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Antihypertensive Therapy in Preeclampsia: A Secondary Hospital Perspective on Prescribing Behavior and Patient Safety

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Abstract
Hypertensive disorders in pregnancy remain a leading cause of maternal and neonatal morbidity and mortality worldwide, including in Indonesia. Preeclampsia contributes significantly to maternal deaths due to uncontrolled blood pressure and inappropriate drug use. This study aims to evaluate the prescribing behavior, therapeutic outcomes, and safety of antihypertensive drugs used in preeclampsia management in secondary hospitals. A retrospective cohort study was conducted among 832 hospitalized patients with preeclampsia in Yogyakarta, Indonesia, from 2018 to 2024. Analytical and descriptive methods were employed to examine both patient characteristics and treatment variables. This study found that complete recommended therapy was predominantly administered among patients in the third trimester (100%) and those with gravida <3 (72.9%). Nifedipine was the most frequently prescribed drug (63.2%). In terms of effectiveness, nifedipine monotherapy achieved target blood pressure in 48.4% of patients, compared to 15.6% in methyldopa monotherapy, while combination therapy (nifedipine–methyldopa) achieved 6.1%. These findings are consistent with current clinical guidelines, where methyldopa is considered a safe first-line antihypertensive, while nifedipine serves as an effective alternative to achieve optimal maternal and fetal outcomes.

Keywords: Drug safety; Hypertension; Pregnant women; Preeclampsia; Prescription pattern.

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Terapi Antihipertensi pada Preeklamsia: Perspektif Rumah Sakit Sekunder terhadap Perilaku Peresepan dan Keamanan Pasien

Abstrak
Gangguan hipertensi pada kehamilan masih menjadi penyebab utama morbiditas dan mortalitas ibu serta bayi di seluruh dunia, termasuk di Indonesia. Preeklamsia berkontribusi besar terhadap kematian ibu akibat tekanan darah tinggi yang tidak terkontrol dan penggunaan obat antihipertensi yang kurang tepat. Penelitian ini bertujuan untuk mengevaluasi perilaku peresepan, luaran terapi, dan keamanan obat antihipertensi yang digunakan dalam penatalaksanaan preeklamsia di rumah sakit sekunder. Studi kohort retrospektif dilakukan terhadap 832 pasien preeklamsia yang dirawat di rumah sakit di Yogyakarta, Indonesia, selama periode 2018–2024. Analisis deskriptif dan analitik digunakan untuk mengevaluasi karakteristik pasien serta variabel pengobatan. Hasil penelitian menunjukkan bahwa terapi yang direkomendasikan secara lengkap paling banyak diberikan pada pasien trimester ketiga (100%) dan pada pasien dengan jumlah gravida kurang dari tiga (72,9%). Nifedipin merupakan obat antihipertensi yang paling sering diresepkan (63,2%). Ditinjau dari efektivitasnya, monoterapi nifedipin mencapai target tekanan darah pada 48,4% pasien, dibandingkan dengan 15,6% pada monoterapi metildopa, sedangkan terapi kombinasi nifedipin–metildopa mencapai 6,1%. Temuan ini sejalan dengan pedoman klinis terkini, yang menempatkan metildopa sebagai antihipertensi lini pertama yang aman, sedangkan nifedipin merupakan alternatif yang efektif untuk mencapai luaran maternal dan fetal yang optimal.

Kata Kunci: Keamanan obat; Hipertensi; Ibu hamil; Preeklamsia; Pola peresepan.

1. Introduction

Hypertension in pregnancy can affect up to 10% of pregnancies globally, with 3-5% of pregnancies experiencing complications.[1] Hypertension in pregnant women can lead to adverse outcomes such as low birth weight, impaired fetal development, and even neonatal mortality. Preeclampsia is one of hypertensive disorders that frequently occur during pregnancy and cause of 50,000 maternal deaths worldwide.[2] Throughout 2022, maternal deaths in Indonesia reached 3,572, and 801 of them died due to hypertension in pregnancy.[3] Preeclampsia, according to the International Society for the Study of Hypertension in Pregnancy (ISSHP), is characterized by high blood pressure, specifically a systolic blood pressure of 140 mmHg or higher and a diastolic blood pressure of 90 mmHg or higher, occurring at a gestational age of more than 20 weeks.[4] Preeclampsia is linked to specific risk factors that manifest either before or after the 34th week of pregnancy.[5] Common risk factors associated with preeclampsia include chronic hypertension, diabetes mellitus, kidney disease, and obesity.[2] In the first decade following a preeclampsia-affected pregnancy, the risk of cardiovascular disease-related complications such as heart failure, stroke, and mortality is becoming more significant.[5]

The adverse outcomes associated with hypertension in pregnancy can be mitigated through appropriate antihypertensive therapy.[6] The Indonesian Guideline for Medical Services (PNPK) recommends the use of antihypertensive agents to control blood pressure, magnesium sulfate to prevent seizures, and corticosteroids to promote fetal lung maturation prior to delivery in patients with preeclampsia.[7] Therefore, selecting antihypertensive therapy that is safe, effective, and rational is essential to achieve optimal maternal and fetal outcomes.[8] In Indonesia, the burden of preeclampsia remains substantial, with 1,077 cases reported among 7,389 pregnant women in 2021 and 412 maternal deaths due to hypertension among 3,994 pregnant women in 2023.[9,10]

Despite the availability of clinical guidelines, evidence regarding real-world prescribing practices for antihypertensive therapy in Indonesian hospital settings remains limited. Most existing studies primarily focus on clinical outcomes or guideline recommendations, with insufficient data describing actual prescribing behavior in routine care.[8-10] Furthermore, there is a lack of comparative insight into the effectiveness of different antihypertensive regimens used in real-world settings, particularly in secondary hospitals where prescribing patterns and resource availability may differ from tertiary care.[15]

Therefore, this study aims to evaluate prescribing behavior, therapeutic outcomes, and the safety profile of antihypertensive drugs among hospitalized preeclampsia patients in secondary hospitals in Yogyakarta, Indonesia. In addition, this study provides real-world evidence on the effectiveness of commonly prescribed antihypertensive regimens and their safety classification based on the United States Food and Drug Administration (US FDA) and the Australian Therapeutic Goods Administration (AU TGA). This study also explores the potential impact of the COVID-19 pandemic on preeclampsia management in these settings.

2. Methods

2.1. Study Design

This study utilized a retrospective cohort design to analyze prescribing patterns for pregnant women with preeclampsia during hospitalization until discharge. The study protocol was approved by the Health Research Ethics Committee of PKU Muhammadiyah Hospital, Yogyakarta (Ethical Clearance No. 158/KEP-PKU/VIII/2024). This study included hospitalized pregnant women diagnosed with preeclampsia at secondary hospitals in Yogyakarta between 2018 and 2024 with complete medical records on demographics, gestational age, blood pressure, and prescribed antihypertensive therapy. Patients with chronic hypertension, eclampsia, HELLP syndrome, incomplete records, or transferred cases were excluded.

2.2. Data Collection

Data collection was carried out retrospectively at the secondary hospitals in Yogyakarta, which provide specialized obstetric care. This study involved 832 hospitalized pregnant women with preeclampsia who met the inclusion criteria. All patients included in this study were hospitalized with a primary diagnosis of preeclampsia as documented in their medical records. Data were gathered from 2018-2024, encompassing prescription analysis and patient characteristics such as age, BMI, gestational age, gravida status, and blood pressure records. Information on comorbid conditions, when available, was also collected; however, detailed classification of comorbidities was limited due to the retrospective nature of the data.

The BMI record was obtained from the initial antenatal visit data to document the presence of obesity at the early stage of pregnancy. The blood pressure records were also obtained from the initial antenatal check and the first day of hospitalization due to preeclampsia. The timing of blood pressure data collection aimed to

capture the history of high blood pressure at the early stages of pregnancy, as a risk factor, and to analyze the blood pressure trend on the first day of admission for preeclampsia.

2.3. Clinical Outcomes

This study primarily evaluated prescribed treatment patterns and therapeutic outcomes among patients with preeclampsia. Complete recommended therapy was operationally defined as the administration of antihypertensive agents in combination with at least one adjunct therapy, including anticonvulsants (e.g., magnesium sulfate) or corticosteroids, in accordance with the Indonesian National Guideline for Medical Services (PNPK) on preeclampsia management issued by the Indonesian Society of Obstetrics and Gynecology (POGI). Patients were considered clinically eligible to receive complete recommended therapy if they had no documented contraindications to antihypertensive therapy, anticonvulsants, or corticosteroids, and had complete medical records supporting treatment evaluation. Patients were categorized as achieving target therapy if their blood pressure decreased to <140/90 mmHg after receiving treatment during hospitalization. The safety profile of antihypertensive drugs was assessed based on the classification criteria of the United States Food and Drug Administration (US FDA) and the Australian Therapeutic Goods Administration (AU TGA)[47,48], as these are widely recognized international references for evaluating drug safety in pregnancy and are commonly used in clinical research.

2.4. Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA).[46] A descriptive analysis was performed to determine patients characteristics in this study. Categorical variables were described as absolute numbers and percentages. For continuous variables, normally-distributed variables were described as mean. Chi-square or Fisher's exact test was employed to compare the number of patients who received the complete recommended therapy and achieved target therapy across each relevant patient variable. A p-value < 0.05 was considered statistically significant. Multivariate analysis was not performed in this study due to the retrospective nature of the data and limitations related to incomplete documentation of potential confounding variables, which may affect the robustness of multivariable modeling.

3. Results

A comprehensive analysis was conducted on the medical records of 832 pregnant women diagnosed with preeclampsia across two secondary hospitals. Table 1 indicates that the average age of patients with preeclampsia was 32.61±5.63 years, with an obesity BMI category of 31.22±5.64 kg/m² noted at their initial antenatal visit. The mean gestational age at the onset

Table 1. Basic characteristics of patients with preeclampsia

Variable	%	Mean (SD)	p-value of Normality test
Age (N=832)		32.61 (5.63)	0.200
Gestational Age (N=832)			
1st Trimester (N=8)	0.96		
2nd Trimester (N=33)	3.97	36.56 (3.33)	0.200
3rd Trimester (N=791)	95.07		
BMI (N=832)			
Underweight (N=0)	0		
Normal (N=95)	11.42	31.22 (5.64)	0.200
Overweight (N=257)	30.89		
Obesity (N=480)	57.69		
Gravida state (N=832)			
1 (N=317)	38.10		
2 (N=257)	30.89		<0.001
≥3 (N=258)	31.01		
Systolic at admission (N=832)		156.87 (21.83)	<0.001
Diastolic at admission (N=832)		97.04 (13.31)	0.200
Admission Period (N=832)			
Pre COVID-19 Pandemic (2019) (N=303)	36.42		
During COVID-19 Pandemic (2020-2021) (N=307)	36.90		<0.001
Post COVID-19 Pandemic (2022-2024) (N=222)	26.68		

Table 2. Prescribing patterns among hospitalized patients with preeclampsia

Prescribing Behavior	% (n)
ACEI	0
ARB	1.7 (14)
CCB	59.3 (493)
Beta Blocker	0.5 (4)
Diuretic	19.1 (159)
Anticonvulsant	61.4 (511)
Corticosteroid	33.1 (275)
Antibiotic	84.3 (701)
NSAID	74.6 (621)
Antifibrinolytic	13.2 (110)
Antiemetic	19.9 (166)
Analog prostaglandin	21.2 (176)
Electrolyte	55.9 (465)
Hormone synthesis	29.7 (247)

of preeclampsia was 36.56±3.33 weeks, with the majority of patients in their third trimester (95.07%). This study found that preeclampsia predominantly occurred in patients during their first gravida state (38.10%), followed by those in their second gravida state (30.89%). The average SBP/DBP recorded at the initial antenatal visit was 134/85, categorizing it as stage 1 hypertension.[43] Subsequently, the average recorded upon in-hospital admission was 156/97, indicating stage 2 hypertension.[43] This study compares the number of preeclampsia patients before, during, and after the COVID-19 pandemic to assess its impact. The findings indicate that cases were higher before (303 cases) and during (307 cases) the pandemic compared to after (222 cases) the pandemic. The data indicate that preeclampsia cases may not be influenced by the COVID-19 pandemic. Table 2 displays the utilization of the most often prescribed drugs at both hospitals for preeclampsia mothers. This study unexpectedly revealed that antibiotics were predominantly administered to 701 (84.3%) preeclampsia patients, followed by NSAIDs to 621 (74.6%) patients with preeclampsia. Anticonvulsants, calcium channel blockers, and electrolytes were also prescribed to hospitalized patients with preeclampsia.

Table 3 presents the patient characteristics correlated with the number of patients who received the complete recommended therapy for preeclampsia at both secondary hospitals. The study findings revealed that complete recommended therapy for preeclampsia was mostly prescribed to the preeclampsia patients with age under 35 years old (59.3%) and 100% of them were at their 3rd trimester. As many as 72.9% of the patients with less than three gravida state were also receiving the complete recommended therapy. By comparing

Table 3. Patients' characteristics linked to receiving complete recommended therapy for preeclampsia patients

Variable	Patients Receiving Complete Recommended Therapy N (%)	p-value
Age		
<35 years old (N=536)	318 (59.3)	0.346
≥35 years old (N=296)	120 (40.5)	
Gestational Age		
1st Trimester (N=4)	0 (0)	0.714
2nd Trimester (N=4)	0 (0)	
3rd Trimester (N=824)	824 (100)	
Gravida State		
<3 (N=575)	419 (72.9)	0.464
≥3 (N=257)	70 (27.2)	
COVID-19 Period		
Pre (2019) (N=303)	36 (11.9)	<0.001
During (2020-2021) (N=307)	99 (32.2)	
Post (2022) (N=222)	124 (55.9)	

Table 4. Prescribed antihypertensive drugs among preeclamptic patients with achieved target therapy (≤140/90)

Antihypertensive Therapy	Achieved Target Therapy (≤140/90)	
	N (%)	p-value
Monotherapy		
Nifedipine (N=192)	93 (48.4)	0.010
Amlodipine (N=38)	5 (13.2)	0.991
Methyldopa (N=327)	51 (15.6)	0.454
Dual therapy		
Nifedipine + Methyldopa (N=169)	10 (6.1)	<0.001
Nifedipine + amlodipine (N=10)	1 (10)	0.481
Nifedipine + Telmisartan (N=10)	0 (0)	0.154
Amlodipine + Methyldopa (N=66)	7 (10.5)	0.195
Triple therapy		
Amlodipine + Methyldopa + Valsartan (N=10)	0 (0)	0.154
Nifedipine + Nebivolol + Telmisartan (N=10)	0 (0)	0.154

the number of preeclampsia incidence based on the COVID-19 period, 55.9% patients with preeclampsia were prescribed the complete recommended therapy in the period of post COVID-19, while significantly fewer patients were receiving it before (11.9%) and during (32.2%) COVID-19 pandemic. The findings demonstrated a significant difference proportion (p-value <0.001) of preeclampsia patients received a complete recommended therapy between the range periods of COVID-19 pandemic.

According to Table 4, Methyldopa was the most frequently prescribed monotherapy among the preeclampsia patients (327 patients), however, only 15.6% of them could achieve the target therapy. Among patients undergoing monotherapy, those prescribed nifedipine achieved the target therapy most significantly (48.4%, p-value = 0.010) compared to those on monotherapy with amlodipine and methyldopa. The most prescribed dual therapy was the combination of nifedipine and methyldopa (169 patients) and 6.1% of them were significantly achieving the target therapy compared to other dual therapy (p-value ≤0.001). No patients received a combination of three different therapies could reach the targeted therapy (≤140/90).

Table 5 illustrates a comparison between the antihypertensive drugs presently prescribed and the criteria set by the US FDA and AU TGA. This analysis discovered that an enormous number of patients (63.2%) were prescribed nifedipine, which under the safety class C category according to both US FDA and AU TGA guidelines. On the other hand, Methyldopa was administered to 258 (31%) patients, classified as safety category class B based on US FDA guidelines and class A according to AU TGA guidelines. Despite being classified as Category C, nifedipine has demonstrated efficacy in reducing blood pressure in preeclampsia.[11] Nevertheless, careful risk-benefit monitoring remains essential during its administration in patients with preeclampsia.

4. Discussion

This study aimed to evaluate prescribing patterns, therapeutic outcomes, and the safety of antihypertensive drugs among hospitalized patients with preeclampsia in secondary hospitals. The findings showed that nifedipine was the most frequently prescribed antihypertensive, while methyldopa and combination therapy with nifedipine were associated with achieving target blood pressure.

Table 5. Prescribed Antihypertensive Therapy among Preeclamptic Patients According to Safety Category

Drug Name	US FDA* Category	AU TGA** Category	% (n)
Methyldopa oral	B	A	31 (258)
Nifedipine	C	C	63.2 (526)
Amlodipine	C	C	4.2 (35)
Nebivolol (Linoven)	Fetal risk cannot be ruled out	C	0.4 (3)
Valsartan	Fetal risk cannot be ruled out	D	0.4 (3)
Telmisartan (Tinov)	Fetal risk cannot be ruled out	D	0.8 (7)

** United States Food and Drug Administration (US FDA) pregnancy categories*
***Australian Therapeutic Goods Administration (AU TGA) pregnancy categories*

Complete recommended therapy was more commonly administered among patients in the third trimester and those with lower gravida status. In addition, most prescribed antihypertensive drugs were classified as category C, highlighting the importance of careful risk–benefit consideration in clinical practice.

Hypertension in pregnancy is a significant global health issue that can lead to mortality for both the mother and the fetus. The data in this study signified that the average age of most preeclampsia patients was 32 years old (Table 1). This finding aligns with the previous study conducted by Nurizawati et al. (2021), indicating that most preeclampsia patients hospitalized at the age range of 25 and 35 years old. Since women in this age range are thought to be in their prime years for reproduction and productivity, many factors need to be taken into account while making decisions about their pregnancies and postpartum periods, particularly for working mothers. This circumstance puts them under stress and increases their risk of developing preeclampsia.12 Preeclampsia is most commonly seen in the third trimester of pregnancy, usually at 36.5 weeks of gestation, according to this study. According to a study conducted by Satish Kumar et al. (2016), 76% of preeclampsia cases occurred during this trimester which attributed to many variables, including nulliparity (never having given birth), stress, a family history of preeclampsia, and carrying multiple fetuses.[13]

This study uncovered that 57.69% of the patients belonged to the obese BMI category, with an average BMI of 31.2 kg/m2 since their first antenatal visit. Maintaining appropriate weight gain during pregnancy can significantly reduce the risk of developing preeclampsia, as excessive weight gain is correlated with increased risk.14 Weight management helps mitigate factors like hyperinsulinemia, insulin resistance, and systemic inflammation, which are crucial in preventing endothelial dysfunction and the clinical manifestations of preeclampsia.[14,15] Prior to treatment, the average blood pressure of patients was averagely measured as hypertension stage 1 at the initial antenatal visit and stage 2 at the hospitalized admission. Aligns with the previous study conducted by Ramadhan et al. (2022), reporting that preeclampsia patients typically found to have higher blood pressure since the beginning of their pregnancy and even more than 140/90 mmHg upon their admission to the hospital due to preeclampsia.[15]

This study found that the incidence of preeclampsia was elevated prior to and during the COVID-19 pandemic in comparison to the post-pandemic period. However, the proportion of preeclampsia patients receiving complete recommended therapy was significantly higher in the post-pandemic period. This situation indicates that the COVID-19 pandemic may not directly induce preeclampsia among mothers, but the lesson learn during the pandemic can influence the overall treatment practices at the hospital. Rapid discharge of stable patients16 and applying the standard of medication[17] are some of the post COVID-19 lesson learn as reported by previous studies, which then may affect the hospital staff more focus to give the optimal treatment during hospitalization. The COVID-19 pandemic has also transformed therapy delivery in hospitals by accelerating technological innovations and fostering greater collaboration among healthcare professionals. Despite initial challenges, these changes have the potential to make therapy more comprehensive by expanding access through virtual platforms and integrating family-centered care.

The low prescription rates of ACEI (0%) and ARB (1.4%) observed among preeclampsia patients in this study may be interpreted as a primary effort to mitigate the possible risks these medications pose to the developing fetus. People who take ACEI or ARB run the most prominent risk during the second and third trimesters because they might change the way the fetal kidneys work, which can be highly dangerous.18 Although both beta-blockers (BB) and calcium channel blockers (CCB) effectively lower blood pressure during pregnancy, it is documented that the use of BB may result in a reduction of birth weight.[19] Conversely, the administration of CCBs may diminish the probability of developing preeclampsia and eclampsia, while not affecting the incidence of gestational diabetes or the infant's birth weight.[20] Thus, CCB observed as the most prescribed antihypertension among the preeclampsia patients involved in this study (59.3%).

This study recorded the utilization rate of magnesium sulfate as anticonvulsants for the preeclampsia patients was found dominant as much as 61.4% (Table 2). Magnesium sulfate effectively prevents and treats preeclampsia-related complications by inducing cerebral vasodilation to counteract ischemia from vasospasm, blocking calcium-mediated neuromuscular excitability to avert seizures, and improving endothelial function through prostacyclin stimulation and platelet inhibition, ultimately halving eclampsia risk and reducing maternal mortality by 46%.[18,21,22] As recommended by the updated guideline, magnesium sulfate could also effectively acts on the central nervous system by blocking NMDA receptors.[23,24]

This study revealed that antibiotics were the most frequently prescribed drug in both hospitals, prescribed to 701 (84.3%) preeclampsia patients. Previous study also reported that approximately 80% of all

prescriptions during pregnancy were for antibiotics, and as many as 20–25% of pregnant women will be prescribed antibiotics.[4] Urinary tract infections (UTIs) are the most common diseases during pregnancy, followed by pyelonephritis, sexually transmitted infections (STIs), and upper respiratory tract infections (URTIs)[25] which might contribute to the high rates of prescribed antibiotics in this population. While the decision to use drugs during pregnancy involves considering the potential benefits against the risks, it is crucial to note that untreated infections pose significant dangers to the fetus, such as spontaneous abortion, premature birth, and low birth weight.[26,27] Unnecessary antibiotics during pregnancy are associated with increased risks of various health issues in children, including gastrointestinal infections, asthma, food allergies, obesity, inflammatory bowel disease, cerebral palsy, cancer, and neurodevelopmental disorders.[28] These risks are higher with third-trimester use or repeated antibiotic courses, as antibiotics can harm the mother's gut microbiota, potentially impairing the newborn's immune system development and resistance to infections.[29]

The utilization rate of NSAIDs in this study was 74.6%. NSAIDs are commonly recommended during pregnancy to alleviate symptoms such as fever, pain, or inflammation. However, according to AU TGA, the use of NSAIDs is classified as category C. NSAID should be avoided during pregnancy after 20 weeks gestation due to risks of fetal kidney problems leading to low amniotic fluid (oligohydramnios) and after 30 weeks due to risk of premature closure of the ductus arteriosus, with the exception of low-dose aspirin (81 mg/day) which is specifically recommended for prevention of preeclampsia in high-risk women when started between 12-16 weeks gestation.[30,31]

The administration of electrolyte fluids in this study was 55.9%, a relatively high percentage. It is due to the fact that blood electrolyte concentrations during pregnancy often undergo fluctuations that can go below or exceed the normal range.[32] Preeclampsia is usually characterized by an abnormality in the distribution of water and electrolytes, leading to sodium retention and potassium depletion. This imbalance results in a rise in peripheral vascular resistance and the development of hypertension. Administering electrolytes during pregnancy can aid in early detection and treatment of preeclampsia, as well as mitigate any detrimental impact on the pregnancy.[21]

As found in this study, a previous study also reported approximately one third of preeclampsia mothers were administered antenatal corticosteroids at the most appropriate time.[33] The recommendation of optimal timing for administering antenatal corticosteroids to mothers with pre-eclampsia is between 24 hours and 7 days before delivery, could significantly reduce the risk of respiratory distress syndrome, neonatal mortality, and perinatal mortality.[33] Strategic utilization of antenatal corticosteroids can save the condition for both the mother and the fetus.[33,34]

Pregnant women in the third trimester have a higher likelihood of developing preeclampsia due to the significant metabolic changes and its effect to lead hypertension event.[35] This study found that the majority of preeclampsia patients received completed therapy within their third trimester (824 out of 832 patients). Consistent with current study, earlier studies have also recommended the administration of comprehensive antihypertensive, anticonvulsant, and corticosteroid treatment to preeclampsia patients during the third trimester of pregnancy, as this timing optimally balances the risks of preterm birth with the severity of the condition and fetal health.[36,37] A study conducted by Hurrell et al. (2022) in the UK, 250 of 1632 preeclampsia patients gave birth before reaching 35 weeks of gestation.[33] Healthcare providers are advised to extend the pregnancy of preeclampsia patients to a minimum of 37 weeks, if feasible, to facilitate optimal fetal development while vigilantly monitoring maternal and fetal health; however, earlier delivery may be warranted if preeclampsia escalates or complications emerge that jeopardize the lives of the mother or infant.[38,39]

Table 4 portrays the administration of antihypertensive drugs to preeclampsia patients who have reached their desired treatment goal. It included the use of monotherapy and combination therapy. The majority of patients with preeclampsia in this study were given monotherapy of nifedipine (n = 192) and methyldopa (n = 327). In pregnant women, the recommended use of antihypertensive drugs begins by selecting a monotherapy, typically labetalol, nifedipine, or methyldopa, to prevent adverse effects and drug interactions, with the adjusted dosage as advised.[7,11] The use of nifedipine monotherapy results the effective dilation of both coronary and peripheral arteries without causing any anomalies in the fetal heart.[15] Moreover, Nifedipine is deemed to possess similar effectiveness as methyldopa in controlling mild to moderate hypertension during pregnancy, making it a viable choice for patients intolerant to methyldopa.[40] The higher effectiveness of nifedipine observed in this study may be explained by its rapid onset of action and potent vasodilatory effect on peripheral arteries, which allows faster reduction of blood pressure compared to centrally acting agents such as methyldopa. In addition, nifedipine is widely recommended in clinical guidelines due to its favorable efficacy profile in managing hypertension during pregnancy.[45]

According to findings from a systematic analysis of a Randomized Controlled Trial (RCT), nifedipine was found more effective than labetalol or other drugs at the same group, in reducing blood pressure with noticeable results occurring roughly one hour after the initial delivery.[7]

Through the bivariate test utilizing the chi-square test, this study demonstrated a noteworthy correlation between the administration of methyldopa monotherapy and the attainment of a therapeutic goal, yielding a p-value of 0.010. Methyldopa belongs to the central α2 agonist group, which functions by reducing the elevation of norepinephrine in smooth muscle receptors. It leads to a vasodilatory effect and makes it an effective and safe drug for lowering blood pressure during pregnancy.41 As per the POGI 2016 report, methyldopa is considered to have a wide safety margin, making it the safest option classified as safety category B by the US FDA and category A by the AU TGA.

As listed in Table 4, this study discovered a significant association between the use of combination nifedipine + methyldopa in achieving blood pressure ≤140/90 mmHg as the targeted therapy (p <0.001). The combination of methyldopa and nifedipine was the most utilized among 169 of 832 preeclampsia patients in this study. According to the PNPK guidelines 7, the concurrent use of nifedipine and methyldopa results in a synergistic interaction. A prior study compared monotherapy with Methyldopa to the combination of Nifedipine and Methyldopa, revealing the better efficacy of combination therapy over the monotherapy in lowering both systolic and diastolic blood pressure.44 Table 5 presents a comparison between the antihypertensive drugs prescribed to patients in this study based on the criteria set by the US FDA and the safety category established by the AU TGA. Angiotensin II receptor blockers (ARBs) such as valsartan and telmisartan have been classified by the US FDA and TGA as having a potential risk to the fetus, meaning that there is a possibility of harm when these drugs are prescribed.

The use of ARBs is generally not recommended during pregnancy due to their potential fetal toxicity.[42] However, the presence of ARB prescriptions in this study may reflect real-world clinical practice, where certain patients with severe or refractory hypertension are managed based on individual clinical judgment. In rare and specific cases, ARBs may be considered when the benefits of controlling severe hypertension outweigh the potential risks, particularly when first-line antihypertensive agents such as calcium channel blockers (e.g., nifedipine), beta-blockers (e.g., labetalol), methyldopa, or hydralazine are ineffective or contraindicated.[42] This would typically occur only if other first-line medications, such as calcium channel blockers (e.g., nifedipine), beta-blockers (e.g., labetalol), methyldopa, or hydralazine, are ineffective or contraindicated. In such scenarios, the patient must be fully informed about the potential risks to the fetus, including possible renal failure, lung dysplasia, cranial hypoplasia, limb contractures, and even fetal or neonatal death. Continuous and careful monitoring of both maternal and fetal health is essential, and the pregnancy should be allowed to proceed as long as clinically feasible to optimize outcomes. Ultimately, the use of ARBs during pregnancy should be a last resort, and the decision should involve a thorough discussion between the patient and healthcare provider, considering all available evidence and guidelines.

It is important to interpret these findings with caution due to the observational nature of this study. The absence of multivariate analysis limits the ability to control for potential confounding variables, such as disease severity and clinical indication, which may influence treatment selection and outcomes. For example, patients receiving combination therapy may have had more severe conditions, which could explain the lower proportion of achieving target blood pressure. Therefore, the observed associations should not be interpreted as causal relationships. The findings of this study have important clinical implications, particularly in supporting evidence-based prescribing practices in secondary hospital settings. Understanding real-world prescribing patterns and treatment outcomes may assist clinicians in selecting appropriate antihypertensive therapies while considering both effectiveness and safety for pregnant women with preeclampsia.

This study has several strengths. It provides real-world evidence from a relatively large sample size of 832 patients across multiple years, reflecting actual clinical practice in secondary hospitals. In addition, the study evaluates both prescribing patterns and treatment outcomes, as well as drug safety classification based on internationally recognized guidelines (US FDA and AU TGA), which enhances the relevance of the findings.

This study has limitations that specifically examined the prescribing behavior of preeclamptic patients during the hospitalization until they were discharged and analyzed the success of achieving the target blood pressure of 140/90 or lower when the patients went home. However, the study did not evaluate the duration of time required to lower the blood pressure based on the treatment received. Furthermore, the precise understanding of drugs suitable for use during pregnancy remains intricate due to

the scarcity of information regarding the potential benefits of these drugs for both the mother and fetus. This lack of data arose from the infrequent inclusion of pregnant women in clinical studies.

5. Conclusion

This results of study demonstrated that methyldopa and nifedipine have been mostly prescribed for the treatment of preeclampsia mothers at the secondary hospitals. Both are acknowledged for their effectiveness in reducing blood pressure and attaining the target therapy for patients with preeclampsia, while simultaneously safeguarding the fetus from the risk of impaired growth. These findings reinforce the importance of evidence-based prescribing practices to optimize maternal and fetal outcomes in preeclampsia treatment. Further research should be undertaken to ascertain the advantages of providing an effective and a complete recommended therapy for preeclampsia mothers while also focusing on keeping both the mother and fetus wellness. Thus, health workers have a crucial role in evaluating risks and selecting the most effective drugs to prevent and solve preeclampsia condition among the pregnant mothers while also enhance maternal health.

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Conflict of Interest

All authors declared that there was no conflict of interest.

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