Is Low Dose Aspirin Reduced the Risk of Preeclampsia?

Era Kurniati[1], Bhisma Murti[1], Eti Poncorini Pamungkasari[2]

[1]Master's Program in Public Health, Universitas Sebelas Maret
[2]Faculty of Medicine, Universitas Sebelas Maret

ABSTRACT

Background: The maternal mortality rate is the number of maternal deaths resulting from pregnancy, childbirth and postpartum processes, which is an indicator of women's health status. Efforts that can be made to accelerate the reduction in maternal mortality are by ensuring that every mother is able to access quality health services. Low-dose aspirin has been proven to be a safe and effective primary prevention of preeclampsia. This study aimed to determine the effect of low dose aspirin on the incidence of preeclampsia.

Subjects and Method: Cross sectional research was conducted at the Community Health Center, Blora, Central Java, Indonesia. A sample of 200 pregnant women was selected randomly. The dependent variable was preeclampsia. The independent variables were age, income, aspirin consumption, primigravida, multigravida and hypertension. Data were collected by questionnaire and analyzed by multiple logistic regression.

Results: The results of logistic regression analysis in this study concluded that the risk of preeclampsia increased at age <20 years or ≥35 years (OR= 4.62; 95% CI= 1.89 to 11.28; p= 0.001), gravida 2-3 (OR= 3.03; CI 95 %= 1.01 to 9.05; p= 0.047), gravida ≥3 (OR= 4.41; 95% CI= 1.07 to 18.18; p= 0.040) and history of hypertension (OR= 2.41; 95% CI= 1.02 to 5.69; p= 0.005). The risk of preeclampsia decreased with income >IDR 2,000,000 (OR= 0.44; 95% CI= 0.22 to 0.87; p= 0.019) and administration of low-dose aspirin (OR= 0.13; 95% CI= 0.05 to 0.35; p <0.001).

Conclusion: The risk of preeclampsia increases with age, gravida 2-3, gravida ≥3 and history of hypertension. The risk of preeclampsia decreases with high income and administration of low-dose aspirin.

Keywords: preeclampsia, maternal age, hypertension.

Correspondence:
Era Kurniati. Masters Program in Public Health, Universitas Sebelas Maret. Jl. Ir. Sutami 36A, Surakarta, Central Java 57126, Indonesia. Email: erakurnia3@gmail.com. Mobile: 081325639317.

BACKGROUND

Maternal Mortality Rate is an indicator of a country's health development. Basically, pregnancy, childbirth and postpartum are natural and physiological conditions, but in the process it is possible that these conditions will turn into pathological conditions that can threaten the lives of the mother and baby. In order for natural conditions to remain in a safe position, continuous efforts

are needed from the government, private sector, family and community. As an illustration of maternal health, it can be seen from the number of maternal deaths collected from the family health program records at the Ministry of Health in 2021, which was 7,389 cases, this data has increased compared to 2020, namely 4,627 deaths in Indonesia. This number shows an increase of 3,122 deaths, most of which were caused by Covid-19 cases. However, as the Covid-19 pandemic ended, the maternal mortality rate began to decline in 2022, namely 207/100,000 live births. Based on causes, the majority of maternal deaths in 2022 will be caused by bleeding, namely 30% and preeclampsia 25% (Ministry of Health, 2022). Maternal mortality in Central Java Province in 2020 was 98.60/100,000 live births and increased in 2021, namely 199/100,000 thousand live births and decreased significantly in 2022 to 84.60/100,000 live births (Central Java Provincial Health Office 2022).

The condition of the maternal mortality rate which is still fluctuating also occurs in the Blora Regency area where in 2020 the number of maternal deaths was 15 cases and increased in 2021 due to the impact of the Covid 19 pandemic which increased to 22 cases but decreased in 2022 to 10 cases. The highest cause of maternal death in Blora Regency is preeclampsia, namely 45%, followed by comorbidities such as bleeding and infection. The prevalence of preeclampsia is increasing due to multifactorial factors, one of which is hypertension in pregnancy (Blora District Health Service 2022).

Hypertension in pregnancy is a health problem that contributes to high mortality and morbidity rates. The prevalence rate of hypertension in pregnancy ranges from 5–15% and is one of three causes of mortality and morbidity in childbirth apart from

infection and bleeding (Roberge et al., 2018). The incidence of preeclampsia worldwide is around 31.4%. The incidence of preeclampsia in Indonesia in 2020 was 9.4%, while in Central Java Province in 2019 it was 27.27% from 575,485 deliveries and in 2020 it was 30.88% from 568,295 deliveries (Ministry of Health, 2021), while in Blora Regency in 2020 the prevalence of preeclampsia was 1.4% of 11,600 pregnant women and in 2021 the percentage will increase to 1.7% of 11,300 pregnant women. However, the highest contributing factor to maternal deaths in Blora Regency is preeclampsia, which is 45% in 2022 (Blora District Health Service, 2022).

Efforts that can be made to accelerate the reduction in MMR are by ensuring that every mother is able to access quality health services. Complications that occur during pregnancy can be caused by conditions before pregnancy and conditions during pregnancy. The impact of pregnancy complications on the mother and baby is difficult to estimate because the pregnancy complications that occur vary in severity. However, with existing data, opportunities can be identified to prevent and manage pregnancy complications and improve care for pregnant women (Ministry of Health, 2022).

Low-dose aspirin has been proven to be a safe and effective primary prevention of preeclampsia. In Indonesia, its use has also been recommended as primary and secondary prevention of preeclampsia in high-risk women. Low-dose aspirin can reduce this risk, especially in high-risk pregnancies. This therapy inhibits thromboxane-mediated vasoconstriction and prevents failure of physiological transformation of the spiral arteries. Its use is not associated with significant complications (Wright et al., 2018). Based on previous research, aspirin is effective when given in the right dose, namely between 60-150 mg/day (Berliana,

2020). The use of aspirin in Blora Regency has not yet become a routine program so cases of preeclampsia in pregnancy are still high.

<div align="center">SUBJECTS AND METHOD</div>

1. Study Design

The research design used in this research is an observational analytical research study using a cross sectional approach. Multivariate analysis was carried out using logistic regression analysis. This research was conducted in November and was located in Blora Regency.

2. Population and Sample

Population is a target with the same characteristics and can be clearly defined, namely a collection of subjects. In this study, the population was pregnant women who were in the working area of the Community Health Center in Blora District, Central Java. The sampling technique in this research is random sampling. The sample size is 200 subjects.

3. Study Variables

The dependent variable is Preeclampsia. The independent variables are aspirin, hypertension, maternal age, parity, and family income.

4. Operational Definition of Variables

Preeclampsia was hypertension caused by pregnancy, characterized by hypertension with systolic/diastolic ≥140/90 mmHg and proteinuria ≥300 mg/24 hours after the 20th week of pregnancy.

Low-Dose Aspirin was low-dose aspirin given daily during pregnancy is effective in preventing preeclampsia.

Hypertension was an increase in systolic blood pressure is above the normal limit, namely more than 140 mmHg and diastolic blood pressure is more than 90 mmHg.

Maternal Age was the age of pregnant women is calculated based on the date of birth written on the questionnaire.

Parity was the number of living children or the number of pregnancies that produce fetuses capable of surviving outside the womb, at risk if nullipara or grande-multipara, no risk if primipara or multipara.

Family Income was total income of mother (wife) and father (husband), based on regional/ provincial minimum wage (UMR).

5. Study Instruments

Data collection, including questionnaires, weighing and measurements, is carried out in the work area of the puskesmas according to the schedule of each puskesmas.

6. Data Analysis

Univariate analysis was carried out to describe the characteristics of research subjects which were described in n and percent (%), while continuous data were described in mean, SD, minimum and maximum.

Bivariate analysis was carried out to analyze the relationship between the independent variables and the dependent variable. The test used is the difference in proportions test, namely chi-square with a confident interval and a significance level of $p<0.05$.

Multivariate analysis is carried out to see the relationship between the independent variables and the dependent variable as well as other variables that can influence them together. The statistical test used is multiple logistic regression analysis which is a statistical method used to find the best model of a problem and analyze the influence between variables, namely several independent variables on the dependent variable.

7. Research Ethics

Research ethics including informed consent, anonymity, and confidentiality, were handled carefully throughout the research process. A letter of approval for research ethics permission was obtained from the Research Ethics Committee of Dr. Regional

General Hospital. Moewardi, Indonesia, No. 1,940/X /HREC/2023, on October 31, 2023.

RESULTS

1. Sample Characteristics

The univariate characteristics of the research sample explain the distribution of research subjects based on independent variables, namely age, income, aspirin use, primigravida, multigravida, history of hypertension and the dependent variable, namely preeclampsia.

2. Univariate Analysis

Table 1 shows that the age variable with 200 research subjects has an average value of 31.60 (Mean= 31.60; SD= 6.53) with the lowest value being 17 and the highest value being 46. Family income with 200 research subjects has an average value of 2,706,750 (Mean= 2,706,750; SD= 3,342,240) with the lowest value being IDR 500,000 and the highest value being IDR 30,000,000.

Table 2 shows the variables of multi-gravida pregnant women with 2-3 preg-nancies, showing the number of research subjects was 141 or (70.5). Meanwhile, pregnant women with multi-gravida ≥3 pregnancies were 175 research subjects or (87.5%). Then, pregnant women who did not experience hypertension were 148 research subjects or (74%). Lastly, there were 131 pregnant women with non-preeclamptic status or (65.5%).

Table 1. Sample characteristics (continuous data)

Variable	N	Mean	SD	Min.	Maks.
Pregnant Woman's Age	200	31.60	6.53	17	46
Income	200	2,706,750	3,342,240	500,000	30,000,000

Table 2. Sample characteristics (categorical data)

Variable	Frequency (n)	Percentage (%)
Pregnant Woman's Age		
20-35 years	119	59.5
<20 or >=35 years	81	40.5
Family Income		
Low (<Rp 2,000,000)	94	47
High (≥Rp 2,000,000)	106	53
Use of Aspirin		
No Aspirin	124	62
Low Dose	76	38
Multi gravida 2-3		
<2 times	59	29.5
2-3 times	141	70.5
Multi gravida ≥3		
<3 times	175	87.5
≥3 times	25	12.5
History of Hypertension		
No	148	74
Yes	52	26
Preeclampsia		
No	131	65.5
Yes	69	34.5

3. Bivariate Analysis

Bivariate analysis in this study aims to explain the influence of independent variables, namely age, income, aspirin, primigravida, multigravida, hypertension on preeclampsia. The analytical test used in bivariate analysis is chi-square with a confidence level of 95% (p<0.05).

a. The effect of age on preeclampsia

Table 3 presents the results of chi-square analysis with (OR= 2.50; p= 0.002). Based on these results, it can be concluded that there is an influence between age on preeclampsia and it is statistically significant. Pregnant women aged <20 or ≥ 35 years are 2.50 times more likely to experience preeclampsia than pregnant women aged 20-35 years.

b. The effect of income on preeclampsia

Table 3 presents the results of chi-square analysis with (OR= 0.38; p= 0.002). Based on these results, it can be concluded that there is an influence between income on preeclampsia and it is statistically significant. Pregnant women with income ≥Rp 2,000,000 are 0.38 times more likely to experience preeclampsia than pregnant women with income <Rp 2,000,000.

c. Effect of aspirin on preeclampsia

Table 3 presents the results of chi-square analysis with (OR= 0.39; p= 0.005). Based on these results, it can be concluded that there is an influence between the use of low dose aspirin on preeclampsia and it is statistically significant. Pregnant women who take low-dose aspirin are 0.39 times more likely to experience preeclampsia than pregnant women who do not take aspirin.

d. Effect of multi gravida 2-3 on preeclampsia

Table 3 presents the results of chi-square analysis with (OR= 1.44; p= 0.274). Based on these results, it can be concluded that there is an influence between multigravida status and 2-3 pregnancies on preeclampsia and it is not statistically significant. Pregnant women with multigravida status with 2-3 pregnancies are 1.44 times more likely to experience preeclampsia compared to pregnant women with multigravida status with <2 pregnancies..

e. The effect of multiple gravida >3 on preeclampsia

Table 3 presents the results of chi-square analysis with (OR= 1.91; p= 0.129). Based on these results, it can be concluded that there is an influence between multigravida status and >3 pregnancies on preeclampsia and it is not statistically significant. Pregnant women with 2nd gravida status with ≥3 pregnancies are 1.91 times more likely to experience preeclampsia than pregnant women with <3 pregnancies.

f. The influence of a history of hypertension on preeclampsia

Table 3 presents the results of chi-square analysis with (OR= 2.44; p= 0.006). Based on these results, it can be concluded that there is an influence between hypertension and preeclampsia and it is statistically significant. Pregnant women with hypertension are 2.44 times more likely to experience preeclampsia than pregnant women without hypertension.

4. Multivariat Analysis

Multivariate analysis in this study aims to explain the influence of independent variables, namely age, income, aspirin use, gravida, hypertension on preeclampsia. The analytical test used in this multivariate analysis is logistic regression analysis.

a. The influence of age on preeclampsia

Logistic regression analysis in Table 4 shows that there is an influence between the age of a pregnant woman on the risk of preeclampsia and it is statistically significant. Pregnant women aged <20 or >35 years have a risk of experiencing preeclampsia

4.62 times compared to those aged 20-35 years (OR= 4.62; 95% CI= 1.89 to 11.28; p= 0.001).

b. The effect of income on pre-eclampsia

Logistic regression analysis in Table 4 shows that there is an influence between income and the risk of preeclampsia and it is statistically significant. Pregnant women with income ≥Rp. 2,000,000 are effective in reducing the risk of preeclampsia by 0.44 compared to pregnant women with income <Rp. 2,000,000 (OR= 0.44; 95% CI= 0.22 to 0.87; p= 0.019).

c. Effect of aspirin on preeclampsia

Logistic regression analysis in Table 4 shows that there is an effect between administering low-dose aspirin on pereclampsia and it is statistically significant. Giving low-dose aspirin to pregnant women is effective in reducing the risk of preeclampsia 0.13 times compared to pregnant women who are not given aspirin (OR= 0.13; 95% CI= 0.05 to 0.35; p <0.001).

d. Effect of multi gravida 2-3 on preeclampsia

Logistic regression analysis in Table 4 shows that there is an influence between pregnant women with multigravida status 2-3 on pereclampsia and it is statistically significant. Pregnant women with multigravida status 2-3 have a risk of preeclampsia 3.03 times compared to pregnant women with primi gravida status (OR= 3.03; 95% CI= 1.01 to 9.05; p= 0.047).

Table 3. Effect of age, income, aspirin, primigravida, multigravida, hypertension on preeclampsia

Independent Variable	Preeclampsia						OR	p
	No		Yes		Total			
	n	(%)	n	(%)	n	(%)		
Pregnant Woman's Age								
20-35 years	88	74	31	26	119	100	2.50	0.002
<20 or >35 years	43	53	38	47	81	100		
Income								
Low (<Rp 2,000,000)	51	54	43	46	94	100	0.38	0.002
High (≥Rp 2,000,000)	80	75.4	26	24.6	106	100		
Aspirin								
No Aspirin	72	58	52	42	124	100	0.39	0.005
Low Dose	59	78	17	22	76	100		
Multi gravida 2-3								
<2 times	42	71	17	29	59	100	1.44	0.274
2-3 times	89	63	52	37	141	100		
Multi gravida >3								
<3 times	118	67.4	57	32.6	175	100	1.91	0.129
≥3 times	13	52	12	48	25	100		
Hypertension								
No	105	70.95	43	29.05	148	100	2.44	0.006
Yes	26	50	26	50	52	100		

e. Effect of multiple gravida ≥3 on preeclampsia

Logistic regression analysis in Table 4 shows that there is an influence between pregnant women with multigravida status ≥3 on preeclampsia and it is statistically significant. Pregnant women with multigravida status ≥3 have a risk of preeclampsia 4.41

times compared to pregnant women with gravida status <3 (OR= 4.41; 95% CI= 1.07 to 18.18; p= 0.040).

f. The influence of a history of hypertension on preeclampsia

Logistic regression analysis in Table 4 shows that there is an influence between pregnant women with a history of hypertension on preeclampsia and it is statistically significant. Pregnant women with a history of hypertension have a risk of preeclampsia 2.41 times compared to pregnant women without a history of hypertension (OR= 2.41; CI 95%= 1.02 to 5.69; p= 0.005).

Table 4. Results of logistic regression analysis between the effect of age, income, aspirin, primigravida, multigravida, hypertension on preeclampsia

Independent Variable	OR	CI 95%		p
		Lower Limit	Upper Limit	
Pregnant mother's age (<20 years or ≥ 35 years)	4.62	1.89	11.28	0.001
Income (≥Rp 2,000,000)	0.44	0.22	0.87	0.019
Low Dose Aspirin	0.13	0.05	0.35	<0.001
Multi gravida (2-3 times)	3.03	1.01	9.05	0.047
Multi gravida (>3 times)	4.41	1.07	18.18	0.040
History of Hypertension	2.41	1.02	5.69	0.005
n Observation=200				
Log likelihood = -104.19				
Negelkerke R^2= 19.14%				

DISCUSSION

1. Effect of age on preeclampsia

The results of the multivariate analysis showed that there was a significant relationship between age and preeclampsia with a value (OR= 4.62; 95% CI= 1.89 to 11.28; p= 0.001) meaning that age <20 years or ≥35 years had a 4.62 times risk of experiencing preeclampsia compared to age 20- 35 years old. This is in line with research by Rosmiati (2014) which states that there is a relationship between maternal age and preeclampsia. Ages under 20 years and over 35 years are considered to be at risk because at the age of under 20 years the reproductive organs have not yet matured, whereas if over 35 years the reproductive organs' function has decreased. This is in line with research conducted by Julianti (2014) which shows that mothers who are 35 years old are at risk of experiencing preeclampsia 1.9 times greater than mothers who are not at risk. Mothers aged 35 years are more at risk of preeclampsia, this is because at age <20 years it is thought to be

immunological as well as endocrine and genetic, while preeclampsia at age ≥35 years is thought to be due to hypertension which is exacerbated by pregnancy (Cuningham, 2010). Pregnant women who have a history of hypertension are at risk of developing preeclampsia 2.34 times greater than pregnant women who do not have a history of hypertension (Julianti, 2014).

In theory, ages under 20 years and over 35 years are also known as high risk ages for experiencing pregnancy complications. At <20 years of age, the size of the uterus has not yet reached the normal size for pregnancy, so there is a possibility of pregnancy disorders such as preeclampsia. At the age of ≥35 years, a degenerative process occurs which results in structural and functional changes in peripheral blood vessels which are responsible for changes in blood pressure, making them more susceptible to preeclampsia (Cunningham, 2010).

2. Effect of income on preeclampsia

The research found that there was a

relationship between family income and the incidence of preeclampsia (OR= 0.44; 95% CI= 0.22 to 0.87; p= 0.019). The family's economic level is related to the mother's family's ability to access good and adequate health facilities as well as the ability to fulfill nutrition during pregnancy. Pregnant women from a high economic background will find it easier to access better health services.

The results of this study are in accordance with research conducted by Tika (2015) which states that there is a relationship between economic status and the incidence of preeclampsia, mothers who give birth with high economic status have a greater chance of not getting preeclampsia 2.34 times compared to mothers who give birth with low family economic status. The results of Rozikhan's research (2007) stated that subjects with an income of <Rp. 500,000 were 1.35 times more at risk than subjects with an income of ≥Rp. 500,000. Ramesh's (2013) research states that monthly household income is related to the incidence of preeclampsia. In this study, case subjects earned <Rs 4000 more, namely 80% compared to control subjects (37%).

3. Effect of aspirin on preeclampsia

Logistic regression analysis in Table 4.4 shows that there is an effect between administering low-dose aspirin on pereclampsia and it is statistically significant. Giving low-dose aspirin to pregnant women is effective in reducing the risk of preeclampsia 0.13 times compared to pregnant women who are not given aspirin (OR= 0.13; 95% CI= 0.05 to 0.35; p<0.001). These results are supported by research from Duley et al (2018) which states that low-dose aspirin slightly reduces the risk of preeclampsia and its complications, but guarantees regarding the safety of higher doses of aspirin or other antiplatelet agents need further research. Low-dose aspirin that serves as prophylaxis starting in high-risk patients before 16 weeks of gestation is considered more effective in preventing preeclampsia.

4. Effect of multi gravida on preeclampsia

a. Multi gravida with 2-3 pregnancies
Logistic regression analysis in Table 4 shows that there is an influence between pregnant women with multigravida status 2-3 on pereclampsia and it is statistically significant. Pregnant women with multigravida status 2-3 pregnancies have a risk of preeclampsia 3.03 times compared to pregnant women with primigravida status (OR= 3.03; 95% CI= 1.01 to 9.05; p= 0.047).

b. Multi gravida with ≥3 pregnancies
Logistic regression analysis in Table 4. shows that there is an influence between pregnant women with gravida status ≥3 on pereclampsia and it is statistically significant. Pregnant women with gravida status ≥3 have a risk of preeclampsia 4.41 times compared to pregnant women with gravida status <3 (OR= 4.41; 95% CI= 1.07 to 18.18; p= 0.040).

Based on the research results, there are still multigravids who experience preeclampsia due to a previous history of preeclampsia, age at risk and other diagnoses in the mother such as: anemia, hyperemesis gravidarum, polyhydramnios, chronic hypertension, incomplete abortion, oligo hydramnios and thrombocytopenia.

The results of this research are in line with research by Rahmawati (2019) with the title research on the risk of age and parity of pregnant women on the incidence of preeclampsia and eclampsia. The results showed a significant relationship between parity and the incidence of preeclampsia. Therefore, pregnant women should carry out early detection to avoid complications in obstetric conditions which can cause preeclampsia and attend classes for pregnant women, furthermore, according to research by Renita et al. (2018) stated that there is a

relationship between parity and pre-eclampsia, especially in primiparas. Because primiparas often experience stress because they are facing childbirth. Stress will give rise to uncontrolled emotions that can disrupt the performance of the heart organ in pumping blood throughout the body. This will cause an increase in blood pressure.

5. Effect of a history of hypertension on preeclampsia

Based on the research results, it shows that pregnant women with a history of hypertension have a risk of preeclampsia 2.41 times compared to pregnant women who do not have a history of hypertension (OR= 2.41; 95% CI= 1.02 to 5.69; p= 0.005). This is in accordance with the theory which states that pregnant women with a history of hypertension will have a greater risk of experiencing superimposed preeclampsia. This is because hypertension suffered since before pregnancy has resulted in disturbance or damage to the body's important organs and, with pregnancy, the body's work will become more difficult, which can result in even more severe disturbance or damage with the emergence of edema and osteoporosis (Wiknjosastro, 2008) .

In Mariza's study, mothers who had a history of hypertension in case subjects (33.7%) were higher than in control subjects (8.7%). Kartika's research (2016) also stated similarly that a history of hypertension was related to the incidence of preeclampsia. In this study, a history of hypertension was related because some mothers were obese, namely 40.3%.

AUTHOR CONTRIBUTION

All authors have made significant contributions to data analysis as well as preparing the final manuscript.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

REFERENCE

Berliana A (2020). Aspirin dosis rendah untuk mencegah preeklampsia pada kehamilan. Jurnal Ilmiah Kesehatan Sandi Husada (Low dose aspirin to prevent preeclampsia in pregnancy. Sandi Husada Health Scientific Journal). 12(2): 1029–1036. https://doi.org/10.35816/jiskh.v12i2.458

Cendekia MS, Nurdin I, Hartati S (2019). Metodologi penelitian sosial (Social research methodology). Media Sahabat Cendekia.

Murti B (2018). Prinsip dan Metode Riset Epidemiologi (5th ed.) (Principles and Methods of Epidemiological Research (5th ed)). Program Studi Ilmu Kesehatan Masyarakat, Program Pascasarjana, Universitas Sebelas Maret.

Rahayu AM, Astuti AW, Utami FS (2020). Pengalaman ibu dengan riwayat preeklampsia dalam kehamilan (Experiences of mothers with a history of preeclampsia in pregnancy). Jurnal Riset Kebidanan Indonesia. 3(2): 56–68. https://doi.org/10.32536/jrki.v3-i2.55

Roberge S, Bujold E, Nicolaides KH (2018). Meta-analysis on the effect of aspirin use for prevention of preeclampsia on placental abruption and antepartum hemorrhage. J Obstet Gynaecol, 218 (5): 483–489. https://doi.org/10.10-16/j.ajog.2017.12.238

Wright D, et al. (2018). Aspirin for evidence-based preeclampsia prevention

trial: effect of aspirin on length of stay in the neonatal intensive care unit. J Obstet Gynaecol. 218(6): 612.e1-612.e6. https://doi.org/10.1016/j.ajog.2018.02.014

Rosmiyati (2014). Faktor-faktor yang berhubungan dengan kejadian Preeklamsia di Rumah Sakit Umum Menggala Kabupaten Tulang Bawang (Factors associated with the incidence of preeclampsia at Menggala General Hospital, Tulang Bawang Regency). Jurnal Kesehatan Holistik. 8(3): 105-109.

Rahmawati, et al. (2022). Literature review: faktor-faktor risiko terjadinya preeklampsia pada ibu hamil (Literature review: risk factors for preeclampsia in pregnant women). Journal of Borneo Holistic Health. 5 (2): 122-132.

Renita (2018). Faktor yang mempengaruhi kejadian preeklamsia pada ibu bersalin di Puskesmas Sirampong Kabupaten Brebes 2(3) (Factors influencing the incidence of preeclampsia in mothers giving birth at the Sirampong Community Health Center, Brebes Regency 2(3). http://journal.unnes.ac.id/sju/index.php/higeia

Kementerian Kesehatan (2022). DataIndonesia.id/Kesehatan/detil/jumlah-kematian-ibu-di-Indonesia-meningkat-5969-pada-2021.

Dinas Kesehatan Provinsi Jawa Tengah (2022). Httpps//ppid.dinkesjatengprov.go.id/ppid/wpcontent/uploads/2023/03/LKJIP-DINKES-2022.pdf

Dinas Kesehatan Kabupaten Blora (2022). Data profil Kesehatan Kabupaten Blora tahun 2022 (Blora Regency Health profile data for 2022).