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Bio Statement

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TITLE AND ABSTRACT

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

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.

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Overview Of Antihypertensive Medicines Use In Preeclampsia Cases

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Abstract

Approximately 2-8% of all pregnancy problems are caused by preeclampsia, which is hypertension that may occur during pregnancy. Globally, there are more than 50,000 maternal deaths and nearly 500,000 infant deaths. The purpose of this study was to determine the pattern of medicine use and the appropriateness of the use of antihypertensive medicines in preeclampsia patients. This study employs a non-experimental, cross-sectional design with a retrospective descriptive approach, utilizing medical records. This study was conducted from August to December 2024. The sampling technique used in this study employed a total sampling approach. Data analysis was carried out descriptively and compared with the POGI 2016 reference standard. The results showed that of 52 preeclampsia patients at the Indonesian Christian University Hospital who were at risk of developing preeclampsia were those aged over 35 years (50%) with a gestational age in the third trimester (94.2%) with a diagnosis of mild preeclampsia (80.8%). In mild preeclampsia, the most frequently used treatment was nifedipine monotherapy (92.9%). In severe preeclampsia, monotherapy with nifedipine (50%) is the most commonly used treatment. The percentage of appropriate antihypertensive medicine use shows appropriate indication (100%), appropriate medicine (100%), appropriate dose (100%), appropriate patient (100%), and rational use of antihypertensive medicines (100%).

Keyword: Preeclampsia, Antihypertensives, Treatment Rationale, Nifedipine, Pregnancy

INTRODUCTION

Pregnancy disorders known as preeclampsia are characterized by placental damage and a maternal response to systemic inflammation with endothelial activation and coagulation. Preeclampsia can be categorized into two categories: mild and severe (Kemenkes 2022). Pregnancy-specific high blood pressure and organ dysfunction at more than 20 weeks of gestation are diagnostic of preeclampsia. Worldwide, 2% to 8% of pregnancy disorders are caused by preeclampsia, a condition characterized by increased blood pressure during pregnancy. (Fujiko, Nurdin, and Aman 2024). Globally, infant deaths average around half a million, while maternal deaths exceed 50,000. Approximately 16% occur in developed countries, while 9% - 26% occur in developing countries (Karrar, Martingano, and Hong 2024).

Commented [B1]: 1. Align title–objectives–methods–results. The objective "pattern & appropriateness of antihypertensive use" is appropriate, but the analysis is still purely descriptive; add analytics that assess appropriateness operationally (the 4T definition: right indication/drug/dose/patient) and influencing factors.
2. Define "appropriateness" operationally based on standards (the POGI 2016 you mentioned; also mention the latest global comparator) + examples of borderline cases (e.g., when nifedipine alone is considered appropriate in mild/severe PE).
3. Analytical improvements are needed, at a minimum: display 95% CIs for proportions; test of association (χ^2/Fisher) between PE severity and medication pattern; simple logistic model for predictors of drug combinations (age ≥35, TM III, comorbidities).
4. Consistency of numbers & categories. Correct blood pressure thresholds (<140/80 mmHg in the table appears incorrect; 140/90 is common) and synchronize totals/percentages in Tables 1–3; The title of Table 4 mentions "severe," but the N=52 (all cases).
5. Refine the reporting structure and guidelines: use STROBE for observational studies; add a sample selection flow diagram.
6. Ethics and administration: add ethics approval number, secondary informed consent statement, funding/COI, data availability.
7. Discussion should be critical, not simply a rehash of results. Discuss why nifedipine is dominant (availability, ease of titration, safety profile) and its implications, as well as biases/limitations (retrospective, documentation, single-center).
8. Journal language and format: improve grammar ("medicine" → "medications/drugs"), terminology consistency (trimester, gravidity), and remove word processor artifacts ("PAGE * MERGEFORMAT").

Commented [B2]: Suggested title: "Patterns and Appropriateness of Antihypertensive Use in Preeclampsia: A Retrospective Study at a Jakarta Tertiary Hospital (2022–2024)". The title highlights the scope, location, and period.

Commented [B3]: Abstract (IMRaD structure):
1. Background: burden of PE (1–2 sentences sufficient).
2. Methods: design, location, period, N, variables, definition of appropriateness (4Ts), analysis (proportion + 95% CI; test of association).
3. Results: main proportion (e.g., nifedipine 92.9% in mild PE, 50% in severe PE; nifedipine–methyldopa combination 40% in severe PE), figures with 95% CI.
4. Conclusion: clinical & research implications.
5. Add 5–6 MeSH/DeCS keywords: Preeclampsia; Antihypertensive Agents; Nifedipine; Drug Utilization; Pregnancy; Guideline Adherence.

There remains a significant problem with maternal mortality rates in developing countries, with more than 300 deaths for every 100,000 live births, according to data from the 2017 Indonesian Demographic and Health Survey (SDKI). At the same time, there were at least 32 infant mortality rates (IMR) for every 1,000 live births. Indonesia has a relatively high prevalence of preeclampsia, with 5.3% of cases reported annually (Anon 2025b). 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 (Anon 2025a)

Antihypertensive medicines in the calcium channel blocker, beta-blocker, and methyldopa classes are recommended for the treatment of preeclampsia by the Indonesian Obstetrics and Gynecology Association (POGI) in 2016. The recommended medicines are nifedipine, labetalol, atenolol, and methyldopa. Treatment of hypertension during pregnancy requires extra caution to avoid complications such as eclampsia, which can harm the mother and fetus. To achieve the desired results, medicine selection must be appropriate in terms of safety, efficacy, and rationality. 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)

Given the above data on the prevalence of morbidity and mortality, it is necessary to assess the effectiveness of medications prescribed by hospitals and community health centers as primary healthcare providers in combating preeclampsia. Therefore, the author is interested in examining the description of antihypertensive medication use in preeclampsia cases at the Indonesian Christian University Hospital for the period from January 2022 to October 2024.

This study aimed to determine the description of the use of antihypertensive medicines in cases of preeclampsia, reviewed from the perspective of indication accuracy, patient accuracy, medicine accuracy, and dosage accuracy in patients at the Indonesian Christian University Hospital

METHODS

This study used a retrospective method and was not experimental. Medical record data is an example of secondary data used in data collection. Based on the 2016 POGI recommendations, the data were evaluated, and their rationality was determined. The Indonesian Christian

Commented [B4]: Introduction (Focus & Gaps) :
Trimming repeated global statistics; highlighting local gaps: few audits of antihypertensive PE fidelity in Indonesia, variation in drug choice across PE grades, and lack of guideline adherence audits. Conclude with the primary objective (pattern & fidelity of the 4Ts) and secondary objective (factors associated with monotherapy vs. combination therapy).

University General Hospital was the site of this research. The medical record data used in this study covered the period from January 2022 to October 2024 and were collected between August and December 2024. The population consisted of patients diagnosed with preeclampsia and using antihypertensive medicines who were undergoing treatment at the Indonesian Christian University Hospital during the period January 2022 - October 2024. The sample was collected using a total sampling technique, comprising a total of 52 participants who met the inclusion and exclusion criteria. The research instrument in the form of medical records of preeclampsia patients treated with antihypertensive medicines at the Indonesian Christian University Hospital from January 2022 to October 2024 served as a secondary data source in this study. Data analysis was conducted using the SPSS (Statistical Package for the Social Sciences) program in this study. The results were then analyzed univariately. Univariate analysis aims to determine the quantitative and qualitative frequency distribution of each variable. This is achieved by examining the prevalence of preeclampsia in relation to age, gestational age, gravid status, and comorbidities. Additionally, an analysis will be conducted to explore the reasons for using antihypertensive medication, considering appropriate indications, suitable patients, effective treatment, and optimal dosages, in accordance with the 2016 POGI guidelines

RESULTS

The Indonesian Christian University Hospital served as the study site. 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 collected to determine the characteristics and distribution of the sample population. 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.

Commented [B5]: Methods (improve scientific credibility)

What's good: retrospective design, total sampling, clear period (January 2022–October 2024).
What needs to be added/improved:

Inclusion/exclusion criteria (gestational age ≥20 mg, evidence of proteinuria/definition of PE, exclusion of chronic kidney disease, etc.).

Definition of PE severity (cite blood pressure and proteinuria thresholds used in medical records; avoid 140/80).

Operational definition of the 4Ts (appropriateness):

Right indication: therapy is given when blood pressure criteria/PE diagnosis are met.

Right drug: recommended drug class; include if first-line is not available/contraindicated.

Right dose: dose range—e.g., nifedipine 10 mg immediate-release q8–12h; methyldopa 250–500 mg q8–12h—and how you assess appropriateness (interval, titration).

Right patient: Consider comorbidities (diabetes mellitus/asthma), allergies, and gestational age.

Name the assessor (pharmacist/obgyn), double-check, and agreement (kappa) if possible.

Sample size & power: Explain that this is a total-sampling audit study; still report precision (CI) to allow readers to assess uncertainty.

Statistical analysis:

Proportion + 95% CI (Wilson).

χ^2/Fisher: PE grade (mild/severe) × monotherapy/combination.

Bivariable → multivariable logistic: Combined predictors (age ≥35, TM III, chronic hypertension, proteinuria ≥+2).

Sensitivity analysis: Exclude cases with incomplete data.

Commented [B6]: Results (improve figures & add analytical value)

Table coherence:

Table 1: Check the sum of "Types of Concomitant Diseases" (sum & % should be 17 and 100%).

Blood pressure: Change categories to <140/90, ≥140/90, ≥160/110 (clearly mutually exclusive).

Table 3: Uniformize % (92.9 instead of 92.8).

Table 4: Change title to "All preeclampsia cases (N=52)" or separate by PE degree.

Add association table: PE degree × type of therapy (monotherapy vs. combination) with p-value & OR (95% CI).

Summary graphs: bar chart of drug patterns per degree; forest plot of OR of combination predictors.

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*
Types of Concomitant Diseases		
Hypertension	*8*	*47.1*
HDK	*4*	*23.5*
Preeclampsia	*1*	*5.9*
Hypertension + Allergies	*1*	*5.9*
Hypertension + Type 2 Diabetes	*1*	*5.9*
Hypertension + Cholesterol 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 less than 140/80 mmHg	*10*	*19.2*
Blood pressure of at least 140/90 mmHg	*32*	*61.5*
Blood pressure of at least 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 +*	*1*	2.4
Methyldopa				
Severe Preeclampsia				
Monotherapy				
Nifedipine			*5*	*50*
Amlodipine			*1*	10
Two-Medicine	*Combination*	*Nifedipine +*	*4*	40
Methyldopa				

Table 4. Percentage of Appropriate Use of Antihypertensive Medications in Severe Preeclampsia Patients at the Indonesian Christian University Hospital for the Period January 2022 – October 2024

	Appropriate		***Not Exactly***	
Criteria	***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*

DISCUSSION

Table 1, data shows that between January 2022 and October 2024, 26 patients (or 50% of the total) were diagnosed with preeclampsia at the Indonesian Christian University Hospital. The next largest age group was patients between 25 and 35 years old, comprising 24 patients (or 46.2% of the total). Two patients (3.8% of the total) were under 25 years old. This finding supports 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). 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 and 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 and 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. Therefore, pregnant women must undergo comprehensive prenatal monitoring, including frequent and adequate Antenatal Care (ANC) appointments, to reduce the possibility of potential risk factor.

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, Pont, and Purwanti 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 and 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. 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, Ismansyah, and Siregar 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 (Amalina, Kasoema, and Mardiah 2022).

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 the 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 and 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, Rahmawati, and Yasin 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, Ulfa, and Jannah 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 and 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 and 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 and 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 (Andriana, Utami, and Sholihat 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.

Commented [B7]: Discussion (depth & balance)

Key interpretations: why nifedipine is dominant—safety profile, availability, onset, ease of administration; rationale for combination in severe PE (BP targets, suboptimal response).

Compare with Indonesian & international research (mention differences in practice, availability of labetalol, etc.).

Discuss the claim of 100% accuracy: explain the audit process (who assessed, how borderline prescriptions were handled), acknowledge the potential for classification bias.

Limitations: retrospective, single hospital, did not assess maternal-neonatal outcomes and adverse events; did not measure time to BP control.

Implications: the need for prospective drug use evaluation, bundled PE management, and periodic guideline compliance audits.

CONCLUSIONS

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 preeclampsia patients were over 35 years old and in their third trimester. The use of antihypertensives in all patients met rational criteria based on four main parameters: appropriate indication, appropriate drug, appropriate dose, and appropriate patient, and was in accordance with the 2016 POGI guidelines. These findings emphasize the importance of implementing rational, guideline-based therapy to improve maternal and fetal safety in cases of preeclampsia.

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Standardize the style (APA) according to the target journal, capitalize the title, italicize the journal name, and add the DOI if applicable.

Prioritize ≥60% of references from the last 5 years that are directly relevant (drug audit in PE, practice guideline for hypertensive disorders in pregnancy).

Overview Of Antihypertensive Medicines Use In Preeclampsia Cases

Track Record Article

Accepted:

Published:

Abstract

Approximately 2-8% of all pregnancy problems are caused by preeclampsia, which is hypertension that may occur during pregnancy. Globally, there are more than 50,000 maternal deaths and nearly 500,000 infant deaths. The purpose of this study was to determine the pattern of medicine use and the appropriateness of the use of antihypertensive medicines in preeclampsia patients. This study employs a non-experimental, cross-sectional design with a retrospective descriptive approach, utilizing medical records. This study was conducted from August to December 2024. The sampling technique used in this study employed a total sampling approach. Data analysis was carried out descriptively and compared with the POGI 2016 reference standard. The results showed that of 52 preeclampsia patients at the Indonesian Christian University Hospital who were at risk of developing preeclampsia were those aged over 35 years (50%) with a gestational age in the third trimester (94.2%) with a diagnosis of mild preeclampsia (80.8%). In mild preeclampsia, the most frequently used treatment was nifedipine monotherapy (92.9%). In severe preeclampsia, monotherapy with nifedipine (50%) is the most commonly used treatment. The percentage of appropriate antihypertensive medicine use shows appropriate indication (100%), appropriate medicine (100%), appropriate dose (100%), appropriate patient (100%), and rational use of antihypertensive medicines (100%).

Keyword: Preeclampsia, Antihypertensives, Treatment Rationale, Nifedipine, Pregnancy

INTRODUCTION

Pregnancy disorders known as preeclampsia are characterized by placental damage and a maternal response to systemic inflammation with endothelial activation and coagulation. Preeclampsia can be categorized into two categories: mild and severe (Kemenkes 2022). Pregnancy-specific high blood pressure and organ dysfunction at more than 20 weeks of gestation are diagnostic of preeclampsia. Worldwide, 2% to 8% of pregnancy disorders are caused by preeclampsia, a condition characterized by increased blood pressure during pregnancy. (Fujiko, Nurdin, and Aman 2024). Globally, infant deaths average around half a million, while maternal deaths exceed 50,000. Approximately 16% occur in developed countries, while 9% - 26% occur in developing countries (Karrar, Martingano, and Hong 2024). There remains a significant problem with maternal mortality rates in developing countries, with more than 300 deaths for every 100,000 live births, according to data from the 2017 Indonesian Demographic and Health Survey (SDKI). At the same time, there were at least 32 infant mortality rates (IMR) for every 1,000 live births. Indonesia has a relatively high prevalence of preeclampsia, with 5.3% of cases reported annually (Anon 2025b). 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 (Anon 2025a)

Antihypertensive medicines in the calcium channel blocker, beta-blocker, and methyldopa classes are recommended for the treatment of preeclampsia by the Indonesian Obstetrics and Gynecology Association (POGI) in 2016. The recommended medicines are nifedipine, labetalol, atenolol, and methyldopa. Treatment of hypertension during pregnancy requires extra caution to avoid complications such as eclampsia, which can harm the mother and fetus. To achieve the desired results, medicine selection must be appropriate in terms of safety, efficacy, and rationality. 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)

Given the above data on the prevalence of morbidity and mortality, it is necessary to assess the effectiveness of medications prescribed by hospitals and community health centers as primary healthcare providers in combating preeclampsia. Therefore, the author is interested in examining the description of antihypertensive medication use in preeclampsia cases at the Indonesian Christian University Hospital for the period from January 2022 to October 2024.

This study aimed to determine the description of the use of antihypertensive medicines in cases of preeclampsia, reviewed from the perspective of indication accuracy, patient accuracy, medicine accuracy, and dosage accuracy in patients at the Indonesian Christian University Hospital

METHODS

This study used a retrospective method and was not experimental. Medical record data is an example of secondary data used in data collection. Based on the 2016 POGI recommendations, the data were evaluated, and their rationality was determined. The Indonesian Christian University General Hospital was the site of this research. The medical record data used in this study covered the period from January 2022 to October 2024 and were collected between August and December 2024. The population consisted of patients diagnosed with preeclampsia and using antihypertensive medicines who were undergoing treatment at the Indonesian Christian University Hospital during the period January 2022 - October 2024. The sample was collected using a total sampling technique, comprising a total of 52 participants who met the

inclusion and exclusion criteria. The research instrument in the form of medical records of preeclampsia patients treated with antihypertensive medicines at the Indonesian Christian University Hospital from January 2022 to October 2024 served as a secondary data source in this study. Data analysis was conducted using the SPSS (Statistical Package for the Social Sciences) program in this study. The results were then analyzed univariately. Univariate analysis aims to determine the quantitative and qualitative frequency distribution of each variable. This is achieved by examining the prevalence of preeclampsia in relation to age, gestational age, gravid status, and comorbidities. Additionally, an analysis will be conducted to explore the reasons for using antihypertensive medication, considering appropriate indications, suitable patients, effective treatment, and optimal dosages, in accordance with the 2016 POGI guidelines

RESULTS

The Indonesian Christian University Hospital served as the study site. 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 collected to determine the characteristics and distribution of the sample population. 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*
Types of Concomitant Diseases		
Hypertension	*8*	*47.1*
HDK	*4*	*23.5*
Preeclampsia	*1*	*5.9*
Hypertension + Allergies	*1*	*5.9*
Hypertension + Type 2 Diabetes	*1*	*5.9*
Hypertension + Cholesterol 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 less than 140/80 mmHg	*10*	*19.2*
Blood pressure of at least 140/90 mmHg	*32*	*61.5*
Blood pressure of at least 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*	+	*4*	40
Methyldopa					

Table 4. Percentage of Appropriate Use of Antihypertensive Medications in Severe Preeclampsia Patients at the Indonesian Christian University Hospital for the Period January 2022 – October 2024

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*

DISCUSSION

Table 1, data shows that between January 2022 and October 2024, 26 patients (or 50% of the total) were diagnosed with preeclampsia at the Indonesian Christian University Hospital. The next largest age group was patients between 25 and 35 years old, comprising 24 patients (or 46.2% of the total). Two patients (3.8% of the total) were under 25 years old. This finding supports 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). 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 and 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 and 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. Therefore, pregnant women must undergo comprehensive prenatal monitoring, including frequent and adequate Antenatal Care (ANC) appointments, to reduce the possibility of potential risk factor.

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, Pont, and Purwanti 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 and 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. 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, Ismansyah, and Siregar 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 (Amalina, Kasoema, and Mardiah 2022).

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)

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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 and 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, Rahmawati, and Yasin 2022).

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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 and 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 (Andriana, Utami, and Sholihat 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.

CONCLUSIONS

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 preeclampsia patients were over 35 years old and in their third trimester. The use of antihypertensives in all patients met rational criteria based on four main parameters: appropriate indication, appropriate drug, appropriate dose, and appropriate patient, and was in accordance with the 2016 POGI guidelines. These findings emphasize the importance of implementing rational, guideline-based therapy to improve maternal and fetal safety in cases of preeclampsia.

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COMMENTS:

Title and Abstract

- Title: The title is concise but could be more specific. Consider specifying the study design and location, e.g., "A Retrospective Descriptive Study on Antihypertensive Use in Preeclampsia at a Tertiary Hospital in Indonesia."
- Abstract:
  - The abstract structure is acceptable but requires refinement. The sentence "This study was conducted from August to December 2024" is confusing as it appears to be the data analysis period, not the study period.
  - The finding of 100% appropriateness across all criteria is highly unusual and requires contextualization in the abstract. A brief mention of the study's limitation (e.g., small sample size, single-center design) would provide balance.

Introduction and Literature Review

- Research Problem: The global and local burden of preeclampsia is well-established. However, the specific research problem—why this particular audit at this specific hospital is needed—is not clearly defined.
- Gap Identification: The introduction fails to identify a clear gap in the literature. It states the need to "assess the effectiveness of medications" but the study conducted is a descriptive drug utilization review, not an effectiveness study. The gap should be reframed to highlight the importance of continuous audit and feedback to ensure adherence to clinical guidelines in local settings.
- References: The references are a mix of international sources (e.g., Karrar et al., 2024) and local Indonesian literature, which is appropriate. However, citing "Anon 2025a/b" for current data is problematic as these are not proper references and the year 2025 is in the future. These must be replaced with correctly cited, verifiable sources.
- The objective is clear and specific: to describe the pattern and appropriateness of antihypertensive use. It aligns with the descriptive nature of the study.

Methodology

- Study Design: The non-experimental, retrospective, cross-sectional design is correctly stated and appropriate for a drug utilization study.
- Sample Size and Sampling: The use of total sampling (N=52) is justified for a retrospective audit over a defined period. However, the inclusion and exclusion criteria are not stated in the manuscript. This is a critical omission and must be detailed.
- Data Collection and Variables: The source of data (medical records) is clear. The variables (indication, drug, dose, patient) are well-defined according to the POGI 2016 standard.
- Data Analysis: The analysis is not sufficiently rigorous. The exclusive use of univariate descriptive analysis (frequencies/percentages) is a major weakness. For a sample of 52, basic inferential statistics (e.g., Chi-square or Fisher's exact test) should be employed to explore potential associations between patient characteristics (e.g., age, severity of preeclampsia) and the choice of antihypertensive therapy. This would significantly strengthen the scientific contribution.
- Ethical Considerations: This is a critical omission. The manuscript must state whether ethical approval was obtained from an Institutional Review Board (IRB) or Ethics Committee for the use of patient medical record data. If an exemption was granted, this should be stated with the reference number. This is a mandatory requirement for publication.

Results

- The results are presented clearly with appropriate tables. The demographic and clinical characteristics of the cohort are well-described.
- The finding of 100% appropriateness across all criteria is statistically remarkable and warrants careful scrutiny. The results section should simply present the data; the interpretation belongs in the discussion.

Discussion

- Interpretation of Results: The discussion is largely a repetition of the results with supporting or contrasting literature. It lacks critical depth.
  - The 100% adherence rate must be discussed critically. Is this a true reflection of perfect practice, or could it be influenced by limitations such as small sample size, incomplete medical record documentation, or the audit's methodological design? This requires honest and transparent analysis.
  - The discussion on why nifedipine is the preferred choice is good, but it should be linked more strongly to international guidelines (e.g., FIGO, SOMANZ, NICE) in addition to POGI to provide a broader context.
- Comparison with Literature: Comparisons are made, but the reasons for discrepancies (e.g., with Yani et al.) are speculative and not sufficiently explored.
- Limitations: The discussion must include a dedicated "Limitations" section. Key limitations include the retrospective design, small sample size from a single center, potential for documentation bias in medical records, and the absence of maternal or fetal outcome data. The lack of inferential statistical analysis is also a methodological limitation.

Conclusion and Implications

- The conclusions are too strong given the study's limitations. Stating that the findings "emphasize the importance of implementing rational, guideline-based therapy" is not fully supported, as the study found that such therapy was already being implemented perfectly.
- The implications are weak. Instead, the conclusion should focus on the value of the audit in confirming local guideline adherence and recommend future studies with larger samples, multicenter designs, and correlation with clinical outcomes (e.g., time to blood pressure control, maternal/fetal adverse events).

Quality of Writing and Structure

- The manuscript requires thorough editing for English grammar, syntax, and academic style. There are numerous instances of awkward phrasing and repetition (e.g., "Based on the table..." is used repeatedly). Professional language editing is recommended.
- The structure is generally coherent but would benefit from clearer subsection headings within the Methodology and Discussion.

References

- The reference list has significant issues. Citations like "Anon 2025" are unacceptable. All references must be complete, verifiable, and accurately formatted according to the target journal's specific guidelines. The use of sources such as university repositories (e.g., Bulqies, 2021) for a journal article should be minimized in favor of peer-reviewed publications.

Overview Of Antihypertensive Medicines Use In Preeclampsia Cases

Track Record Article

Accepted:

Published:

Abstract

Approximately 2-8% of all pregnancy problems are caused by preeclampsia, which is hypertension that may occur during pregnancy. Globally, there are more than 50,000 maternal deaths and nearly 500,000 infant deaths. The purpose of this study was to determine the pattern of medicine use and the appropriateness of the use of antihypertensive medicines in preeclampsia patients. This study employs a non-experimental, cross-sectional design with a retrospective descriptive approach, utilizing medical records. This study was conducted from August to December 2024. The sampling technique used in this study employed a total sampling approach. Data analysis was carried out descriptively and compared with the POGI 2016 reference standard. The results showed that of 52 preeclampsia patients at the Indonesian Christian University Hospital who were at risk of developing preeclampsia were those aged over 35 years (50%) with a gestational age in the third trimester (94.2%) with a diagnosis of mild preeclampsia (80.8%). In mild preeclampsia, the most frequently used treatment was nifedipine monotherapy (92.9%). In severe preeclampsia, monotherapy with nifedipine (50%) is the most commonly used treatment. The percentage of appropriate antihypertensive medicine use shows appropriate indication (100%), appropriate medicine (100%), appropriate dose (100%), appropriate patient (100%), and rational use of antihypertensive medicines (100%).

Keyword: Preeclampsia, Antihypertensives, Treatment Rationale, Nifedipine, Pregnancy

INTRODUCTION

Pregnancy disorders known as preeclampsia are characterized by placental damage and a maternal response to systemic inflammation with endothelial activation and coagulation. Preeclampsia can be categorized into two categories: mild and severe (Kemenkes 2022). Pregnancy-specific high blood pressure and organ dysfunction at more than 20 weeks of gestation are diagnostic of preeclampsia. Worldwide, 2% to 8% of pregnancy disorders are caused by preeclampsia, a condition characterized by increased blood pressure during pregnancy. (Fujiko, Nurdin, and Aman 2024). Globally, infant deaths average around half a million, while maternal deaths exceed 50,000. Approximately 16% occur in developed countries, while 9% - 26% occur in developing countries (Karrar, Martingano, and Hong 2024). There remains a significant problem with maternal mortality rates in developing countries, with more than 300 deaths for every 100,000 live births, according to data from the 2017 Indonesian Demographic and Health Survey (SDKI). At the same time, there were at least 32 infant mortality rates (IMR) for every 1,000 live births. Indonesia has a relatively high prevalence of preeclampsia, with 5.3% of cases reported annually (Anon 2025b). 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 (Anon 2025a)

Antihypertensive medicines in the calcium channel blocker, beta-blocker, and methyldopa classes are recommended for the treatment of preeclampsia by the Indonesian Obstetrics and Gynecology Association (POGI) in 2016. The recommended medicines are nifedipine, labetalol, atenolol, and methyldopa. Treatment of hypertension during pregnancy requires extra caution to avoid complications such as eclampsia, which can harm the mother and fetus. To achieve the desired results, medicine selection must be appropriate in terms of safety, efficacy, and rationality. 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)

Given the above data on the prevalence of morbidity and mortality, it is necessary to assess the effectiveness of medications prescribed by hospitals and community health centers as primary healthcare providers in combating preeclampsia. Therefore, the author is interested in examining the description of antihypertensive medication use in preeclampsia cases at the Indonesian Christian University Hospital for the period from January 2022 to October 2024.

This study aimed to determine the description of the use of antihypertensive medicines in cases of preeclampsia, reviewed from the perspective of indication accuracy, patient accuracy, medicine accuracy, and dosage accuracy in patients at the Indonesian Christian University Hospital

METHODS

This study used a retrospective method and was not experimental. Medical record data is an example of secondary data used in data collection. Based on the 2016 POGI recommendations, the data were evaluated, and their rationality was determined. The Indonesian Christian University General Hospital was the site of this research. The medical record data used in this study covered the period from January 2022 to October 2024 and were collected between August and December 2024. The population consisted of patients diagnosed with preeclampsia and using antihypertensive medicines who were undergoing treatment at the Indonesian Christian University Hospital during the period January 2022 - October 2024. The sample was

collected using a total sampling technique, comprising a total of 52 participants who met the inclusion and exclusion criteria. The research instrument in the form of medical records of preeclampsia patients treated with antihypertensive medicines at the Indonesian Christian University Hospital from January 2022 to October 2024 served as a secondary data source in this study. Data analysis was conducted using the SPSS (Statistical Package for the Social Sciences) program in this study. The results were then analyzed univariately. Univariate analysis aims to determine the quantitative and qualitative frequency distribution of each variable. This is achieved by examining the prevalence of preeclampsia in relation to age, gestational age, gravid status, and comorbidities. Additionally, an analysis will be conducted to explore the reasons for using antihypertensive medication, considering appropriate indications, suitable patients, effective treatment, and optimal dosages, in accordance with the 2016 POGI guidelines

RESULTS

The Indonesian Christian University Hospital served as the study site. 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 collected to determine the characteristics and distribution of the sample population. 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*
Types of Concomitant Diseases		
Hypertension	*8*	*47.1*
HDK	*4*	*23.5*
Preeclampsia	*1*	*5.9*
Hypertension + Allergies	*1*	*5.9*
Hypertension + Type 2 Diabetes	*1*	*5.9*
Hypertension + Cholesterol 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 less than 140/80 mmHg	*10*	*19.2*
Blood pressure of at least 140/90 mmHg	*32*	*61.5*
Blood pressure of at least 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*	+	*4*	40
Methyldopa					

Table 4. Percentage of Appropriate Use of Antihypertensive Medications in Severe Preeclampsia Patients at the Indonesian Christian University Hospital for the Period January 2022 – October 2024

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*

DISCUSSION

Table 1, data shows that between January 2022 and October 2024, 26 patients (or 50% of the total) were diagnosed with preeclampsia at the Indonesian Christian University Hospital. The next largest age group was patients between 25 and 35 years old, comprising 24 patients (or 46.2% of the total). Two patients (3.8% of the total) were under 25 years old. This finding supports 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). 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 and 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 and 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. Therefore, pregnant women must undergo comprehensive prenatal monitoring, including frequent and adequate Antenatal Care (ANC) appointments, to reduce the possibility of potential risk factor.

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, Pont, and Purwanti 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 and 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. 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, Ismansyah, and Siregar 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 (Amalina, Kasoema, and Mardiah 2022).

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 the 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 and 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, Rahmawati, and Yasin 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, Ulfa, and Jannah 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 and 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 and 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 and 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 (Andriana, Utami, and Sholihat 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.

CONCLUSIONS

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 preeclampsia patients were over 35 years old and in their third trimester. The use of antihypertensives in all patients met rational criteria based on four main parameters: appropriate indication, appropriate drug, appropriate dose, and appropriate patient, and was in accordance with the 2016 POGI guidelines. These findings emphasize the importance of implementing rational, guideline-based therapy to improve maternal and fetal safety in cases of preeclampsia.

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REVIEW:

1. Title: add design, setting, and timeframe for indexing clarity, e.g., “Drug-Use Evaluation of Antihypertensives in Preeclampsia: A Retrospective Study at an Indonesian Tertiary Hospital, 2022–2024.”
2. Abstract: structure is present but tighten language, align numerators/denominators, and report key statistics consistently (mean/SD or %, plus 95% CIs where relevant). Ensure timeline consistency (data period Jan 2022–Oct 2024; collection Aug–Dec 2024) and avoid method slippage (cross-sectional vs retrospective).
3. Keywords are relevant; consider adding “drug-use evaluation,” “guideline adherence,” “Indonesia” to improve discoverability.
4. The problem statement is clear and contextualised with national indicators, but sources labelled “Anon 2025a/b” are weak; replace with authoritative reports (national vital statistics/SDKI/WHO) and align years.
5. You cite POGI 2016 recommendations; briefly contrast with other contemporary guidance and explain any differences relevant to local practice (e.g., first-line choices, dosing ranges, in-labour management), to justify your audit yardstick.
6. Conclude the introduction with a sharper gap statement and a measurable objective linked to prespecified indicators (e.g., “≥90% correct dose per POGI 2016”).
7. Current aim is descriptive. Recast as audit questions with targets: (i) proportion receiving guideline-recommended agent by severity; (ii) proportion dosed within recommended range; (iii) patterns of mono- vs combination-therapy by severity; (iv) safety signals (AEs). This will sharpen your narrative and tables.
8. Design: clearly retrospective, medical-record based; keep terminology consistent (avoid “cross-sectional” unless you justify it).
9. Setting/period/sample: define inclusion/exclusion precisely (diagnostic criteria for mild/severe preeclampsia; inpatient/outpatient; multiple gestation; co-treatments such as magnesium sulfate). Provide a flow diagram with numbers screened/included/excluded.
10. Variables/indicators: operationalise “appropriate indication/drug/dose/patient” with exact POGI thresholds (e.g., nifedipine IR 10 mg q8–12h; what counts as “appropriate patient” beyond absence of contraindications?). Predefine severity strata and proteinuria/blood-pressure cut-offs you used.

11. Data collection: specify who abstracted data, training, and inter-rater reliability. Note how proteinuria was measured (dipstick vs 24-h urine), and how BP was verified.
12. Sample size/statistics: justify n=52 (power for estimating proportions with desired precision). Move beyond univariate counts—add exact binomial 95% CIs for key proportions; consider simple comparisons (e.g., mild vs severe) if appropriate.
13. Ethics: add IRB approval ID and consent waiver statement for retrospective records research. (Not currently reported in this manuscript.)
14. Present a study flow (n screened→eligible→analysed). Provide a baseline table (age, GA, BP, proteinuria, comorbidities) with clear denominators and missingness. Current descriptive results can be tightened and tabulated.
15. Drug-use patterns are central; consolidate Table 3 and the narrative to highlight the key messages (e.g., “Nifedipine monotherapy in 92.9% of mild cases; 50.0% of severe cases, with 40.0% nifedipine+methyldopa”). Add 95% CIs to these percentages.
16. For the “100% appropriate” indicators, report numerators/denominators and the exact definitions applied; if any cases were borderline or unknown (e.g., missing dose frequency), state how you handled them. Consider a second reviewer audit on a 10–20% subsample.
17. Interpret practice patterns (dominance of nifedipine) against your local formulary, availability, and on-call workflows; acknowledge why labetalol/methyldopa use was lower.
18. Discuss clinical implications carefully—your data are on prescribing appropriateness, not maternal/foetal outcomes. Avoid efficacy claims; instead, recommend system-level actions (order sets, dosing protocols, audit-and-feedback).
19. Add a structured Limitations paragraph: single-centre; retrospective design; potential misclassification bias; lack of denominators for all pregnant patients with hypertension; absence of safety/adverse-event data; reliance on one guideline year; no outcome linkage (e.g., time-to-BP control, eclampsia, NICU).
20. Conclusions: Temper language to reflect audit findings rather than therapeutic effectiveness. Offer 2–3 concrete practice recommendations (e.g., maintain nifedipine first-line with dosing protocol; add labetalol availability for severe cases; implement quarterly DUE with agreed targets).

21. Undertake thorough language editing to UK academic English and remove visible formatting artefacts (“Page PAGE * MERGEFORMAT”). Standardise decimal points, units, and percent formatting; keep tables consistent (headings, alignment, significant figures).
22. Shorten repetitive prose in Results; let well-designed tables carry the detail. Ensure table captions are self-contained (population, period, denominator).
23. Add a dedicated Ethics subsection (approving body, approval number, consent waiver, confidentiality safeguards).
24. Upgrade references: replace “Anon 2025a/2025b” with full authoritative citations; ensure every in-text guideline claim is supported (complete authors, year, title, publisher/DOI). Align all entries to the journal’s style and fix inconsistencies (capitalisation, journal names, page ranges).

Page PAGE * MERGEFORMAT

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

Track Record Article

Accepted:

Published:

Abstract

Background: *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.* ***Methods:*** *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.* ***Results:*** *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.* ***Conclusion:*** *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 is a pregnancy-specific hypertensive disorder characterized by abnormal placentation followed by a maternal systemic inflammatory response, endothelial dysfunction, and activation of the coagulation cascade. Clinically, preeclampsia is diagnosed after 20 weeks of gestation and is classified into mild and severe forms based on blood pressure levels and the presence of target organ involvement (Kemenkes, 2022). Pregnancy-specific high blood pressure and organ dysfunction at more than 20 weeks of gestation are diagnostic of preeclampsia. Worldwide, 2% to 8% of pregnancy disorders are caused by preeclampsia, a condition characterized by increased blood pressure during pregnancy. (Fujiko, Nurdin, and Aman 2024). Globally, infant deaths average around half a million, while maternal deaths

exceed 50,000. Approximately 16% occur in developed countries, while 9% - 26% occur in developing countries (Karrar, Martingano, and Hong 2024).

Although the global burden of preeclampsia has been widely reported, excessive reliance on global statistics often obscures context-specific challenges. In Indonesia, preeclampsia continues to contribute substantially to maternal deaths. National data indicate that maternal mortality remains high, exceeding 300 deaths per 100,000 live births, with hypertensive disorders of pregnancy consistently ranked among the leading causes. 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)

Pharmacological management plays a central role in preventing progression to severe complications such as eclampsia, stroke, and maternal–fetal morbidity. 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, evidence regarding real-world prescribing practices for antihypertensive therapy in preeclampsia in Indonesia remains 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. The lack of institutional audits on guideline adherence represents an important gap in the optimization of maternal care.

Given these gaps, evaluating antihypertensive prescribing patterns at the hospital level is crucial to support evidence-based practice and quality improvement. Therefore, this study was conducted at the Indonesian Christian University Hospital during the period from January 2022 to October 2024.

The primary objective of this study was to assess the pattern and fidelity of antihypertensive use in preeclampsia based on the 4Ts principle. The secondary objective was to identify factors associated with the use of monotherapy versus combination antihypertensive therapy among patients with different grades of preeclampsia.

METHODS

Commented [a1]: Ethical Clearance?

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 study population consisted of all pregnant women diagnosed with preeclampsia who received antihypertensive therapy at the Indonesian Christian University General Hospital during the study period. A total sampling technique was applied, and all eligible cases were included. A total of 52 patients met the inclusion and exclusion criteria and were analyzed.

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

Inclusion and Exclusion Criteria

Inclusion criteria were:

1. Pregnant women with a gestational age of ≥20 weeks.
2. A diagnosis of preeclampsia documented in the medical record, defined as: Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on at least two measurements, and Evidence of proteinuria (≥+1 on dipstick or ≥300 mg/24 hours), in accordance with the POGI 2016 guideline.

3. Patients who received at least one antihypertensive medication during hospitalization or outpatient care.

Exclusion criteria were:

1. Pregnant women with chronic hypertension diagnosed before pregnancy or before 20 weeks of gestation.
2. Patients with chronic kidney disease, lupus nephritis, or other secondary causes of hypertension documented in the medical record.
3. Incomplete medical records, particularly those lacking blood pressure measurements, antihypertensive drug details, or gestational age.

Commented [a2]: Inclusion and exclusion criteria are included in the descriptive paragraph.

Definition of Preeclampsia Severity

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

- Mild preeclampsia: blood pressure ≥140/90 mmHg but <160/110 mmHg with proteinuria.
- Severe preeclampsia: 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

Secondary data were obtained from patients' medical records, including 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).

Operational Definition of Appropriateness (4Ts Criteria)

The appropriateness of antihypertensive drug use was evaluated using the **4Ts framework**, based on the POGI 2016 guideline:

1. **Right Indication**

   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**

   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**

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**. Prescriptions were considered appropriate if the dose, frequency, and titration were within recommended ranges.

4. **Right Patient**

   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.

Assessment Process

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

Statistical Analysis

Data were analyzed using SPSS software. Descriptive statistics were 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.

RESULTS

The Indonesian Christian University Hospital served as the study site. 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 collected to determine the characteristics and distribution of the sample population. 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*
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*	+	*1*	*2.4*
Methyldopa					
Severe Preeclampsia					
Monotherapy					
Nifedipine				*5*	*50*
Amlodipine				*1*	*10*
Two-Medicine	*Combination*	*Nifedipine*	+	*4*	*40*
Methyldopa					

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

	Appropriate		***Not Exactly***	
Criteria	***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*

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; $p < 0.05$), indicating a statistically significant association between disease

severity and treatment pattern. The wide confidence interval reflects the limited number of severe preeclampsia cases

DISCUSSION

Table 1 shows that between January 2022 and October 2024, 26 patients (or 50% of the total) were diagnosed with preeclampsia at the Indonesian Christian University Hospital. The next largest age group was patients between 25 and 35 years old, comprising 24 patients (or 46.2% of the total). Two patients (3.8% of the total) were under 25 years old. This finding supports 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). 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 and 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 and 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. Therefore, pregnant women must undergo comprehensive prenatal monitoring, including frequent and adequate Antenatal Care (ANC) appointments, to reduce the possibility of potential risk factor. 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, Pont, and Purwanti 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 and 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. 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, Ismansyah, and Siregar 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 (Amalina, Kasoema, and Mardiah 2022).

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 the 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 and 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, Rahmawati, and Yasin 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, Ulfa, and Jannah 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 and 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 and 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 and 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 (Andriana, Utami, and Sholihat 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.

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. 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. 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. 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. 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.

CONCLUSIONS

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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Commented [a3]: All article citations must include a DOI, using APA 7th format in accordance with the template requirements. A minimum of 25 references is required, and please double-check that the citations in the article are also included in the references.

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

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Abstract

Background: *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.* ***Methods:*** *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.* ***Results:*** *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.* ***Conclusion:*** *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 is a pregnancy-specific hypertensive disorder characterized by abnormal placentation followed by a maternal systemic inflammatory response, endothelial dysfunction, and activation of the coagulation cascade. Clinically, preeclampsia is diagnosed after 20 weeks of gestation and is classified into mild and severe forms based on blood pressure levels and the presence of target organ involvement (Kemenkes, 2022). Pregnancy-specific high blood pressure and organ dysfunction at more than 20 weeks of gestation are diagnostic of preeclampsia. Worldwide, 2% to 8% of pregnancy disorders are caused by preeclampsia, a condition characterized by increased blood pressure during pregnancy. (Fujiko, Nurdin, and Aman 2024). Globally, infant deaths average around half a million, while maternal deaths

exceed 50,000. Approximately 16% occur in developed countries, while 9% - 26% occur in developing countries (Karrar, Martingano, and Hong 2024).

Although the global burden of preeclampsia has been widely reported, excessive reliance on global statistics often obscures context-specific challenges. In Indonesia, preeclampsia continues to contribute substantially to maternal deaths. National data indicate that maternal mortality remains high, exceeding 300 deaths per 100,000 live births, with hypertensive disorders of pregnancy consistently ranked among the leading causes. 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)

Pharmacological management plays a central role in preventing progression to severe complications such as eclampsia, stroke, and maternal–fetal morbidity. 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, evidence regarding real-world prescribing practices for antihypertensive therapy in preeclampsia in Indonesia remains 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. The lack of institutional audits on guideline adherence represents an important gap in the optimization of maternal care.

Given these gaps, evaluating antihypertensive prescribing patterns at the hospital level is crucial to support evidence-based practice and quality improvement. Therefore, this study was conducted at the Indonesian Christian University Hospital during the period from January 2022 to October 2024.

The primary objective of this study was to assess the pattern and fidelity of antihypertensive use in preeclampsia based on the 4Ts principle. The secondary objective was to identify 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 study population consisted of all pregnant women diagnosed with preeclampsia who received antihypertensive therapy at the Indonesian Christian University General Hospital during the study period. A total sampling technique was applied, and all eligible cases were included. A total of 52 patients met the inclusion and exclusion criteria and were analyzed.

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

Inclusion and Exclusion Criteria

Inclusion criteria were:

1. Pregnant women with a gestational age of ≥20 weeks.
2. A diagnosis of preeclampsia documented in the medical record, defined as: Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on at least two measurements, and Evidence of proteinuria (≥+1 on dipstick or ≥300 mg/24 hours), in accordance with the POGI 2016 guideline.

3. Patients who received at least one antihypertensive medication during hospitalization or outpatient care.

Exclusion criteria were:

1. Pregnant women with chronic hypertension diagnosed before pregnancy or before 20 weeks of gestation.
2. Patients with chronic kidney disease, lupus nephritis, or other secondary causes of hypertension documented in the medical record.
3. Incomplete medical records, particularly those lacking blood pressure measurements, antihypertensive drug details, or gestational age.

Definition of Preeclampsia Severity

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

- Mild preeclampsia: blood pressure ≥140/90 mmHg but <160/110 mmHg with proteinuria.
- Severe preeclampsia: 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

Secondary data were obtained from patients' medical records, including 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).

Operational Definition of Appropriateness (4Ts Criteria)

The appropriateness of antihypertensive drug use was evaluated using the **4Ts framework**, based on the POGI 2016 guideline:

1. **Right Indication**

   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**

   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**

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**. Prescriptions were considered appropriate if the dose, frequency, and titration were within recommended ranges.

4. **Right Patient**

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.

Assessment Process

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

Statistical Analysis

Data were analyzed using SPSS software. Descriptive statistics were 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.

RESULTS

The Indonesian Christian University Hospital served as the study site. 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 collected to determine the characteristics and distribution of the sample population. 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*
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*	+	*1*	*2.4*
Methyldopa					
Severe Preeclampsia					
Monotherapy					
Nifedipine				*5*	*50*
Amlodipine				*1*	*10*
Two-Medicine	*Combination*	*Nifedipine*	+	*4*	*40*
Methyldopa					

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*

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; $p < 0.05$), indicating a statistically significant association between disease

severity and treatment pattern. The wide confidence interval reflects the limited number of severe preeclampsia cases

DISCUSSION

Table 1 shows that between January 2022 and October 2024, 26 patients (or 50% of the total) were diagnosed with preeclampsia at the Indonesian Christian University Hospital. The next largest age group was patients between 25 and 35 years old, comprising 24 patients (or 46.2% of the total). Two patients (3.8% of the total) were under 25 years old. This finding supports 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). 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 and 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 and 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. Therefore, pregnant women must undergo comprehensive prenatal monitoring, including frequent and adequate Antenatal Care (ANC) appointments, to reduce the possibility of potential risk factor. 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, Pont, and Purwanti 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 and 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. 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, Ismansyah, and Siregar 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 (Amalina, Kasoema, and Mardiah 2022).

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 the 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 and 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, Rahmawati, and Yasin 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, Ulfa, and Jannah 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 and 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 and 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 and 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 (Andriana, Utami, and Sholihat 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.

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. 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. 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. 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. 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.

CONCLUSIONS

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

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Abstract

Background: *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.* ***Methods:*** *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.* ***Results:*** *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.* ***Conclusion:*** *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 is a pregnancy-specific hypertensive disorder characterized by abnormal placentation followed by a maternal systemic inflammatory response, endothelial dysfunction, and activation of the coagulation cascade. Clinically, preeclampsia is diagnosed after 20 weeks of gestation and is classified into mild and severe forms based on blood pressure levels and the presence of target organ involvement (Kemenkes, 2022). Pregnancy-specific high blood pressure and organ dysfunction at more than 20 weeks of gestation are diagnostic of preeclampsia. Worldwide, 2% to 8% of pregnancy disorders are caused by preeclampsia, a condition characterized by increased blood pressure during pregnancy. (Fujiko et al., 2024). Globally, infant deaths average around half a million, while maternal deaths exceed 50,000.

Approximately 16% occur in developed countries, while 9% - 26% occur in developing countries (Karrar et al., 2024).

Although the global burden of preeclampsia has been widely reported, excessive reliance on global statistics often obscures context-specific challenges. In Indonesia, preeclampsia continues to contribute substantially to maternal deaths. National data indicate that maternal mortality remains high, exceeding 300 deaths per 100,000 live births, with hypertensive disorders of pregnancy consistently ranked among the leading causes. 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)

Pharmacological management plays a central role in preventing progression to severe complications such as eclampsia, stroke, and maternal–fetal morbidity. 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, evidence regarding real-world prescribing practices for antihypertensive therapy in preeclampsia in Indonesia remains 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. The lack of institutional audits on guideline adherence represents an important gap in the optimization of maternal care.

Given these gaps, evaluating antihypertensive prescribing patterns at the hospital level is crucial to support evidence-based practice and quality improvement. Therefore, this study was conducted at the Indonesian Christian University Hospital during the period from January 2022 to October 2024.

The primary objective of this study was to assess the pattern and fidelity of antihypertensive use in preeclampsia based on the 4Ts principle. The secondary objective was to identify 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 study population consisted of all pregnant women diagnosed with preeclampsia who received antihypertensive therapy at the Indonesian Christian University General Hospital during the study period. A total sampling technique was applied, and all eligible cases were included. A total of 52 patients met the inclusion and exclusion criteria and were analyzed.

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

Inclusion and Exclusion Criteria

This study included pregnant women with a gestational age of ≥20 weeks who were diagnosed with preeclampsia, as documented in the medical records. Preeclampsia was defined 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). Eligible participants were further required to 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 were excluded if they had a history of chronic hypertension diagnosed before pregnancy or before 20 weeks of gestation, 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 excluded to minimize confounding factors that could influence blood pressure control and antihypertensive selection. Medical records that 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:

- Mild preeclampsia: blood pressure ≥140/90 mmHg but <160/110 mmHg with proteinuria.
- Severe preeclampsia: 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

Secondary data were obtained from patients' medical records, including 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).

Operational Definition of Appropriateness (4Ts Criteria)

The appropriateness of antihypertensive drug use was evaluated using the **4Ts framework**, based on the POGI 2016 guideline:

1. **Right Indication**

   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**

   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**

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**. Prescriptions were considered appropriate if the dose, frequency, and titration were within recommended ranges.

4. **Right Patient**

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.

Assessment Process

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

Statistical Analysis

Data were analyzed using SPSS software. Descriptive statistics were 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

This research has passed ethical approval with the number: No. 652/UKI.LPPM/PPM.00.00/ET.2024.

RESULTS

The Indonesian Christian University Hospital served as the study site. 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 collected to determine the characteristics and distribution of the sample population. 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*
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*	+	*1*	*2.4*
Methyldopa					
Severe Preeclampsia					
Monotherapy					
Nifedipine				*5*	*50*
Amlodipine				*1*	*10*
Two-Medicine	*Combination*	*Nifedipine*	+	*4*	*40*
Methyldopa					

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*

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; $p < 0.05$), indicating a statistically significant association between disease severity and treatment pattern. The wide confidence interval reflects the limited number of severe preeclampsia cases

DISCUSSION

Table 1 shows that between January 2022 and October 2024, 26 patients (or 50% of the total) were diagnosed with preeclampsia at the Indonesian Christian University Hospital. The next largest age group was patients between 25 and 35 years old, comprising 24 patients (or 46.2% of the total). Two patients (3.8% of the total) were under 25 years old. This finding supports 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). 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. Therefore, pregnant women must undergo comprehensive prenatal monitoring, including frequent and adequate Antenatal Care (ANC) appointments, to reduce the possibility of potential risk factor. 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 mild 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. 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 the 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.

CONCLUSIONS

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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