design

A retrospective observational study design was applied, utilizing secondary data obtained from medical records of inpatients diagnosed with congestive heart failure (CHF) with comorbid chronic kidney disease (CKD) at RSUD Kabupaten Kediri during 2022. The sampling technique used was total sampling.

Population and Sample

The population included all hospitalized patients diagnosed with CHF and CKD during the study period. The sample consisted of all patients who met the inclusion criteria.

The inclusion criteria were: (1) patients diagnosed with CHF and CKD, (2) hospitalized during the study period (January–December 2022), and (3) having complete data on age, sex, body weight, serum creatinine levels, and medication records.

The exclusion criteria were: (1) patients with incomplete or missing medical records, and (2) patients discharged against medical advice or referred to other healthcare facilities before completing therapy.

Research Procedure

Research Permission Application

The research permission request was submitted to the Faculty of Pharmacy and approved by the Dean of the Faculty of Pharmacy at Institut Ilmu Kesehatan Bhakti Wiyata Kediri. The approval letter was then submitted to the Director of RSUD Kabupaten Kediri to obtain institutional permission. Subsequently, authorization was granted through the Medical Records Department for data collection.

Data Collection

Data were collected using a structured data collection form. The variables recorded included patient demographics (age, sex, body weight), laboratory data (serum creatinine levels), comorbidities, and pharmacological therapy administered during hospitalization.

Data Analysis

Data were analysed descriptively to present patient characteristics, patterns of drug therapy, and dose appropriateness. Descriptive analysis was selected as the study aimed to provide an overview of real-world prescribing practices without examining causal relationships between variables. Dose appropriateness was evaluated based on renal function using the estimated glomerular filtration rate (eGFR), calculated with the Cockcroft–Gault equation, which incorporates patient age, body weight, sex, and serum creatinine levels.

The calculated eGFR values were then used to classify renal function and determine whether the prescribed drug doses were appropriate. Dose evaluation was performed by comparing the prescribed dose, frequency, and contraindications with standard references, including *The Renal Drug Handbook*, UpToDate Lexidrug and KDIGO (kidney disease: Improving Global Outcomes) guidelines.

Each prescribed medication was assessed individually to determine whether dose adjustment, dose reduction, or drug avoidance was required based on the patient's renal function. A dose was

considered appropriate if it was consistent with guideline recommendations and had been adjusted according to the patient's glomerular filtration rate (GFR). Inappropriate if it deviated from recommended dosing, including overdosing, underdosing, or use of contraindicated drugs in patients with impaired renal function.

RESULT AND DISCUSSION

The results of this study included a total sample of 72 hospitalized patients diagnosed with CHF accompanied by comorbid CKD during the January–December 2022 period.

Patient Characteristics

The patient characteristics in this study begin with the distribution of patients by sex, as presented in the following table:

Tabel 1. Patient distribution based on gender

Gender	Number (n)	Presentage (%)
Female	39	54,17
Male	33	45,83
Total	**72**	**100**

In this study, the proportion of patients with CHF and comorbid CKD was higher in females (54.17%) than in males (45.83%). Epidemiologically, heart failure is a clinical condition whose prevalence increases with advancing age and is frequently accompanied by multiple comorbidities. The higher prevalence observed in females compared to males may be influenced by several factors, one of which is hormonal changes. Advancing age is commonly associated with a decline in estrogen levels. Estrogen is known to exert various cardioprotective effects on the cardiovascular system. Reduced estrogen levels in women may contribute to extracellular matrix remodeling, endothelial dysfunction, and chronic inflammation [10]. Other studies have also reported that early menopause is associated with an increased incidence of CHF [11]. However, this difference is relatively small, suggesting that gender may not be the primary determinant, and other factors such as comorbidities and disease severity likely play a more significant role.

Table 2. Patient distribution based on age

Age (year)	Number (n)	Percentage (%)
15-24	1	1,39
25-34	2	2,79
35-44	7	9,72
45-54	30	41,67
55-64	19	26,39
65-74	11	15,28
>75	2	2,78
Total	**72**	**100**

The majority of patients were aged 45–54 years (41.67%). These findings are consistent with a study by Fajriansyah et al. (2016), which reported that 92% of heart failure patients were aged over 45 years. This result indicates that the risk of developing CHF increases with advancing age. The aging process contributes to reduced cardiac capacity, particularly impaired ventricular function, which subsequently increases susceptibility to CHF [12].

Table 3. Patient distribution based on Length of Stay (LOS)

Day	Number (n)	Percentage (%)
1-7	45	62,50
8-14	22	30,56
15-21	5	6,94
Total	**72**	**100**

Most patients (62.5%) had a length of stay of 1–7 days. which may reflect adequate short-term clinical stabilization; however, it does not necessarily indicate optimal long-term disease control or prevention of rehospitalization [13].

Table 4. Patient distribution based on comorbidity

Comorbidities	Number (n)	Type of Comorbidities	Patient Number	Percentage (%)
1 comorbidity	35	Anemia	2,3,4,6,9,11,12,15,19,20,22,24,31,36,37,40,42,43,44,46,47,48,51,56,58,59,61,62,63,64,65,67,69,70	73,61
	1	Bradycardia	52	
	2	Aterosclerotic	25, 30	
	1	Ischemic cardiomyopathy	66	
	3	Septic	13, 28, 53	
	3	Hypokalemia	7, 10, 60	
	1	Supraventricular tachycardia	23	
	1	Stroke	57	
	1	ARDS	29	
	1	Diabetes mellitus	72	
	3	Protein metabolism disorders	17, 18, 35	
2 comorbidity	1	Gastroesophageal reflux disease without esophagitis	39	5,56
	2	Mitral and Tricuspid Valve Regurgitation	8,14	
	1	Hyperuricemia + Tophaceous	5	
	1	Elevated transaminase levels + Lactate dehydrogenase	71	
3 comorbidity	1	Encephalitis + Myelitis + Encephalomyelitis	1	1,39
Total	**58**			**80,56**
Without comorbidity	14		16,21,26,27,32,33,34,38,41,45,49,50,54,55,68	19,44
Total	**72**			**100**

Comorbidity was observed in 80.56% of patients, with anemia being the most common. This is consistent with the known pathophysiology of CHF and CKD, where reduced erythropoietin production and chronic inflammation contribute to anemia [14,15]. The high prevalence of anemia further complicates pharmacotherapy, as it may influence drug response and overall clinical outcomes.

Table 5. Patient distribution based on chronic kidney failure stage

Stage	eGFR (ml/min/1,73 m^2)	Number (n)	Percentage (%)
3	30-59	3	4,17
4	15-29	13	18,07
5	<15	56	77,78
Total		**72**	**100**

A large proportion of patients (77.78%) were classified as CKD stage 5. This finding indicates that most patients were in advanced renal impairment, which significantly increases the complexity of pharmacotherapy and the need for strict dose adjustment. Reduced renal perfusion in CHF contributes to decreased GFR, reinforcing the close interaction between cardiac and renal dysfunction [16].

Patient therapy profile

The profile of drug use in CHF patients treated at RSUD Kabupaten Kediri can be described as follows:

Table 6. Distribution of Drug Usage Patterns in Patients with CHF

Number of Medications	Class Therapy	Number of Patients (n)	Percentage (%)
1 drug	ARB	9	12,5
	Diuretic	7	9,72
	Vasodilator	1	1,39
Total		**17**	**23,61**
2 drugs	Diuretic + β Blokers	3	4,17
	Diuretic + Vasodilator	1	1,39
	Diuretic + ARB	10	13,89
	ARB + β Blokers	3	4,17
	ARB + Vasodilator	3	4,17
	Aldosterone antagonist + ARB	1	1,39
	Aldosterone antagonist + Vasodilator	1	1,39
Total		**22**	**30,57**
3 drugs	Diuretic + ARB + β Blokers	7	9,72
	Diuretic + ARB + Vasodilator	4	5,56
	Diuretic + ACEI + Vasodilator	1	1,39
	Diuretic + β Blokers + Vasodilator	1	1,39
	Diuretic + Aldosterone antagonist + β Blokers	1	1,39
	ARB + β Blokers + Inotropic	1	1,39

Number of Medications	Class Therapy	Number of Patients (n)	Percentage (%)
Total		**15**	**20,84**
4 drug	Diuretic + ARB + β Blokers + Vasodilator	2	2,78
	Diuretic + ARB + β Blokers + Inotropic	1	1,39
	Diuretic + Aldosterone antagonist + ARB + β Bloker	1	1,39
	Diuretic + Aldosterone antagonist + β Blokers + Vasodilator	1	1,39
	ARB + β Blokers + Vasodilator + Inotropic	2 1	2,78 1,39
	Aldosterone antagonist + ARB + β Blokers + Vasodilator		
Total		**8**	**11,12**
5 drug	Diuretik + Aldosterone antagonist + ARB + *β Bloker* + Vasodilator	1	1,39
Total		**1**	**1,39**
No therapy heart failure	-	9	12,5
Total		**9**	**12,5**
Total		**72**	**100**

As shown in Table 6, the most frequently used combination therapy consisted of two medications, administered to 22 patients (30.57%). The most commonly prescribed drug class combination was diuretics plus angiotensin receptor blockers (ARBs), used in 10 patients (13.89%).

Table 7. Drug Utilization Profile in Patients with CHF

Class Therapy	Drug	Number (n)	Percentage (%)
Diuretic	Furosemid	46	29,30
Aldosterone Antagonist	Spironolacton	7	4,45
Angiotensin Converting Enzym Inhibitor (ACEI)	Lisinopril	1	0,63
*Angiotensin receptor Blockers (*ARB)	Candesartan	1	0,63
	Valsartan	10	6,37
	Telmisartan	9	5,73
	Irbesartan	32	20,38
ß-Blockers	Bisoprolol	26	16,56
	Propranolol	2	1.27
Vasodilator	Isosorbide dinitrate	19	12,10
Inotropic	Digoxin	4	2,54
Total		**157**	**100**

The most common therapy pattern was a two-drug combination (30.57%), particularly diuretics and ARBs. These findings are consistent with guideline recommendations, where ARBs are used

as alternatives to ACE inhibitors and diuretics are essential for managing fluid overload [1,13]. Loop diuretics are the recommended class of diuretics for this purpose. Furosemide is the first-line agent within this class due to its effectiveness in reducing congestive symptoms through the reduction of fluid retention [1,17].

Evaluation of Dose Appropriateness

The results of the dose appropriateness evaluation in the 72 patients were as follows:

Table 8. Evaluation of Dose Appropriateness in Patients with CHF

Appropriateness Dose	Number (n)	Percentage (%)
Appropriate dose	69	95,83
Inappropriate dose	3	4,17
Total	**72**	**100**

Dose evaluation showed that 95.83% of patients received appropriate dosing, while 4.17% were inappropriate. Although the proportion of inappropriate dosing was relatively small, this finding remains clinically significant. Several factors may explain the occurrence of inappropriate dosing, including variability in prescriber adherence to guidelines, limited consideration of renal function during prescribing, and the complexity of managing patients with multiple comorbidities and polypharmacy. In addition, incomplete clinical monitoring or delayed dose adjustment may also contribute to this issue [18].

Table 9. Evaluation of Dose-Inappropriate Medications Based on Patients' eGFR Values

Patient number	Drug	The prescribed dose (mg)	eGFR (ml/menit/1,73 m^2)	Adjustment dose
47	Spironolactone	25	6,5	Contraindicated
66	Spironolactone	25	9,02	Contraindicated
35	Acarbose	50	23,54	Contraindicated

Table 9 presents medications that were prescribed at inappropriate doses based on the patients' eGFR values. Based on existing literature, spironolactone is contraindicated in patients with an estimated GFR (eGFR) of 10 mL/min/1.73 m^2 [19]. From a clinical perspective, the inappropriate use of spironolactone in patients with severely reduced eGFR poses a high risk of hyperkalemia. As a potassium-sparing diuretic, spironolactone reduces potassium excretion, which can lead to life-threatening arrhythmias in patients with impaired renal function [20,21]. Therefore, its use should be avoided or strictly monitored in advanced CKD.

Similarly, the use of acarbose in patients with low eGFR is not recommended due to increased systemic exposure. In patients with severe renal impairment, the drug's plasma concentration and AUC may increase significantly, leading to an exaggerated pharmacological effect and a higher risk of adverse events [22]. This highlights the importance of considering pharmacokinetic changes in CKD patients when prescribing medications [19,23].

Overall, this study demonstrates that while most patients received appropriate dosing, a small proportion of inappropriate prescribing still exists and may have serious clinical consequences. Compared to previous studies reporting higher rates of inappropriate dosing, the lower proportion observed in this study may reflect better adherence to guidelines in the study setting. Nevertheless, continuous evaluation and monitoring of drug therapy remain essential to improve patient safety.

CONCLUSIONS

This study demonstrates that the majority of hospitalized patients with CHF and comorbid CKD at RSUD Kabupaten Kediri received pharmacological therapy with doses appropriately adjusted to their renal function. However, a small proportion of inappropriate dosing was still identified, particularly involving drugs that require strict consideration of renal function.

These findings highlight the importance of routine evaluation of renal function and careful dose adjustment in patients with CHF and CKD to minimize the risk of drug-related toxicity. From a practical perspective, healthcare professionals especially physicians and pharmacists should consistently consider estimated glomerular filtration rate (eGFR) when prescribing and reviewing medications, as well as adhere to established clinical guidelines.

Furthermore, interdisciplinary collaboration and periodic medication review are essential to ensure optimal and safe pharmacotherapy in this patient population. Continuous monitoring and evaluation of drug use are recommended to improve the quality of care and patient safety in clinical practice.

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