Patterns and Appropriateness of Antihypertensive Use in Preeclampsia: A Retrospective Study at a Jakarta Tertiary Hospital (2022–2024)

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Abstract

Preeclampsia (PE) complicates approximately 2–8% of pregnancies worldwide and remains a leading cause of maternal and perinatal morbidity and mortality, contributing to more than 50,000 maternal deaths and nearly 500,000 neonatal deaths annually. Appropriate antihypertensive therapy is essential to prevent disease progression and adverse outcomes. This non-experimental, cross-sectional, retrospective study was conducted at the Indonesian Christian University Hospital from August to December 2024. All medical records of patients with preeclampsia during the study period were included using total sampling (N = 52). Variables included patient characteristics, type of antihypertensive therapy, and appropriateness of drug use. Appropriateness was evaluated using the 4Ts criteria (appropriate indication, appropriate drug, appropriate dose, and appropriate patient) based on the POGI 2016 guideline. Data were analyzed as proportions with 95% confidence intervals (CI), and associations between preeclampsia severity and antihypertensive patterns were explored descriptively. Most patients were aged >35 years (50%), in the third trimester of pregnancy (94.2%), and diagnosed with mild preeclampsia (80.8%). In mild preeclampsia, nifedipine monotherapy was the most frequently prescribed antihypertensive (92.9%; 95% CI: approximately 80–99%). In severe preeclampsia, nifedipine monotherapy was used in 50% of cases (95% CI: approximately 19–81%), whereas nifedipine–methyldopa combination therapy accounted for 40% (95% CI: approximately 13–74%). Evaluation of antihypertensive use showed 100% appropriateness for indication, drug selection, dose, and patient suitability, indicating entirely rational use in accordance with guidelines. Antihypertensive prescribing patterns for preeclampsia in this hospital largely adhered to clinical guidelines, with nifedipine as the mainstay therapy for both mild and severe cases. These findings support the effectiveness of guideline-based pharmacotherapy for the management of preeclampsia and highlight the need for further multicenter studies to evaluate clinical outcomes and long-term maternal-fetal safety.

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Keywords: Preeclampsia, Antihypertensive Agents, Nifedipine, Drug Utilization, Pregnancy, Guideline Adherence.

INTRODUCTION

Preeclampsia occurs during pregnancy, and it is characterized by high blood pressure and protein in the urine. The condition is followed by a maternal systemic inflammatory response, endothelial dysfunction, and activation of the coagulation cascade. Preeclampsia is seen after 20 weeks of gestation and is classified into mild and severe forms based on blood pressure levels (Kemenkes, 2022). During pregnancy, if a woman has experienced high blood

pressure and organ dysfunction for more than twenty weeks, it might be preeclampsia. Preeclampsia can cause pregnancy disorders, and 2% to 8% of its cases are found worldwide (Fujiko et al., 2024). This condition is bad because it can cause infant deaths. Approximately, around half a million infants worldwide dying from this, while maternal deaths exceed 50,000. 16% often occur in developed countries, while 9% - 26% occur in developing countries (Karrar et al., 2024). It means preeclampsia during pregnancy can be seen more often in developing countries.

There seems to be an awareness of preeclampsia as it has been reported widely on global statistics. Preeclampsia has been seen to be a cause of maternal deaths in Indonesia. Of 100,000 live births, 300 of them are maternal deaths caused by preeclampsia, signified by hypertensive disorders of pregnancy. Regional data from DKI Jakarta also demonstrate a persistent burden, with an increasing number of maternal deaths related to pregnancy complications, including preeclampsia, over recent years. These figures highlight that preeclampsia remains a critical public health concern at both national and local levels (Ryan et al., n.d.). Based on data from the 2021 DKI Jakarta Provincial Health Profile, 152 mothers died during childbirth in the DKI Jakarta area. This number increased from 117 mothers in 2020. In 2021, there were 73. maternal deaths per 100,000 live births. The neonatal mortality rate was 1.33 per 1,000 live births, and the infant mortality rate was 1.64 per 1,000 live births recorded in the DKI Jakarta region in 2021. In 2020, the AKN was 1.8, and the IMR was 2.54 (Widyaputri et al., 2022). The increasing number of maternal deaths caused by preeclampsia cannot be overlooked anymore. Necessary efforts need to be made to overcome this.

One of the preventive measures is Pharmacological Management in preventing progression to severe complications such as eclampsia, stroke, and maternal–fetal morbidity. Besides, the Indonesian Obstetrics and Gynecology Association (POGI) recommends several antihypertensive agents for the treatment of preeclampsia, including calcium channel blockers, beta-blockers, and centrally acting agents such as methyldopa. Commonly recommended drugs include nifedipine, labetalol, atenolol, and methyldopa. However, antihypertensive treatment during pregnancy requires careful consideration due to physiological changes in maternal pharmacokinetics, the potential for placental drug transfer, and the risk of adverse fetal effects. Consequently, rational prescribing, ensuring the right patient, indication, drug, and dosage, is essential to optimize outcomes. However, due to the risk of teratogenic effects and physiological changes that occur in the mother during pregnancy, treatment during pregnancy requires extra attention. Medications taken by pregnant women have the potential to cross the placental barrier and reach the developing fetus's bloodstream (Maisarah, 2021).

Despite the availability of national guidelines, real-world prescribing practices for antihypertensive therapy in preeclampsia in Indonesia remain limited. Few studies have systematically audited the fidelity of antihypertensive use to clinical guidelines, particularly using structured frameworks such as the 4Ts (right patient, right indication, right drug, right dose). In addition, variations in drug selection between mild and severe preeclampsia have been reported anecdotally, yet formal evaluations comparing monotherapy and combination therapy across disease severity are scarce. One of the reasons is the lack of institutional audits on guideline adherence represents an important gap in the optimization of maternal care.

Considering the issues above, it is important to evaluate antihypertensive prescribing patterns at the hospital level to support evidence-based practice and quality improvement. This study was conducted at the Indonesian Christian University Hospital during the period from January 2022 to October 2024. This study aims to assess the pattern and fidelity of antihypertensive use in preeclampsia based on the 4Ts principle. It also aims to see the factors associated with the use of monotherapy versus combination antihypertensive therapy among patients with different grades of preeclampsia.

METHODS

Study Design and Setting

This study employed a non-experimental, retrospective, cross-sectional drug utilization audit. The study was conducted at the Indonesian Christian University General Hospital. Medical record data covered the period from January 2022 to October 2024, while data extraction and analysis were performed between August and December 2024.

Study Population and Sample

The participants of this study include pregnant women diagnosed with preeclampsia who received antihypertensive therapy at the Indonesian Christian University General Hospital during the study period. A total of 52 patients met the inclusion and exclusion criteria through purposive sampling

Since this study was designed as an audit of prescribing practices, no formal sample size calculation or power analysis was carried out. To account for statistical precision and uncertainty, proportions were reported with 95% confidence intervals (CI).

Inclusion and Exclusion Criteria

The inclusion criteria for the participants in this study are pregnant women with a gestational age of ≥20 weeks diagnosed with preeclampsia, as documented in their medical records. The presence of Preeclampsia was analyzed based on the criteria established in the

2016 Indonesian Society of Obstetrics and Gynecology (POGI) guideline, namely systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on at least two measurements, accompanied by evidence of proteinuria (≥+1 on urine dipstick examination or ≥300 mg in a 24-hour urine collection). Besides, the participants must have received at least one antihypertensive medication, either during hospitalization or in an outpatient setting, to ensure the availability of data related to antihypertensive prescribing patterns.

Patients with a history of chronic hypertension diagnosed before pregnancy or before 20 weeks of gestation were excluded from the study, as this condition represents a distinct clinical entity from preeclampsia. In addition, pregnant women with chronic kidney disease, lupus nephritis, or other documented secondary causes of hypertension were also excluded to minimize confounding factors that could influence blood pressure control and antihypertensive selection. Also, their medical records were incomplete, particularly those lacking essential information such as blood pressure measurements, details of antihypertensive therapy, or gestational age, were also excluded from the analysis to maintain data validity and reliability.

Definition of Preeclampsia Severity

Preeclampsia severity was classified based on clinical documentation in the medical records and aligned with the POGI 2016 criteria below:

- Pregnant women experiencing mild preeclampsia have blood pressure ≥140/90 mmHg but <160/110 mmHg with proteinuria.
- Pregnant women experiencing severe preeclampsia have systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg, with or without severe features such as heavy proteinuria, neurological symptoms, or signs of organ dysfunction.

Data Collection

The primary data were obtained from the participants that have met the inclusion and exclusion criteria. Researcher have made sure that the participants are the most suitable ones to answer the research questions. For the secondary data in this study, the data were obtained from patients' medical records, including their age, gestational age, gravida status, comorbidities, blood pressure values, degree of proteinuria, type and dose of antihypertensive therapy, and treatment regimen (monotherapy or combination therapy). With these data, the researchers expected that the findings could be interpreted effectively and could answer the research questions well.

Operational Definition of Appropriateness (4Ts Criteria)

In this study, the researchers followed the 4Ts framework to evaluate the appropriateness of antihypertensive drug use. This consideration has been made based on the POGI 2016

guideline. There are four of them, namely right indication, right drug, right dose, and right patient:

1. **Right Indication**

   First, the right indication. It means the antihypertensive therapy was considered appropriate if it was prescribed to patients who met diagnostic criteria for preeclampsia with blood pressure values requiring pharmacological intervention.

2. **Right Drug**

   Second, the right drug. It means the prescribed antihypertensive agent was considered appropriate if it belonged to the recommended drug class for preeclampsia (e.g., nifedipine or methyldopa). The use of alternative agents was considered appropriate when first-line drugs were contraindicated, unavailable, or not tolerated.

3. **Right Dose**

   Third, the right dose. Dosage appropriateness was assessed by comparing prescribed doses and dosing intervals with guideline recommendations, including: Nifedipine immediate-release: **10 mg every 8–12 hours**, with dose titration as clinically indicated; Methyldopa: **250–500 mg every 8–12 hours**. It means prescriptions were considered appropriate if the dose, frequency, and titration were within recommended ranges.

4. **Right Patient**

   Finally, the right patient. It means therapy was considered appropriate if patient-specific factors such as gestational age, comorbidities (e.g., diabetes mellitus, asthma), history of drug allergy, and contraindications were taken into account.

These four criteria were used to help the researchers in analyzing the data.

Assessment Process

In the assessment process, the evaluation of appropriateness was independently conducted by a clinical pharmacist and an obstetrician–gynecologist. Discrepancies were resolved through discussion to reach a consensus. Inter-rater agreement was assessed descriptively; formal kappa analysis was planned but limited by sample size.

Statistical Analysis

To analyze the data effectively, the SPSS software was used. Descriptive statistics were also used to summarize patient characteristics and prescribing patterns. Proportions were reported with 95% confidence intervals (Wilson method). Bivariate analysis using the χ^2 test or Fisher's exact test (as appropriate) was performed to examine associations between

preeclampsia severity (mild vs. severe) and antihypertensive regimen (monotherapy vs. combination therapy). Variables with potential clinical relevance, including maternal age ≥35 years, third-trimester gestation, chronic hypertension history, and proteinuria ≥+2, were further explored using bivariable and multivariable logistic regression models. A sensitivity analysis was conducted by excluding cases with incomplete data.

Ethical Clearance

Since this study involved humans as its participants. Ethical clearance is an important part that cannot be overlooked. Thus, this study has passed ethical approval with the number: No. 652/UKI.LPPM/PPM.00.00/ET.2024.

RESULT

In this study, the Indonesian Christian University Hospital served as the study site. When collecting the data, fifty-two patients diagnosed with preeclampsia were identified between January 2022 and October 2024. Data on characteristics, including age, gestational age, gestational status, comorbidities, blood pressure, proteinuria, medicine classes, and patterns of medicine use, were also collected to determine the characteristics and distribution of the sample population. After that, data on medicine distribution were classified into monotherapy and two-medicine combinations. Data on the rationality of antihypertensive use were assessed based on the accuracy of indication, medicine, patient, and dose. The data were collected and processed through data editing, coding, data entry, and data cleaning. Statistical analysis was then performed using univariate tests (qualitative and quantitative).

Table 1 presents data on the frequency distribution based on several characteristics, including Age, Gestational Age, Gravida Status, Accompanying Diseases, and Type of Accompanying Diseases in Preeclampsia Patients at the Indonesian Christian University Hospital for the Period January 2022 – October 2024.

Table 1. Frequency Distribution of Several Characteristics

Characteristics	Frequency	Percentage
Age		
< 25 years	2	3.8
25 -35 years	24	46.2
≥ 35 years	26	50.0
Gestational Age		
Trimester 1	2	3.8
Trimester 2	1	2.0
Trimester 3	49	94.2
Gravida Status		
Primigravida	26	50
Multigravida	26	50

Concomitant Diseases		
There is no	35	67.3
There is	17	32.7
Characteristics	**Frequency**	**Percentage**
Types of Concomitant Diseases		
Hypertension	8	47.0
HDK	4	23.5
Preeclampsia	1	5.9
Hypertension + Allergies	1	5.9
Hypertension + Type 2 Diabetes	1	5.9
Hypertension + Cholesterol	1	5.9
HDK + Asthma	1	5.9

Table 2. Distribution of Examination Results in Preeclampsia Patients at the Indonesian Christian University Hospital for the Period January 2022 – October 2024

Types	**Frequency**	**Percentage**
Diagnosis		
Mild Preeclampsia	42	80.8
Severe Preeclampsia	10	19.2
Blood pressure		
Blood pressure <140/90 mmHg	10	19.2
Blood pressure ≥140/90 mmHg	32	61.5
Blood pressure ≥160/110 mmHg	10	19.2
Proteinuria		
Negative	6	11.5
Positive (+1)	36	69.5
Positive (+2)	4	7.7
Positive (+3)	6	11.5

Table 3. Frequency Distribution of Antihypertensive Medicine Use in Preeclampsia Patients at the Indonesian Christian University Hospital for the Period January 2022–October 2024

Antihypertensive Medicine	**Frequency**	**Percentage**
Mild Preeclampsia		
Monotherapy		
Nifedipine	39	92.8
Amlodipine	2	4.8
Two-Medicine Combination Nifedipine + Methyldopa	1	2.4
Severe Preeclampsia		
Monotherapy		
Nifedipine	5	50
Amlodipine	1	10
Two-Medicine Combination Nifedipine + Methyldopa	4	40

Table 4. Percentage of All preeclampsia cases (N=52)

Criteria	Appropriate		Not Exactly	
	Frequency	Percentage	Frequency	Percentage
Indication Accuracy	52	100	0	0
Medicine Accuracy	52	100	0	0
Dosage Accuracy	52	100	0	0
Patient Accuracy	52	100	0	0

Table 5. Association Between Degree of Preeclampsia and Type of Antihypertensive Therapy

Degree of Preeclampsia	Monotherapy n (%)	Combination Therapy n (%)	OR (95% CI)	p-value
Mild preeclampsia	41 (97.6)	1 (2.4)	Reference	—
Severe preeclampsia	6 (60.0)	4 (40.0)	27.33 (2.60–287.43)	<0.05

Based on the analysis, it can be seen that patients with severe preeclampsia had 27.3 times higher odds of receiving combination antihypertensive therapy compared with those with mild preeclampsia (OR = 27.33; 95% CI: 2.60–287.43; $p < 0.05$). The findings indicate a statistically significant association between disease severity and treatment pattern. The wide confidence interval reflects the limited number of severe preeclampsia cases.

DISCUSSION

In Table 1, we can see that between January 2022 and October 2024, 26 patients (or 50% of the total) were diagnosed with preeclampsia at the Indonesian Christian University Hospital. Also, the next largest age group was patients between 25 and 35 years old, comprising 24 patients (or 46.2% of the total), and two patients (3.8% of the total) were under 25 years old. These findings support the findings of Nurul Azizah et al., who found that pregnant women over 35 years old have an increased risk of pregnancy problems (Gayatri et al., 2022), and Preeclampsia is very common in women over 35 years old. There are several explanations for why this occurs. The risk of preeclampsia increases as the degenerative process in peripheral blood vessels begins after age 35. This process changes their structure and function (Arwan & Sriyanti, 2020). Due to less-than-ideal uterine health, the risk factors for preeclampsia are not limited to those over 35 years of age, but can occur in mothers under 20 years of age (Ertiana & Wulan, 2019). Many variables can cause preeclampsia between the ages of 25 and 35, but one of them is pregnant women who do not know or do not care about the benefits of prenatal check-ups.

From these findings, it is suggested that pregnant women must undergo comprehensive prenatal monitoring, including frequent and adequate Antenatal Care (ANC) appointments, to reduce the possibility of potential risk factors.

Based on Table 1, the gestational age at diagnosis of preeclampsia was most often in the third trimester, with 49 patients (94.2%), followed by the first trimester, with 2 patients (3.8%). Meanwhile, in the second trimester, there was one patient (1.9%). The findings in the table are in line with research conducted by Dewie A. et al., namely that preeclampsia generally occurs in the third trimester (Dewie et al., 2020). Preeclampsia most often occurred in the third trimester with 122 patients (99.3%), according to research by Simatupang A and Ida Bagus Sutha Dwipajaya. This finding is consistent with their research (Simatupang & Dwipajaya, 2021). One of the risk factors for preeclampsia is gestational age. The most common form of preeclampsia, which occurs in the third trimester, is caused by placental ischemia and a mismatch between fetal metabolism and the mother's supply needed for growth and development. The finding suggests that knowing whether preeclampsia will occur early or late in pregnancy is crucial, as the severity of this condition is related to complications for both the mother and the baby (Sitohang et al., 2023).

Based on the data in Table 1, 26 patients (or 50% of the total) were classified as primigravidas, and 26 patients (or 50% of the total) were classified as multigravidas. Other researchers have demonstrated that gestational status does not correlate with the occurrence of preeclampsia. The findings of Rahman AANF et al., who investigated the correlation between gestational status and the incidence of preeclampsia, provide conclusive evidence of this (Rahman et al., 2023).

Although some studies have shown no association between primigravida and preeclampsia, others have found that this condition is highly prevalent in pregnant women who were initially exposed to chorionic villi during their first pregnancy. This occurs when the immunological mechanism for forming blocking antibodies, mediated by HLA-G (Human Leukocyte Antigen G) against placental antigens, has not fully developed in these women. As a result, the process of trophoblast implantation into the mother's decidual tissue is disrupted. Experiencing stress during childbirth can trigger cortisol production, which can also affect primigravida. Increased cardiac output is a side effect of cortisol's action on the sympathetic nervous system (Bulqies, 2021).

Based on the data from Table 1, of the 17 patients with a history of comorbidities, the highest results were obtained in patients with a history of hypertension, as many as eight patients (47.1%), then followed by patients with a history of hypertension in pregnancy (HDK)

as many as four patients (23.5%). For patients with a history of preeclampsia, there was one patient (5.9%), patients with a history of hypertension and allergies were one patient (5.9%), patients with a history of hypertension and Type 2 Diabetes Mellitus (DM) were one patient (5.9%), patients with a history of hypertension and cholesterol were one patient (5.9%). Patients with a history of hypertension in pregnancy (HDK) and asthma were one patient (5.9%). This study is in accordance with the results of Maisarah RH, et al. where almost all pregnant women in this study did not have a history of increased blood pressure/hypertension, namely 20 patients (40%) then with a history of hypertension in the family (36%) (Maisarah, 2021). Research shows that preeclampsia occurs more frequently in mothers with a history of hypertension. Preeclampsia and other pregnancy problems are 3.5 times more likely to occur in women with a history of high blood pressure (Kristanti et al., 2023).

According to Table 2, 42 patients (82.7%) were diagnosed with mild preeclampsia, while 10 patients (17.3%) were diagnosed with severe preeclampsia. This finding corroborates those of Kencana Dewi. Seventeen patients (29.31%) were diagnosed with severe preeclampsia, while 41 patients (70.69%) were diagnosed with mild preeclampsia. According to the data in the table, 32 patients (61.5%) had blood pressure of at least 140/90 mmHg, while 10 patients (19.2%) had blood pressure below 140/80 mmHg. At the same time, ten patients (19.2%) had blood pressure of at least 160/110 mmHg. According to the table, the highest prevalence was proteinuria +1, with 36 patients (69.2%), followed by proteinuria +3, with six patients (11.5%). Meanwhile, six patients (11.5%) had negative proteinuria results, and four patients (7.7%) had proteinuria +2. Blood pressure readings and proteinuria levels are used to diagnose severe or mild preeclampsia. Patients with mild preeclampsia have a blood pressure of 140/90 mmHg or higher and a proteinuria level of 300 mg or more per 24 hours, or a proteinuria score of 1+ when tested with a dipstick. Proteinuria levels of 5 g per 24-hour urine volume, along with systolic and diastolic blood pressures of 160/90 mmHg, are characteristic of severe preeclampsia (Dewi, 2021).

The purpose of proteinuria testing during pregnancy is to identify kidney abnormalities and differentiate between preeclampsia and less severe forms of hypertension. Tubular protein reabsorption and glomerular filtration contribute to the development of proteinuria. Proteinuria develops in preeclampsia as a result of a decreased glomerular filtration rate. Low-molecular-weight proteins, which are normally filtered but end up in the urine due to reabsorption, are present in this case, along with aberrant albumin excretion. Although certain low-molecular-weight proteins that normally pass through glomerular filtration are reabsorbed and thus

undetectable in the urine when the body is not pregnant, high-molecular-weight proteins remain undetectable (Prawirohardjo, 2010)

Based on Table 3, in 42 patients diagnosed with mild preeclampsia, the most frequently used treatment was nifedipine monotherapy, used in 39 patients (92.9%), followed by amlodipine in 2 patients (4.8%). Meanwhile, in the two-drug combination, nifedipine and methyldopa were used in 1 patient (2.4%). Based on the table, in 10 patients diagnosed with severe preeclampsia, the most frequently used treatment was nifedipine monotherapy, used in 5 patients (50%), followed by nifedipine and methyldopa combination treatment in 4 patients (40%). Furthermore, the most frequently used drug for monotherapy was methyldopa, used in 1 patient (10%). Nifedipine is the drug of choice for patients with mild to severe preeclampsia. If preeclampsia is suspected, the first line of defense is to administer nifedipine (Rakhmawati & Bismantara, 2020). Nifedipine is a popular CCB. This drug is safe for use as an antihypertensive during pregnancy because its mechanism of action is to reduce systemic vascular resistance. It also increases urine output by increasing blood flow to the kidneys and inhibiting the production of antidiuretic hormone (Widayani et al., 2022).

The data in this study found 100% indication accuracy, as shown in the table. Similar findings were also found by Saputri GAR et al., where an indication accuracy of 83.33% was achieved in this study (Saputri et al., 2020). These findings align with the study by Simatupang A. and Ida Bagus Sutha Dwipajaya, which showed an indication accuracy rate of 91.9% (Simatupang & Dwipajaya, 2021). Patients were prescribed antihypertensive medications based on the diagnosis of preeclampsia, which was based on the patient's blood pressure and proteinuria readings according to the 2016 POGI reference standards. This indicates that the indication was valid.

Based on the table, the medication accuracy in this study was 100%. Medication accuracy is considered correct because the medications used followed the 2016 POGI recommendations. 1 The results of a study conducted by Yani YA et al. showed different results, where in that study, the medication accuracy percentage was only 69.04%. However, the results of research conducted by Simatupang A and Ida Bagus Sutha Dwipajaya showed similar results to those obtained by researchers, where the study found a drug accuracy percentage of 86.7% (Simatupang & Dwipajaya, 2021). One possible explanation for this difference is that the gestational age had reached full term (Yani, 2021).

The table shows that this study had a 100% dose accuracy rate. Non-significant differences were also demonstrated by Yani YA et al. in their comparable study. This study found an 80.96% accuracy rate in dosing. 30 If the nifedipine dose is 10 mg two to three times daily, the

amlodipine dose is 10 mg daily, and the methyldopa dose is 250 to 500 mg two to three times daily, as specified in the 2016 POGI reference standard, then the drug dosage is considered accurate.

In this study, the patient accuracy rate was 100%, as shown in the table above. Non-significant differences were also demonstrated by Yani YA et al. in their comparable study. Specifically, this study found that patient accuracy reached 80.96%. 30 A study conducted by Simatupang A. and Ida Bagus Sutha Dwipajaya corroborates these findings. The patient accuracy rate in this study was 96.9% (Simatupang & Dwipajaya, 2021) Patient accuracy is considered accurate if the administration of drugs does not have side effects on pregnant women and the prescribed drugs are in accordance with the physiological and pathological conditions of the patient. In all cases of preeclampsia, data showed that antihypertensive drug use was 100% rational. Similar findings were also produced by research conducted by Andriana DD et al. This study found that rational use of antihypertensive drugs was 77.65% of cases (Dwi Andriana et al., 2018). Patients engaged in rational drug use when they received the drugs at the right time and according to their needs, and when they met all existing criteria. "Right indication, right drug, right patient, right dose" was the guiding principle of this study.

Patient Characteristics and Clinical Context

The majority of patients in this study were aged ≥35 years, consistent with evidence indicating that advanced maternal age is associated with increased risk of preeclampsia due to age-related vascular degeneration and endothelial dysfunction. However, cases were also observed in younger age groups, reflecting that preeclampsia is a multifactorial condition influenced by vascular, immunological, and behavioral factors, including suboptimal antenatal care. The predominance of third-trimester diagnoses aligns with the pathophysiological progression of placental ischemia and systemic maternal response, which typically become clinically evident in late pregnancy (Tyas et al., 2019)

The equal distribution between primigravida and multigravida patients supports previous findings that gravidity alone is not a consistent predictor of preeclampsia. Nonetheless, immunological mechanisms related to first exposure to placental antigens may partly explain the susceptibility observed in some primigravida women. Comorbid conditions—particularly chronic hypertension—were common, reinforcing their role as established risk factors for preeclampsia and highlighting the importance of early risk stratification during antenatal care.

Dominance of Nifedipine in Antihypertensive Therapy

Nifedipine was the most frequently prescribed antihypertensive agent across both mild and severe preeclampsia. Several factors may explain this dominance. First, nifedipine has a favorable safety profile in pregnancy, with minimal adverse effects on uteroplacental blood flow. Second, it offers rapid onset of action, particularly in immediate-release formulations, making it suitable for acute blood pressure control. Third, nifedipine is widely available in Indonesian healthcare settings and can be administered orally, facilitating ease of use in both inpatient and outpatient contexts (S et al., 2022). These advantages collectively support its position as a first-line agent in national and international guidelines.

Rationale for Combination Therapy in Severe Preeclampsia

The higher proportion of combination therapy observed in severe preeclampsia reflects clinical necessity rather than prescribing variability. In severe cases, blood pressure targets are stricter, and monotherapy may be insufficient to achieve rapid and sustained control. The combination of nifedipine and methyldopa provides complementary mechanisms of action, peripheral vasodilation, and central sympathetic inhibition, allowing for more effective blood pressure reduction while minimizing dose escalation and potential adverse effects (Ernawati et al., 2023). This practice aligns with the principle of individualized therapy based on disease severity and response.

Comparison with Indonesian and International Studies

The prescribing patterns observed in this study are consistent with several Indonesian studies reporting nifedipine as the most commonly used antihypertensive in preeclampsia. However, international studies, particularly from high-income settings, often report greater use of labetalol, reflecting differences in drug availability, cost, and institutional protocols. In Indonesia, limited availability of intravenous labetalol and clinician familiarity may contribute to the preference for oral nifedipine and methyldopa (Ekawati et al., 2021). These contextual differences underscore the importance of interpreting guideline adherence within local healthcare realities.

Interpretation of 100% Appropriateness Findings

This study reported 100% accuracy across all 4Ts domains. This finding should be interpreted cautiously. The audit was conducted retrospectively by the research team using standardized criteria derived from the 2016 POGI guidelines. Prescriptions were classified as appropriate if they met all explicit criteria for indication, drug choice, dosage, and patient suitability. Borderline cases, such as dose adjustments within acceptable ranges, were adjudicated through consensus discussion (Hadi et al., 2008). While this structured approach

strengthens internal consistency, the possibility of classification bias cannot be excluded, particularly in retrospective reviews that rely on the completeness of documentation.

Study Limitations

Several limitations should be acknowledged. First, the retrospective design limits causal inference and depends on the accuracy of medical records. Second, this study was conducted in a single hospital, which may limit generalizability to other healthcare settings in Indonesia. Third, clinical outcomes such as time to blood pressure control, maternal–neonatal outcomes, and adverse drug events were not assessed. Finally, the study did not evaluate dynamic treatment adjustments or patient adherence, which are important determinants of real-world effectiveness.

Clinical and Research Implications

Despite these limitations, the findings provide important insights into antihypertensive prescribing practices in preeclampsia. The high level of guideline fidelity observed supports the feasibility of rational drug use in routine clinical practice. Future efforts should focus on prospective drug use evaluations, integration of bundled preeclampsia management protocols, and periodic guideline compliance audits to ensure sustained quality of care. Additionally, incorporating outcome-based indicators will be essential to link prescribing fidelity with meaningful maternal and neonatal benefits.

CONCLUSION

This study shows that nifedipine is the most frequently used antihypertensive in patients with preeclampsia, both mild and severe, at the Indonesian Christian University Hospital. The majority of cases received nifedipine; 4T fidelity was high according to internal, guideline-based operational criteria, but prospective audit and comparison across drug classes are needed.

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