

Profile of Antihypertensive Drug Use in Patients with Coronary Artery Disease at Prof. Dr. I.G.N.G. Ngoerah General Hospital (RSUP) in 2023

Jeanan Aulia Arifin*, Ida Ayu Alit Widhiartini, I Made Jawi

Universitas Udayana, Indonesia

Email: jeananaulia@gmail.com*

ABSTRACT

Cardiovascular disease is the leading cause of death worldwide, with Coronary Heart Disease (CHD) as the major contributor. Hypertension, a primary risk factor for CHD, shows high global prevalence and requires comprehensive management through lifestyle changes and pharmacological therapy. This study aims to determine the profile of antihypertensive drug use in CHD patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital (RSUP) in 2023. A descriptive cross-sectional study was conducted using retrospective data from CHD patients' medical records after approval from relevant authorities. The study population comprised 774 CHD patients, with a sample of 100 selected using the Slovin formula (95% confidence level, 10% margin of error). Data were analyzed using IBM SPSS version 26 with univariate descriptive statistics. Most patients were male (88%), aged 56–65 years (36%), and resided in Denpasar (42%). Common comorbidities included hypertension (29.2%), type 2 diabetes mellitus (15.8%), and chronic kidney disease. Beta-blockers were the most frequently used antihypertensive agents (32.3%), followed by diuretics (24.4%) and ACE inhibitors (19.6%). Triple-drug combination therapy was most common (40%), mainly the ACEi + BB + Diuretics regimen, typically administered once daily (OD). In conclusion, CHD patients were predominantly older males with multiple comorbidities. The frequent use of beta-blockers and combination therapy reflects an individualized treatment approach consistent with evidence-based cardiovascular pharmacotherapy.

KEYWORDS

Antihypertensive Drugs, Combination Therapy, Coronary Heart Disease



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INTRODUCTION

Cardiovascular disease has become the leading cause of death worldwide, with Coronary Heart Disease (CHD) being the largest contributor (Ananth et al., 2023). According to World Health Organization (WHO) data in 2021, as many as 41 million people worldwide died from Non-Communicable Diseases (NCDs), of which 43.6% were caused by heart disease, with a death rate of 17.9 million people (Minister of Health of the Republic of Indonesia, 2023). Globally, it is estimated that in 2020 there were around 244.11 million people living with ischemic heart disease (IHD), with a higher prevalence in men than in women, at 141.0 million and 103.1 million cases, respectively (Tsao et al., 2022).

Hypertension, as the main risk factor for CHD, also shows an alarming global prevalence. Based on WHO data in 2021, an estimated 1.28 billion adults worldwide suffer from hypertension, with two-thirds of them living in developing countries. This condition is of serious concern, considering that uncontrolled hypertension can accelerate the atherosclerosis process and increase the risk of major cardiovascular events (World Health Organization, 2021).

Coronary Heart Disease (CHD) is a clinical condition caused by narrowing or blockage of the coronary arteries—the main blood vessels that supply oxygen and nutrients to the heart muscle—resulting in an imbalance between myocardial oxygen demand and supply (Lestari et al., 2020). This imbalance leads to myocardial ischemia, which can manifest as chest pain or

angina. Based on symptoms, angina is divided into typical and atypical forms. Typical angina has three main characteristics: chest pain radiating to the neck, jaw, or arms; pain triggered by physical activity; and relief within five minutes of rest or nitrate administration (Neumann et al., 2020).

In Indonesia, the prevalence of CHD has shown an alarming trend. The Institute for Health Metrics and Evaluation (IHME) reported that in 2019, ischemic heart disease accounted for 28.3% of all deaths in Indonesia (Minister of Health of the Republic of Indonesia, 2023). Hospital Information System (SIRS) data in 2015 recorded 51,160 hospitalized CHD cases, with a higher proportion in men (32,314 cases) compared to women (18,846 cases) (Sawu et al., 2022a). Based on Basic Health Research (Riskesdas) data, the highest prevalence of CHD was observed in East Java Province at 1.3% or approximately 337,127 people. Riskesdas 2018 further noted that in Indonesia, more than 650 thousand adults were diagnosed with hypertension, including 11,242 in Bali Province (Amisi et al., 2018).

Atherosclerosis is the main cause of CHD and represents a chronic process involving the accumulation of atheromatous plaques containing fats, platelets, and inflammatory cells such as neutrophils and macrophages within the coronary arterial walls. These plaques narrow the arterial lumen and restrict blood flow to the heart muscle (Wongkar & Yalume, 2019). CHD is multifactorial and influenced by both non-modifiable factors age, gender, family history and modifiable ones, including smoking, dyslipidemia, obesity, diabetes mellitus, lack of physical activity, and hypertension.

Hypertension is one of the most frequently observed major risk factors in CHD patients. It is a chronic condition characterized by an increase in systolic blood pressure ≥ 140 mmHg and/or diastolic pressure ≥ 90 mmHg. Long-term elevated blood pressure damages the vascular endothelium, accelerates atherosclerosis, and increases the risk of cardiovascular events such as myocardial infarction, stroke, and heart failure (Ministry of Health of the Republic of Indonesia, 2018).

The relationship between hypertension and CHD is reciprocal and mutually aggravating. Chronic hypertension damages vascular structures and increases cardiac workload, eventually leading to myocardial ischemia (Barrios et al., 2020). Yani et al. (2020) reported that hypertensive patients have a 2.6-fold higher risk of developing CHD than normotensive individuals. Moreover, disease duration matters patients with hypertension for more than 10 years face nearly triple the risk of developing CHD compared with those newly diagnosed (Tulung et al., 2020).

Effective management of hypertension and CHD is key to preventing and controlling cardiovascular diseases. Interventions can be nonpharmacological or pharmacological. Nonpharmacological strategies include lifestyle modifications dietary regulation, regular exercise, weight control, limiting salt and alcohol intake, smoking cessation, and stress management. Pharmacological therapy involves administering antihypertensive drugs that play a strategic 13000educingg blood pressure, cardiac workload, and risks of further complications.

Antihypertensive drugs are categorized into several major classes: Angiotensin-Converting Enzyme Inhibitors (ACE-I) such as lisinopril and ramipril; Angiotensin Receptor Blockers (ARB) such as valsartan and candesartan; Beta Blockers such as bisoprolol and metoprolol; Calcium Channel Blockers (CCB) such as amlodipine and nifedipine; and diuretics

such as hydrochlorothiazide and furosemide. Each class has a distinct mechanism of action, chosen according to the patient's clinical profile (McEvoy et al., 2024).

Previous research on antihypertensive drug use has emphasized adherence to updated hypertension therapy guidelines. Nurjannah et al. (2009) evaluated antihypertensive drug use in CHD patients at Southeast Sulawesi Provincial Hospital and found that 79.8% of patients received ACE inhibitors, either as monotherapy or in combination. Four-drug combinations were used by 38.5% of patients. Therapeutic outcomes demonstrated a significant reduction in blood pressure ($p < 0.001$), though 21.2% experienced side effects.

Mahottama, Karmaya, and Muliani (2021) reported that 77.9% of CHD patients with hypertension at Sanglah Hospital Denpasar were men, while only 22.1% were women, with the 56–65-year age group being the largest (35.4%). Similarly, Santi, Nelwan, and Langi (2022) at Prof. Dr. R. D. Kandou Manado Hospital found that CHD patient distribution was dominated by men (73%) compared to women (27%).

The clinical complexity of CHD patients, often with comorbidities like diabetes, heart failure, or dyslipidemia, necessitates careful drug selection to minimize side effects and interactions. Given the strong association between hypertension and CHD—and the critical role of antihypertensive therapy—it is vital to understand the profile of antihypertensive drug use. Appropriate drug type, combination, and dosage selection greatly determine therapeutic effectiveness.

Research on the profile of antihypertensive use is essential to identify hospital therapy trends, guideline compliance, and potential drug interactions or adverse effects. However, no study has specifically examined the profile of antihypertensive drug use in CHD patients at Prof. Dr. I.G.N.G. Ngoerah Hospital, Bali Province, one of Indonesia's national referral hospitals.

As the main referral hospital in Bali, Prof. Dr. I.G.N.G. Ngoerah Denpasar Hospital manages a high number of CHD and hypertension cases. Yet, data on antihypertensive drug use in these patients remain limited. Therefore, this study aims to identify antihypertensive drug types, combination patterns, and evaluate their impact on the clinical management of CHD patients at Prof. Dr. I.G.N.G. Ngoerah Denpasar Hospital.

Based on the aforementioned background, this research aims to comprehensively analyze the profile of antihypertensive drug use in patients with coronary heart disease at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar in 2023. Specifically, the objectives are: (1) to identify demographic and clinical characteristics of CHD patients receiving antihypertensive therapy; (2) to determine the most frequently prescribed types and classes of antihypertensive drugs; (3) to analyze single and combination therapy patterns; and (4) to evaluate dosage and frequency regimens.

The benefits of this research are multifaceted. For the scientific community, it contributes to cardiovascular pharmacotherapy knowledge, particularly regarding rational drug use in complex clinical cases. For healthcare professionals, including physicians and pharmacists, the findings provide evidence-based insights that support clinical decisions for more effective, guideline-concordant hypertensive therapy. For Prof. Dr. I.G.N.G. Ngoerah Hospital, this research offers valuable input for policy evaluation and development on antihypertensive drug use, potentially supporting quality improvement in cardiovascular care services.

Furthermore, the results are expected to enhance treatment effectiveness through rational, evidence-based therapeutic decisions, facilitate optimized therapy protocols, identify training needs for medical personnel, support the implementation of updated clinical guidelines, and provide preliminary data for future studies evaluating antihypertensive therapy safety and effectiveness in patients with cardiovascular comorbidities. By achieving a comprehensive understanding of the profile of antihypertensive drug use in CHD patients, this study is anticipated to promote therapy optimization—focusing not only on blood pressure reduction but also on long-term cardiovascular protection and improved patient quality of life.

METHOD

This study employed a descriptive observational design with a cross-sectional approach to determine the profile of antihypertensive drug use in patients with coronary heart disease. The research was conducted at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar, Bali Province, Indonesia, which serves as the main tertiary referral hospital in the region. Data collection was performed retrospectively by reviewing medical records of CHD patients hospitalized during the period from January to December 2023, after obtaining ethical clearance and permission from the hospital research ethics committee and relevant authorities.

The target population in this study is all patients suffering from coronary heart disease at Prof. Dr. I.G.N.G. Ngoerah Denpasar Hospital. The affordable population is patients with coronary heart disease at Prof. dr. I.G.N.G. Ngoerah Hospital Denpasar from January to December 2023, totaling 774 patients based on hospital medical record data.

The research sample consisted of CHD patients who received antihypertensive drug therapy at Prof. Dr. I.G.N.G. Ngoerah Denpasar Hospital during the study period. The research sample was patients with coronary heart disease who received antihypertensive drug therapy at Prof. dr. I.G.N.G. Ngoerah Denpasar Hospital in the period from January to December 2023. The inclusion criteria include: (1) Patients with coronary heart disease at Prof. dr. I.G.N.G. Ngoerah Denpasar Hospital from January to December 2023, (2) Patients with coronary heart disease who receive antihypertensive drug therapy, and (3) Patients who have complete medical records containing information on demographics, diagnosis, comorbidities, blood pressure measurements, and prescribed antihypertensive medications.

Exclusion criteria include: (1) Patients with coronary heart disease who do not receive antihypertensive drug therapy, and (2) Patients with coronary heart disease who are not hospitalized or have incomplete medical record documentation. An affordable population is known to be 774 patients with CHD at Prof. Dr. I.G.N.G. Ngoerah Hospital in 2023, so the sample size calculation was carried out using the Slovin formula with a confidence level of 95% and a margin of error of 10%, so that a sample of 89 patients was obtained. However, in this study, 100 samples were successfully collected that met the criteria.

The sampling technique employed was consecutive sampling, a non-probability sampling method where all patients meeting the inclusion and exclusion criteria during the study period were included until the desired sample size was achieved. This approach ensures adequate representation while maintaining feasibility within the study timeframe.

Data was collected using an instrument in the form of a data collection matrix that recorded information about gender, age, city of origin, comorbidities, blood pressure measurements, severity of disease, and the type of antihypertensive drugs used including drug

names, dosages, dosage forms, and frequency of administration. The data collection process involved the following steps: (1) identification of eligible patients from hospital medical record databases using ICD-10 codes for coronary heart disease (I20-I25), (2) retrieval of complete medical records for patients meeting inclusion criteria, (3) systematic extraction of relevant data using standardized data collection forms, (4) verification of data completeness and accuracy, and (5) coding and entry of data into electronic databases for analysis. Data quality was ensured through double-checking by two independent researchers and resolution of discrepancies through consensus.

The primary data source for this study was secondary data obtained from medical records of CHD patients at Prof. Dr. I.G.N.G. Ngoerah Hospital Denpasar. Medical records provided comprehensive information including patient demographics, admission and discharge dates, primary and secondary diagnoses, comorbid conditions, vital signs including blood pressure measurements, laboratory results, prescribed medications with detailed dosing information, and clinical progress notes.

The data was then processed using IBM SPSS statistical software version 26. Data analysis uses univariate analysis to describe the frequency distribution of each collected variable presented in the form of frequency tables and percentages. Descriptive statistics including measures of central tendency (mean, median) and measures of variability (standard deviation, range) were calculated for continuous variables such as age and blood pressure. For categorical variables including gender, drug classes, combination therapy patterns, and dosage regimens, frequency distributions and percentages were computed. Data were presented using tables and narrative descriptions to facilitate interpretation of antihypertensive drug use patterns in the study population.

RESULTS AND DISCUSSION

Characteristics of Patients with Coronary Heart Disease

The exploration of data on the use of antihypertensive drugs in patients with Coronary Heart Disease (CHD) at Prof. Dr. I.G.N.G. Ngoerah Hospital in 2023 succeeded in collecting 774 patients recorded in medical record data as inpatients with a diagnosis of Coronary Heart Disease. Data selection was carried out with the criteria that patients have a coronary heart history of >1 year, receive antihypertensive therapy during 2023, with complete medical record data. Based on calculations using the Slovin formula:

$$n = N / (1 + N \times e^2)$$

Where:

1. n = sample size
2. N = population size (774)
3. e = margin error (10% or 0.1)

$$n = 774 / (1 + 774 \times 0.1^2) = 774 / (1 + 7.74) = 774 / 8.74 = 88.6 \approx 89$$

Although the calculations showed the need for a minimum of 89 samples, the study managed to collect 100 patients who met the inclusion and exclusion criteria, thus providing better statistical strength.

Table 1. Demographic Characteristics of Patients with Coronary Heart Disease (CHD) at Prof. Dr. I.G.N.G. Ngoerah Hospital in 2023

Characteristics	Category	Quantity (n)	Percentage (%)
Gender	Man	88	88,0
	Woman	12	12,0
Age	26-35 years old (early adult)	1	1,0
	36-45 Years (Late Adult)	6	6,0
	46-55 Years (Early Seniors)	29	29,0
	56-65 Years (Late Seniors)	36	36,0
	>65 Years Old (Senior)	28	28,0
Origin City	Denpasar	42	42,0
	Gianyar	15	15,0
	Tabanan	11	11,0
	Badung	8	8,0
	Bangli	6	6,0
	Karangasem	5	5,0
	Cities/Regencies Outside Bali	4	4,0
	Jembrana	3	3,0
	Klungkung	3	3,0
	São Paulo	3	3,0
	Normal (<130/<85 mmHg)	46	46,0
	Normal Tinggi (130-139/85-89 mmHg)	25	25,0
Blood pressure	Hypertension Grade 1 (140-159/90-99 mmHg)	25	25,0
	Hypertension Grade 2 ($\geq 160/\geq 100$ mmHg)	4	4,0
Number of Comorbidities	No Comorbidities	12	12,0
	There are 1 Comorbidities	37	37,0
	There are 2 Comorbidities	34	34,0
	There are 3 Comorbidities	15	15,0
	There are 4 Comorbidities	1	1,0
	There are 5 Comorbidities	1	1,0
Total		100	100,0

Based on Table 1, the characteristics of patients with CHD showed a significant dominance in the male sex by 88% (88 people) compared to 12% (12 people) in women. The age distribution showed that the age group of 56-65 years (the final elderly) was the most with 36% (36 people), followed by the age group of 46-55 years (early elderly) at 29% (29 people), and the age group >65 years (seniors) at 28% (28 people). An interesting finding is the discovery of 1% (1 person) of CHD cases at a young age (26-35 years), which shows the importance of early detection of cardiovascular risk factors in the young population.

The geographical distribution of patients shows that the majority come from Denpasar City at 42% (42 people), followed by Gianyar Regency 15% (15 people), and Tabanan Regency 11% (11 people). This reflects the accessibility of Prof. Dr. I.G.N.G. Ngoerah Hospital as the main referral hospital in Bali Province, with a dominant referral pattern from urban areas and its surroundings.

Table 2. Comorbid Distribution of Patients with Coronary Heart Disease

Comorbid	Quantity (n)	Percentage (%)
Hypertension	50	29,2
Diabetes Mellitus Type 2	27	15,8
ACKD (Acute on Chronic Kidney Disease)	11	6,4
AKI (Acute Kidney Injury)	11	6,4
Dyslipidemia	11	6,4
Hyperuricemia	10	5,8
Hyperglycaemia	6	3,5
Stroke	5	2,9
Cardiac arrhythmias	4	2,3
Hypokalemia	4	2,3
Heart Failure	3	1,8
Anemia	2	1,2
Hypoalbuminaemia	2	1,2
Osteoarthritis	2	1,2
TBC Paru	2	1,2
CKD (Chronic Kidney Disease)	1	0,6
Dyspepsia	1	0,6
Hepatitis	1	0,6
Hypothyroidism	1	0,6
HIV	1	0,6
Leukocytosis	1	0,6
Obesity	1	0,6
Transaminitis	1	0,6
Xerosis Cutis	1	0,6
No Comorbidities	12	7,0
Comorbid Total	171	100,0

Comorbidity analysis showed that 88% of patients (88 out of 100 patients) had at least one comorbidity, with a total of 171 comorbid diagnoses recorded. Hypertension dominated as the main comorbid with 29.2% (50 cases), followed by type 2 diabetes mellitus at 15.8% (27 cases). Renal disorder conditions, both acute and chronic, showed a significant prevalence with ACKD and AKI at 6.4% each (11 cases), reflecting the cardio-renal complications that often occur in CHD patients.

Profile of Antihypertensive Drug Use in CHD Patients

Table 3. Distribution of Proportions of Antihypertensive Drugs

Drug Classes	Total Usage (n)	Percentage (%)
Beta Blocker (BB)	94	32,3
Diuretic	71	24,4
ACE Inhibitor (ACEi)	57	19,6
Angiotensin Receptor Blocker (ARB)	38	13,1
Calcium Channel Blocker (CCB)	31	10,7
Total Drug Use	291	100,0

Table 3 shows the distribution of the use of 291 antihypertensive drug regimens in 100 CHD patients. Beta-blockers dominated the use with 32.3% (94 uses), followed by diuretics at 24.4% (71 uses), and ACE inhibitors at 19.6% (57 uses). Angiotensin Receptor Blocker (ARB) was used in 13.1% of cases (38 uses), while Calcium Channel Blocker (CCB) was the group with the lowest use at 10.7% (31 uses).

Table 4. Variations in the Number of Antihypertensive Drug Therapy Combinations

Types of Therapy	Number of Patients (n)	Percentage (%)
Monotherapy (1 Drug)	8	8,0
2-Drug Combination Therapy	24	24,0
3-Drug Combination Therapy	40	40,0
4-Drug Combination Therapy	7	7,0
Therapy with Group Repetition	21	21,0
Total	100	100,0

Analysis of therapy patterns showed that 3-drug combination therapy was the most dominant approach, applied to 40% of patients (40 people). 2-drug combination therapy came in second place with 24% (24 patients), while monotherapy was applied to only 8% of patients (8 people). An interesting finding was that 21% of patients (21 people) received therapy with a repeat of the same class of drugs, especially diuretics, indicating the complexity of the clinical condition that required intensification of therapy.

Table 5. Specific Patterns of Use of Antihypertensive Drug Combinations

Drug Combinations	Number of Patients (n)	Percentage (%)
Monotherapies		
ACEi	3	3,0
BB	4	4,0
Diuretic	1	1,0
2-Drug Combination Therapy		
ACEi + BB	16	16,0
ARB + BB	7	7,0
ACEi + Diuretics	1	1,0
3-Drug Combination Therapy		
ACEi + Diuretics + BB	13	13,0
ACEi + CCB + BB	11	11,0
ARB + CCB + BB	8	8,0
ARB + Diuretics + BB	7	7,0
ACEi + ARB + BB	1	1,0
4-Drug Combination Therapy		
ACEi + CCB + Diuretics + BB	2	2,0
ARB + CCB + Diuretics + BB	5	5,0
Therapy with Relapse		
ARB + BB + Diuretics + Diuretics	7	7,0
ACEi + BB + Diuretics + Diuretics	8	8,0
ARB + BB + CCB + Diuretics + Diuretics	2	2,0
ACEi + BB + CCB + Diuretics + Diuretics	2	2,0
ARB + CCB + Diuretics + Diuretics	1	1,0
BB + Diuretics + Diuretics	1	1,0
Total	100	100,0

The combination of ACEi + BB was the most dominant combination therapy pattern with 16% (16 patients), followed by ACEi + Diuretics + BB at 13% (13 patients), and ACEi + CCB + BB at 11% (11 patients). The use of combination with repeated diuretics shows significant prevalence, especially in patients with conditions that require strict fluid volume control.

Analysis of Dosage Regimen by Antihypertensive Drug Group

Table 6. ACE Inhibitor Regimen Distribution

Drug Name	Dose	Preparation Form	Frequency	Quantity (n)	Percentage (%)
Ramipril	5 mg	Tablet	1x day (OD)	25	43,9
Ramipril	2,5 mg	Tablet	1x day (OD)	17	29,8
Ramipril	10 mg	Tablet	1x day (OD)	11	19,3
Captopril	25 mg	Tablet	3x day (TID)	1	1,8
Captopril	12,5 mg	Tablet	3x day (TID)	1	1,8
Lisinopril	10 mg	Tablet	1x day (OD)	1	1,8
Ramipril	5 mg	Tablet	2x day (BID)	1	1,8
Total				57	100,0

Tabel 7. Distribution of Regimen Angiotensin Receptor Blocker (ARB)

Drug Name	Dose	Preparation Form	Frequency	Quantity (n)	Percentage (%)
Candesartan	16 mg	Tablet	1x day (OD)	10	26,3
Candesartan	8 mg	Tablet	1x day (OD)	10	26,3
Candesartan	32 mg	Tablet	1x day (OD)	4	10,5
Valsartan	50 mg	Tablet	2x day (BID)	4	10,5
Candesartan	4 mg	Tablet	1x day (OD)	2	5,3
Valsartan	80 mg	Tablet	1x day (OD)	2	5,3
Irbesartan	150 mg	Tablet	1x day (OD)	1	2,6
Telmisartan	80 mg	Tablet	1x day (OD)	1	2,6
Valsartan	100 mg	Tablet	2x day (BID)	1	2,6
Valsartan	160 mg	Tablet	1x day (OD)	1	2,6
Valsartan	160 mg	Tablet	2x day (BID)	1	2,6
Valsartan	80 mg	Tablet	2x day (BID)	1	2,6
Total				38	100,0

Table 8. Distribution of Beta-Blocker Regimen

Drug Name	Dose	Preparation Form	Frequency	Quantity (n)	Percentage (%)
Bisoprolol	2,5 mg	Tablet	1x day (OD)	39	41,5
Bisoprolol	5 mg	Tablet	1x day (OD)	34	36,2
Bisoprolol	1,25 mg	Tablet	1x day (OD)	8	8,5
Carvedilol	6,25 mg	Tablet	2x day (BID)	4	4,3
Bisoprolol	10 mg	Tablet	1x day (OD)	2	2,1
Bisoprolol	7,5 mg	Tablet	1x day (OD)	2	2,1
Carvedilol	3,125 mg	Tablet	2x day (BID)	2	2,1
Bisoprolol	3,75 mg	Tablet	1x day (OD)	1	1,1
Carvedilol	12,5 mg	Tablet	2x day (BID)	1	1,1
Total				94	100,0

Tabel 9. Distribution of Regimen Calcium Channel Blocker (CCB)

Drug Name	Dose	Preparation Form	Frequency	Quantity (n)	Percentage (%)
Amlodipine	5 mg	Tablet	1x day (OD)	24	77,4
Amlodipine	10 mg	Tablet	1x day (OD)	6	19,4
Nifedipine	60 mg	Tablet	1x day (OD)	1	3,2
Total				31	100,0

Table 10. Diuretic Regimen Distribution

Drug Name	Dose	Preparation Form	Frequency	Quantity (n)	Percentage (%)
Spironolactone	25 mg	Tablet	1x day (OD)	31	43,7
Furosemide	40 mg	Tablet	If the complaint (K/P)	14	19,7
Furosemide	40 mg	Tablet	1x day (OD)	10	14,1
Spironolactone	50 mg	Tablet	1x day (OD)	5	7,0
Furosemide	40 mg	Tablet	2x day (BID)	4	5,6
Furosemide	20 mg	Tablet	If the complaint (K/P)	2	2,8
Furosemide	120 mg	IV Injection	Continuum	1	1,4
Furosemide	360 mg	IV Injection	Continuum	1	1,4
Furosemide	40 mg	IV Injection	1x day (OD)	1	1,4
Furosemide	5 mg	IV Injection	Continuum	1	1,4
Hydrochlorothiazide	25 mg	Tablet	1x day (OD)	1	1,4
Total				71	100,0

Discussion of Demographic and Clinical Characteristics of Patients

The dominance of the male sex (88%) in this study is consistent with the epidemiology of CHD globally. Mahottama, Karmaya, and Muliani (2021) reported similar results at Sanglah Hospital Denpasar with 77.9% of CHD patients with hypertension being men. Research at Prof. Dr. R. D. Kandou Manado Hospital by Santi, Nelwan, and Langi (2022) also showed a similar distribution with 73% of male patients. The high prevalence in men is associated with biological and behavioral factors, including greater exposure to cardiovascular risk factors such as smoking, alcohol consumption, a high-fat diet, and higher levels of job stress.

Biologically, women have hormonal protection in the form of estrogen before menopause which plays a role in maintaining vascular endothelial function and lipid metabolism. Estrogen increases the production of nitric oxide which is vasoprotective, decreases the expression of adhesion molecules, and has an anti-inflammatory effect on the walls of blood vessels (Regitz-Zagrosek, 2012). After menopause, the risk in women increases significantly, but remains lower than in men of the same age.

The age distribution showed a peak incidence in the 56-65 year old group (36%), which is in line with the research of Mahottama et al. (2021) which recorded that 35.4% of CHD patients with hypertension were in a similar age range. This reflects a progressive degenerative process of the cardiovascular system, including decreased vascular elasticity, increased arterial stiffness, and accumulated endothelial damage due to long-term exposure to risk factors. The discovery of CHD cases at a young age (26-35 years) although only 1%, underscores the importance of early detection and preventive intervention in the productive age population.

The dominance of patients from Denpasar (42%) reflects the demographic pattern and accessibility of tertiary health services. As the provincial capital, Denpasar has a high population density, intensive urbanization rate, and greater exposure to a sedentary lifestyle. Socio-economic factors in urban areas also contribute to increased consumption of processed foods, low physical activity, and higher levels of psychosocial stress (World Health Organization, 2018).

Comorbidity Profile Analysis

The high prevalence of comorbidities (88% of patients have at least one comorbidity) with a total of 171 comorbid diagnoses indicates the clinical complexity of CHD patients. Hypertension as the dominant comorbid (29.2%) strengthens the evidence of a pathophysiological relationship between hypertension and CHD. Underlying mechanisms include acceleration of atherosclerosis due to shear stress in the endothelium, activation of the renin-angiotensin-aldosterone system, increased left ventricular afterload load, and stimulation of systemic inflammatory processes.

Type 2 diabetes mellitus as the second most common comorbid (15.8%) indicates a metabolic syndrome that often accompanies CHD. Chronic hyperglycemia leads to protein glycation, endothelial dysfunction, acceleration of atherosclerosis, and increased platelet aggregation. The combination of diabetes and hypertension creates synergistic cardiovascular risk, with an increased risk of major events up to 2-4 times that of the normal population.

The high prevalence of renal disorders (ACKD 6.4%, AKI 6.4%) reflects a complex cardio-renal syndrome. Impaired renal function in CHD patients may occur as a result of renal hypoperfusion secondary to decreased cardiac output, nephrotoxic effects of contrast media on catheterization procedures, or as a manifestation of systemic atherosclerosis involving the renal arteries.

Discussion of the Profile of Antihypertensive Drug Use

The dominance of beta-blockers (32.3%) in the profile of antihypertensive drug use in this study was in accordance with evidence-based medicine recommendations for CHD patients. The European Society of Cardiology (ESC) 2024 places beta-blockers as the primary therapy in patients with specific cardiovascular indications, including CHD, post-myocardial infarction, heart failure, and rhythm disorders (McEvoy et al., 2024). Beta-blockers work through beta-1 receptor antagonism in the heart, producing negative chronotropic (decreased heart rate), negative inotropic (decreased contractility), and negative dromotropic (AV conduction slowdown) effects.

The cardioprotective mechanism of beta-blockers in CHD includes: (1) Reduction of myocardial oxygen consumption through a decrease in heart rate-pressure product, (2) Extension of the diastole phase that increases coronary perfusion, (3) Inhibition of sympathetic activity that reduces coronary vasospasm, (4) Antiarrhythmic effect that reduces the risk of sudden cardiac death, and (5) Slowing down of left ventricular remodeling after myocardial infarction. A meta-analysis by Gai-gai Ma et al. (2020) showed beta-blockers reduced mortality by 22% (RR = 0.78; 95% CI 0.71-0.86) in heart failure patients with atrial fibrillation.

The use of diuretics as the second most common therapy (24.4%) reflects a comprehensive approach in the management of hypertension and volume overload. Spironolactone as the dominant diuretic (43.7% of the total diuretic) showed a preference for aldosterone antagonists that had additional cardioprotective effects. The PATHWAY-2 study by Williams et al. (2015) demonstrated the superiority of spironolactone in lowering blood pressure in resistant hypertension compared to beta-blockers and alpha-blockers.

Spironolactone acts through competitive antagonism of mineralocorticoid receptors, producing natriuretic, potassium-sparing, and anti-fibrotic effects on the myocardium. RALES

and EMPHASIS-HF research showed that spironolactone decreased mortality and rehospitalization in heart failure, especially through modulation of aldosterone pathways that play a role in myocardial fibrosis and ventricular remodeling.

Analysis of Combination Therapy Patterns

The dominance of 3-drug combination therapy (40% of patients) reflects the implementation of the ESC 2024 guidelines which recommend combination strategies from the early stages of hypertension management. The ESC 2024 algorithm suggests fixed-dose dual therapy (ACE inhibitor/ARB + CCB) as the first line, followed by triple therapy with the addition of thiazide-like diuretics if the blood pressure target has not been achieved (Visseren et al., 2024).

The combination of ACEi + BB as the most frequent pattern (16%) showed a synergistic approach in cardioprotection. ACE inhibitors inhibit the conversion of angiotensin I to angiotensin II, resulting in vasodilation, decreased aldosterone secretion, and renoprotective effects. Combination with beta-blockers provides additional protection through afterload reduction (ACEi) and preload reduction as well as heart rate control (beta-blocker). The HOPE and EUROPA studies show ACE inhibitors lower major cardiovascular events in high-risk patients, including CHD.

The use of combination with diuretic repetition (21% of patients) indicated clinical Complexity requiring intensive fluid volume control. The combination of spironolactone and furosemide exerts synergistic effects through different mechanisms: furosemide (loop diuretic) inhibits NKCC2 in Henle's ascending limb, while spironolactone (potassium-sparing diuretic) antagonists aldosterone in the collecting duct. This strategy is effective in patients with fluid retention who are resistant to diuretic monotherapy.

Discussion of Dosage Regimen and Frequency of Administration

The dominance of the once-daily (OD) regimen in all classes of antihypertensive drugs reflects efforts to optimize therapeutic adherence. Ramipril 5 mg OD (43.9% of ACEi), Bisoprolol 2.5 mg OD (41.5% of beta-blockers), and Amlodipin 5 mg OD (77.4% of CCB) showed a preference for long-acting formulations that provide 24-hour blood pressure control with a single dose.

Pharmacoeconomic studies show that the once-daily regimen increases medication adherence by 20-30% compared to twice-daily or multiple-daily dosing. This is especially relevant in CHD patients who generally require long-term polypharmacy. Poor adherence to antihypertensive therapy increases the risk of major cardiovascular events, rehospitalization, and mortality.

The selection of Ramipril 5 mg as the dominant dose is in line with evidence from the HOPE study that used similar doses and showed a significant reduction in composite endpoints (cardiovascular death, MI, stroke) of 22% in high-risk patients. This dose is within the optimal therapeutic range that provides maximum antihypertensive effects with a tolerable side effect profile.

Bisoprolol 2.5-5 mg OD as the dominant beta-blocker regimen is in accordance with the recommendation of gradual titration in CHD patients. This dose provides optimal selective beta-1 blockade without excessive bradycardia or excessive negative inotropic effects. CIBIS-

II and MERIT-HF studies show bisoprolol at therapeutic doses lowers mortality in ischemic heart failure.

Clinical Implications and Compliance with the Guidelines

The profile of the use of antihypertensive drugs in this study shows good compatibility with the ESC 2024 guidelines for hypertension management in CHD patients. The use of beta-blockers as the primary therapy, followed by combination with ACE inhibitors and diuretics, reflects the implementation of evidence-based medicine in daily clinical practice.

However, there are some areas that need further attention. Relatively low use of ARBs (13.1%) may be optimized as an alternative to ACE inhibitors in patients with intolerance (such as dry cough). CCB as the class with the lowest use (10.7%) may also be considered for intensification of therapy, especially in patients with isolated systolic hypertension or vasospastic angina.

The high prevalence of complex combination therapy (>3 drugs) indicates the need for close monitoring of side effects, drug interactions, and kidney function. Significant use of spironolactone requires regular monitoring of electrolytes, especially serum potassium, to prevent potentially life-threatening hyperkalaemia.

Research Limitations and Constraints

This study has several limitations that need to be considered in the interpretation of the results. First, retrospective design limits the ability to evaluate long-term clinical outcomes and causality. Second, the lack of detailed laboratory data (such as eGFR, electrolyte, HbA1c) limits the analysis of factors influencing drug selection. Third, there are no data on blood pressure achievement targets and cardiovascular endpoints which are important parameters for assessing the effectiveness of therapy.

Nevertheless, this study provides the first comprehensive overview of the profile of the use of antihypertensive drugs in CHD patients at Prof. Dr. I.G.N.G. Ngoerah Hospital, which can be the basis for the development of more optimal therapy protocols and evaluation of the quality of cardiovascular services in the future.

CONCLUSION

The profile of antihypertensive drug use in patients with coronary heart disease at Prof. Dr. I.G.N.G. Ngoerah Hospital in 2023 demonstrates several key findings that reflect evidence-based clinical practice and guideline adherence. First, the demographic profile reveals that the majority of CHD patients are elderly males (88% male, 36% aged 56-65 years) with significant comorbidities, particularly hypertension (29.2%), type 2 diabetes mellitus (15.8%), and renal disorders (12.8% combined ACKD and AKI), highlighting the complex clinical management required in this population. Second, beta-blockers emerged as the most frequently prescribed antihypertensive class (32.3%), followed by diuretics (24.4%) and ACE inhibitors (19.6%), reflecting appropriate implementation of cardiovascular protection strategies in accordance with ESC 2024 guidelines. Third, the predominance of combination therapy, particularly triple-drug regimens (40% of patients), with ACEi + BB combination being the most common pattern (16%), demonstrates a comprehensive approach to blood pressure management and cardiovascular risk reduction. Fourth, the widespread use of once-daily dosing regimens,

especially ramipril 5 mg OD, bisoprolol 2.5 mg OD, and amlodipine 5 mg OD, indicates a patient-centered approach aimed at optimizing medication adherence and therapeutic outcomes. These findings collectively suggest that antihypertensive therapy in CHD patients at Prof. Dr. I.G.N.G. Ngoerah Hospital is generally aligned with current evidence-based guidelines, emphasizing individualized treatment approaches based on patient characteristics, comorbidities, and clinical conditions. The results of this study provide a foundation for continuous quality improvement initiatives, including the development of standardized therapy protocols, enhancement of medication safety monitoring systems, identification of professional development needs for healthcare providers, and establishment of benchmarks for future comparative effectiveness research. Future prospective studies are recommended to evaluate long-term clinical outcomes, medication adherence rates, achievement of blood pressure targets, and the cost-effectiveness of different antihypertensive regimens in CHD patients with multiple comorbidities.

REFERENCES

- Amisi, M. D., Maramis, F. R., & Kandou, J. M. (2018). Hubungan antara umur, jenis kelamin dan hipertensi dengan kejadian penyakit jantung koroner pada pasien rawat inap di RSUP Prof. Dr. R. D. Kandou Manado periode Juli 2015-Juni 2016. *Jurnal e-Clinic*, 6(1), 48-52.
- Ananth, C. V., Rutherford, C., Rosenfeld, E. B., Brandt, J. S., Graham, H., Kostis, W. J., & Keyes, K. M. (2023). Epidemiologic trends and risk factors associated with the decline in mortality from coronary heart disease in the United States, 1990-2019. *American Heart Journal*, 263, 46–55.
- Barrios, V., Escobar, C., & Ruilope, L. M. (2020). Blood pressure targets in patients with coronary artery disease. *European Cardiology Review*, 15, e14. <https://doi.org/10.15420/ecr.2019.11>
- Gai-gai, M., Xin, L., Qiang, L., & Jin-wen, W. (2020). β -blockers for the treatment of atrial fibrillation in patients with heart failure: A meta-analysis. *BMC Cardiovascular Disorders*, 20(1), 1-9. <https://doi.org/10.1186/s12872-020-01456-w>
- Lestari, I. A., Wulandari, Y., & Setiati, S. (2020). Diagnosis dan tatalaksana penyakit jantung koroner. *Jurnal Penyakit Dalam Indonesia*, 7(1), 41–49. <https://doi.org/10.7454/jpdi.v7i1.123>
- Mahottama, A. A., Karmaya, I. N. M., & Muliani. (2021). Prevalensi hipertensi pada penderita penyakit jantung koroner (PJK) di RSUP Sanglah Denpasar Maret–September 2019. *E-Jurnal Medika Udayana*, 10(4), 1–5. <https://doi.org/10.24843/MU.2021.V10.i4.P01>
- McEvoy, J. W., McCarthy, C. P., Bruno, R. M., Brouwers, S., Canavan, M. D., Ceconi, C., & Khamidullaeva, G. A. (2024). 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *European Heart Journal*, 45(38), 3912–4018. <https://doi.org/10.1093/eurheartj/ehae178>
- Neumann, F. J., Sousa-Uva, M., Ahlsson, A., Alfonso, F., Banning, A. P., Benedetto, U., Byrne, R. A., Collet, J. P., Falk, V., Head, S. J., Jüni, P., Kastrati, A., Koller, A., Kristensen, S. D., Niebauer, J., Richter, D. J., Seferovic, P. M., Sibbing, D., Stefanini, G. G., Windecker, S., Yadav, R., & Zembala, M. O. (2020). 2018 ESC/EACTS Guidelines

- on myocardial revascularization. *European Heart Journal*, 41(4), 407-477. <https://doi.org/10.1093/eurheartj/ehz467>
- Nurjannah, N., Suwantika, A. A., & Abdulah, R. (2009). Evaluasi penggunaan obat antihipertensi pada pasien penyakit jantung koroner di Rumah Sakit Umum Daerah Provinsi Sulawesi Tenggara. *Majalah Farmasi Indonesia*, 20(4), 186-192.
- Regitz-Zagrosek, V. (2012). Sex and gender differences in cardiovascular disease. *Circulation Research*, 110(11), 1341-1344. <https://doi.org/10.1161/CIRCRESAHA.111.249305>
- Santi, M. N., Nelwan, J. E., & Langi, F. L. F. G. (2022). Gambaran penderita penyakit jantung koroner di RSUP Prof. Dr. R. D. Kandou Manado periode Januari 2019-Desember 2020. *Jurnal e-Clinic*, 10(1), 126-131. <https://doi.org/10.35790/ec1.v10i1.35891>
- Sawu, D. A. D., Nurjanah, N., & Puspitasari, I. M. (2022a). Pola penggunaan obat antihipertensi pada pasien penyakit jantung koroner dengan hipertensi di rumah sakit. *Pharmaceutical Sciences and Research*, 9(1), 34-44. <https://doi.org/10.7454/psr.v9i1.1234>
- Tsao, C. W., Aday, A. W., Almarzooq, Z. I., Alonso, A., Beaton, A. Z., Bittencourt, M. S., Boehme, A. K., Buxton, A. E., Carson, A. P., Commodore-Mensah, Y., Elkind, M. S. V., Evenson, K. R., Eze-Nliam, C., Ferguson, J. F., Generoso, G., Ho, J. E., Kalani, R., Khan, S. S., Kissela, B. M., ... & Martin, S. S. (2022). Heart disease and stroke statistics—2022 update: A report from the American Heart Association. *Circulation*, 145(8), e153-e639. <https://doi.org/10.1161/CIR.0000000000001052>
- Tulung, M., Karundeng, A., & Panelewen, S. (2020). Hubungan antara durasi hipertensi dengan kejadian penyakit jantung koroner di RSUP Prof. Dr. R. D. Kandou Manado. *Jurnal Biomedik (JBM)*, 12(3), 134–140. <https://doi.org/10.35790/jbm.12.3.2020.30123>
- Visseren, F. L. J., Mach, F., Smulders, Y. M., Carballo, D., Koskinas, K. C., Bäck, M., & ESC Scientific Document Group. (2024). 2024 ESC Guidelines for the management of arterial hypertension. *European Heart Journal*, 45(12), 1083–1161. <https://doi.org/10.1093/eurheartj/ehae207>
- Williams, B., MacDonald, T. M., Morant, S., Webb, D. J., Sever, P., McInnes, G., & Brown, M. J. (2015). Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension. *The Lancet*, 386(10008), 2059–2068. [https://doi.org/10.1016/S0140-6736\(15\)00257-3](https://doi.org/10.1016/S0140-6736(15)00257-3)
- Wongkar, M. C., & Yalume, Y. T. (2019). Gambaran klinis dan faktor risiko penyakit jantung koroner. *Jurnal E-Biomedik (eBm)*, 7(2), 71–77. <https://doi.org/10.35790/ebm.7.2.2019.25773>
- World Health Organization. (2018). *Noncommunicable diseases country profiles 2018*. Geneva: World Health Organization.
- World Health Organization. (2021). *Hypertension fact sheet*. Retrieved from <https://www.who.int/news-room/fact-sheets/detail/hypertension>
- Yani, J., Polii, J., & Adiguna, M. (2020). Hubungan hipertensi dengan kejadian penyakit jantung koroner di RSUP Prof. Dr. R. D. Kandou Manado. *Jurnal Ilmiah Perioperatif*, 5(2), 116–122. <https://doi.org/10.35790/jip.5.2.2020.29456>

