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Reproductive Status Affecting the Incidence of Hypertension in Pregnancy at Prof. Dr. Chairuddin P. Lubis Educational Hospital, Medan City

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Abstrak: Hypertension in pregnancy is one of the leading causes of maternal mortality, with a global prevalence of 5–10% (Khedagi & Bello, 2021). This study aims to analyze the effect of reproductive status—maternal age, gravidity, and parity—on the incidence of hypertension in pregnancy at Prof. Dr. Chairuddin P. Lubis Educational Hospital, Medan. A case-control design was employed with 96 respondents, consisting of 48 cases and 48 controls. Bivariate analysis revealed that pregnant women aged ≥35 years have a 2.839-fold higher risk of developing hypertension compared to those aged <35 years (OR=2.839; 95% CI: 1.123–7.177; p=0.027). First pregnancy (primigravida) increases the risk by 2.742 times compared to multigravida (OR=2.742; 95% CI: 1.047–7.178; p=0.040), while nulliparous women have a 2.714-fold higher risk compared to those who have given birth (OR=2.714; 95% CI: 1.101–6.693; p=0.030). Multivariate analysis identified maternal age ≥35 years and nulliparity as the most significant predictors (p=0.005). These findings align with studies by Wiranto & Putriningtyas (2021), Hinkosa et al. (2020), and Luo et al. (2020), which confirmed that advanced maternal age and nulliparity increase the risk of pregnancy complications. The novelty of this research lies in integrating all three reproductive status factors as simultaneous predictors of hypertension risk, providing a new perspective compared to previous studies focused on single variables. Based on these findings, early detection and targeted health education for high-risk mothers are strongly recommended.

Keywords: hypertension in pregnancy, maternal age, primigravida, nulliparity, reproductive status, risk predictors

1. INTRODUCTION

World Health Organization data reports that the global maternal mortality rate in 2020 was 223 deaths per 100,000 live births. This is equal to nearly 800 maternal deaths every day or one maternal death every two minutes (WHO, 2023b). This high maternal mortality rate remains an important public health problem that requires a reduction of 11.6 per cent annually between 2021 and 2030 to achieve the Sustainable Development Goals (SDGs) target of less than 70 deaths per 100,000 live births worldwide to ensure healthy lives and improved well-being for all people at all ages (WHO, 2023a).

Indonesia is the fourth country in the Southeast Asian region with the highest maternal mortality rate in 2020 after Timor-Leste, Cambodia and Myanmar, at 173 deaths per 100,000 live births (WHO, 2023b). From 2022 to 2023, the number of maternal deaths in Indonesia was reported to increase from 3,572 deaths to 4,482 deaths (Kemenkes RI, 2024). Almost 75 per cent of all maternal deaths globally are caused by complications during pregnancy and after delivery, especially hypertension in pregnancy, which are preventable (WHO, 2024).

Hypertension in pregnancy is estimated to affect 5-10% of pregnancies worldwide and is one of the main causes of maternal mortality that is still increasing (Khedagi & Bello, 2021). Global Burden Disease data states that the incidence of hypertension in pregnancy has

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increased by 10.92% worldwide from 1990 to 2019 (Wang et al., 2021). In Indonesia, despite the decreased number of cases, hypertension in pregnancy is still the leading cause of maternal death, with 801 cases in 2022 (Kemenkes RI, 2023) and 412 cases in 2023 (Kemenkes RI, 2024). North Sumatra Province is one of the provinces in Indonesia with an increase in the maternal mortality rate per 100,000 live births from 50.60 deaths in 2022 to 88.44 deaths in 2023. Medan City, located in North Sumatra Province, also reported that in 2023, 20% of pregnant women suffered from pregnancy complications, including hypertension in pregnancy, and this number increased to 20.6% in 2024 (Kemenkes RI, 2024).

The high maternal mortality rate caused by complications during pregnancy and after delivery, including hypertension in pregnancy, is influenced by various direct and indirect factors. Factors that directly affect the incidence of hypertension in pregnancy include reproductive status, which includes maternal age at pregnancy, parity, and gravidity (McCarthy & Maine, 1992). Pregnant women aged 35 years and above have a significantly higher incidence of pregnancy complications than pregnant women of younger ages. The incidence of gestational hypertension and preeclampsia/eclampsia was found to be higher in nulliparous pregnant women aged 35 years or older compared to nulliparous pregnant women aged 20-29 years (Luo et al., 2020). First-pregnancy (primigravida) and nulliparous women were also reported to be independently associated with a higher prevalence of hypertension in pregnancy (Hinkosa et al., 2020).

The results of the preliminary survey conducted by the researchers showed that Prof. Dr Chairuddin P. Lubis Educational Hospital is one of the hospitals in Medan City that reported a significant increase in hypertension cases in pregnant women by 8% from 2023 to 2024. In 2023, it was reported that there were 12% (109 cases) of hypertension in pregnancy out of a total of 944 pregnant women patients. From January to August 2024, there were 20% (125 cases) of hypertension in pregnancy out of a total of 642 pregnant women who received health services in this hospital. Based on the preliminary survey results showing an increase in cases, we were interested in examining the characteristics of reproductive status among patients with hypertension in pregnancy and its effect on hypertension in pregnancy at Prof. Dr Chairuddin P. Lubis Educational Hospital.

2. METHODS

This study is a quantitative study with a case-control design. The study population included all inpatients and outpatients of pregnant women at Prof. Dr. Chairuddin P. Lubis Educational Hospital. Based on the calculation of sample size using the formula of Lemeshow

et al. (1990), the number of samples in this study was determined as 48 people in each case and control group. Sample selection was done by consecutive sampling, in which samples met the inclusion criteria and were willing to become respondents by signing informed consent. The case inclusion criteria were third-trimester pregnant women with hypertension (based on a doctor's diagnosis or systolic blood pressure ≥140 mmHg and/or diastolic ≥90 mmHg after being examined by a doctor or health worker). In comparison, the inclusion criteria in the control group were third-trimester pregnant women who did not have hypertension (based on a doctor's diagnosis or had a systolic blood pressure <140 mmHg and diastolic <90 mmHg after being examined by a doctor or health worker), meanwhile, the exclusion criteria for cases and controls were third-trimester pregnant women who had poor general condition, having mental or psychiatric disorders, or having hearing impairment, unable to communicate well, and unwilling to be interviewed directly.

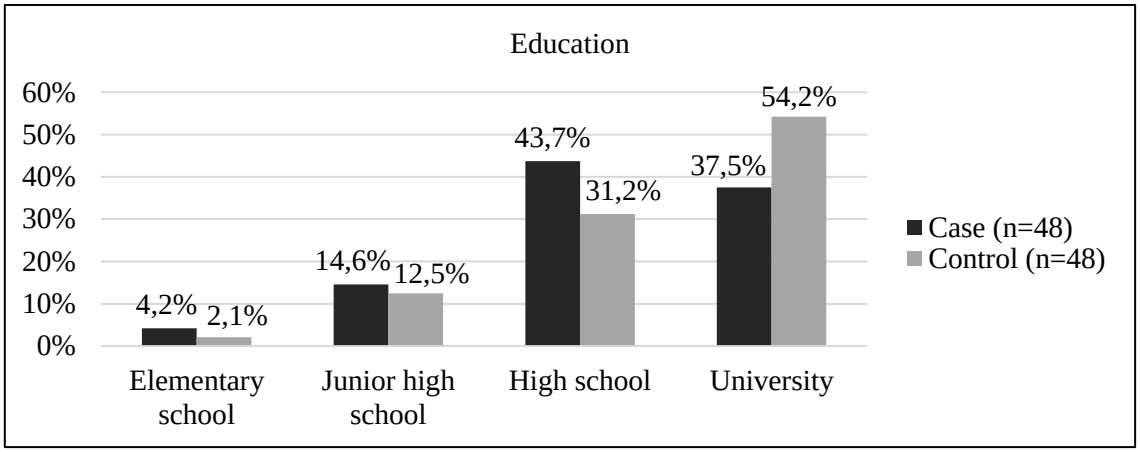
The dependent variable in this study was the incidence of hypertension in pregnancy, while the independent variables were reproductive status factors consisting of age, gravidity, and parity. Maternal age at pregnancy was determined through a questionnaire and categorized into <35 years and ≥35 years. Gravidity was the total number of pregnancies the mother had experienced (including the current pregnancy) regardless of the outcome of the pregnancy (abortion, live birth, stillbirth), which was also known through a questionnaire and further categorized into primigravida (first pregnancy) and multigravida. Meanwhile, parity was the number of deliveries the mother had experienced in giving birth to a neonate regardless of whether the child was viable or nonviable (stillbirth), which was known through a questionnaire and categorized into two categories: nulliparous (never given birth) and primiparous/multiparous (had given birth ≥1 time).

Furthermore, the data obtained is analyzed through univariate, bivariate, and multivariate. The univariate analysis describes the characteristics of respondents; bivariate analysis is used to determine the effect of each independent variable on the dependent variable with a simple logistic regression test, while multivariate analysis aims to test the effect of independent variables simultaneously on the dependent variable to determine the characteristics of reproductive status that most significantly affect the incidence of hypertension in pregnancy using multiple logistic regression test. The significance level was 95% or had a significant effect if the p-value was <0.05.

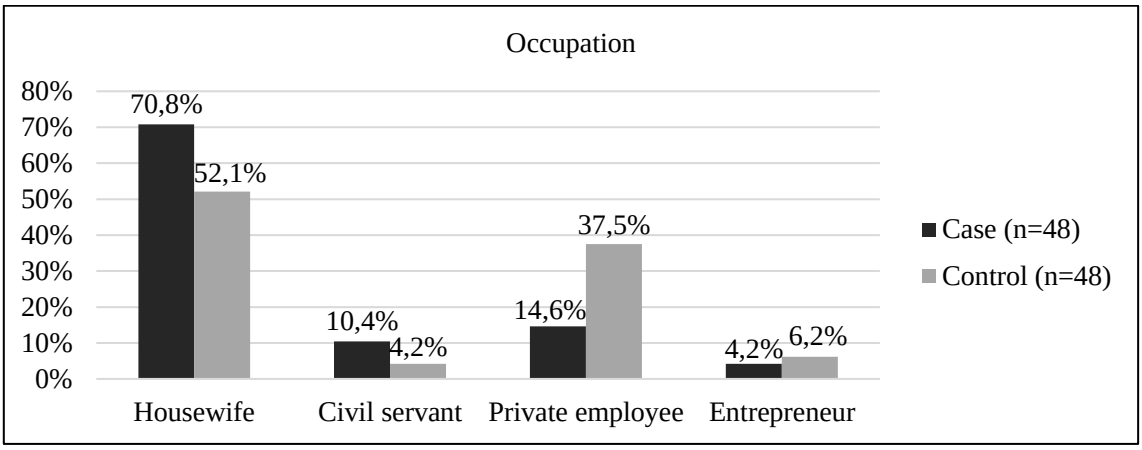
3. RESULTS

The following results were obtained based on data collected from each of the 48 pregnant women patients in the case and control groups.

Univariate Analysis



(a)



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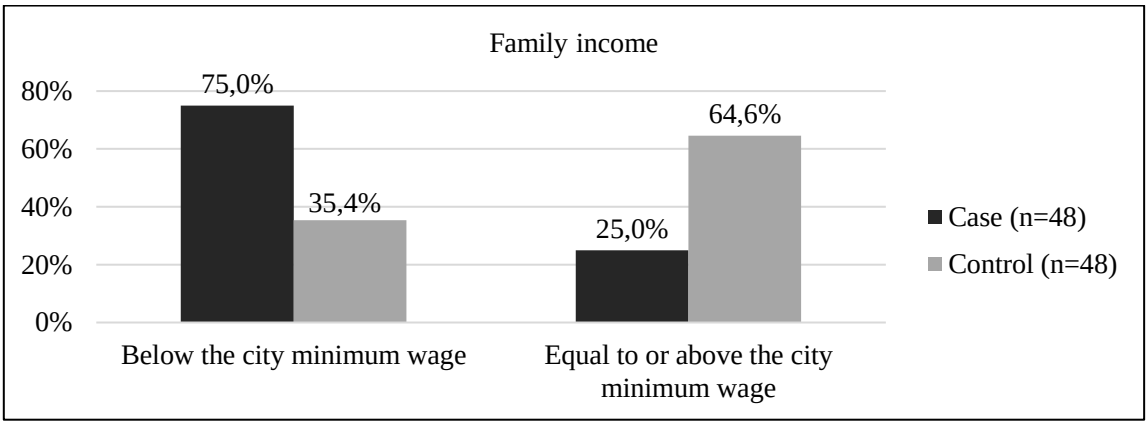

(c)

Figure 1. Characteristics of pregnant women patients at Prof. Dr. Chairuddin P. Lubis Educational Hospital based on (a) latest education, (b) occupation, and (c) family income

As shown in Figure 1, the study's results show that most pregnant women had a high school education in the case group, 43.7% (21 respondents) and university, 37.5% (18 respondents). In contrast, the most educated pregnant women in the control group were university, 54.2% (26 respondents), followed by high school education, 31.2% (15 respondents). The majority of pregnant women in the case group were homemakers, at 70.8 per cent (34 respondents), while the rest worked as private employees (14.6%), civil servants (10.4%), and entrepreneurs (4.2%). Meanwhile, in the control group, most pregnant women were also housewives at 52.1% (25 respondents), followed by private employees (37.5%), and a few worked as entrepreneurs (6.2%) and civil servants (4.2%). Based on income, most pregnant women in the case group had family income below the Medan city minimum wage (IDR 3,769,082.00) at 75% (36 respondents). In contrast, in the control group, most pregnant women had family income equal to or above the Medan city minimum wage at 64.6 per cent (31 respondents).

Bivariate Analysis

The bivariate analysis results with a simple logistic regression test to determine the effect of each independent variable (age, gravidity, and parity) on the dependent variable (incidence of hypertension in pregnancy) are presented below.

Table 1. The effect of age on the incidence of hypertension in pregnancy at Prof. Dr. Chairuddin P. Lubis Educational Hospital Medan City

Age	The incidence of hypertension in pregnancy				p	OR	95% CI
	Case		Control				
	n	%	n	%			
≥35 years	19	39.6	9	18.8	0.027	2.839	1.123–7.177
<35 years	29	60.4	39	81.2			
Total	48	100	48	100			

Based on the information in Table 1, it is seen that most of the pregnant women patients were less than 35 years old in the case (60.4%) and control (81.2%) groups, while pregnant women aged ≥35 years were more in the case group (39.6%) compared to the control group (18.8%). The results showed that age affected the incidence of hypertension in pregnancy with a p-value of 0.027 ($p<0.05$) and an OR of 2.839, which means that the risk of hypertension in pregnant women aged 35 years and over is 2.839 times greater than those under 35 years of age.

Table 2. The effect of gravidity on the incidence of hypertension in pregnancy at Prof. Dr. Chairuddin P. Lubis Educational Hospital Medan City

Gravidity	The incidence of hypertension in pregnancy				p	OR	95% CI
	Case		Control				
	n	%	n	%			
Primigravida	17	35.4	8	16.7	0.040	2.742	1.047–7.178
Multigravida	31	64.6	40	83.3			
Total	48	100	48	100			

As shown in Table 2, the study's results show that most pregnant women in the case (64.6%) and control (83.3%) groups were multigravida. In comparison, primigravida pregnant women in the case group (35.4%) were more than the control group (16.7%). Bivariate analysis showed a significant effect of gravidity on the incidence of hypertension in pregnancy (p=0.040) with an OR value of 2.742, which means that the risk of hypertension in primigravida pregnant women is 2.742 times greater than in multigravida.

Table 3. The effect of parity on the incidence of hypertension in pregnancy at Prof. Dr. Chairuddin P. Lubis Educational Hospital Medan City

Parity	The incidence of hypertension in pregnancy				p	OR	95% CI
	Case		Control				
	n	%	n	%			
Nuliparous	20	41.7	10	20.8	0.030	2.714	1.101–6.693
Primiparous/Multiparous	28	58.3	38	79.2			
Total	48	100	48	100			

Table 3 shows most pregnant women were primiparous/multiparous in the case (58.3%) and control (79.2%) groups. Meanwhile, there were more nulliparous pregnant women in the case group (41.7%) compared to the control group (20.8%). The results showed that parity also affected the incidence of hypertension in pregnancy with a p-value of 0.030 ($p<0.05$) and an OR of 2.714, which indicated that the risk of hypertension in pregnant women who had never given birth (nulliparous) was 2.714 times greater than those who had given birth before (primiparous or multiparous).

Multivariate Analysis

The results of multivariate analysis using multiple logistic regression tests to determine the effect of reproductive status (age, gravidity, and parity) on the incidence of hypertension in pregnancy are presented below.

Table 4. Multivariate analysis results

	Variables	B	p	OR	95% CI	
					Lower	*Upper*
Step 1	Age	1.458	0.005	4.299	1.568	11.785
	Gravidity	0.460	0.657	1.585	0.208	12.085
	Parity	1.023	0.299	2.783	0.403	19.229
	Constant	–0.858	0.009	0.424		
Step 2	Age	1.452	0.005	4.274	1.558	11.721
	Parity	1.404	0.005	4.072	1.522	10.892
	Constant	–0.856	0.010	0.425		

The results of the multivariate analysis, as presented in Table 4 above, show that when tested together, the reproductive status factor that most significantly affects the incidence of hypertension in pregnancy is the maternal age at pregnancy with a p-value of 0.005 ($p<0.05$) and an OR value of 4.274 which indicates that the risk of hypertension in pregnant women aged 35 years and over is 4.274 times greater than those under 35 years of age.

4. DISCUSSION

The results showed that age is the reproductive status factor that most significantly affects the incidence of hypertension in pregnancy (p=0.005), with the risk of hypertension in pregnant women aged 35 years and over 2.839 times greater than that of pregnant women under 35 years of age. This is consistent with the results of Wiranto & Putriningtyas's (2021) research on pregnant women in the Gunungpati Health Center working area in Semarang City, which found that maternal age 35 years or older during pregnancy was associated with an increased risk of hypertension in pregnancy (p=0.021). Hinkosa et al. (2020), in a case-control study conducted in Ethiopia, also suggested that the risk of hypertension in pregnant women aged 35 years or more was 2.508 times greater than that of pregnant women under 35 years of age (OR=2.508 (95% CI: 1,078–5,832); p<0.001). Another study by Febyan & Pemaron (2020) also stated that maternal age was associated with the incidence of hypertension at Bhayangkara Denpasar Hospital (OR=2.770 (95% CI: 1,410–5,430); p=0.004). Specifically, Aziz et al. (2022), in their research conducted at Hasan Sadikin Hospital Bandung, found that pregnant women aged older than 35 years were more at risk of developing preeclampsia compared to pregnant women aged 35 years or younger (p=0.042).

Pregnant women older than 35 years of age are reported to be more likely to suffer from various pregnancy complications, such as gestational diabetes, hypertension in pregnancy, preterm birth, stillbirth, caesarean delivery, and maternal and neonatal morbidity and mortality.

These risks increase with advancing maternal age. Although many studies are showing that older pregnant women are at higher risk of developing hypertension in pregnancy, the biological mechanisms underlying the relationship of whether age independently or indirectly causes this condition are not well known (Luo et al., 2020; Lopian et al., 2023).

Several factors associated with the development of pregnancy-induced hypertension are found in older pregnant women, such as endothelial dysfunction, increased levels of anti-angiogenic factors, and an elevated inflammatory state. The normal ageing process induces various changes, including decreased vascular elasticity and endothelial dysfunction, that may hinder the physiological adaptation of the cardiovascular system during pregnancy. Another mechanism proposed in theories to explain the independent effect of maternal ageing on the incidence of hypertension in pregnancy is an increased inflammatory state and oxidative stress. Studies have also shown that older women have increased resistance in the uterine arteries during the first trimester of pregnancy, reduced endometrial spiral artery volume, and increased levels of anti-angiogenic factors, such as sFlt-1, all of which are associated with impaired placental function in the development of pregnancy-induced hypertension. Additionally, the increased risk of various other placenta-mediated conditions, such as retarded fetal growth and stillbirth in older pregnant women, adds to the evidence that placentation disorders, such as those in the pathophysiology of hypertension in pregnancy, are more prone to occur with advancing maternal age. Maternal age as a risk factor for hypertension in pregnancy is suggested to not only play an independent role but may be mediated by the increased prevalence of comorbidities in older pregnant women. Various comorbidities, such as chronic hypertension, DM, obesity, renal disease, and autoimmune diseases that are pre-existing in older pregnant women have been shown to indirectly increase the risk of developing hypertension in pregnancy (Lopian, Kashani-Ligumsky & Many, 2023; Wang et al., 2021).

The results of this study also show that gravidity has an independent effect on the incidence of hypertension in pregnancy (p=0.040), with the risk of hypertension in primigravida pregnant women 2.742 times greater than that of multigravida. This is in line with research conducted by Arikah et al. (2020) on pregnant women in the working area of the Kramat Jati Health Center, East Jakarta, which found that gravidity was associated with the incidence of hypertension in pregnant women (OR = 2.556 (95% CI: 1.097–5.956); p = 0.047). A case-control study conducted by Hinkosa et al. (2020) also showed that in the case group (pregnant women who suffered from hypertension in pregnancy), most (54.8%) were the first pregnancy (primigravida) and the risk of hypertension in pregnancy in primigravida pregnant

women was 3.392 times greater than that of multigravida (OR=3.392 (95% CI: 2.159–5.330); p<0.001). Haile et al. (2021) in their research also stated that among the factors related to the obstetric status of pregnant women tested simultaneously in multivariate analysis, primigravida is a significant factor affecting the risk of preeclampsia. The risk of developing preeclampsia in pregnant women with primigravida status was reported to be 5.41 times higher than that of multigravida (OR=5.41 (95% CI: 2.85–10.29); p <0.001).

Based on the results of this study, it was also found that there was an independent effect of parity on the incidence of hypertension in pregnancy (p=0.030), with the risk of hypertension in pregnant women who had never given birth (nulliparous) 2.714 times greater than those who had given birth (primiparous or multiparous). This is consistent with the case-control study by Hinkosa et al. (2020), which showed that nulliparity is one of the factors that increase the risk of hypertension in pregnancy (OR = 4.35 (95% CI: 2.36–8.03); p <0.001). Harris et al. (2024) in their study found that the incidence of preeclampsia was more common among nulliparous pregnant women (2.6%) compared to primiparous or multiparous (1.5%). The results of the study also stated that the risk of preeclampsia in pregnant women without a history of previous childbirth was reported to be 3.61 times higher than that of pregnant women who had given birth before (OR = 3.61 (95% CI: 2.67–4.94); p <0.001). Another study conducted by Dai et al. (2023) also showed that nulliparity had a significant effect on the incidence of gestational hypertension and preeclampsia with increasing risk with advancing maternal age (p-value<0.05).

Gravidity and parity have been widely suggested as contributing factors to the development of hypertension in pregnant women. First-time pregnant women (primigravida) are reported to have a higher incidence of hypertension in pregnancy (Upadya & Rao, 2018). Some studies have also concluded that nulliparous women have a higher risk of developing hypertension during their pregnancy compared to primiparous and multiparous women. Although not fully understood, studies have suggested immune maladaptation, angiogenic factor imbalance, genetic predisposition, or oxidative stress as mechanisms that may explain this association (Phipps et al., 2019; Chang, Seow, & Chen, 2023).

Maternal immune tolerance is necessary during pregnancy due to the semiallogenic nature of the fetus, which has genetic material from both the mother and father and thus can be perceived as an antigen (foreign body) by the maternal immune system. During normal pregnancy, the mechanisms that regulate the mother's immune response must be able to adapt towards fetal-derived tissues, including the placenta, while maintaining maternal immunity

from various infectious organisms. Maladaptation of maternal immunological response to fetal-derived trophoblasts in early pregnancy may lead to abnormal placentation and initiate the development of hypertension in pregnancy. The higher risk of pregnancy-induced hypertension in both primigravida and nulliparous is associated with the mother's first exposure to chorionic villi, particularly fetal-derived trophoblasts. Failure of immune tolerance or immune maladaptation at this first exposure is suggested to be one of the mechanisms contributing to the increased risk of hypertension in pregnancy in primigravida compared to multigravida women as a successful first pregnancy without incident hypertension in pregnancy may induce adaptive changes that sustain immune tolerance in subsequent pregnancies (Lokki et al., 2018).

The first pregnancy is also associated with maternal vulnerability to experiencing a greater burden of psychological stress, which can indirectly affect the increase in cortisol levels that induce vasoconstriction and the release of inflammatory cytokines that can aggravate oxidative stress and endothelial dysfunction, which all contribute to the pathomechanism of the development of hypertension in pregnancy (Hinkosa et al., 2020). Moreover, primigravida and nulliparous women were found to have an angiogenic imbalance characterized by relatively higher levels of sFlt-1 and sFlt- 1/PIGF ratio in the circulation, which is likely due to the process of angiogenesis (formation of new vascularization to supply blood to the placenta) that could contribute to their tendency to develop pregnancy-induced hypertension (Chang, Seow, & Chen, 2023). A study conducted by Bdolah et al. (2014) found that sFlt-1 levels and sFlt- 1/PIGF ratio were similar in the primigravida-nulliparous women group and the multigravida-nulliparous group. This finding suggests that nulliparous women who have had previous abortions are not protected from the risk of hypertension in subsequent pregnancies, indicating that the mechanism of angiogenic imbalance may be more influenced by parity than gravidity.

Parity is also shown to influence the physiological adaptation of the cardiovascular system during pregnancy to fulfil the needs of the developing fetus. Blood pressure, especially in early pregnancy, was found to be higher in nulliparous than multiparous pregnant women. Research also shows that nulliparous women have a higher risk of experiencing decreased blood flow in the uterus compared to multiparous. This finding is suggested to be explained by the effect of parity on the spiral artery. During early placentation, trophoblast cells invade the thick-walled spiral artery and convert it into thin-walled blood vessels that can dilate and facilitate increased uteroplacental blood flow. These modifications may persist in the maternal vasculature and alter its suitability in subsequent pregnancies such that the incidence of

hypertension in multiparous women is less reported than nulliparous (Rurangirwa et al., 2012). In addition, differences between nulliparous and multiparous pregnant women regarding other risk factors, such as age at pregnancy, history of diabetes mellitus, multiple pregnancies, stress levels, etc., may also indirectly explain the effect of parity on the incidence of hypertension in pregnancy (Chang, Seow, & Chen, 2023).

5. CONCLUSION

This study reveals that reproductive status, including maternal age, gravidity, and parity, significantly influences the incidence of hypertension in pregnancy. The findings highlight that maternal age ≥35 years, first pregnancy (primigravida), and nulliparity notably increase the risk of developing hypertension during pregnancy. Multivariate analysis indicates that maternal age is the most dominant factor, with a 4.27-fold higher risk of hypertension in pregnant women aged ≥35 years compared to those under 35. These factors are important indicators for preventing and managing hypertensive disorders in pregnancy at healthcare facilities such as Prof. Dr. Chairuddin P. Lubis Educational Hospital in Medan.

The significance of this research lies in its contribution to expanding the understanding of the relationship between reproductive status and hypertension in pregnancy, particularly within the context of the Medan population. Previous studies have highlighted the roles of maternal age and obstetric status in increasing the risk of hypertension. However, this study provides a new perspective by emphasizing the cumulative risk of combining these three factors. Compared to earlier research that predominantly focused on one or two variables, this study demonstrates novelty by simultaneously integrating multivariate analysis of the three primary reproductive status factors. This approach strengthens existing scientific evidence and provides relevant contextual data for developing local health policies.

From a practical perspective, these findings encourage implementing more intensive health education programs for prospective mothers, especially those aged ≥35, primigravida, and nulliparous. These programs may include counselling on hypertension risk factors and the importance of regular antenatal check-ups. Additionally, strengthening early detection services and preconception counselling can be an effective strategy to reduce hypertension in high-risk groups. Prof. Dr. Chairuddin P. Lubis Educational Hospital is also advised to enhance the capacity of healthcare providers to identify these risk factors early, ensuring timely and appropriate interventions.

As a closing remark, this study underscores that reproductive status is a critical aspect of maternal health that requires serious attention. The contribution of this research lies in

identifying risk factors for hypertension in pregnancy and offering preventive strategies that can be widely implemented. By understanding and managing these identified risk factors, the incidence of pregnancy-related hypertension can be minimized, ultimately contributing to the reduction of maternal mortality in Indonesia.

REFERENCE

Abalos, E., Cuesta, C., Grosso, A. L., Chou, D., & Say, L. (2013). Global and regional estimates of preeclampsia and eclampsia: a systematic review. European journal of obstetrics & gynaecology and reproductive biology, 170(1), 1-7.

Andraweera, P. H., Dekker, G. A., & Roberts, C. T. (2012). The vascular endothelial growth factor family in adverse pregnancy outcomes. *Human reproduction update*, 18(4), 436-457.

Antwi, E., Amoakoh-Coleman, M., Vieira, D. L., Madhavaram, S., Koram, K. A., Grobbee, D. E., ... & Klipstein-Grobusch, K. (2020). A systematic review of prediction models for gestational hypertension and preeclampsia. *PLoS One*, 15(4), e0230955.

Arikah, T., Rahardjo, T. B. W., & Widodo, S. (2020). Faktor risiko kejadian hipertensi pada ibu hamil di Puskesmas Kramat Jati Jakarta Timur tahun 2019. *Jurnal Penelitian dan Pengembangan Kesehatan Masyarakat Indonesia*, 1(2), 115–124.

Aziz, M. A., Wibowo, A., Almira, N. L., & Sutjighassani, T. (2022). Relationship of Age, Body Mass Index, Gravida, and Parity in Pregnant Women with the Incidence Preeclampsia. Indonesian Journal of Obstetrics & Gynecology Science, 5(2), 208–216.

Bartsch, E., Medcalf, K. E., Park, A. L., & Ray, J. G. (2016). Clinical risk factors for preeclampsia determined in early pregnancy: systematic review and meta-analysis of large cohort studies. *Bmj*, 353.

Bdolah, Y., Elchalal, U., Natanson-Yaron, S., Yechiam, H., Bdolah-Abram, T., Greenfield, C., Goldman-Wohl, D., Milwidsky, A., Rana, S., Karumanchi, S. A., Yagel, S., & Hochner-Celnikier, D. (2014). The relationship between nulliparity and preeclampsia may be explained by altered circulating soluble fms-like tyrosine kinase 1. *Hypertension in Pregnancy*, 33(2), 250–259.

Bdolah, Y., Lam, C., Rajakumar, A., Shivalingappa, V., Mutter, W., Sachs, B. P., ... & Karumanchi, S. A. (2009). Twin Pregnancy and the Risk of Preeclampsia: Bigger Placenta or Relative Ischemia? Obstetric Anesthesia Digest, 29(3), 135.

Benschop, L., Duvekot, J. J., & van Lennep, J. E. R. (2019). Future risk of cardiovascular disease risk factors and events in women after a hypertensive disorder of pregnancy. *Heart*, 105(16), 1273-1278.

Burton, G. J., Redman, C. W., Roberts, J. M., & Moffett, A. (2019). Preeclampsia: pathophysiology and clinical implications. *Bmj*, 366.

Carpentier, C., Guerby, P., Camiré, B., Tapp, S., Boutin, A., & Bujold, E. (2022). Aspirin responsiveness at a dose of 80 mg and its impact on birth weight when used in twin pregnancies: the GAP Pilot Randomized Trial. *American Journal of Perinatology*, 39(13), 1396-1400.

Chang, K.-J., Seow, K.-M., & Chen, K.-H. (2023). Preeclampsia: Recent advances in predicting, preventing, and managing the maternal and fetal life-threatening condition. International Journal of Environmental Research and Public Health, 20(4), 2994.

Chappell, L. C., Cluver, C. A., & Tong, S. (2021). Preeclampsia. *The Lancet*, 398(10297), 341-354.

Dai, J., Shi, Y., Wu, Y., Guo, L., Lu, D., Chen, Y., Wang, Y., Lai, H., & Kong, X. (2023). The interaction between age and parity on adverse pregnancy and neonatal outcomes. Frontiers in Medicine, 10(February), 1–13.

Dewi, I. S., Rahmadi, M. A., Nasution, H., Mawar, L., & Sari, M. (2024). Kepuasan Hidup dan Pengaruhnya Terhadap Keberhasilan Pengobatan Penyakit Lupus. *Jurnal Ventilator*, 2(3), 300-322.

Duley, L., Meher, S., Hunter, K. E., Seidler, A. L., & Askie, L. M. (2019). Antiplatelet agents for preventing preeclampsia and its complications. *Cochrane database of systematic reviews*, (10).

English, F. A., Kenny, L. C., & McCarthy, F. P. (2015). Risk factors and effective management of preeclampsia. Integrated blood pressure control, 7–12.

Febyan, & Pemaron, I. B. R. (2020). Tinjauan faktor risiko kejadian hipertensi dalam kehamilan di Rumah Sakit Bhayangkara Denpasar. *Indonesian Journal of Obstetrics & Gynecology Science*, 3(1), 21–26.

Fox, R., Kitt, J., Leeson, P., Aye, C. Y., & Lewandowski, A. J. (2019). Preeclampsia: risk factors, diagnosis, management, and the cardiovascular impact on the offspring. *Journal of Clinical Medicine*, 8(10), 1625.

Garovic, V. D., Dechend, R., Easterling, T., Karumanchi, S. A., McMurtry Baird, S., Magee, L. A., ... & August, P. (2022). Hypertension in pregnancy: diagnosis, blood pressure goals, and pharmacotherapy: a scientific statement from the American Heart Association. *Hypertension*, 79(2), e21-e41.

Haile, T. G., Assefa, N., Alemayehu, T., Mariye, T., Geberemeskel, G. G., Bahrey, D., Mebrahtom, G., Demisse, B., Gebrekidan, H., & Getachew, T. (2021). Determinants of preeclampsia among women attending delivery services in Public Hospitals of Central Tigray, Northern Ethiopia: A case-control study. *Journal of Pregnancy*, 2021, 1–8.

Harris, J. M., Franck, L., Green, B., & Michie, S. (2014). The psychological impact of providing women with risk information for preeclampsia: a qualitative study. *Midwifery*, 30(12), 1187-1195.

Harris, K., Xu, L., Woodward, M., De Kat, A., Zhou, X., Shang, J., Hirst, J. E., & Henry, A. (2024). Early pregnancy maternal blood pressure and risk of preeclampsia: Does the

association differ by parity? Evidence from 14,086 women across 7 countries. *Pregnancy Hypertension*, 37(2024), 101136.

Hinkosa, L., Tamene, A., & Gebeyehu, N. (2020). Risk factors associated with hypertensive disorders in pregnancy in Nekemte referral Hospital, from July 2015 to June 2017, Ethiopia: case control study. *BMC Pregnancy and Childbirth*, 20(16), 1–9.

Jeyabalan, A. (2023). Epidemiology of preeclampsia: impact of obesity. *Nutrition Reviews*, 71(suppl_1), S18-S25.

Kemenkes RI. (2023). Profil Kesehatan Indonesia 2022.

Kemenkes RI. (2024). Profil Kesehatan Indonesia 2023.

Khaliq, O. P., Konoshita, T., Moodley, J., & Naicker, T. (2020). The role of LNPEP and ANPEP gene polymorphisms in the pathogenesis of preeclampsia. European Journal of Obstetrics & Gynecology and Reproductive Biology, 252, 160–165.

Khedagi, A. M., & Bello, N. A. (2021). Hypertensive disorders of pregnancy. *Cardiology Clinics*, 39(1), 77–90.

Komladzah, E. (2021). Maternal and Perinatal Outcomes Among Pregnant Women with Hypertensive Disorders in the Volta Region (Doctoral dissertation, University of Cape Coast).

Lemeshow, S., Jr, D. W. H., Klar, J., & Lwanga, S. K. (1990). Adequacy of sample size in health studies. John Wiley & Sons Ltd.

Li, C., Luo, J., Yang, Y., Wang, Q., Zheng, Y., & Zhong, Z. (2023). The relationship between cadmium exposure and preeclampsia: a systematic review and meta-analysis. *Frontiers in Medicine*, 10, 1259680.

Lokki, A. I., Heikkinen-Eloranta, J. K., & Laivuori, H. (2018). The immunogenetic conundrum of preeclampsia. *Frontiers in Immunology*, 9(NOV), 1–8.

Lopian, M., Kashani-Ligumsky, L., & Many, A. (2023). A balancing act: Navigating hypertensive disorders of pregnancy at very advanced maternal age, from preconception to postpartum. *Journal of Clinical Medicine*, 12(14), 4701.

Luo, J., Fan, C., Luo, M., Fang, J., Zhou, S., & Zhang, F. (2020). Pregnancy complications among nulliparous and multiparous women with advanced maternal age: a community-based prospective cohort study in China. *BMC Pregnancy and Childbirth*, 20(1), 581.

Luo, Z. C., An, N., Xu, H. R., Larante, A., Audibert, F., & Fraser, W. D. (2007). The effects and mechanisms of primiparity on the risk of preeclampsia: a systematic review. *Paediatric and perinatal epidemiology*, 21, 36-45.

Magee, L. A., Pels, A., Helewa, M., Rey, E., & von Dadelszen, P. (2014). Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. *Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health*, 4(2), 105-145.

Mawar, L., Rahmadi, M. A., Nasution, H., & Sari, M. (2024). Efek Kecemasan Sosial pada Pengobatan Penyakit Behçet. *Vitalitas Medis: Jurnal Kesehatan dan Kedokteran*, 1(4), 198-221.

Mawar, L., Rahmadi, M. A., Nasution, H., & Sari, M. (2024). Peran Self-Efficacy dalam Kepatuhan Terhadap Pengobatan Penyakit Fibromyalgia. *OBAT: Jurnal Riset Ilmu Farmasi dan Kesehatan*, 2(5), 363-385.

Mawar, L., Rahmadi, M. A., Nasution, H., Dewi, I. S., & Sari, M. (2024). Pengaruh Emosi Positif Terhadap Hasil Pengobatan Penyakit Rheumatoid Arthritis. *Jurnal Ventilator*, 2(3), 352-374.

Mawar, L., Rahmadi, M. A., Nasution, H., Dewi, I. S., Nasution, R., & Sari, M. (2024). Efek Stres terhadap Pengobatan Asthma. Termometer: *Jurnal Ilmiah Ilmu Kesehatan dan Kedokteran*, 2(4), 86-112.

Mawar, L., Rahmadi, M. A., Nasution, H., Sihombing, N., Nasution, R., & Sari, M. (2024). Peran Kecerdasan Emosional dalam Pengobatan Cystic fibrosis. *Detector: Jurnal Inovasi Riset Ilmu Kesehatan*, 2(4), 60-90.

McCarthy, J., & Maine, D. (1992). A Framework for Analyzing the Determinants of Maternal Mortality. *Studies in Family Planning*, 23(1), 23.

McClure, E. M., Garces, A. L., Hibberd, P. L., Moore, J. L., Goudar, S. S., Saleem, S., ... & Goldenberg, R. L. (2020). The Global Network Maternal Newborn Health Registry: a multi-country, community-based registry of pregnancy outcomes. *Reproductive health*, 17, 1-11.

Muti, M., Tshimanga, M., Notion, G. T., Bangure, D., & Chonzi, P. (2015). Prevalence of pregnancy-induced hypertension and pregnancy outcomes among women seeking maternity services in Harare, Zimbabwe. *BMC Cardiovascular Disorders*, 15, 1-8.

Nasution, H., Rahmadi, M. A., Mawar, L., & Sari, M. (2024). Efek Depresi terhadap Efektivitas Pengobatan Penyakit Crohn. *Jurnal Ventilator*, 2(3), 240-260.

Nasution, H., Rahmadi, M. A., Mawar, L., & Sari, M. (2024). Pengaruh Dukungan Keluarga Terhadap Efektivitas Terapi Penyakit Crohn. *Jurnal Anestesi*, 2(4), 356-381.

Nasution, H., Rahmadi, M. A., Mawar, L., Dewi, I. S., & Sari, M. (2024). Efek Emosi Negatif pada Pengobatan Penyakit Endometriosis. *Observasi: Jurnal Publikasi Ilmu Psikologi*, 2(4), 218-244.

Nasution, H., Rahmadi, M. A., Mawar, L., Dewi, I. S., Nasution, R., & Sari, M. (2024). Peran Kepuasan Hidup dalam Pengelolaan Penyakit Systemic Sclerosis. *Termometer: Jurnal Ilmiah Ilmu Kesehatan dan Kedokteran*, 2(4), 195-224.

Nasution, H., Rahmadi, M. A., Mawar, L., Sihombing, N., Nasution, R., & Sari, M. (2024). Hubungan Dukungan Sosial dalam Pengobatan Sklerosis Multipel. *Detector: Jurnal Inovasi Riset Ilmu Kesehatan*, 2(4), 121-151.

Nasution, R., Rahmadi, M. A., Nasution, H., Mawar, L., Dewi, I. S., & Sari, M. (2024). Pengaruh Intervensi Emosi Positif pada Pengobatan Fibromyalgia. *Termometer: Jurnal Ilmiah Ilmu Kesehatan dan Kedokteran*, 2(4), 277-302.

Nasution, R., Rahmadi, M. A., Nasution, H., Mawar, L., Dewi, I. S., & Sari, M. (2024). Hubungan antara Perasaan Bersalah dan Keberhasilan Pengobatan Lupus. *An-Najat*, 2(4), 179-206.

Nobles, C. J., Mendola, P., Mumford, S. L., Naimi, A. I., Yeung, E. H., Kim, K., ... & Schisterman, E. F. (2018). Preconception blood pressure levels and reproductive outcomes in a prospective cohort of women attempting pregnancy. *Hypertension*, 71(5), 904-910.

Phipps, E. A., Thadhani, R., Benzing, T., & Karumanchi, S. A. (2019). Preeclampsia: pathogenesis, novel diagnostics and therapies. *Nature Reviews Nephrology*, 15(5), 275–289.

Phipps, E., Prasanna, D., Brima, W., & Jim, B. (2016). Preeclampsia: updates in pathogenesis, definitions, and guidelines. *Clinical Journal of the American Society of Nephrology*, 11(6), 1102-1113.

Rahmadi, M. A., Nasution, H., Mawa, L., Nasution, R., & Sari, M. (2024). Peran Harapan dalam Kepatuhan Pengobatan Kanker Kolorektal. *OBAT: Jurnal Riset Ilmu Farmasi dan Kesehatan*, 2(6), 38-64.

Rahmadi, M. A., Nasution, H., Mawar, L., & Sari, M. (2024). Pengaruh Kecemasan Terhadap Kepatuhan Pengobatan Kanker Payudara. *Jurnal Medika Nusantara*, 2(3), 325-350.

Rahmadi, M. A., Nasution, H., Mawar, L., Dewi, I. S., & Sari, M. (2024). Peran Motivasi Internal dalam Pengobatan Penyakit Fibromyalgia. *Jurnal Anestesi*, 2(4), 257-283.

Rahmadi, M. A., Nasution, H., Mawar, L., Dewi, I. S., Nasution, R., & Sari, M. (2024). Hubungan Motivasi terhadap Keberhasilan Pengobatan Endometriosis. *Termometer: Jurnal Ilmiah Ilmu Kesehatan dan Kedokteran*, 2(4), 225-253.

Rana, S., Lemoine, E., Granger, J. P., & Karumanchi, S. A. (2019). Preeclampsia: pathophysiology, challenges, and perspectives. *Circulation Research*, 124(7), 1094-1112.

Roberts, J. M., & Cooper, D. W. (2001). Pathogenesis and genetics of preeclampsia. *The Lancet*, 357(9249), 53–56.

Rurangirwa, A. A., Gaillard, R., Steegers, E. A. P., Hofman, A., & Jaddoe, V. W. V. (2012). Hemodynamic adaptations in different trimesters among nulliparous and multiparous pregnant women; the generation R study. *American Journal of Hypertension*, 25(8), 892–899.

Sava, R. I., March, K. L., & Pepine, C. J. (2018). Hypertension in pregnancy: Taking cues from pathophysiology for clinical practice. *Clinical cardiology*, 41(2), 220–227.

Sibai, B., Dekker, G., & Kupferminc, M. (2005). Preeclampsia. The Lancet, 365(9461), 785-799.

Steegers, E. A., Von Dadelszen, P., Duvekot, J. J., & Pijnenborg, R. (2010). *Preeclampsia. The Lancet*, 376(9741), 631-644.

Teirilä, L., Heikkinen-Eloranta, J., Kotimaa, J., Meri, S., & Lokki, A. I. (2019). Regulation of the complement system and immunological tolerance in pregnancy. *Seminars in immunology*, 45, 101337.

Tesfa, E., Nibret, E., Gizaw, S. T., Zenebe, Y., Mekonnen, Z., Assefa, S., ... & Munshea, A. (2020). Prevalence and determinants of hypertensive disorders of pregnancy in Ethiopia: A systematic review and meta-analysis. *PLoS One*, 15(9), e0239048.

Thilaganathan, B., & Kalafat, E. (2019). Cardiovascular system in preeclampsia and beyond. Hypertension, 73(3), 522-531.

Upadya, M., & Rao, S. (2018). Hypertensive disorders in pregnancy. *Indian Journal of Anaesthesia*, 62(9), 675–681.

Valensise, H., Vasapollo, B., Gagliardi, G., & Novelli, G. P. (2008). Early and late preeclampsia: two different maternal hemodynamic states in the latent phase of the disease. *Hypertension*, 52(5), 873-880.

Wang, W., Xie, X., Yuan, T., Wang, Y., Zhao, F., Zhou, Z., & Zhang, H. (2021). Epidemiological trends of maternal hypertensive disorders of pregnancy at the global, regional, and national levels: a population-based study. *BMC Pregnancy and Childbirth*, 21(1), 1–10.

Wang, Y. A., Chughtai, A. A., Farquhar, C. M., Pollock, W., Lui, K., & Sullivan, E. A. (2016). Increased incidence of gestational hypertension and preeclampsia after assisted reproductive technology treatment. *Fertility and sterility*, 105(4), 920–926.

Webster, K., Fishburn, S., Maresh, M., Findlay, S. C., & Chappell, L. C. (2019). Diagnosis and management of hypertension in pregnancy: summary of updated NICE guidance. *Bmj*, 366.

WHO. (2023a). Targets of Sustainable Development Goal 3.

WHO. (2023b). Trends in maternal mortality 2000 to 2020: estimates by WHO, UNICEF, UNFPA, World Bank Group and UNDESA/Population Division.

WHO. (2024). Maternal Mortality.

Wiranto, & Putriningtyas, N. D. (2021). Faktor risiko kejadian hipertensi pada ibu hamil. *Indonesian Journal of Public Health and Nutrition*, 1(3), 759–767.

Wu, P., Haththotuwa, R., Kwok, C. S., Babu, A., Kotronias, R. A., Rushton, C., ... & Mamas, M. A. (2017). Preeclampsia and future cardiovascular health: a systematic review and meta-analysis. Circulation: Cardiovascular Quality and Outcomes, 10(2), e003497.

Xiang, C., Sui, L., Ding, X., Cao, M., Li, G., & Du, Z. (2024). Maternal adiposity measures and hypertensive disorders of pregnancy: a meta-analysis. *BMC Pregnancy and Childbirth*, 24(1), 675.