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RESEARCH ARTICLE

# Cost-effectiveness analysis of amlodipine and candesartan in the inpatient setting at Mataram University Hospital in Indonesia, 2021

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## Abstract

**Background:** Hypertension requires ongoing treatment, which could be costly. There are different single-drug therapy options available, such as amlodipine or candesartan, which have varying costs. **Objective:** This study aimed to analyse the cost-effectiveness of amlodipine and candesartan in hypertensive patients by determining the Average Cost Effectiveness Ratio (ACER) and Incremental Cost Effectiveness Ratio (ICER) ratios from a hospital perspective. **Method:** This study used probability sampling of retrospective data from 2021 for the analysis. All inpatients who were given single therapy with amlodipine of 10 mg or candesartan of 16 mg were included. Direct medical costs were collected, including medicine and room costs, doctor visits, medical procedures, labour and administration. The effectiveness of the therapy was measured by blood pressure reduction from each therapy. ACER and ICER analyses were conducted to determine the most cost-effective therapy. **Result:** A total of 18 samples met the inclusion criteria, 14 patients received amlodipine therapy and four patients received candesartan therapy. The results showed that the cost-effectiveness of antihypertensive therapy with amlodipine and candesartan, as measured by ACER, was IDR 74,851.15 and IDR 87,809.25, respectively. The ICER value obtained was IDR 362,768. **Conclusion:** The results may suggest that amlodipine is more cost-effective than candesartan.

## Introduction

Hypertension continues to be the leading cause of death worldwide, resulting in 10.4 million deaths annually. Cases of high mortality caused by hypertension can be reduced by administering antihypertensive therapy, which can be done pharmacologically or non-pharmacologically (Unger *et al.*, 2020). Several factors, including patient demographics like age, sex, race, and the availability of evidence-based guidelines, influence the treatment of hypertension. Furthermore, the cost-effectiveness of treatment is closely tied to social determinants (Davari *et al.*, 2022). Patients with hypertension will require long-term or lifelong therapy, which demands a high cost of treatment. The varying effectiveness of antihypertensive medications and the wide range of prices for different types of

antihypertensives also impact the overall cost of treatment (Baroroh *et al.*, 2019). JNC VIII recommends several pharmacological therapies as first-line antihypertensives, such as thiazides, calcium channel blockers (CCB), angiotensin-converting enzyme inhibitors (ACE-I), and/or angiotensin receptor blockers (ARBs) (James *et al.*, 2014).

ARBs, such as valsartan and candesartan, belong to a newer and safer class of medications used for treating hypertension. They are especially beneficial for individuals who cannot tolerate angiotensin-converting enzyme inhibitors due to their efficacy and improved tolerability (Barreras & Gurk-Turner, 2003). However, due to their short half-lives, some patients may require twice-daily dosing of ARBs to control blood pressure, leading to increased costs effectively. In the CCB group,

amlodipine is one of the most frequently prescribed drugs due to several favourable pharmacodynamic and pharmacokinetic properties. These properties include high bioavailability, a prolonged half-life, and an extended duration of action. Consequently, patients can conveniently take the medication once per day (Wu *et al.*, 2013).

In previous research conducted in West Nusa Tenggara, it was discovered that amlodipine was the most commonly prescribed drug for hypertension. There were also other hypertension drugs prescribed, including angiotensin receptor blockers such as candesartan and valsartan (Lestari *et al.*, 2021; Puspitasari *et al.*, 2022).

Mataram University Hospital is a Type C teaching hospital in Indonesia with a minimum of 100 beds. According to data from the Indonesian Hospital Association, Type C hospitals are the most common type of hospital in Indonesia (PERSI, 2020). In addition, chronic diseases that cannot be treated at first-level health facilities in Indonesia are referred to the next-level facility, which is Type C hospitals.

The study was conducted at Mataram University Hospital, thus potentially reflecting prescription practices in similar healthcare settings. However, no pharmaco-economic research has been conducted at Mataram yet. Based on the initial survey, amlodipine and candesartan were the two most commonly used antihypertensive agents at the University of Mataram Hospital.

Therefore, a pharmaco-economic analysis is necessary to compare the cost-effectiveness of amlodipine and candesartan. This study aims to analyse the cost-effectiveness of amlodipine and candesartan in hypertensive patients by determining the Average Cost-Effectiveness Ratio (ACER) and Incremental Cost-Effectiveness Ratio (ICER) from a hospital perspective.

## Methods

### Design

As an observational study with a cross-sectional research design, this study used cost-effectiveness as an analysis approach using a hospital perspective. The research output was the effectiveness of therapy in the form of the difference in blood pressure reduction during the patient's treatment period until discharged from the hospital.

### Material

The research data were financial and medical record data from all hypertensive patients at the Mataram

University Hospital Inpatient Installation in 2021. The data was collected between January and March 2022.

### Inclusion and exclusion criteria

This study's population included all hypertensive patients (ICD 10: I10) who were prescribed amlodipine or candesartan at the inpatient installation at the Mataram University Hospital in 2021. Inclusion criteria were all hypertensive patients hospitalised in 2021 who were given single therapy using 10 mg of amlodipine or 16 mg of candesartan. Patients on combination therapy of the two drugs, COVID-19 patients, and patients referred to other hospitals were excluded.

### Data analysis

Data were analysed by calculating the effectiveness or outcome of therapy: the percentage (%) decrease in blood pressure of patients who reached the target after treatment with amlodipine or candesartan. Furthermore, ACER and ICER analyses were carried out to determine the most cost-effective therapy. Data were also analysed to examine the difference in blood pressure decrease and the average cost. This was done by the Mann-Whitney test because the data were not normally distributed.

$$ACER = \frac{\Delta \text{treatment cost (Indonesian rupiah)}}{\Delta \text{treatment effectivity (\%)}}$$

$$ICER = \frac{\text{treatment cost A} - \text{treatment cost B (Indonesian rupiah)}}{\text{treatment effectivity A} - \text{treatment effectivity B (\%)}}$$

## Results

The sampling of 78 patients was carried out based on the inclusion and exclusion criteria detailed above. The final sample number obtained during the study comprised of 18 patients. Of the 18 samples, 14 patients were treated with 10 mg of amlodipine and four patients were treated with candesartan of 16 mg.

Table I illustrates that the majority of patients with hypertension in this research were male. Based on the age category, the results showed that patients aged 45-64 years experienced the highest incidence of hypertension, at 94.44%. The results of this study showed that most of the patients (17 patients) spent no more than ten days in hospitals. Based on the distribution of types of facilities/classes of treatment, the majority of patients came from class three treatment rooms.

**Table I: Patient characteristics**

Characteristics	Total number of patients (n = 18)		Total	Percentage (%)
	Amlodipine (n = 14)	Candesartan (n = 4)		
<b>Sex</b>				
Male	8	3	11	61.11
Female	6	1	7	38.89
<b>Age</b>				
20-44 years old	6	0	6	33.33
45-64 years old	5	3	8	44.45
≥65 years old	4	0	4	22.22
<b>Length of stay</b>				
1-10 days	14	3	17	94.44
11-20 days	0	1	1	5.56
≥ 20 days	0	0	0	0.00
<b>Room class type</b>				
VIP	2	2	4	22.23
1 <sup>st</sup> Class	3	0	3	16.67
2 <sup>nd</sup> Class	4	1	5	27.77
3 <sup>rd</sup> Class	5	1	6	33.33

Table II shows the average reduction in systolic and diastolic blood pressure from the provision of amlodipine of 10 mg and candesartan of 16 mg. The data shows that the average decrease in amlodipine was greater than that of candesartan. Statistically, there were no differences between systole and diastole for both drugs.

**Table II: Average blood pressure reduction (mmHg)**

Cardiac cycle	Average blood pressure reduction (mmHg ± SD)		P
	Amlodipine	Candesartan	
Systole	21.43 ± 13.73	20.75 ± 12.60	0.915
Diastole	13.85 ± 10.37	7.00 ± 3.80	0.287

Based on Table III, the total direct medical costs were calculated based on the average of each cost component. Patients in this study were divided into groups of patients who received 10 mg of amlodipine and 16 mg of candesartan respectively. The cost of each drug per tablet at Mataram University Hospital was IDR 2,300.00 for 10 mg of amlodipine and IDR 1,200.00 for 16 mg of candesartan.

A comparative test between the cost components of different antihypertensive therapies, namely amlodipine and candesartan, was carried out using a the Mann-Whitney test. In terms of the difference

between the cost components of amlodipine and candesartan, there were insignificant differences ( $p = 0.056$ ).

**Table III: Average cost in Indonesian Rupiah (IDR)**

Cost component	Average cost in Indonesian Rupiah (IDR) + SD		P
	Amlodipine 10 mg	Candesartan 16 mg	
Medicine	283,800	59,300	0.241
Room cost	10,645,000	10,860,000	0.454
Doctor visit	3,560,000	2,400,000	0.157
Medical procedures	33,309,000	11,288,000	0.396
Laboratorium analysis	14,427,250	9,661,400	0.089
Administration	5,135,000	855,000	0.487
Total cost	67,360,050	35,123,700	0.056
Average	4,811,432 ± 5,652,022	8,780,925 ± 5,091,443	0.056

Table IV shows the calculation of the effectiveness as well as the ACER and ICER values of amlodipine and candesartan. The amlodipine ACER value was IDR 74,851.15, while the candesartan ACER obtained was IDR 87,809.25. The ICER value was IDR 362,768 per effectiveness.

**Table IV: ACER and ICER values**

Antihypertensive	Average cost (IDR)	ACER (IDR)	ICER (IDR)
Amlodipine	4,811.432	74,851.15	362,768
Candesartan	8,780.925	87,809.25	

**Discussion**

Indonesia is a large archipelagic country, making it difficult to gather comprehensive data on a national level. To our knowledge, this study represents the first pharmaco-economic research comparing amlodipine and candesartan in the West Nusa Tenggara region, Indonesia.

Monotherapy is rarely used in the treatment of hypertension (James *et al.*, 2014). Nevertheless, it is crucial to analyse the effects of various antihypertensive medications when used alone, based on real-world data (Alruthia *et al.*, 2021). This will help in devising an efficient treatment strategy for essential hypertension.

This study found that more patients were prescribed amlodipine than candesartan. Several researches revealed no statistical difference in efficacy between both drugs ( $p = 0.969$ ) (Ogihara *et al.*, 2008) since both candesartan and amlodipine are effective at reducing blood pressure in moderate hypertension (Althanoon & Thanoon, 2022). The prescription pattern in Lower-Middle Income Countries, like Indonesia, indicate the tendency to use Calcium Channel Blockers as one of the choices for hypertensive therapy (Arshad *et al.*, 2021).

The data demonstrated that amlodipine could lower the patient's blood pressure more than candesartan. These results are in line with previous research regarding the analysis of the cost-effectiveness of amlodipine and candesartan at Jambi Hospital in 2019 which stated that the percentage of amlodipine was more significant than that of candesartan in lowering blood pressure (Perawati *et al.*, 2021).

The average cost comparison shows that the cost of candesartan is greater than amlodipine. The biggest cost component incurred by patients during hospitalisation is influenced by the severity experienced by the patient in the process of the action performed on each patient. The difference in direct medical costs for patients is due to the patient's length of stay in the hospital and the chosen treatment class (Perawati *et al.*, 2021).

The results of the analysis in this study are expressed as the ratio of ACER and ICER. ACER is the value of the average cost-effectiveness, which aims to show a 1%

increase in the effectiveness of therapy for the costs incurred by ACER. The ICER ratio is the additional cost required to obtain 1% of the effectiveness of therapy.

Based on the ratio of the ACER values of amlodipine and candesartan, the ACER of amlodipine is lower than that of candesartan, thereby indicating that the effectiveness of amlodipine therapy is higher than that of candesartan. The results obtained were supported by similar studies regarding the analysis of the cost-effectiveness of amlodipine and candesartan, in which the ACER of amlodipine was lower than that of candesartan, namely IDR 7,611 for amlodipine and IDR 24,992 for candesartan (Perawati *et al.*, 2021).

The resulted ICER value illustrates the amount of additional costs required to obtain a one-unit change in effectiveness in hypertensive patients. If the ICER calculation shows negative results or gets smaller, the alternative therapy is said to be cheaper and can be used as the best therapeutic option (Nalang *et al.*, 2018). The ICER value obtained in this study was IDR 362,768 or approximately \$23.

To date, we have not found any research that compares the cost effectiveness of amlodipine and candesartan therapy. However, there are several studies that compare amlodipine with other angiotensin receptor blocker (ARB) groups. Research conducted by Chan *et al.* (2016) in Taiwan compared the cost effectiveness of amlodipine and valsartan. The study found that amlodipine was more cost effective than valsartan, resulting in a cost reduction of NT\$2251 (\$81) per year (Chan *et al.*, 2016). Similar results were obtained from research conducted by Wu *et al.* (2013) in China, which showed that amlodipine was more cost-effective than valsartan, resulting in reduced costs of ¥2033 or \$599 (Wu *et al.*, 2013).

Pharmaco-economic perspectives consider who pays the costs and who receives the benefits. Moreover, the values of saving money for society may be perceived differently by private third-party payers, administrators, healthcare providers, governmental agencies, or even individual patients (Rai & Goyal, 2018). This research focuses on the healthcare perspective. In Indonesia, the National Insurance Service (BPJS) determines the rates for health service packages that cover all aspects of hospital costs. These packages include non-medical services and medical procedures based on Indonesia Case Based Groups (INA CBGs). The insurance coverage value can vary depending on the type of hospital. Therefore, it is important to conduct research at Type C hospitals, such as Mataram University Hospital, which serves as a referral centre after primary care. Excessive costs incurred by the hospital can lead to financial losses. Additionally, the findings of this research are expected

to be applicable to other similar type C hospitals, which are dominant in Indonesia.

Amlodipine and candesartan are primarily used in conjunction with other medications (James *et al.*, 2014). Therefore, it was not easy to identify patients who were only taking a single antihypertensive medication. Additionally, the research was conducted during the ongoing COVID-19 pandemic, which required us to exclude all COVID-19 patients in order to minimise bias. As a result, the sample size became very limited.

Several limitations in this study were the limited number of samples because some of the patient data obtained during the study were excluded and retrospective data used, thus making the results of the study heavily dependent on information obtained based on medical record data.

## Conclusion

Based on the results of the study, it can be concluded that amlodipine therapy is more cost-effective than candesartan which can be seen from the ratio of ACER and ICER amlodipine that is lower than that of candesartan.

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