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Research Article

Identification of Rationality and Potential Drug Interactions in Preeclampsia Patients with Comorbidities

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Abstract: Preeclampsia is one of the pregnancy complications that constitutes a major cause of maternal and fetal morbidity and mortality. Its management requires the rational and safe use of medications, as there is a potential for drug interactions that may affect therapeutic outcomes. This study aimed to evaluate the rationality of drug use and potential drug interactions in preeclampsia patients in the inpatient ward of Pertiwi Mother and Child Hospital, Makassar. This research employed a descriptive method with a retrospective approach, utilizing medical records of preeclampsia patients from January 2024 to January 2025. The evaluation of rationality was based on the "four rights" principle: right indication, right drug, right dose, and right time of administration. The results of this study showed that the majority of patients received rational pharmacotherapy, with nifedipine being the most commonly used antihypertensive drug. The potential drug interactions identified were predominantly of moderate severity. The findings indicate that, overall, drug use among preeclampsia patients in this hospital has not yet been fully rational, and the presence of potential drug interactions requires careful consideration in clinical practice.

Keywords: preeclampsia; rational drug use; drug interactions

1. INTRODUCTION

Pregnancy is a physiological process that may be accompanied by complications such as preeclampsia, the second leading cause of maternal death after hemorrhage [1]. Preeclampsia is hypertension occurring after the 20th week of gestation, accompanied by proteinuria and impaired placental function [2]. Hypertension in pregnancy is a global health problem and is classified into four categories according to the ISSHP: gestational hypertension, preeclampsia–eclampsia, chronic hypertension, and preeclampsia superimposed on chronic hypertension [3]. Hypertension during pregnancy can occur in all pregnant women and may lead to organ damage and maternal death [4]. High blood pressure in pregnancy is one of the leading causes of maternal mortality worldwide, with Indonesia's maternal mortality ratio reaching 420 per 100,000 live births [5]. In Indonesia, hypertension is the second leading cause of maternal death after hemorrhage, with gestational hypertension accounting for nearly 30% of maternal deaths (Ministry of Health of the Republic of Indonesia).

Preeclampsia, as a form of gestational hypertension, is a major cause of maternal morbidity and mortality [6]. It accounts for approximately 70,000 maternal deaths and 500,000 fetal or neonatal deaths annually [7]. South Sulawesi is among the provinces with a high maternal mortality rate, which increased from 133 cases in 2020 to 195 cases in 2021, largely due to limited access to healthcare

services and preeclampsia. Risk factors for hypertensive disorders of pregnancy include maternal age, parity, multiple pregnancies, a history of hypertension, and obesity [4]. The management of preeclampsia involves the use of antihypertensive agents such as nifedipine, methyldopa, and magnesium sulfate ($MgSO_4$), with careful consideration to ensure that drug selection is both safe and rational [8][9].

Medications can affect uteroplacental blood flow, making drug selection crucial [10], and the use of a single agent is generally recommended [11]. Drug Utilization (DUE) is essential to prevent irrational prescribing and potential drug interactions [12], as such interactions may reduce therapeutic effectiveness and increase the risk of morbidity [13][14][15]. Based on these considerations, the authors conducted a study on drug use in preeclampsia patients in the inpatient ward of Pertiwi Mother and Child Hospital, Makassar, assessing the appropriateness of indication, drug selection, dosage, duration, and potential drug interactions.

2. MATERIALS AND METHODS

2.1. Research Design

This study employed a descriptive observational design with a retrospective approach and quantitative analysis, using secondary data from the medical records of preeclampsia patients in the inpatient ward of Pertiwi Mother and Child Hospital, Makassar. The data reviewed included demographics, therapy (drug name, dosage, and time of administration), symptoms, drug interactions, and diagnoses. The assessment of drug use rationality encompassed the appropriateness of indication, drug selection, dosage, and timing of administration.

2.2. Study Period and Location

The study was carried out at Pertiwi Mother and Child Hospital, Makassar, Indonesia, over the period of February to March 2025.

2.3. Study Population and Sample

The population comprised all preeclampsia patients in the inpatient ward of Pertiwi Mother and Child Hospital, Makassar, from January 2024 to February 2025. The sample was selected using a total sampling technique based on the inclusion criteria: patients diagnosed with preeclampsia, blood pressure ≥140/90 mmHg, receiving antihypertensive therapy, having complete medical records, with or without comorbidities. The exclusion criteria were non-preeclampsia patients and incomplete medical records.

2.4. Data Analysis

Potential drug interactions were analyzed using the database at www.drugs.com and processed with SPSS, presented in tables descriptively to determine the frequency and percentage of patient characteristics, patterns of drug use, and drug interactions.

3. RESULTS AND DISCUSSION

This study employed secondary data from 66 preeclampsia patients who were hospitalized at Pertiwi Mother and Child Hospital, Makassar, between January 2024 and January 2025. Patient characteristics were analyzed based on age, educational level, occupation, blood pressure, parity, comorbidities, number of medications, and length of hospital stay.

3.1. Respondent Characteristics

The majority of respondents were aged 20–35 years (69.7%), had a senior high school education (60.6%), worked as housewives (56.1%), experienced severe preeclampsia (47.0%), were classified as

multigravida (39.4%), had no comorbidities (57.6%), and were hospitalized for 1–3 days (57.6%). In contrast, the smallest proportions were in the categories of age <20 years (4.5%), elementary school education (3.0%), unemployed (4.5%), mild preeclampsia (19.7%), grandemultigravida (27.3%), comorbidity in the form of hypertension (30,3%), and a length of hospital stay of 4–8 days (42.4%).

Table 1. Frequency Distribution of Preeclampsia Patient Characteristics by Age, Education Level, Occupation, Preeclampsia Classification, Parity, Comorbidities and Length of Hospital Stay

No		Characteristic	Frequency (n)	Percentage (%)
1.	Age	<20 Years	3	4.5
		20-35 Years	46	69.7
		>35 Years	17	25.8
		Total	66	100
2.	Education Level	Elementary School	2	3
		Junior High School	12	18.2
		Senior High School	40	60.6
		Diploma/Bachelor's Degree	12	18.2
		Total	66	100
3.	Occupation	Unemployed	3	4.5
		Honorary Worker	4	6.1
		Housewife	37	56.1
		Private Employee	9	13.6
		Civil Servant	4	6.1
		Entrepreneur	9	13.6
		Total	66	100
4.	Preeclampsia Classification	Mild PE : 140/90 mmHg-149/90mmHg	13	19.7
		Moderate PE : 150/100 mmHg-159/109 mmHg	22	33.3
		Severe PE : ≥160/110 mmHg	31	47
		Total	66	100
5.	Parity	Primigravida	22	33.3
		Multigravida	26	39.4
		Grandemultigravida	18	27.3
		Total	66	100
6.	Comorbidities	No. Comorbiditi	38	57.6
		Asthma	6	9.1
		Hypertension	20	30.3
		Heart Disease	1	1.5
		Tuberculosis	1	1.5
		Total	66	100
7.	Length of Hospital Stay	1-3 Days	38	57.6
		4-8 Days	28	42.4
		Total	66	100

Source : Secondary Data, 2025

Notes: Preeclampsia Classification = Mild Preeclampsia : 140/90 mmHg-149/99 mmHg; Moderate Preeclampsia : 150/100 mmHg-159/109 mmHg; Severe Preeclampsia : ≥160/110 mmHg ⏐Parity Characteristics = Primigravida : Woman in her first pregnancy; Multigravida : Woman in her second to fourth pregnancy; Grandemultigravida : Woman with more than five pregnancies

Based on Table 1, the majority of patients were in the 20–35-year age group (69.7%). Although this age group is considered the safe reproductive age, the results indicate that preeclampsia does not occur exclusively in high-risk age groups (<20 years and >35 years). This finding is consistent with Rumampuk, who stated that age is not the sole risk factor for severe preeclampsia [7]. In terms of education, most patients had completed senior high school (60.6%), indicating a potential limitation in understanding health information, which may affect preeclampsia prevention. However, these results also demonstrate that both higher and lower educational levels remain at risk of developing preeclampsia. Rumampuk emphasized that a mother's knowledge and attitudes are not solely determined by formal education but also by decision-making abilities [7].

In terms of occupation, the majority of patients were housewives (56.1%). Domestic work, which is often perceived as light, still poses risks due to potential stress and excessive physical activity. Sartika and Wardani emphasized that a mother's workload is not solely derived from employment outside the home [16]. The distribution of blood pressure showed that nearly half of the patients (47%) experienced severe preeclampsia (≥160/110 mmHg). Blood pressure during pregnancy is strongly influenced by lifestyle and genetic factors. Handayani highlighted the importance of early detection and appropriate management [17].

Based on parity, multigravida (second to fifth pregnancy) constituted the largest group (39.4%). Although primigravida is often associated with preeclampsia, these findings indicate that the risk remains high in subsequent pregnancies, particularly in those with a history of preeclampsia. Supiani and Wirastri stated that the reproductive system of mothers who have experienced previous pregnancies may also contribute to an increased risk. A total of 18.2% of patients had comorbidities, with hypertension being the most prevalent (12.1%). This reinforces that comorbidities, particularly chronic hypertension, are major risk factors for preeclampsia. Halim highlighted the importance of early detection to reduce the risk of complications for both mother and fetus [18].

In terms of length of stay, the majority of patients were hospitalized for 1–3 days (57.6%). Length of stay is strongly influenced by the presence of comorbidities, fetal abnormalities, and postnatal conditions. Cases of severe preeclampsia tend to require longer hospitalization [19]. Polypharmacy was observed in 87.9% of patients, reflecting the high complexity of preeclampsia management. While polypharmacy is often necessary to control symptoms and prevent complications, it can increase the risk of drug interactions, adverse effects, and prolonged hospitalization. Kusuma Wardhany and Rizki emphasized that polypharmacy in patients with complications should be managed with caution due to its potential to cause drug interactions [20], [21].

3.2. Characteristics of Drug Use Rationality and Potential Drug Interactions

Of the 66 preeclampsia patients, 50 (75.8%) received rational treatment, while 16 (24.2%) received irrational treatment. A total of 62 respondents (93.9%) experienced potential drug interactions, whereas 4 respondents (6.1%) did not. Among the 64 identified drug interactions, the majority were classified as moderate (43 cases; 67.5%), followed by minor (12 cases; 18.5%) and major (9 cases; 14.0%). Of the 69 interactions, 47 (68.2%) were pharmacodynamic and 22 (31.8%) were pharmacokinetic. Based on the number of drugs used, most respondents (87.9%) received ≥5 types of drugs, while 12.1% received <5 types of drugs.

Table 2. Distribution of Drug Use Rationality and Potential Drug Interactions

No.	Characteristic		Frequency (n)	Percentage (%)
1.	Drug Use Rationality	Rational	50	75.8
		Not Rational	16	24.2
		Total	66	100
2.	Potential Drug Interactions	Interaction Occurred	62	93.9
		Not Interaction	4	6.1
		Total	66	100
3.	Types of Drug Interactions	Major	9	14
		Moderate	43	67.5
		Minor	12	18.5
		Total	64	100
4.	Mechanisms of Drug Interactions	Pharmacodynamic	47	68.2
		Pharmacokinetic	22	31.8
		Total	69	100
5.	Polypharmacy	<5 Drugs	8	12.1
		≥5 Drugs	58	87.9
		Total	66	100

Source : Secondar Data, 2025

Notes: Characteristics of drug interaction types = Minor: Represents a mild severity level that does not cause significant clinical impact and generally does not require therapeutic intervention; Moderate: Represents a moderate severity level that may affect the patient's clinical condition and may require therapy adjustment or closer monitoring; Major: Represents a severe severity level that has the potential to cause serious impact, endanger life, or require discontinuation or major changes in therapy

Table 2 shows that the assessment of drug use rationality was based on the "four rights" principle: right indication, right drug, right dose, and right time of administration. Treatment was categorized as rational if all these aspects were fulfilled. For the right indication aspect, all patients met the criteria as they had been diagnosed with preeclampsia with blood pressure ≥140/90 mmHg, and drugs such as nifedipine and methyldopa were administered according to the indication. Regarding the right drug aspect, most therapies were in accordance with clinical guidelines; however, the use of mefenamic acid was still found in pregnant women with hypertension, which may cause serious adverse effects [22].

For the right dose and time aspects, most patients received appropriate dosages and dosing intervals, particularly nifedipine 10 mg three times daily (Irghi Fahrezy et al., 2025), although some inconsistencies in time recording were noted. A total of 62 patients (93.9%) experienced drug interactions, with moderate severity being the most frequent (64 cases or 57.1%), followed by minor (30 cases) and major (18 cases). The most common interaction occurred between nifedipine and mefenamic acid, which can increase the risk of acute kidney failure [15]. Based on the mechanism, pharmacodynamic interactions predominated (69.1%), while pharmacokinetic interactions were less common (30.9%). Understanding these mechanisms is essential for determining strategies to manage drug interactions [23].

3.3. Drug Use by Therapeutic Class and Drug Name

The most frequently used drug in preeclampsia patients was nifedipine (56 respondents/84.8%), followed by paracetamol (47 respondents/71.2%), mefenamic acid, and Livron B-Plex (each 45 respondents/68.2%). The least frequently used drugs, each administered to only one

respondent (1.5%), were candesartan, cefazolin, cefotaxime, fentanyl, phenobarbital, metoclopramide, bromhexine, ambroxol, OBH, and oral contraceptive pills.

Table 3. Distribution of Drug Use by Therapeutic Class and Drug Name in Preeclampsia Patients (n=66)

No.	Drug Class	Drug Name	Frequency (n)	Percentage (%)
1.	Antihypertensive (Calcium Channel Blocker)	Nifedipine	56	10.9
		Amlodipine	4	0.8
	Antihypertensive (Alpha-2 receptor agonist)	Methyldopa (Dopamet)	2	0.4
	Antihypertensive (Angiotensin II Receptor Blocker)	Candesartan	1	0.2
2.	Analgesic & Antipyretic	Paracetamol	47	9.1
	Analgesic (NSAID)	Mefenamic Acid	45	8.7
		Ketoprofen (Pronalges)	30	5.8
		Ketorolac	9	1.7
	Opoid Analgesic	Tramadol	9	1.7
		Fentanyl	1	0.2
3.	Antibiotics (First Generation Cephalosporins)	Cefadroxil	38	7.4
		Cefazolin	1	0.2
	Antibiotics (Third Generation Cephalosporins)	Cefixime	2	0.4
		Cefotaxime	1	0.2
		Ceftriaxone	37	7.2
	Antibiotics (Penicillin)	Amoxicillin	3	0.6
4.	Antibiotik & Antiprotozoa	Metronidazole	23	4.5
	Anticonvulsants & Electrolytes	Magnesium Sulfate (MgSO4)	36	7
	Anticonvulsant (Barbiturate)	Phenobarbital	1	0.2
5.	Antiemetic (5-HT3 Receptor Antagonist)	Ondansetron	7	1.4
	Antiemetic & Prokinetic	Metoclopramide	1	0.2
6.	Mucolytic	Bromhexine (Solvinex)	1	0.2
		Ambroxol	1	0.2
7.	H2 Receptor Antagonist	Ranitidine	7	1.4
8.	Proton Pump Inhibitor	Omeprazole	2	0.4
9.	Local Anesthetic	Bupivacaine (Bucain)	3	0.6
10.	Sympathomimetic	Ephedrine	2	0.4
11.	Uterotonic (Ergot Alkaloid)	Methylergometrin	9	1.7
	Uterotonic (Prostaglandin E1 Analog)	Misoprostol	4	0.8
	Uterotonic (Oxytocin)	Oxytocin	47	9.1
12.	Corticosteroid	Dexamethasone	17	3.3
13.	Diuretic (Loop Diuretic	Furosemide	4	0.8
14.	Antifibrinolytic (Hemostatic)	Tranexamic Acid	7	1.4
15.	Expectorant & Antitussive	OBH	1	0.2
16.	Vitamin B Complex Supplement	Livron B-Plex	45	8.7

	Vitamin A Supplement	Vitamin A	10	1.9
17.	Hormonal Contraceptive (Estrogen-Progestin)	Oral Contraceptive Pill	1	0.2
Total			576	100

Source : Secondary Data, 2025

Table 3 shows that the most frequently used antihypertensive therapy was the Calcium Channel Blocker class, specifically nifedipine, administered to 56 patients (10.9%). Nifedipine is used as the first-line therapy in preeclampsia patients because it is effective in reducing blood pressure, creatinine, urea, and 24-hour urinary protein without disrupting arterial blood flow. It also carries a low risk of hypotension, is cost-effective, easily accessible, and does not require special storage conditions [24].

Some patients did not receive antihypertensive therapy and were directly administered an anticonvulsant, namely magnesium sulfate ($MgSO_4$). In such cases, seizure prevention becomes the primary priority; therefore, $MgSO_4$ is administered immediately, even before or concurrently with antihypertensive drugs. As explained by Amalia (2023), when preeclampsia progresses to seizures, the condition is defined as eclampsia. Eclampsia may occur in cases of severe preeclampsia, characterized by systolic blood pressure ≥160 mmHg and diastolic blood pressure ≥110 mmHg, accompanied by proteinuria exceeding 5 g/24 hours. Primary management focuses on preventing seizures in preeclampsia–eclampsia, which can be achieved through the administration of $MgSO_4$. Magnesium sulfate has been used for over a century to treat preeclampsia and eclampsia, and it remains the anticonvulsant of choice for both seizure prophylaxis in preeclampsia and seizure control in eclampsia [24].

3.4. Relationship between Patient Characteristics and The Incidence of Drug Interaction

Of the 66 preeclampsia patients, 28 (42.4%) had comorbidities, among whom 24 (36.4%) experienced drug interactions and 4 (6.1%) did not. In contrast, all 38 patients (57.6%) without comorbidities experienced drug interactions. Statistical analysis showed a significant association between comorbidities and the occurrence of drug interactions ($p = 0.016$).

Table 4. Association between Comorbidities and the Occurrence of Drug Interactions in Preeclampsia Patients

Characteristic	Drug Interaction Occurred n (%)	No Drug Interaction n (%)	Total	P-value
With Comorbidities	24 (36.4%)	4 (6.1%)	28 (42.4%)	0.016
Without Comorbidities	38 (57.6%)	0 (0%)	38 (57.6%)	
Total	62 (93.9%)	4 (6.1%)	66 (100%)	

Source : Secondary Data, 2025

Table 4 presents the relationship between the presence of comorbidities and the occurrence of potential drug interactions among preeclampsia patients. The statistical analysis revealed a significant association ($p = 0.016$), indicating that comorbidities play an important role in the likelihood of drug interactions. Among the 28 patients with comorbidities, 24 (36.4%) experienced potential drug interactions, while 4 (6.1%) did not. In contrast, all 38 patients (57.6%) without comorbidities experienced at least one potential drug interaction [25].

Of the 66 preeclampsia patients, 58 (87.9%) experienced polypharmacy, and 57 of them (86.4%) had drug interactions. Conversely, among the 8 patients without polypharmacy, 5 (7.5%) experienced drug interactions, while 3 (4.5%) did not. There was a significant association between polypharmacy and drug interactions (p = 0.001).

Table 5. Association between Polypharmacy and the Occurrence of Drug Interactions in Preeclampsia Patients

Characteristic	Drug Interaction Occurred n(%)	No Drug Interaction n(%)	Total	P-Value
Polypharmacy	57 (86.4%)	1 (1.5%)	58 (87.9%)	
No Polypharmacy	5 (7.5%)	3 (4.5%)	8 (12.1%)	0.001
Total	62 (93.9%)	4 (6.1%)	66 (100%)	

Source : Secondary Data, 2025

Table 5 shows a significant association between polypharmacy (≥5 drugs) and drug interactions (p = 0.001). The greater the number of drugs used, the higher the potential for interactions [21]. In addition to polypharmacy, Table 7 indicates that drug use rationality also influences the occurrence of drug interactions (p = 0.015). Of the 62 patients who experienced drug interactions, 49 (79.0%) were in the irrational drug use group. This suggests that non-adherence to the "four rights" principle contributes to the risk of drug interactions, as explained by Ilmi [26].

Of the 66 patients, 50 (75.8%) received rational treatment and 16 (24.2%) received irrational treatment. In the rational group, 49 (74.2%) experienced drug interactions and 1 (1.5%) did not. In the irrational group, 13 (19.7%) experienced drug interactions and 3 (4.5%) did not. There was a significant association between treatment rationality and drug interactions (p = 0.005).

Table 6. Association between Drug Use Rationallity and Drug Interactions in Preeclampsia Patients

Characteristic	Drug Interaction Occurred n (%)	No Drug Interaction n (%)	Total	P-Value
Rational	49 (74.2%)	1 (1.5%)	50 (75.8%)	
Irrational	13 (19.7%)	3 (4.5%)	16 (24.2%)	0.005
Total	62 (93.9%)	4 (6.1%)	66 (100%)	

Source : Secondary Data, 2025

Table 6 out of 66 patients, 50 patients (75.8%) received rational treatment, while 16 patients (24.2%) received treatment categorized as irrational. In the rational drug use group, 49 patients (74.2%) experienced drug interactions, whereas 1 patient (1.5%) did not. Meanwhile, in the irrational drug use group, 13 patients (19.7%) experienced drug interactions, and only 3 patients (4.5%) did not. Statistical analysis showed a significant association between the rationality of drug use and the occurrence of drug interactions, with a p-value of 0.005 ($p < 0.05$) [27].

4. CONCLUSION

This study indicates that drug use in preeclampsia patients at Pertiwi Mother and Child Hospital, Makassar, is not yet fully rational, as some drugs contraindicated in pregnant women were still used. Potential drug interactions were found in the majority of patients (93.9%), with most interactions classified as moderate in severity and primarily pharmacodynamic in mechanism. Patient characteristics such as age, parity, blood pressure, and comorbidities contribute to therapy complexity and the risk of polypharmacy. Healthcare professionals, especially physicians and

pharmacists, need to enhance monitoring of potential drug interactions to ensure patient safety. The hospital is advised to optimize periodic evaluations of drug use rationality through the involvement of clinical pharmacy teams. Further research is expected to include analyses of the clinical effects of drug interactions on maternal and neonatal outcomes, as well as to cover a broader population.

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