

Preterm birth risk in mother with hypertensive disorders of pregnancy

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ABSTRACT

Preterm birth (PTB) is a major public health concern and is the leading cause of under-5 child mortality. Some studies suggest that hypertension disorders of pregnancy (HDP) play an important role in causing PTB. HDP is a term that includes chronic hypertension (CH), gestational hypertension (GH), and pre-eclampsia (PE). The association between the various types of HDP and PTB has not been studied specifically in prior research, yet. Therefore, the purpose of this study is to analyze risk differences among HDP types. This study was carried out in Makassar's Maternal and Child Hospital using a case-control study design. A sample consisting of 138 cases and 276 controls was collected from the medical record data. Odds ratio and logistic regression test analysis were used to obtain both crude OR (COR) and adjusted OR (AOR). The finding shows that regardless of its type, HDP is a major risk factor for preterm birth. The findings also indicated that PTB risk differs depending on the type of HDP suffered. CH had the highest risk (COR=5.61; AOR=6.58), followed by PE (COR=3.36; OR=3.18) and GH (COR=3.46; AOR=3.09), which have fairly similar risks. CH which has the greatest risk needs to be considered to be the focus of prevention. While in the context of preventing preterm delivery, GH and PE need to receive the same attention. However, prevention and treatment must still be adjusted depending on the type of hypertension suffered.

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1. INTRODUCTION

Preterm birth is still a major global health concern nowadays. Preterm birth is the leading cause of death among children under five years of age globally [1]–[3]. Around 16% of child deaths and 35% of newborn deaths are caused by preterm birth [4]. It is estimated that 14.8 million babies are born preterm each year worldwide, with a global preterm birth rate of 10.6% [5].

Preterm births are higher in low and middle-income countries, especially in Southeast Asia [1], [6]. Asian countries account for more than half (52.9%) of global preterm births, which Indonesia ranked fifth highest worldwide and the highest in Southeast Asia (3.5%) [5]. Preterm birth is a live birth that occurs before 37 weeks of gestation [1]. Babies who are born preterm will not only have an increased risk of mortality, but they're also at risk of long-term adverse health conditions [7]. All of that may lead to the

emergence of emotional and economic burdens for the family [8]. Preterm birth is a complex health problem with a variety of risk factors [9]. The mechanism of preterm birth is still uncertain, but some studies suggest that maternal medical conditions, especially hypertension disorders of pregnancy (HDP), may play an important role in causing preterm birth [9], [10]. HDP can disrupt nutrient delivery to the fetus, which leads to intrauterine growth restriction (IUGR) and vascular damage to the placenta, causing placental abruption, which can lead to preterm birth [9], [11].

HDP is one of the three leading causes of maternal morbidity and mortality worldwide, with an incidence ranging from 4 to 25% [12]. Various references and health organizations divided HDP into at least three main types, which are chronic hypertension or pre-existing hypertension, gestational hypertension, and pre-eclampsia [8], [13], [14]. The role of HDP in the incidence of preterm birth has been explained in numerous retrospective studies over the past 20 years and obtained significant results [15].

However, it turns out that previous studies have not looked at the relationship between various types of hypertension to preterm birth specifically. Most studies use the term pregnancy-induced hypertension (PIH), which is defined as hypertension that appears after 20 weeks of gestation or more with or without proteinuria [11], [16]–[19]. That term combines gestational hypertension with pre-eclampsia into one term, so the relationship obtained is not specific. In addition, PIH does not consider the presence of pre-existing hypertension or chronic hypertension. Gestational hypertension and pre-eclampsia are two different things. Apart from differences in diagnosis, gestational hypertension and pre-eclampsia also have differences in terms of epidemiology, including differences in causative factors, pathophysiology, and impact [20]. Pre-eclampsia is associated with more adverse outcomes with higher severity than gestational hypertension [21].

Therefore, it is necessary to conduct more specific research on hypertension as the risk factor for preterm birth to address the risk of each HDP type to preterm birth and whether there is a risk difference between the types of HDP. The results of this study will provide more specific data about HDP risk to preterm birth (PTB) as a step to determine and adjust for the appropriate intervention. To date, scientific data and information on the distribution, frequency, and determinants of preterm birth at Makassar are unavailable, as preterm birth data are not routinely collected through surveillance systems. This suggests that preterm birth is not yet considered a serious health problem. As a result, it is hoped that the findings of this study will not only provide a useful scientific basis for preterm birth and the risk of HDP in particular as a step toward determining appropriate interventions but will also raise public and government awareness of preterm births.

2. RESEARCH METHOD

This study used a case-control study design and was conducted in August–September 2022 at Maternal and Child Special Regional Hospitals Pertiwi and Siti Fatimah, the only mother-and-child special hospitals owned by the government in Makassar. The population of this study was all born alive babies in the hospital during 2021, with a total sample of 414 consisting of 138 mothers who gave birth pretermly as case samples (total sampling) and 276 mothers who gave birth termly as control samples (matching cases) with a ratio of 1:2. Research data was collected from hospital medical records because the data itself is the result of a medical examination by certain medical personnel and was recorded in the medical record. The availability of the sample's medical record data at the hospital, which means that all information about the respondents' identities and characteristics as well as their anamnesis, diagnoses and laboratory test results, is fully available to obtain, uses as the inclusion criterion for this study's sample.

Measurement of the dependent variable, which is preterm birth, is taken based on the results of the diagnosis by the medical personnel (doctor, nurse, and midwife) on the patient's medical record and its suitability with the gestational age at delivery. The independent variables consisted of chronic hypertension (CH), gestational hypertension (GH), and pre-eclampsia (PE). Data on CH will be collected by looking at the history of hypertension, while for GH, it will be done by looking at the diagnosis and the results of blood pressure checks, and seeing the time of examination to ensure that the correct gestational age is >20 weeks, and for PE, it will be done by looking at the diagnosis, results of blood pressure checks, and laboratory proteinuria checks. The odds ratio (OR) analysis used in this study assesses the value of the HDP Crude OR (COR) to preterm birth. To obtain the adjusted OR (AOR) value, multivariate regression logistic test analysis is also performed. In order to adjust the risk value of HDP when the effects of other variables were taken into account, numerous control variables (parity, history of unfavorable pregnancy outcomes, and history of other chronic conditions) were used in this study.

3. RESULTS AND DISCUSSION

Table 1 shows the characteristics of respondents, including age, religion, ethnicity, and occupation. There are no significant differences between the case and control group respondents based on the characteristics. It shows that most of the respondents in both the case and control groups were in the age

group of 20 to 35 years (76.8%), the majority religion was Islam (>90%), came from the Makassar tribe (>65%), and had a job as a housewife (>80%).

Table 1. Frequency distribution of respondent characteristics

Respondent's characteristics	Study subject			
	Cases (N=138)		Controls (N=276)	
	n	%	n	%
Age (Years)				
<20	5	3.6	10	3.6
20-35	106	76.8	212	76.8
>35	27	19.6	54	19.6
Religion				
Islam	136	98.6	257	93.2
Katolik	1	0.7	12	4.3
Protestan	1	0.7	7	2.5
Ethnic				
Bugis	30	21.7	57	20.7
Makassar	101	73.3	189	68.4
Toraja	2	1.4	11	4
Others	5	3.6	19	6.9
Occupation				
Civil servant	2	1.4	9	3.3
Private employee	6	4.3	10	3.6
Entrepreneur	12	8.7	26	9.4
Housewife	116	84.2	227	82.3
Others	2	1.4	4	1.4

It is shown in Table 2 that, among the 138 respondents who gave birth preterm, most were experiencing moderate to late preterm (80.4%) or mothers who gave birth at 33-37 weeks of gestation, with an average gestational age of 34 weeks. As shown in Table 3, there is a difference in the proportion of HDP based on its type. However, the proportion of hypertension incidence was higher in the case group than the control group in all types of HDP (CH 4.3% to 1.1%; GH 8.7% to 3.6%; PE 26.8% to 10.9%).

Table 2. Distribution by prematurity categories

Prematurity categories	Preterm births (N=138)		$\bar{X} \pm SD$
	n	%	
Extreme Preterm (<28 Weeks)	2	1.5	
Very Preterm (28-32 Weeks)	25	18.1	34.4 ± 2.4
Moderate to Late Preterm (33-37 Weeks)	111	80.4	

Table 3. Distribution by preterm birth risk factors

Risk factor	Study subject			
	Cases (N=138)		Controls (N=276)	
	n	%	n	%
Dependent variable				
Type of hypertension				
Chronic hypertension (CH)	6	4.3	3	1.1
Gestational hypertension (GH)	12	8.7	10	3.6
Pre-eclampsia (PE)	37	26.8	30	10.9
Normotensive	83	60.2	233	84.4
Control variable				
Parity				
0 and ≥3	74	53.6	115	41.6
1-2	64	46.4	161	58.4
History of adverse pregnancy outcome (Preterm, LBW, Stillbirth, Fetal Death)				
Yes	49	35.5	63	22.8
No	89	64.5	213	77.2
Other Chronic Condition/Disease (DM, Obesity, Asthma)				
Yes	9	6.5	9	3.3
No	129	93.5	267	96.7

Figure 1 shows that most of the respondents experienced moderate to late preterm (33-37 weeks), whatever the HDP type. Then, the proportion of very preterm events (28-32 weeks) was higher in respondents with gestational hypertension. Lastly, the only extreme preterm events (<28 weeks) occurred in respondents with pre-eclampsia.

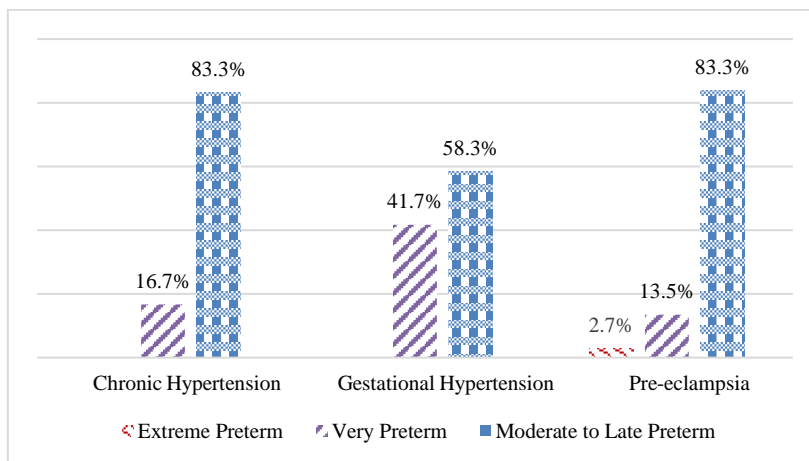


Figure 1. Comparison of prematurity proportion by hypertension type

There are differences in the OR of preterm birth based on the type of HDP experienced before and after controlling for other variables as shown in Table 4. The results of the analysis showed that there was a big difference in the value of the risk of preterm birth based on the type of HDP suffered. The highest risk came from CH (COR=5.61 vs. AOR=6.58), followed by pre-eclampsia (COR=3.36 vs. AOR=3.18) and gestational hypertension (COR=3.46 vs. AOR=3.09).

Table 4. Risk analysis of hypertension disorders of pregnancy to preterm birth

Type of hypertension	Study subject				COR (95%CI)	AOR (95%CI)
	Cases (N=138)		Controls (N=276)			
	n	%	n	%		
Chronic hypertension	6	4.3	3	1.1	5.614 (1.373-22.959)	6.580* (1.584-27.974)
Gestational hypertension	12	8.7	10	3.6	3.369 (1.403-8.088)	3.184* (1.301-7.792)
Pre-eclampsia	37	26.8	30	10.9	3.462 (2.019-5.958)	3.095* (1.776-5.395)
Normotensive	83	60.2	233	84.4	1 (Ref)	1 (Ref)

*) OR after adjusting parity, adverse pregnancy outcome and other chronic disease

3.1. Discussion

The results showed that there are differences in the proportion of hypertension in pregnancy based on the type of hypertension. However, the proportion of hypertension incidence was higher in the case group compared to the control group in all types of hypertension in pregnancy. This makes it clear that preterm births tend to occur in respondents or mothers who suffer from hypertension in pregnancy, regardless of whether it is chronic hypertension, gestational hypertension, or pre-eclampsia.

These results are in line with research by Bateman *et al.* [22], [23] and Berger *et al.* [24] for chronic hypertension (CH), which also found that the proportion of chronic hypertension was higher in the group of mothers who gave birth pretermly. In populations where maternal age at delivery is increasing, the association of hypertension with advanced age will inevitably contribute to a greater prevalence of chronic hypertension [25], [26]. For GH, this result is in line with research done by Huang *et al.* [27] and Premkumar *et al.* [15] which found that preterm births were more common in respondents who suffered from gestational hypertension during pregnancy. Gestational hypertension occurs in about 6% of all pregnancies [28]. Gestational hypertension commonly occurs in women with first pregnancy, twin pregnancies, women over 35 years of age, women with chronic hypertension or who have had hypertension in previous

pregnancies, and women with diabetes [29]. And for PE, Research by Pragitara *et al.* [30] and Saleha *et al.* [31] also obtained similar results, where the proportion of pre-eclampsia was higher in mothers who gave birth preterm. Pre-eclampsia occurs in 3% of all pregnancies and more than 10% of women will experience it in their first pregnancy [32]. This figure is smaller than the results of studies that found that among all types of HDP, pre-eclampsia has the highest proportion (>20%). Some other factors that can cause pre-eclampsia include a previous history of pre-eclampsia, type 1 and 2 diabetes, pregnancy >3, and twin pregnancy [21].

The results also showed that pre-eclampsia had a greater proportion of incidence in the group of cases when compared to other types of hypertension in pregnancy. This can be caused because women with proteinuria can develop severe pre-eclampsia and have a higher rate of preterm birth compared to women who suffer from hypertension but without proteinuria [33]. In addition, many respondents in this research suffered from gestational hypertension early and then developed pre-eclampsia later in their pregnancy. No cases of eclampsia were found in this study, so the amount or proportion was purely derived from pre-eclampsia cases.

Furthermore, the findings showed that the risk of preterm birth varied depending on the type of pregnancy in which hypertension was present. The greatest risk comes from chronic hypertension, followed by pre-eclampsia and gestational hypertension. CH has the lowest proportion among other types of HDP. Nevertheless, CH has the highest OR (COR=5.61 (1.373-22.959); AOR=6.58 (1.584-27.974)). After adjusting for confounding variables, the risk of preterm birth is 6.58 times higher in mothers with chronic hypertension. Similar results were obtained from studies conducted by Berger *et al.* [24] and Premkumar *et al.* [15]. Although it has a smaller risk value, the study also found that respondents or mothers who had chronic hypertension have 3.8 (95%CI 3.54-4.10) and 3.4 (95%CI 3.0-3.9) times higher risk for preterm labor compared to normotensive mothers. The presence of chronic hypertension in pregnant women can disrupt the delivery of oxygen and nutrients to the developing fetus's placenta, which may result in fetal growth restriction that can lead to preterm birth [11]. Preterm birth rates range from 12% to 34% among all women with chronic hypertension. That figure suggests that indeed, mothers with chronic hypertension are at high risk of preterm birth.

Although there are differences in the risk of preterm birth between chronic hypertension and other hypertension, but it turns out the results showed that the risk of pre-eclampsia and gestational hypertension is not much different even to say there is no risk differences between pre-eclampsia and gestational hypertension (COR_{GH}=3.36 vs. COR_{PE}=3.46; AOR_{GH}=3.18 vs. AOR_{PE}=3.09). In terms of GH, Huang *et al.* [27] and Premkumar *et al.* [15] also obtained similar results where respondents or mothers with gestational hypertension were at risk of 5.5 (95%CI 2.59-11.68) and 4.9 (95%CI 4.4-5.4) times giving birth preterm compared to normotensive mothers. In particular, gestational hypertension is a unique disease that seriously harms the health of the mother and baby and is one of the leading causes of death of women and newborns. In addition, women with gestational hypertension also have a significantly increased risk of preterm birth compared to healthy pregnant women [34].

While for PE, Pragitara *et al.* [30] and Saleha *et al.* [31] also found similar results, showing that the value of pre-eclampsia to preterm birth was 2.5 (95%CI 1.34-4.83) and 6.9 (95%CI 1.874-25.849), respectively. Many studies state that preterm birth is a consequence of multifactorial factors. But in fact, Sameshima [35] stated that one-third of preterm births are caused by pre-eclampsia, while the rest are caused by other factors. Moreover, pre-eclampsia can cause fetal death. Pregnant women who are detected to have pre-eclampsia must be treated appropriately to prevent fetal death and one of the ways is to deliver faster than scheduled. This delivery is carried out regardless of gestational age, so babies tend to be born preterm. In addition, placental insufficiency causes blood flow to the placenta to be disrupted, resulting in damage to the placenta, and indirectly impacting preterm labor occurrence [36].

Although the effects of gestational hypertension are typically less severe and usually go away after delivering, it is untrue that gestational hypertension is inherently less concerning than preeclampsia [8], [33]. The CDC [8] also states that women with gestational hypertension are more likely to later acquire chronic hypertension. When hypertension is identified before 32 weeks of gestation, the risk that a woman may subsequently develop proteinuria or preeclampsia increases to between 10 to 50% [33]. The findings of this study suggest that this may be the reason for the lack of a significant difference in risk between preeclampsia and gestational hypertension.

Preventive treatment and care for patients with hypertension in pregnancy need to be altered based on the type of hypertension after identifying the differences in the risk of each type of pregnancy hypertension specifically. Chronic hypertension, which has the highest risk, should start to be taken into account as a target or focus of prevention and attention in subsequent studies. Preventing chronic hypertension is similar to preventing hypertension in general; however, if a woman already has chronic hypertension, it is advised that she continue taking or use antihypertensive medications before pregnancy or after giving birth [37]. To make sure that blood pressure stays normal, regular or at-home monitoring is necessary [38].

In this study, pre-eclampsia was found to carry a fairly high risk and serious consequences than other forms of hypertension. This might be because pre-eclampsia, which is accompanied by proteinuria, is a sign of hypertension that is more severe than other types of hypertension. Preeclampsia typically requires inpatient care; thus, quality and standardized management are essential. This needs to be done in a specialized health facility with the right protocols and qualified medical staff. Intensive care and medication are required for preeclampsia with severe hypertension in order to quickly drop blood pressure [39].

Health professionals advise aspirin for mothers who are thought to be at high risk due to maternal risk factors or clinical prediction models, despite the fact that preeclampsia cannot currently be prevented. An experimental study, which used first-trimester screening to predict the risk of pre-eclampsia, found a 62% reduction in the incidence of preterm birth caused by pre-eclampsia in women taking 150 mg of aspirin daily [40]. Predicting the risk of pre-eclampsia during the first trimester is possible using a variety of non-drug methods, such as maternal blood pressure monitoring and risk factor screening. For the sake of the mother's and the fetus's health, antenatal care (ANC) services are crucial.

Given that studies' findings indicated no significant difference between the risk of preeclampsia and gestational hypertension, both conditions should be the focus of prevention efforts. At this time, the growing theory suggests that preeclampsia is a riskier condition than gestational hypertension, so more attention is required. However, this study shows that there is almost no difference in risk, so gestational hypertension should also be considered in terms of risk factors for preterm birth. Hence, in terms of preeclampsia risk for other pregnancy complications, further research is needed.

4. CONCLUSION

The risk of PTB varies between CH, GH, and PE. However, CH, GH, and PE continue to be the most important and leading risk factors for preterm birth. For CH, which has the highest risk, special consideration is necessary. These findings can serve as a warning to the public, especially pregnant people and medical professionals, that GH poses a risk for preterm delivery that cannot be ignored because it is almost as significant as PE. Early identification of hypertension as a risk factor is one method for accomplishing this. Promotion, education, and improving health workers' abilities in early detection of pregnancy risks as part of high-quality ANC services are required to effectively prevent pregnancy-related problems.





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