



A RATIONALITY STUDY OF ANTIHYPERTENSIVE DRUGS USAGE IN PREECLAMPSIA PATIENTS IN THE PRIVATE HOSPITAL

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Abstract

Preeclampsia is a hypertension that happens in pregnancy of ≥ 20 weeks and occurs with proteinuria. Preeclampsia is also the highest cause of mother's death second place in Indonesia. According to that, a study of rationality is needed concerning medicine usage as one of the efforts to determine which medicine is accepted by the rational patient so that the expected therapeutic effect is achieved and does not harm the lives of the mother and baby. The purpose of this research is to determine the profile and rationality of anti-hypertension medicine usage on pregnant mothers with preeclampsia at a private hospital in Malang. This is an observational descriptive research that uses retrospective data. The sample-taking method of this research is using a total sampling method. This research data is served on a diagram or table and percentage. The result of this research is that 3 kinds of anti-hypertension medicine are used: nifedipine 78%, amlodipine 17%, and candesartan 5%. The rationality study of the use of antihypertensive drugs in this study obtained 78% correct indication, 100% correct drug, 93% correct dose, 62% correct interval of administration, and 100% correct patient. This study shows that the usage of antihypertensive drugs in preeclampsia is rational in several parameters.

Keywords: *rationality, preeclampsia, anti-hypertension, calcium channel blocker, nifedipine*



Background

The maternal mortality rate (MMR) reaches 462/100,000 live births in developing countries and 11/100,000 live births in developed countries (WHO, 2020). In 2020, the number of maternal deaths collected from the recording of family health programs at the Ministry of Health (Kemenkes) showed 4,627 deaths in Indonesia. This number shows an increase compared to 2019 of 4,221 deaths (Ministry of Health, 2021). The maternal mortality rate in East Java province itself also increased, reaching 89.81 per 100,000 live births in 2019 and rising in 2020 to reach 98.39 per 100,000 live births. The highest cause of maternal death in 2020 in East Java province was hypertension in pregnancy, namely preeclampsia by 26.90% (East Java Health Office, 2021).

Preeclampsia is hypertension that arises after 20 weeks of gestation, this hypertension is accompanied by proteinuria, preeclampsia is divided into 2, namely preeclampsia without severe symptoms and severe preeclampsia. The condition of preeclampsia needs to be treated appropriately because preeclampsia can cause serious complications in the mother and fetus. Complications can occur in both the mother and fetus. includes maternal complications and fetal complications that can be life-threatening (Setyawati *et al.*, 2018). Therefore, the handling of preeclampsia needs to be considered so that MMR in Indonesia, especially in East Java, does not increase.

Treatment of preeclampsia can be done with the use of drugs. Drugs or therapies that are generally given to preeclampsia patients are antihypertensives. The use of drugs in the treatment of preeclampsia must be done rationally and with special attention which must be considered safety and side effects so as not to harm the mother and fetus. The rationality of drug use can be done with several parameters, including the right assessment of the patient's condition, correct indications, right diagnosis, right dose, right drug, right administration, right way of administration, being aware of side effects, right duration of administration, drugs must be effective, right information, correct follow-up, right drug delivery, and patient compliance (Directorate of Pharmaceutical Services, 2011).

Previous research conducted by Simatupang and Ida (2021) on the evaluation of the administration and use of antihypertensive drugs in severe preeclampsia patients at RSU X Jakarta was assessed using four parameters obtained results, namely the percentage of administration and use of antihypertensive drugs in severe preeclampsia patients showed 91.9% right indications, 86.72% right drugs, 96.9% right patients and 5.26% right dose. Based on previous research data, it is known that the use of antihypertensive drugs in pregnant women with preeclampsia is still found irrational. Based on this, researchers intend to conduct a study on the rationality of using antihypertensive drugs in pregnant women with preeclampsia in different places using 5 parameters that will be observed through medical record data, consisting of the right indications, right drugs, right doses, right patients, and right intervals of administration. The purpose of this study was to determine the profile and rationality of the use of antihypertensive drugs in pregnant women with preeclampsia.

Material and Methods

Method

This study is an observational study with a retrospective *cross-sectional* study design using medical record data of pregnant women with preeclampsia in one of the private hospitals in Malang for the 2019-2021 period. The total sampling used in this study was medical record data of patients

with preeclampsia who were treated with antihypertensive drugs. This research has received ethical permission with number 038/LE.003/III/03/2022.

Tools and Materials

The tools used are data collection sheets, reference standards for national guidelines for Medical Services 2016, Rational Drug Use Module 2011, *Queensland Clinical Guideline* 2021, and supporting libraries. The material used in this study is medical record data of preeclampsia patients for 2019-2021 at private hospitals in Malang City.

Data Analysis

Data analysis is presented in the form of reports descriptively. The collected data analyzed the profile and rationality of the use of antihypertensive drugs in preeclampsia patients. The data obtained is presented in the form of tables or diagrams and percentages using Microsoft Excel 2010.

Results and discussion

a. Demographics of preeclampsia patients

1. Age

Table I. Age of preeclampsia patients

Age	Number of patients	Percentage
20-35 years	14	78%
<20 years or > 35 years	4	22%

Table I shows that patients aged 20-35 years have the highest percentage at 78%. Age is related to increased or decreased body functions that affect health status. Maternal age is one of the determining factors for maternal and fetal health status during pregnancy. The safest period for pregnancy and childbirth is during reproductive age because, at that age, the risk of complications during pregnancy is lower. This reproductive age is usually in the range of 20-35 years (Novianti, 2016). Age is also a risk factor for preeclampsia, but there are other factors such as genetics, gravida, twin pregnancies, and history of the disease (Pulungan *et al.*, 2020).

2. Gestational Age

Table II. Gestational age of preeclampsia patients

Gestational Age	Number of patients	Percentage
2nd trimester (14-28 weeks)	0	0%
3rd trimester (28-42 weeks)	18	100%

Table II shows that the highest percentage occurs in the 3rd trimester of pregnancy, which is as much as 100%. Trimester 3 is the gestational age ranging from 28-40 weeks to 7-9 months.

Compared to pregnancy aged < 28, trimester 3, or gestational age \geq 28 weeks, mothers have a greater chance of experiencing preeclampsia so mothers are advised to do regular check-ups when the gestational age enters 28 weeks (Dewie, 2020). The older the gestational age, the risk of preeclampsia sufferers will be greater. At 27 weeks gestation and above there can be an increase in blood pressure and an increase in body weight due to the increasing volume of the uterus, especially in the 3rd trimester of pregnancy (Manalu, 2015). The results of this study are the same as the results of previous research conducted by Simatupang (2021), namely the highest percentage of preeclampsia incidence occurs in the 3rd trimester of pregnancy at 99.3%.

3. Diagnosis

Table III. Diagnosis of preeclampsia patients

Diagnosis	Number of patients	Percentage
Preeclampsia without severe symptoms	1	6%
Severe preeclampsia	17	94%

Table III shows that the highest percentage occurs in patients diagnosed with severe preeclampsia, which is 94%. The more significant percentage of severe preeclampsia compared to the incidence of preeclampsia without severe symptoms can be caused because severe symptoms do not accompany preeclampsia without severe symptoms, so patients are often unaware and too late to be treated (Setyawan, 2019). The results of this study are in accordance with research conducted by another study conducted by Retnosari (2021), which also received similar results, the highest percentage of preeclampsia distribution is severe preeclampsia, which is 58.1%.

b. Profile of Use of Antihypertensive Drug

Table IV. Profile of antihypertensive drug usage

Antihypertensive drug	Number of patients	Percentage %
Nifedipine	14	78%
Amlodipine	3	17%
Candesartan	1	5%

Table IV shows that the widely used antihypertensive therapy is nifedipine with a percentage of 78%. This is in accordance with Saputri's research (2020) which found that the most frequently used monotherapy antihypertensive drug at RSUD Jend. Ahmad Yani Metro in 2019 for severe preeclampsia patients is the *Calcium Channel Blocker* (CCB) group, namely nifedipine. This is also in accordance with the 2016 preeclampsia PNPk therapy guidelines which state that nifedipine is one of the first choice antihypertensives that is safe to use for pregnant women with preeclampsia. According to the 2016 PNPk guidelines, the first choice of antihypertensives for preeclampsia patients other than nifedipine is hydralazine and labetalol parenterally, while other alternative antihypertensive administrations are nitroglycerin and methyldopa. Nifedipine drugs are ideal antihypertensives for the treatment of preeclampsia because nifedipine drugs have a rapid onset, can be given orally, and effectively lower blood pressure without causing harmful side effects.

Nifedipine drugs are ideal antihypertensives for the treatment of preeclampsia because nifedipine drugs have a rapid onset, can be given orally, and effectively lower blood pressure without causing harmful side effects. In contrast to methyldopa, although the antihypertensive drug methyldopa is widely used in preeclampsia patients. However, it has less effect on some patients because the onset of methyldopa is only 3-6 hours so it is often combined with other antihypertensive drugs (Kundarto, 2021). Nifedipine drug therapy in preeclampsia patients is also better when compared to labetalol. In addition to the rapid onset, nifedipine also has a more affordable price. It is easier to administer orally than labetalol which is more expensive and needs to be given intravenously (Tahar *et al.*, 2021). Nifedipine is also more widely used than hydralazine. However, hydralazine and nifedipine are effective at lowering blood pressure for emergency hypertension in pregnancy and there are no significant side effects from either. However, nifedipine therapy is preferred because the dose is fixed, easy to administer, easy to obtain, and the price is relatively cheap (Alatas, 2019).

c. Study of the rationality of the use of antihypertensive drugs

Rational drug use is the process of prescribing, dispensing, and using appropriate drugs by patients for diagnosis, prevention, and treatment of diseases (Mamo, 2020). In upholding the rationality of treatment, there are 14 parameters mentioned in the module on the rational use of medicine. (Directorate of Pharmaceutical Services, 2011). These 14 parameters can be used for various treatments, including antihypertensive treatment in preeclampsia. In the use of antihypertensive drugs in preeclampsia, rationality is established using several parameters, namely: right indications, right drug, right dose, right interval of administration, and right patient.

1. Exact indications

The accuracy of disease indications is the accuracy of choosing drugs that suit the needs of patients based on the diagnosis established (Sa'idah, 2019). The study of the accuracy of indications on the use of antihypertensive drugs in pregnant women with preeclampsia in this study is seen from the accuracy of the selection of antihypertensive drugs in accordance with the diagnosis established based on the patient's clinical condition and listed in **Table V**.

Table V. Antihypertensive therapy is given to pregnant women with preeclampsia at a private hospital in Malang

Medical Record Number (RM)	Class of Antihypertensive Drugs given	PNPK Preeclampsia 2016 Reference Standard	Exact/ Not Precise
xxx055	Nifedipine orally	Nifedipine orally	True
xxx551	Nifedipine orally	Nifedipine orally	True
xxx815	Nifedipine orally	Nifedipine orally	True
xxx268	Nifedipine orally	Nifedipine orally	True
xxx663	Nifedipine orally	Nifedipine orally	True
xxx413	Amlodipine orally	-	Not Exactly
xxx332	Nifedipine orally	Nifedipine orally	True
xxx430	Amlodipine orally	-	Not Exactly
xxx767	Nifedipine orally	Nifedipine orally	True
xxxx587	Amlodipine orally	-	Not Exactly
xxx291	Nifedipine orally	Nifedipine orally	True

xxx166	Nifedipine orally	Nifedipine orally	True
xxx203	Nifedipine orally	Nifedipine orally	True
xxx913	Nifedipine orally	Nifedipine orally	True
xxx825	Nifedipine orally	Nifedipine orally	True
xxx910	Nifedipine orally	Nifedipine orally	True
xxx636	Candesartan orally	-	Not Exactly
xxx803	Nifedipine orally	Nifedipine orally	True

Based on the exact indication study that has been conducted on 18 medical records of pregnant women with preeclampsia, 14 precise medical records of disease indications were obtained with a percentage of 78%. The antihypertensive drug given is oral nifedipine. The results of this study are not much different from the results of research by Saputri *et al.*, (2020) which stated that 83.33% were indicated.

2. Exact drug

Drug accuracy is the accuracy of choosing the type of drug based on the consideration of the magnitude of benefits and risks by paying attention to the effectiveness of the drug (Sa'idah, 2019). The study of the rationality of the use of antihypertensive drugs with the parameters of the accuracy of drug selection in this study is seen from the accuracy of the selection of antihypertensive drug classes that are safe for pregnant women and compared with the 2016 Preeclampsia PNPk reference standard, and seen from whether or not antihypertensive drugs are safely used in pregnant women based on the *Pregnancy Risk Category* of the drug. The exact parameters of this drug were only carried out on 14 medical records that had been declared appropriate indications in the previous parameters with the results of the study listed in **Table VI**.

Table VI. Types of antihypertensives are given to pregnant women with preeclampsia at a private hospital in Malang

Medical Record Number	Diagnosis	Antihypertensive	Pregnancy Risk Category	Drug Class	Exact/ Not Precise
xxx055	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx551	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx815	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx268	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx663	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx332	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx767	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx291	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx166	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx203	Preeclampsia	Nifedipine orally	C	CCB	True
xxx913	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx825	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx910	Severe preeclampsia	Nifedipine orally	C	CCB	True
xxx803	Severe preeclampsia	Nifedipine orally	C	CCB	True

Based on a study of the rationality of using antihypertensive drugs with the right parameters that has been carried out on 14 medical records of pregnant women with preeclampsia, 100% exact

results of the drug were obtained. The antihypertensive drug given is oral nifedipine. Nifedipine is an antihypertensive drug class of *Calcium Channel Blocker* (CCB) which acts as an inhibitory agent of calcium channels and is effective as a safe antihypertensive agent in pregnancy, especially in severe preeclampsia and eclampsia patients. Nifedipine is a drug with a mechanism of action that dilates blood vessels without reducing uteroplacental blood flow and does not cause abnormalities in the fetal heart (POGI, 2016; Lalenoh, 2018).

3. Proper Dosage

Dosage accuracy is the accuracy of drug administration with a dose that is in accordance with the predetermined therapeutic dose standards. If the dose given is excessive or too high, especially in drugs with a narrow therapeutic range, it will be very risky to cause side effects. Conversely, if the dose given is too small, the expected therapeutic effect will not be achieved (Ministry of Health RI, 2011). The study of the rationality of using antihypertensive drugs with dosage accuracy parameters in this study is seen from the accuracy of dosing antihypertensive drugs compared to the 2016 Preeclampsia PNPk reference standard. The accuracy of this dose is only carried out in 14 medical records that have been declared appropriate drugs in the previous parameters and are presented in **Table VII**.

Table VII. Dosage of antihypertensive drugs given to pregnant women with Preeclampsia at a private hospital in Malang

Medical Record Number (RM)	Diagnosis	Antihypertensive	PNPK Preeclampsia 2016 Reference Standard	Exact/ Not Precise
xxx055	Severe preeclampsia	Nifedipine 10 mg, 3x1 orally	10-30 mg/ day	True
xxx551	Severe preeclampsia	Nifedipine 10 mg, 2x1 orally	10-30 mg/ day	True
xxx815	Severe preeclampsia	Nifedipine 10 mg, 2x1 orally	10-30 mg/ day	True
xxx268	Severe preeclampsia	Nifedipine 5 mg, 2x1 orally	10-30 mg/ day	Not Exactly
xxx663	Severe preeclampsia	Nifedipine 10 mg, 2x1 orally	10-30 mg/ day	True
xxx332	Severe preeclampsia	Nifedipine 10 mg, 2x1 orally	10-30 mg/ day	True
xxx767	Severe preeclampsia	Nifedipine 10 mg, 2x1 orally	10-30 mg/ day	True
xxx291	Severe preeclampsia	Nifedipine 10 mg, 3x1 orally	10-30 mg/ day	True

xxx166	Severe preeclampsia	Nifedipine 10 mg, 3x1 orally	10-30 mg/ day	True
xxx203	Preeclampsia	Nifedipine 10 mg, 2x1 orally	10-30 mg/ day	True
xxx913	Severe preeclampsia	Nifedipine 10 mg, 3x1 orally	10-30 mg/ day	True
xxx825	Severe preeclampsia	Nifedipine 10 mg, 2x1 orally	10-30 mg/ day	True
xxx910	Severe preeclampsia	Nifedipine 10 mg, 3x1 orally	10-30 mg/ day	True
xxx803	Severe preeclampsia	Nifedipine 10 mg, 2x1 orally	10-30 mg/ day	True

Based on research on the rationality of using antihypertensive drugs that have been carried out on 14 medical records with dosage accuracy parameters, the results of 13 medical records on dose with a percentage of 93% were obtained. The dose of antihypertensive drugs given is in accordance with the predetermined therapeutic dose range, which is 10-30 mg for the dose of oral nifedipine drugs. The results of the study are not much different from the results of previous research conducted by Andriana (2018), namely Evaluation of the Use of Antihypertensive Drugs in Inpatient Pre-Eclampsia Patients at RSUD Prof. Dr. Margono Soekarjo Purwokerto who got 100% exact dose percentage results.

4. Proper feeding intervals

The accuracy of the administration interval is the accuracy of drug administration in accordance with the interval/frequency of drug use that has been determined (Ministry of Health RI, 2011). The accuracy of this interval was only carried out on 13 medical records that had been declared appropriate doses in the previous parameters. These results are listed in **Table VIII** below:

Table VIII. Frequency of antihypertensive drugs given to pregnant women with preeclampsia at a private hospital in Malang

Medical Record Number (RM)	Diagnosis	Antihypertensive	QCG 2021 Reference Standard	Exact/Not Precise
xxx055	Severe preeclampsia	Nifedipine 10 mg 3x1 orally	2 times a day	It doesn't stop
xxx551	Severe preeclampsia	Nifedipine 10 mg 2x1 orally	2 times a day	True
xxx815	Severe preeclampsia	Nifedipine 10 mg 2x1 orally	2 times a day	True

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xxx663	Severe preeclampsia	Nifedipine 10 mg 2x1 orally	2 times a day	True
xxx332	Severe preeclampsia	Nifedipine 10 mg 2x1 orally	2 times a day	True
xxx767	Severe preeclampsia	Nifedipine 10 mg 2x1 orally	2 times a day	True
xxx291	Severe preeclampsia	Nifedipine 10 mg 3x1 orally	2 times a day	It doesn't stop
xxx166	Severe preeclampsia	Nifedipine 10 mg 3x1 orally	2 times a day	It doesn't stop
xxx203	Preeclampsia	Nifedipine 10 mg 2x1 orally	2 times a day	True
xxx913	Severe preeclampsia	Nifedipine 10 mg 3x1 orally	2 times a day	It doesn't stop
xxx825	Severe preeclampsia	Nifedipine 10 mg 2x1 orally	2 times a day	True
xxx910	Severe preeclampsia	Nifedipine 10 mg 3x1 orally	2 times a day	It doesn't stop
xxx803	Severe preeclampsia	Nifedipine 10 mg 2x1 orally	2 times a day	True

Based on the study of the rationality of using antihypertensive drugs with the right parameters of the interval of administration that has been carried out on 13 medical records of pregnant women with preeclampsia, results were obtained at a 62% proper interval of administration. This is due to the frequency of antihypertensive therapy given to 8 patients' medical records in this study, which is 2 times a day. According to Jhansi 2015, nifedipine can be effective when given in a single dose and can be repeated at a dose of 20 mg.

5. Exact patient

Patient accuracy is the accuracy of drug selection according to the patient's condition by considering the safety of the drug so that it does not cause contraindications. The drugs given must be safe for both pregnant women and the fetus because the use of some drugs can cause disability in the fetus (Sa'idah, 2019). Study of the rationality of using antihypertensive drugs with patient accuracy parameters in this study seen from the antihypertensive drugs used and compared with the patient's disease history. This patient accuracy was only carried out on 8 medical records that had been declared at the right administration interval in the previous parameters. Based on research that has been conducted on 8 medical records of pregnant women with preeclampsia, 100% of patients were obtained according to **Table IX**.

Table IX. History of the disease of pregnant women with preeclampsia at a private hospital in Malang

Medical Record Number (RM)	Categories of Preeclampsia	Antihypertensive	History of the disease	Exact/Not Precise
xxx551	Severe preeclampsia	Nifedipine orally	-	True
xxx815	Severe preeclampsia	Nifedipine orally	-	True
xxx663	Severe preeclampsia	Nifedipine orally	-	True
xxx332	Severe preeclampsia	Nifedipine orally	-	True
xxx767	Severe preeclampsia	Nifedipine orally	-	True
xxx203	Preeclampsia	Nifedipine orally	-	True
xxx825	Severe preeclampsia	Nifedipine orally	-	True
xxx803	Severe preeclampsia	Nifedipine orally	-	True

This is because of 8 medical records of pregnant women patients with preeclampsia none of them have a history of disease. So do not consume drugs that are contraindicated with antihypertensive drug therapy given. Nifedipine is contraindicated in cardiogenic shock, advanced aortic stenosis, acute myocardial infarction, and acute unstable angina, and treatment of angina attacks in chronic stable angina and patients with hypersensitivity to nifedipine (Novianty, 2019).

Conclusion

Based on research on the rationality study of the use of antihypertensive drugs in pregnant women with preeclampsia, conclusions can be drawn that are 78% right indications, 100% right drugs, 93% right doses, 62% right intervals of administration, and 100% right patients. The results suggest that the use of antihypertensive drugs in preeclampsia is rational on the parameters. The results of this study only illustrate the rationality of using antihypertensive drugs in preeclampsia alone without elaboration on the effectiveness of the drug. Therefore, further studies are needed to be able to determine the effectiveness of using antihypertensive drugs to reduce the incidence of preeclampsia in pregnant women.

References

- Alatas, H. (2019) 'Hypertension in Pregnancy', *Herb-Medicine Journal*, 2(2).
- Andriana, D. D., Esti, D. U. and Nia, K. S. (2018) 'Evaluation of the Use of Antihypertensive Drugs in Inpatient Pre-Eclampsia Patients at RSUD Prof. Dr. Margono Soekarjo Purwokerto', *Acta Pharmaciae Indonesia*, 6(1).
- Dewie, A., Anna V. P. and Ayu, P. (2020) 'The Relationship Between Gestational Age and Obesity of Pregnant Women with the Incidence of Preeclampsia in the Working Area of the Kampung Baru Health Center in Luwuk City', *Journal of Public Health*, 10(1).

- Wijaya *et al.* 2023. A Rationality Study of Antihypertensive Drugs Usage in Preeclampsia Patients in the Private Hospital
- Directorate of Pharmaceutical Services. 2011. *Module on Rational Use of Medicine Jakarta: Ministry of Health of the Republic of Indonesia.*
- East Java Provincial Health Office (2021) *East Java Provincial Health Profile in 2020.* Surabaya: East Java Provincial Health Office.
- Indonesian Society of Obstetrics and Gynecology Maternal Feto Medical Association (2016) *National Guidelines for Medical Services for the Diagnosis and Management of Preeclampsia.* Jakarta: POGI.
- Jhansi, C. *et al.* (2015) ‘Comparision Of Efficacy And Safety Of Oral Labetalol And Nifedipine In Preeclampsia: A Prospective Observational Study’, *International Journal of Pharmacy and Pharmaceutical Sciences*, 7(9).
- Kundarto, W. and Riskafiya, N. F. (2021) ‘Evaluation of Antihypertensive Therapy in Severe Preeclampsia Patients in the Inpatient Installation of Dr. Moewardi Hospital for the period January - June 2017’, *Journal of Pharmaceutical Science and Clinical Research*. 2.
- Ministry of Health of the Republic of Indonesia (2011) *Module on Rational Use of Medicine.* Jakarta: Build Pharmaceutical Services.
- Ministry of Health of the Republic of Indonesia (2021) *Indonesia Health Profile in 2020.* Jakarta: Ministry of Health of the Republic of Indonesia.
- Mamo, D. B. and Belete, K. A. (2020) ‘Rational Drug-Use Evaluation Based on World Health Organization Core Drug-Use Indicators in a Tertiary Referral Hospital, Northeast Ethiopia: A Cross-Sectional Study’, *Drug Health Patient Saf*, 12, p. 15-21.
- Manalu, J. S. (2015) ‘Management of Preeclampsia During Childbirth’, *Scientific Journal World of Science*, 1(1).
- Novianti, H. (2016) ‘The Influence of Age and Parity on the Incidence of Pre-Eclampsia at Sidoarjo Regional Hospital’, *Scientific Journal of Health*, 9(1), p. 25-31.
- Novianty., Sutomo, T, and Theodorus. (2019) ‘The Rationality of the Use of Calcium Antagonists in Pregnant Women’, *Biomedical Journal of Indonesia: Biomedical Journal of the Faculty of Medicine, Sriwijaya University*, 5(2).
- Pulungan, P. W. *et al.* (2020) *Obstetrics and gynecology for obstetrics.* Our Foundation Writes.
- Retnosari, A., Ira, T. and Eny S. (2021) ‘The Correlation Of Maternal Age And The Incidence Of Preeclampsia At Aura Syifa Hospital’, *Journal Of Ners And Midwifery*, 8(3).
- Sa'idah, D. *et al.* (2019) ‘Evaluation of the Rationality of Using Antihypertensive Drugs in Outpatient Installations of Dr. Soegiri Lamongan Hospital for the 2017 Period’, *Indonesian Journal of Pharmaceutical Sciences*, 17(1).
- Saputri, G. A. R., Ade, M. U. and Miftahul, J. (2020) ‘Evaluation of the Rationality of Using Antihypertensive Drugs in Inpatient Preeclampsia Patients at RSUD Jend. Ahmad Yani Metro for the 2019 period’, *Journal of Malahayati Pharmacy*, 3(2).

- Setyawan, J. F. D., Ida, A. D. W. and Ni, W. T. (2019) 'Description of Urine Protein Levels in Preeclampsia and Eclampsia Pregnant Women at Sanglah Hospital Denpasar in 2017', *Udayana Medical Journal*, 8(12).
- Setyawati, A., Restuning, W, and Ermiati (2018) 'Factors Associated with the Incidence of Preeclampsia in Indonesia', *Indonesian Journal of Nurses*, 2(1).
- Simatupang, A. and Ida, B. S. D. (2021) 'Evaluation of the Administration and Use of Antihypertensive Drugs in Severe Preeclampsia Patients at RSU X Jakarta', *Indonesian Journal of Pharmacology and Therapeutics*, 2(2).
- Tahar, N. *et al.*, (2021) 'Proper Evaluation of the Use of Antihypertensive First-Line and Second-Line Drugs in Preeclampsia Patients: A Literature Review', *Journal of Midwifery*, 3(2).
- WHO (2020) *Maternal Mortality The Sustainable Development Goals and the Global Strategy for Women's, Children's and Adolescent's Health*. World Health Organization.