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Risk Factors of Body Mass Index and Hypertension on Preeclampsia during the Covid-19 Pandemic

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Preeclampsia, known as the "new onset of persistent hypertension," can increase the morbidity and mortality of mothers and fetus. The Indonesian Health Profile shows that the maternal mortality rate (MMR) due to preeclampsia in Indonesia reaches 25%. The Corona Virus Disease 2019 impacted the access to, and quality health services, including for maternal and neonatal. This study aim to determine the risk factors for preeclampsia at Budhi Asih Hospital during the Covid-19 pandemic. This was a retrospective, observational case-controlled study, using medical records of woman on antenatal care from March 2020 – March 2022. Samples size was 128 participants (64 cases and 64 controls) using a simple random technique. Data analysis used the Chi-square test and logistic regression. The results showed that the variables associated with the incidence of preeclampsia

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were maternal age (p=0.049), parity status (p=0.041), chronic hypertension (p=0.000), and BMI (p=0.003). Variables that were not related to the incidence of preeclampsia were previous history of preeclampsia (p=0.094), pregnancy interval (p=0.367), and family history of preeclampsia (p=0.154). The most dominant variable was chronic hypertension (OR 36.162; 95% CI 4.453-293.655). This study concludes that chronic hypertension, obesity, age at risk (<20 years or >35 years), and nullipara or primipara are risk factors for preeclampsia at Budhi Asih Hospital during the Covid-19 pandemic.

Keywords: BMI; pregnancy hypertension; preeclampsia; Covid-19 pandemic.

1. INTRODUCTION

Preeclampsia is one of five types of gestational hypertension which generally occurs at gestational age >20 weeks or shortly after delivery, with the main sign being "new onset of persistent hypertension," indicated by systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg either with or without proteinuria [1]. Pregnant women with hypertension generally experience headaches when they wake up and other accompanying symptoms such as nausea and vomiting due to increased ICP (intracranial pressure), decreased vision due to hypertensive retinal damage, nocturia, and edema due to increased pressure in the capillaries [2].

Maternal and child morbidity and mortality can be increased, one of them by the incidence of preeclampsia. About 40,000 women who suffer from preeclampsia or eclampsia die each year. Preeclampsia causes around 40-60% of maternal deaths in developing countries, with a prevalence ranging from 1.8% to 16.7% [3]. The maternal mortality rate (MMR) caused by preeclampsia in Southeast Asia is 17%, while in Indonesia, based on the 2015 Indonesian Health Profile, it approaches 25% [4]. It shows that the MMR in Indonesia due to preeclampsia is still relatively high in Southeast Asia [5]. Based on the 2020 Indonesia Health Profile, the causes of maternal death due to hypertension and preeclampsia occupy the second position with 1,100 cases [6]. The proportion of hypertension based on the 2018 Riskesdas data occupies the second highest position of the various disorders/complications that occur during pregnancy, namely 3.3%, with the most in the province of Gorontalo [7].

Some studies state that damage to vascular endothelium and oxidative stress is one of the main pathophysiological pathways of preeclampsia. Cunningham et al. (2010) grouped preeclampsia into four basic theories: abnormal placental implantation, abnormal tolerance and immunological maladaptation, maternal maladaptation in pregnancy, and genetic factors. Preeclampsia is not "One Disease" but involves all maternal, placental, and fetal aspects [8].

According to Sari et al. (2016), factors that can cause hypertension in pregnancy include being overweight, having a history of chronic hypertension, and using contraceptives [9]. According to Anindhita Az Zahra et al. (2016), other factors also support this, such as education level, history of hypertension, weight gain during pregnancy, intake of fat and calcium, and nutritional status ($p < 0.05$). Other factors that were also studied, such as occupation, age, and multi-gravidae, have no evidence that they can affect the incidence of hypertension in pregnancy [10].

The impacts that can be caused by the Covid-19 pandemic (Corona Virus Disease 2019) include limited access to and quality of health services, including for maternal and neonatal. This condition is worrying because it can increase maternal and neonatal mortality and morbidity. Early detection of gestational hypertension is needed for earlier prevention, in this case, by identifying risk factors during the Covid-19 pandemic. Research by Yenny Aulya et al. (2021) reported that age, multiple pregnancies, number of parities, nutritional status, and history of comorbidities influenced the incidence of preeclampsia during the Covid-19 pandemic [11].

Based on the national guidelines used by the Indonesian Obstetrics and Gynecology Association (POGI), preeclampsia is defined as a specific condition in pregnancy characterized by placenta dysfunction and activation of endothelium and coagulation as a maternal response to systemic inflammation [12]. Preeclampsia is now defined as new-onset hypertension with other organ dysfunction indicative of a severe condition without proteinuria [13]. The International Society for the

Study of Hypertension in Pregnancy (ISHHP) defines preeclampsia as gestational hypertension accompanied by one or more of the following new-onset conditions occurring at or after 20 weeks of gestation: [14]. a) Proteinuria (≥ 300 mg/24 hours; or protein/creatinine ratio ≥0.3 mg/dL; or 2+ dipstick); b) Dysfunction of other maternal organs, such as acute kidney injury; liver involvement with or without epigastric pain; neurological complications; or hematological complications; and c) uteroplacental dysfunction.

Based on the onset of occurrence, preeclampsia can be classified into four categories, namely early onset preeclampsia (gestational age <34 weeks), preterm preeclampsia (<37 weeks), late-onset preeclampsia (≥34 weeks), and term preeclampsia (≥37 weeks) [15]. Hypertension requires two measurements 15 minutes apart to make the diagnosis. The minimum blood pressure measurement results are a systolic pressure of 140 mmHg or a diastolic of 90 mmHg when measured twice and diagnosed as hypertension. Severe hypertension is diagnosed if the blood pressure is at least 160 mm Hg systolic or 110 mm Hg diastolic [16]. Hypertensive patients are not diagnosed with preeclampsia without other conditions that meet the criteria.

The global incidence of preeclampsia ranges from 2% -10% of existing pregnancies. WHO estimates that the incidence of preeclampsia in developing countries is seven times higher than in developed countries with the prevalence range of preeclampsia in developed countries is 1.3%-6%, while in developing countries, it is 1.8%-16.7% [17]. The annual incidence of preeclampsia in Indonesia reaches 128,273 (5.3%). Preeclampsia is one of the main caused of maternal and child morbidity and mortality, both globally and in Indonesia. Bleeding is the first leading cause of maternal death in Indonesia, followed by preeclampsia [18]. Based on the 2020 Indonesia Health Profile, the cause of maternal death is hypertension as many as 1,100 cases [19]. The number of these cases has increased when compared to the 2019 Indonesia Health Profile report of 1,066 [20]. Based on data from the DKI Jakarta Provincial Health Office (2015), the most common causes of maternal death in DKI Jakarta in 2015 were severe preeclampsia, postpartum hemorrhage, and antepartum hemorrhage. The most common cause of maternal death in DKI Jakarta in 2020 is bleeding, with a total of 27 mothers, while hypertension in pregnancy occupies the second position, causing 24 maternal deaths and the most in West Jakarta with 9 [21].

The exact etiology of preeclampsia is not yet known. However, several theories state that certain groups can experience preeclampsia, namely mothers with internal factors such as age, because increasing age is more at risk of developing hypertension, in addition to parity, family history, history of pregnancy, and previous preeclampsia [22]. Cunningham et al. (2010) grouped the etiology of preeclampsia into four basic theories, namely: [8]. a) Placental implantation accompanied by abnormal trophoblastic uterine artery invasion; b) Immunological maladaptation in all maternal tissues, placenta, and fetal tissues causes abnormalities in maternal immune tolerance; c) Physiological changes in pregnancy that cannot be adapted by the mother such as cardiovascular and inflammatory changes; and d) Genetic factors. These four etiological groups, in theory, also interact with each other and are supported by other environmental factors. The uncertain etiology of preeclampsia should trigger every researcher and clinician to keep updating information regarding the profile of preeclampsia.

According to Rana's research et al. (2019), various risk factors for developing preeclampsia have been studied. The main risk factors for preeclampsia include a previous history of preeclampsia, chronic hypertension, antiphospholipid syndrome, obesity, and pregestational diabetes mellitus. Other risk factors include increasing maternal age, nulliparity, history of chronic kidney disease, and use of contraceptives. Risk factors are relatively rare, such as a family history of preeclampsia and mothers carrying a fetus with trisomy 13 [23]. Based on the level of involvement, the risk factors for preeclampsia are grouped as follows [24].

It is important to know the risk factors for preeclampsia, especially in the early diagnosis of preeclampsia, including maternal age, parity, previous history of preeclampsia, pregnancy intervals, family history of preeclampsia, comorbidities [25;26;27;28].

Several criteria are often used in classifying preeclampsia, including based on the onset. Based on the onset, preeclampsia was classified as early onset (<34 weeks gestation) and late-onset (≥34 weeks gestation) preeclampsia [15].The onset of preeclampsia is important to

know because it can be associated with short-term and long-term maternal and neonatal morbidity and mortality; for example, neonatal morbidity tends to decrease after reaching 32 weeks and 36 weeks of gestation. [25]. Another classification criterion based on severity is preeclampsia with or without severe features Preeclampsia indicators with severe features (found one or more of the following) [29]. a) Systolic blood pressure ≥160 mmHg, or diastolic blood pressure ≥110 mmHg when checked twice with an interval of 15 minutes on the same arm; b) Thrombocytopenia (platelet count <100,000 per mm3); c) Liver dysfunction, such as elevated liver enzymes (more than twice the upper limit of normal concentration) and/or the presence of severe persistent right quadrant or epigastric pain; d) Renal insufficiency (serum creatinine concentration >1.1 mg/dL or an increase from before in the absence of other renal abnormalities); e) Pulmonary edema; f) Persistent new onset headache; and g) Visual impairment. Many factors support the pathogenesis of preeclampsia, and there are many theories explaining them, such as: [30]. a) Abnormal placental implantation (abnormal trophoblast invasion and spiral arterioles); b) Angiogenic factors; c) Genetic predisposition; d) Immunological phenomena; and e) vascular endothelial damage and oxidative stress.

Table 1 High-medium risk factors for preeclampsia [19]

High-risk factor	Intermediate risk factor
Hypertension in a previous pregnancy	Age ≥40 years
Chronic hypertension	First pregnancy
Chronic kidney disease	Multiple pregnancies
Diabetes mellitus type I/II	Family history
Autoimmune disease (antiphospholipid syndrome)	Pregnancy interval ≥10 years

Recent studies suggest that an imbalance of angiogenic and antiangiogenic factors may play a role in the pathogenesis of preeclampsia. An imbalance of these factors can impair the function of the placenta, causing endothelial dysfunction. Combining the above mechanisms is recognized as possibly responsible for triggering preeclampsia. Soluble Fms-Like Tyrosine Kinase-1 (sFlt-1) antiangiogenic factor levels in the preeclampsia risk group (8-20 weeks' gestation) based on the results of research by Sri Sulistyowati et al. (2015) higher than the control group [31]. Another study by Sri Sulistyowati et al. (2015) found that sFlt-1 levels were higher than Vascular Endothelial Growth Factor (VEGF) in pregnancies with a risk of preeclampsia. sFlt-1 levels increase in the second trimester, starting 4-5 weeks before clinical manifestations of preeclampsia appear [32]. VEGF also plays a role in the pathogenesis of preeclampsia by binding to sFlt-1 so that its levels decrease. It leads to decreased physiological vasodilatation, leading to hypertension. Preeclampsia occurs in 2 stages, namely the first stage is the asymptomatic stage, characterized by abnormal placenta development at the beginning of the first trimester, causing various placental materials to be released into the maternal circulation, and placental insufficiency occurs. The second stage is the symptomatic stage, marked by increased levels of anti-angiogenic factors in the second and third trimesters [23].

The highest complication of preeclampsia is maternal and fetal death. Possible complications of severe preeclampsia include: Maternal Complications (Pulmonary Edema, HELLP Syndrome, and Eclampsia), [25] Fetal Complications (Prematurity and Asphyxia). Preeclampsia can be prevented by various strategies divided into primary, secondary, and tertiary prevention. Primary prevention is an effort to prevent the occurrence of disease. Secondary prevention attempts to stop the process before symptoms or clinical emergencies occur. Tertiary prevention is an effort to prevent the occurrence of various complications [33].

Primary Prevention of Preeclampsia - Various tests performed at the Antenatal Care (ANC) visit can detect various early risk factors that have been proven to increase the risk of preeclampsia. The aim is expected to be able to help with early assessment of the risk of pregnancy at the first ANC visit. Secondary Prevention of Preeclampsia is accomplished through rest, dietary manipulation, antioxidants, and antithrombotic agents [34].

The incidence of hypertension in pregnancy is still relatively high, and the impact on health services that may arise during the Covid-19 pandemic made researchers need to know the characteristics of risk factors for preeclampsia in mothers giving birth during the Covid-19 pandemic at Budhi Asih Hospital. The

formulation of the problem in this study is a) "Is there a relationship between risk factors for the incidence of preeclampsia at Budhi Asih Hospital during the Covid-19 pandemic period March 2020 - March 2022? The study aimed to determine the risk factors the incidence of preeclampsia at Budhi Asih Hospital during the Covid-19 pandemic period March 2020 - March 2022.

2. METHODS

This type of research was a retrospective, observational case-controlled study, using medical records of woman on antenatal care from March 2020 – March 2022. Retrieval of data using secondary data, namely medical record data. The research data was be classified, described, and analyzed by researchers to determine the risk factors for women giving birth with preeclampsia at Budhi Asih Hospital from March 2020 - March 2022. The location of this research is the Medical Record Unit at Budhi Asih Hospital, which has been implemented since May-November 2022. The population of this study was all mothers giving birth at Budhi Asih Hospital from March 2020 - March 2022. Sampling used the simple random sampling method, namely random sampling based on fulfilling the inclusion criteria. This study grouped the sample into two groups: the control group (mothers giving birth without preeclampsia) and the case group (mothers giving birth with preeclampsia). The required sample size in this study was 64 patients, with a 1:1 ratio for each group. The total sample in this study was 128 subjects. The research instrument is a secondary data source, namely the medical records of mothers giving birth at Budhi Asih Hospital in March 2020 - March 2022 which was processed. This study's data collection method was secondary data in the form of medical records of mothers giving birth at Budhi Asih Hospital from March 2020 - March 2022. The data was processed using observational analytic techniques and analyzed to determine the relationship between research variables through univariate, bivariate, and multivariate analysis. The identity of maternity patients at Budhi Asih Hospital from March 2020 - March 2022 was kept confidential and was not included in the publication of research results.

3. RESULTS AND DISCUSSION

Data of 10.52% of 1,616 deliveries in March 2020 - March 2022 were cases of preeclampsia at Budhi Asih Hospital. Patients who met the inclusion criteria were 64 samples who had preeclampsia, then grouped into 61 (95%) patients with severe preeclampsia and 3 (5%) patients without severe features.

The results of the univariate analysis are shown in the frequency distribution table. The frequency distribution table contains the number and percentage of each characteristic of mothers giving birth at Budhi Asih Hospital from March 2020 - March 2022.

Based on Table 2, the sample frequency distribution for the case group was taken as many as 64 people from 170 or 37.64%, while the control sample was taken 64 people from 1,446 or 4.42%.

Based on Table 3, it was found that the proportion of maternal age with preeclampsia was the highest, namely in the non-risk category (20-35 years), amounting to 64.1%, as well as in the control group amounting to 79.7%. These results suggest no difference in the proportion of age at most between the two sample groups.

Table 2. Frequency distribution of cases and controls at budhi asih hospital in 2020 – 2022

Variable	Population	Sample	%
Case (Preeclampsia)	170	64	37.64%
Control (Non Preeclampsia)	1.446	64	4.42%

Table 3. Distribution of profiles of maternity mothers by age group

Age (years)	Preeclampsia		No Preeclampsia		Total	
	n	%	n	%	n	%
At risk (<20 Years and >35 Years)	23	35.9%	13	20.3%	36	28.1%
Not at risk (20-35 Years)	41	64.1%	51	79.7%	92	71.9%
Total	64	100%	64	100%	128	100%

Based on Table 4, the highest proportion of parity status was obtained, namely the nullipara and primipara categories, both in the case and control groups, as much as 64.8%.

Based on Table 5, the highest proportion was obtained in the two groups, namely the category with no history of preeclampsia, as much as 95.3%.

Based on Table 6, the highest proportion of pregnancy intervals was obtained, namely the distant category (≥ two years), as much as 60.2% in both groups. The case group was at most 64.1% for the distant category (≥ two years), while in the control group, it was at most 56.8% for the distant category (≥ two years).

Based on Table 7, the highest proportion was obtained in both groups, as much as 98.4% for the category of no family history of preeclampsia.

Based on Table 8, the highest proportion of chronic hypertension was obtained in the category of no chronic hypertension, namely 81.3%. The case group was 64.1% without chronic hypertension, while the control group was 98.4% without chronic hypertension.

Based on Table 9, the highest proportion was obtained in the obesity category (BMI > 24), namely 88.3% for both groups.

The relationship between risk factors as the independent variable and the incidence of preeclampsia as the dependent variable was analyzed using the Chi-Square test. The Odds Ratio test does a big risk analysis between variables.

Table 10 shows a significant relationship between maternal age and the incidence of preeclampsia in mothers giving birth because the p-value is 0.049 (p <0.05). The Odds Ratio test results show that mothers aged <20 years and >35 years have 2.021 times the risk of experiencing preeclampsia compared to mothers aged 20-35.

Table 11 shows a significant relationship between parity status and the incidence of preeclampsia in women giving birth because the p-value is 0.041 (p <0.05). The results of the Odds Ratio test showed that mothers with nullipara and primipara parity status had a risk of experiencing preeclampsia by 0.465 times compared to mothers with multipara parity status.

Table 4. Distribution of profiles of maternity mothers based on parity status

Parity Status	Preeclampsia		No Preeclampsia		Total	
	n	%	n	%	n	%
Nulliparas and Primiparas	36	56.3%	47	73.4%	83	64.8%
Multipara	28	43.8%	17	26.6%	45	35.2%
Total	64	100%	64	100%	128	100%

Table 5. Distribution of maternity profiles based on previous preeclampsia history

History of Preeclampsia	Preeclampsia		No Preeclampsia		Total	
	n	%	n	%	n	%
There is a history of preeclampsia	5	7.8%	1	1.6%	6	4.7%
No History of Preeclampsia	59	92.2%	63	98.4%	122	95.3%
Total	64	100%	64	100%	128	100%

Table 6. Distribution of maternity profiles based on pregnancy intervals

Pregnancy Interval	Preeclampsia		No Preeclampsia		Total	
	n	%	n	%	n	%
Near (<2 Years)	23	35.9%	28	43.8%	51	39.8%
Far (≥2 Years)	41	64.1%	36	56.3%	77	60.2%
Total	64	100%	64	100%	128	100%

Table 7. Distribution of maternity profiles based on family history of preeclampsia

Family History of Preeclampsia	Preeclampsia		No Preeclampsia		Total	
	n	%	n	%	n	%
There is a family history of preeclampsia	2	3.1%	0	0.0%	2	1,6%
No Family History of Preeclampsia	62	96.9%	64	100.0%	126	98.4%
Total	64	100%	64	100%	128	100%

Table 8. Distribution of maternity profiles based on chronic hypertension history

Variable	Preeclampsia		No Preeclampsia		Total	
	n	%	n	%	n	%
There is Chronic Hypertension	23	35.9%	1	1.6%	24	18.8%
No Chronic Hypertension	41	64.1%	63	98.4%	104	81.3%
Total	64	100%	64	100%	128	100%

Table 9. Distribution of profiles of maternity mothers based on Body Mass Index (BMI)

IMT	Preeclampsia		No Preeclampsia		Total	
	n	%	N	%	n	%
Obesity (>24)	62	96.9%	51	79.7%	113	88.3%
Not obese (20-24)	2	3.1%	13	20.3%	15	11.7%
Total	64	100%	64	100%	128	100%

Table 10. Cross table of age relation to the incidence of preeclampsia

No	Age	Preeclampsia Incidence				P-Value	OR	CI 95%	
		Preeclampsia		No Preeclampsia				Lower	Upper
		n	%	n	%				
1	At risk (<20 Years and >35 Years)	23	35.9%	13	20.3%	0.049	2.021	0.994	4.872
2	Not at risk (20-35 Years)	41	64.1%	51	79.7%				

Table 11. Cross table of the relationship of parity status to the incidence of preeclampsia

No	Parity Status	Preeclampsia Incidence				P-Value	OR	CI 95%	
		Preeclampsia		No Preeclampsia				Lower	Upper
		n	%	n	%				
1	Nulliparas and Primiparas	36	56.3%	47	73.4%	0.041	0.465	0.221	0.977
2	Multipara	28	43.8%	17	26.6%				

Based on Table 12, there is no significant relationship between the previous history of preeclampsia and the incidence of preeclampsia in women giving birth because the p-value is 0.094 (p>0.05). The results of the Odds Ratio test showed that mothers with a history of preeclampsia had 5.339 times the risk of experiencing preeclampsia again compared to mothers without a history of preeclampsia.

Based on Table 13, there is no significant relationship between the interval of pregnancy and the incidence of preeclampsia in women

giving birth because the p-value is 0.367 (p>0.05). Based on the results of the Odds Ratio test, it is known that women with close pregnancy intervals (<2 years) have a 0.721 times risk of experiencing preeclampsia compared to mothers with long gestation intervals (≥ two years).

Based on Table 14, there is no significant relationship between a family history of preeclampsia and the incidence of preeclampsia in women giving birth because the p-value is 0.154 (>0.05). Based on the results of the Odds Ratio test, it is known that mothers with a family history of preeclampsia are at risk of experiencing preeclampsia by 2.032 times compared to mothers without a family history of preeclampsia.

Table 15 shows a significant relationship between chronic hypertension and the incidence of preeclampsia in women giving birth because the p-value is 0.000 (p <0.05). Based on the results of the Odds Ratio test, it is known that mothers with chronic hypertension risk experiencing preeclampsia by 35.341 times compared to mothers without a history of chronic hypertension.

Table 16 shows a significant relationship between BMI and the incidence of preeclampsia in women giving birth because the p-value is 0.003 (p <0.05). Based on the results of the Odds Ratio test, it is known that obese mothers (BMI > 24) have a risk of experiencing preeclampsia by 7.902 times compared to non-obese mothers (IMT 20-24).

Table 12. Cross table of relationship of previous preeclampsia history to preeclampsia incidence

No	Prior history of preeclampsia	Preeclampsia Incidence				P-Value	OR	CI 95%	
		Preeclampsia		No Preeclampsia				Lower	Upper
		n	%	n	%				
1	There is a history of preeclampsia	5	7.8%	1	1.6%	0.094	5.339	0.606	47.051
2	No History of Preeclampsia	59	92.2%	63	98.4%				

Table 13. Cross table of pregnancy interval relationship to preeclampsia incidence

No	Pregnancy Interval	Preeclampsia Incidence				P-Value	OR	CI 95%	
		Preeclampsia		No Preeclampsia				Lower	Upper
		n	%	n	%				
1	Near (<2 Years)	23	35.9%	28	43.8%	0.367	0.721	0.354	1.468
2	Far (≥2 Years)	41	64.1%	36	56.3%				

Table 14. Cross table of the relationship of family history of preeclampsia to the incidence of preeclampsia

No	Family History of Preeclampsia	Preeclampsia Incidence				P-Value	OR	CI 95%	
		Preeclampsia		No Preeclampsia				Lower	Upper
		n	%	n	%				
1	There is a family history of preeclampsia	2	3.1%	0	0.0%	0.154	2.032	1.702	2.427
2	No Family History of Preeclampsia	62	96.9%	64	100.0%				

Table 15. Cross Table of the relationship of chronic hypertension to the incidence of preeclampsia

No	Chronic Hypertension	Preeclampsia Incidence				P-Value	OR	CI 95%	
		Preeclampsia		No Preeclampsia				Lower	Upper
		n	%	n	%				
1	There is Chronic Hypertension	23	35.9%	1	1.6%	0.000	35.341	4.594	271.901
2	No Chronic Hypertension	41	64.1%	63	98.4%				

Table 16. Cross table of the relationship of bmi to the incidence of preeclampsia

No	BMI	Preeclampsia Incidence				P-Value	OR	CI 95%	
		Preeclampsia		No Preeclampsia				Lower	Upper
		n	%	n	%				
1	Obesity (>24)	62	96.9%	51	79.7%	0.003	7.902	1.704	36.643
2	Not obese (20-24)	2	3.1%	13	20.3%				

Using Logistic Regression Analysis, multivariate analysis was performed to determine the most dominant risk factor for preeclampsia. Based on the bivariate analysis above, variables with p-value <0.25 were obtained: age, parity status, previous history of preeclampsia, family history of preeclampsia, chronic hypertension, and BMI. The results of the Logistic Regression Analysis are shown in the Table 17.

Table 17 in Step 1 shows that only chronic hypertension and BMI variables have a p-value <0.05, so other variables must be excluded in Step 2. Table 16 in Step 2 shows the dominant risk factors for preeclampsia, namely chronic hypertension and BMI. The factor that has the greatest influence is chronic hypertension. Chronic hypertension gives an Odds Ratio value of 36,161, while BMI gives an Odds Ratio of 8,267. The most dominant risk factor in this study was chronic hypertension. The following equation is obtained:

$$y = \text{constant} + a1x1 + a2x2 + \ldots\ldots + aixi$$

$$y = -9.055 + 3.588\ (\text{Chronic Hypertension}) + 2.112\ (\text{BMI})$$

Chronic hypertension has a score of 1 if "There is Chronic Hypertension" and a score of 0 if "No Chronic Hypertension." BMI has a value of 1 if "Obesity (BMI> 24)" and a value of 0 if "Not Obese (BMI 20-24). The application of this equation is useful in predicting the chances of experiencing preeclampsia for a mother who gives birth by using the equation:

$$p = 1/(1+e^{-y}) \text{ where } e = 2,7$$

.

Table 17. Table of the relationship of several risk factors for preeclampsia in delivery mothers

	Variable	Koef B	P	OR	CI95%
Step 1	Mother's Age	0.472	0.317	1.603	0.637-4.039
	Parity Status	-0.431	0.340	0.650	0.268-1.575
	Prior history of preeclampsia	1.298	0.280	3.664	0.348-38.596
	Family History of Preeclampsia	18.375	0.999	95535112.880	0.000-NA
	Chronic Hypertension	3.176	0.003	23.953	3.001-191.164
	BMI	2.065	0.037	7.882	1.134-54.812
	Constant	-47.728	0.999	0.000	
Step 2	Chronic Hypertension	3.588	0.001	36.162	4.453-293.655
	BMI	2.112	0.020	8.267	1.386-49.304
	Constant	-9.055	0.000	0.000	

If a delivery mother hasa history of chronic hypertension and BMI > 24, then from the equation above, y = -3.385 will be obtained. Then $p = 1/(1+2,7^{-1,690}) = 0.966$. It means a delivery mother with risk factors for chronic hypertension and BMI > 24 has a 96.6% chance of experiencing preeclampsia.

According to WHO, preeclampsia is higher in developing countries than in developed countries, with a difference of 7 times. The incidence of preeclampsia in Indonesia annually reaches 128,273, or around 5.3%. [14] Other studies that support such as research by Astuti (2015), obtained the same results for the incidence of preeclampsia of 4.74% [35]. It aligns with Marshall's (2000) statement, namely, the incidence of preeclampsia is 5% of total pregnancies [36].

This study yielded 223 cases of preeclampsia from 1,940 deliveries during the Covid-19 pandemic for the 2020-2022 period, whereas before the Covid-19 pandemic for the 2017-2019 period, there were 298 cases of preeclampsia from 4,310 deliveries. This decrease in preeclampsia cases can be linked to the decrease in deliveries during the Covid-19 pandemic compared to before the Covid-19 pandemic.

Based on the number of deliveries at Budhi Asih Hospital during the Covid-19 pandemic for the 2020-2022 period compared to the number of deliveries before the Covid-19 pandemic for the 2017-2019 period, a decrease of 55% was obtained. The number of deliveries per year from 2017 – 2022. This decline could be due to Indonesia's condition when it was declared to be experiencing the Covid-19 pandemic in March 2020, causing anxiety for most people, especially expectant mothers. Based on Septa's research, et al. (2021) found that the mother's anxiety affects the mother's readiness to face childbirth during the Covid-19 pandemic [37]. Other supporting factors, such as pregnant women's access to health services during the Covid-19 pandemic, were limited. Based on Rahmah's research, et al. (2021) found that 14.1% of pregnant women did incomplete health checks, while 44.1% of all pregnant women preferred the hospital as a place for health checks [38]. It shows that there is a need for health services during the Covid-19 pandemic, but people are experiencing difficulty accessing them. A healthcare system that implements strict health protocols needs to be implemented to ensure the safety of health workers and pregnant women from infection with SARS-CoV-2.

The age range of the research subjects was 18-44 years. Pregnancy at <20 years or >35 years is theoretically risky for the mother to experience various complications during pregnancy. The average pregnancy in this study occurred at a safe reproductive age (20-35 years). The profile of the gestational age range in this study was 20-35 years (64.1%), while <20 years and >35 years (35.9%). Similar results were also obtained in the control group, namely ages 20-35 years (79.7%), while those aged <20 years and >35 years (20.3%).

Based on bivariate analysis, it was found that age had a significant relationship with the incidence of preeclampsia at Budhi Asih Hospital in 2020-2022 (p-value 0.049). Pregnant women aged <20 years and >35 years have a 2.021 times greater chance of experiencing preeclampsia than those aged 20-35. The results of this study follow the research conducted by Yenny et al. (2021) that there was a significant relationship between maternal age and the incidence of preeclampsia (p-value 0.010) and the risk of preeclampsia increased for pregnant women aged <20 years and >35 years by 13.2 times [11]. This increased risk of preeclampsia is associated with the maturation of the reproductive organs, which has not fully occurred at the age of <20 years, besides that the psychological factors of the mother who are less stable in terms of readiness for pregnancy can also increase the incidence of hypertension at a young age [25]. Physiological changes to the reproductive organs and the birth canal occur at the age of >35, namely decreased flexibility. Preeclampsia is generally more common in the early (adolescent) and late reproductive years (over 35 years). Decreased cardiovascular function occurs due to the blood vessels in the uterus degenerating, and the arteries lose their elasticity with increasing maternal age.

Preeclampsia is more common in first-born pregnancies than in subsequent pregnancies. According to Gaugler-Senden (2005), preeclampsia is one of the complications of pregnancy in mothers who have had children [39]. This statement is based on the theory that blocking antibodies formed in the placental plasma does not occur completely during the first pregnancy and will experience improvements as the next pregnancy progresses. The results of this study were that the proportion of nulliparous

and primiparous patients who had preeclampsia was 56.3% and 73.4% in non-preeclampsia patients. The proportion of preeclampsia in multiparous patients (give birth > 4 times) was 43.7% and 26.6% in non-preeclampsia patients.

Based on bivariate analysis, it was found that parity status had a significant relationship with the incidence of preeclampsia at Budhi Asih Hospital in 2020-2022 (p-value 0.041). Mothers with nullipara or primipara parity status, compared to multipara parity status, have a 0.465 times greater risk of experiencing preeclampsia.

This study's results agreed with the research result conducted by Yenny et al. (2021), which states that the chance of a mother with primipara parity status is eight times to experience preeclampsia. [11] Similar results by research by Titi Arikah et al. (2019) showed that there is a relationship between parity status and the incidence of hypertension in pregnant women (p-value 0.047) and the OR = 2.5, which means that pregnant women with primigravida parity have a 2.5 times chance of experiencing hypertension compared to multigravida parity [40]. Different results were obtained by Nurfatimah research, et al. (2020), that more hypertension was found in mothers with a history of multiparas. The younger a person's pregnancy (primipara) or, the more a person gives birth (multipara), the greater the chance for a mother to experience preeclampsia. Mothers with multipara parity status are more susceptible to serious complications, one of which is preeclampsia, due to the possibility of a decrease in blood flow to the placenta, which will disrupt fetal growth due to lack of oxygenation. Reports of hypertensive disorders in pregnancy are more severe in multiparous women.

The results of statistical tests showed no significant relationship between the history of preeclampsia and the incidence of preeclampsia in mothers giving birth at Budhi Asih Hospital in 2020-2022 (p-value 0.094). Research conducted by Nuning and Mardiana (2016) also obtained similar results, namely that a history of preeclampsia had a significant relationship with the incidence of preeclampsia (p-value 0.0001) [41]. Another study conducted by Guerrier et al. (2013) found that a history of preeclampsia with the incidence of preeclampsia has a strong relationship, with a risk of 21 times [42]. Univariate analysis found that the proportion of categories with a history of preeclampsia in preeclampsia patients was 7.8%, while the category without a history of preeclampsia was 92.2%. The proportion of categories with a history of preeclampsia in non-preeclampsia patients was 1.6%, while the category without a history of preeclampsia was 98.4%. The Chi-Square test results in this study p-value > 0.05 could be because the proportion of previous preeclampsia history was spread evenly.

Based on the results of bivariate analysis, a p-value of 0.367 was obtained, where the p-value was > 0.05, which means that there was no relationship between the pregnancy interval and the incidence of preeclampsia. Univariate analysis showed an almost even distribution of proportions. This results in no relationship. The proportion of preeclampsia patient pregnancies for the distant category (≥ two years) was 64.1%, while the close category (<2 years) was 35.9%. The distant category (≥2 years) in non-preeclampsia patients was 56.3%, while the close category (<2 years) was 43.8%.

Rimawati et al. (2019) showed a significant relationship between the pregnancy interval and the incidence of preeclampsia. The OR value was 0.329, meaning 0.329 is a greater risk of experiencing preeclampsia in women with close pregnancy intervals (<2 years) [43]. Research by Marlina et al. (2019) also showed a relationship between the interval of pregnancy and the incidence of preeclampsia and obtained an OR > 1. Close pregnancy intervals have a 4.911 chance of experiencing preeclampsia compared to distant pregnancy intervals. According to Marlina (2019), this could be because pregnancies that occur after previous pregnancies at intervals of less than two years will progressively reduce the mother's health [44].

Based on the results of bivariate analysis, it was shown that there was no significant relationship between a family history of preeclampsia and the incidence of preeclampsia (p-value 0.154). It could be due to the almost even distribution of proportions, and there were only two pregnant women with a family history of preeclampsia, only found in the case group.

This research findings are not in agreement with Budi Rahayu's (2019) research, which found a relationship between a family history of preeclampsia and the incidence of preeclampsia (p-value 0.016; OR 2.59) [45]. Research conducted by Prawirohardjo (2013) reported that

daughters of mothers who experience preeclampsia are also 26% likely to experience preeclampsia [46]. The bivariate analysis results showed a significant association between a history of chronic hypertension and the incidence of preeclampsia (p-value 0.000) with a 35 times chance of experiencing preeclampsia compared to mothers without a history of chronic hypertension. Based on multivariate analysis, it is known that chronic hypertension is the main risk factor that has the most influence on causing preeclampsia with a p-value of 0.001 (OR 36.161 95% CI 4.453-293.655).

The incidence of preeclampsia increases in women with a history of chronic hypertension. It is associated with vasospasm in chronic hypertension and can cause persistent vascular damage. This endothelial dysfunction causes poor tissue perfusion in various organs, including placental perfusion, so the placenta experiences ischemia. Mothers with chronic hypertension have a >10-fold risk of developing preeclampsia at ≤33 weeks' gestation and an approximately 5-fold risk at ≥34 weeks gestation.

Septiasih's research (2018) also reported that chronic hypertension was the dominant factor of preeclampsia (p-value 0.000; OR 5.416; 95% CI 2.623-11.186) [47]. Research conducted by Miranda et al. (2021) also obtained similar results that chronic hypertension had a significant relationship with the incidence of preeclampsia (p-value 0.007) and provided a 3.5 times chance of experiencing preeclampsia [48].

Based on the distribution of BMI in this study, it was found that more preeclamptic patients were obese compared to those without preeclampsia. It supports the theory that overweight and obesity are risk factors for preeclampsia. Kesumawati et al. (2020) found that mothers with BMI <20 and >24 had five times the risk of experiencing preeclampsia compared to mothers with BMI 20-24 [49]. Similar results were obtained in a study conducted by Ulfa et al. (2019) that there was a significant relationship between BMI and the incidence of preeclampsia (p-value 0.000), and the OR value of 5.923 meant that obese mothers had five times the chance of experiencing preeclampsia.

The basic mechanism of hypertension in pregnancy is related to high BMI. Dyslipidemia will trigger oxidative stress and lead to endothelial dysfunction. It is associated with increased adipokine production in adipose tissue. The production of adipoksins, for example, leptin, is associated with increased inflammatory events, insulin resistance syndrome, and oxidative stress. Someone who is obese, as well as pregnant women with preeclampsia, have high levels of leptin, which is associated with hypertension because one of the functions of leptin is to stimulate the sympathetic system and increase blood pressure. Factors such as a high-fat diet, inflammation, oxidative stress, dyslipidemia, and insulin resistance are associated with increased levels of ADMA (asymmetric dimethylarginine). ADMA is one of the endogenous inhibitors of NOS, which acts as an inhibitor of arginine to turn into NO, causing a decrease in NO. Endothelial dysfunction will eventually occur due to superoxide anions produced by endothelial NOS, so oxidative stress will increase.

4. CONCLUSION

Based on the results of a study, it is concluded that the characteristics of patients giving birth to mothers with preeclampsia at Budhi Asih Hospital during the Covid-19 pandemic are: a) The number of deliveries during the Covid-19 pandemic has decreased compared to before the Covid-19 pandemic; b) The highest proportion of mothers with preeclampsia were patients aged 20-35 years, nullipara or primipara, no history of preeclampsia, long gestation interval (≥ two years), no family history, no chronic hypertension, and obesity (BMI). >24); c) The risk factors for preeclampsia in women giving birth at Budhi Asih Hospital during the Covid-19 pandemic that had a significant relationship with the incidence of preeclampsia were the mother's age, parity status, chronic hypertension, and BMI; d) Risk factors for the occurrence of preeclampsia in women giving birth at Budhi Asih Hospital during the Covid-19 pandemic were chronic hypertension, BMI (> 24), maternal age (<20 years or > 35 years), and parity status (nullipara or primipara); and e) The most dominant risk factor for preeclampsia in women giving birth at Budhi Asih Hospital during the Covid-19 pandemic was chronic hypertension.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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