

## CLINICAL PROFILE AND CHARACTERISTICS OF HYPERTENSION IN PREGNANT WOMEN

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### ABSTRACT

**Background;** Hypertension in pregnancy contributes to 14% of maternal deaths, with pre-eclampsia as one of the most common complications. Pre-eclampsia is characterized by increased blood pressure and the presence of protein in the urine after 20 weeks of gestation. The selection of antihypertensive therapy in pregnant women requires special consideration because some drugs can increase the risk of teratogenicity in the fetus. This study aims to analyze the profile and clinical characteristics of hypertension (pre-eclampsia) in pregnant women at the South Tangerang City Hospital. **Methods:** This study used a retrospective descriptive method with secondary data obtained from medical records of pre-eclampsia patients from January–December 2023. **Results:** The results showed that 60.5% of patients experienced severe pre-eclampsia, while 39.5% experienced mild pre-eclampsia. The antihypertensives used included nifedipine, methyldopa, amlodipine, and bisoprolol. The characteristics of the most pre-eclampsia patients were mothers aged 26–35 years (40.8%) with a gestational age of 29–42 weeks (81.6%). **Conclusion:** the antihypertensive therapy in pregnancy requires special attention to reduce the risk to the mother and fetus. The accuracy of drug use and routine examinations in pregnant women are important factors in preventing and treating pre-eclampsia.

**Keywords :** pregnancy-induced hypertension, preeclampsia, antihypertensive therapy, drug rationality, pregnancy

### INTRODUCTION

Hypertensive disorders of pregnancy, which affect 5-7% of pregnancies, are a major cause of maternal and fetal morbidity and mortality <sup>1</sup>. These disorders are classified into chronic Hypertension, gestational Hypertension, preeclampsia-eclampsia, and preeclampsia with chronic hypertension <sup>2</sup>. Preeclampsia, which is characterized by Hypertension and proteinuria after 20 weeks of gestation, can progress to eclampsia if left untreated <sup>3</sup>. Hypertension in pregnancy has a detrimental effect on the fetus's health. The choice of drugs is very important because some drugs can harm the fetus <sup>1</sup>. Women with a history of hypertensive disorders during pregnancy have a higher cardiovascular risk later in life, so they require regular evaluation <sup>4</sup>. Thus, a personalized treatment approach is needed, taking into account maternal characteristics and blood pressure variability. It has been reported that the use of antihypertensives in preeclamptic patients has a level of indication accuracy of 80.96%, drug selection accuracy of 69.04%, patient accuracy of 80.96%, dose accuracy of 80.96%, and awareness of drug side effects reaching 100%. These results emphasize the importance of evaluating the rationality of antihypertensive therapy for the mother and fetus <sup>5</sup>.

According to global data, every two minutes, a pregnant woman dies, and her newborn is at high risk of survival due to

pregnancy complications <sup>6,7</sup>. For every maternal death, around 20 to 30 women experience health complications due to pregnancy, including hypertension, which can interfere with organ function and increase the risk of diseases such as kidney failure, diabetes, and stroke <sup>7</sup>. Hypertension in pregnancy is a significant contributor to maternal mortality, affecting 5-15% of pregnancies <sup>8</sup>. The World Health Organization reports that hypertensive disorders contribute to 13-28% of maternal deaths globally <sup>9</sup>. Early detection and treatment of preeclampsia are essential to prevent complications such as eclampsia <sup>10</sup>.

In Indonesia, hypertension in pregnancy (HDK) is the main cause of maternal death, with 801 cases recorded in 2022 <sup>11</sup>. HDK and bleeding are the dominant factors in maternal death <sup>12</sup>. Indonesia is ranked second as the country with the highest maternal mortality in Southeast Asia, one of the causes of which is preeclampsia <sup>13</sup>. HDK is classified into several categories, one of which is pre-eclampsia, a condition characterized by increased blood pressure and proteinuria after 20 weeks of gestation <sup>3</sup>. This condition can cause various complications, including premature birth, fetal growth disorders, and even maternal and perinatal <sup>14</sup>. Management of hypertension in pregnancy requires appropriate antihypertensive therapy to prevent serious complications. In cases of severe preeclampsia that progresses to eclampsia, additional therapy in the form of anticonvulsant drugs is required in

accordance with applicable medical protocols<sup>15</sup>. The use of antihypertensives aims to prevent cerebrovascular disease and maintain the safety of the mother and fetus<sup>16</sup>. However, special attention should be paid, especially in the first trimester of pregnancy, because some antihypertensives have teratogenic effects or can inhibit fetal growth (Hypertensive disorders affect about 10% of pregnancies, posing risks to the mother and fetus<sup>17</sup>. Treatment is recommended for persistent blood pressure  $\geq 150/95$  mmHg or  $>140/90$  mmHg with complications<sup>18</sup>. Methyldopa, Labetalol, and calcium antagonists are the antihypertensives of choice<sup>15,18</sup>. Although treatment reduces the risk of severe hypertension by half, it does not significantly reduce preeclampsia or serious complications in the mother. It increases the effectiveness of treatment and reduces the risk of complications in pregnant women with hypertension<sup>19</sup>.

### **Hypertension in Pregnant Women**

Hypertension in pregnancy is a vascular disorder that can occur before, during, or after pregnancy, with a prevalence reaching 10% among pregnant women worldwide<sup>20</sup>. This condition includes chronic hypertension, gestational hypertension, pre-eclampsia, and eclampsia, which contribute significantly to maternal and perinatal morbidity and mortality<sup>21</sup>. The severity of hypertension in pregnancy is classified as mild-moderate (systolic blood pressure/SBP 140–159 mmHg and diastolic blood pressure/DBP 90–109 mmHg) or severe (SBP  $\geq 160$  mmHg and/or DBP  $\geq 110$  mmHg). Interestingly, the severity of hypertension in pregnant women tends to be lower than in the non-pregnant population, because the risk of hypertensive encephalopathy can occur at lower blood pressures in pregnancy<sup>21</sup>.

Several risk factors have been associated with hypertension in pregnancy, including obesity, family history of hypertension<sup>22</sup>, alcohol consumption, heart failure, stroke, left ventricular hypertrophy, and smoking habits<sup>20</sup>. According to the American College of Obstetricians and Gynecologists (ACOG), hypertension in pregnancy is classified into four main categories: pre-eclampsia/eclampsia, chronic hypertension, chronic hypertension with superimposed pre-eclampsia, and gestational hypertension.

### **Pre-eclampsia**

Pre-eclampsia is a syndrome that occurs at a gestational age of  $>20$  weeks with blood pressure  $\geq 140/90$  mmHg and proteinuria  $>300$  mg/24 hours, with a prevalence of 2-5% of all pregnancies and maternal mortality rates reaching 12-15%<sup>20</sup>. Major risk factors include antiphospholipid syndrome, previous history of pre-eclampsia, type 1 diabetes, multiple pregnancy, nulliparity, family history, obesity, age  $>40$  years, chronic hypertension, and use of assisted reproductive technology<sup>20</sup>.

### **Eclampsia**

Eclampsia is an emergency condition characterized by seizures in women with pre-eclampsia, without any other underlying cause<sup>23</sup>. This condition generally occurs in the last trimester of pregnancy and increases towards delivery. Around 60-75% of eclampsia cases occur before delivery (antepartum), while 40-50% occur during delivery (intrapartum) or within 48 hours after delivery (postpartum)

<sup>21</sup>Eclampsia is often preceded by symptoms such as headache and visual disturbances, followed by episodes of seizures that last for 60-90 seconds<sup>20</sup>.

### **Chronic hypertension**

Chronic hypertension in pregnancy is defined as blood pressure  $\geq 140/90$  mmHg that occurs before pregnancy or is detected before 20 weeks of gestation<sup>24</sup>. This condition is generally essential (primary) hypertension and is found in 3–9% of pregnancies. In addition, chronic hypertension can also be diagnosed for the first time during pregnancy if blood pressure remains high until the postpartum period. Increased blood pressure in chronic hypertension can persist for more than 12 weeks after delivery<sup>20</sup>.

### **Chronic Hypertension with Superimposed Pre-eclampsia**

Women with chronic hypertension before pregnancy have a 4–5 times higher risk of developing pre-eclampsia than normotensive women. Pre-eclampsia occurs in about 25% of pregnancies with chronic hypertension, while in pregnancies without chronic hypertension, the incidence is only around 5%<sup>25</sup>. This condition generally appears at 24–26 weeks of pregnancy and increases the risk of premature birth and low birth weight babies<sup>25</sup>. Women with hypertension who experience proteinuria at around 20 weeks of gestation are at risk of experiencing further complications, such as increased antihypertensive dose requirements, impaired liver function (elevated liver enzymes, thrombocytopenia ( $<100,000$ /mL), epigastric pain, headache, edema, renal impairment (creatinine  $\geq 1.1$  mg/dL), and increased protein excretion<sup>26</sup>.

### **Gestational hypertension**

Gestational hypertension (GH) is defined as high blood pressure that occurs after 20 weeks of gestation without proteinuria, which affects 6-8% of pregnancies<sup>27</sup>. This condition usually improves after delivery, with blood pressure returning to normal within 10 days after delivery in most cases<sup>3</sup>.

## **BAHAN DAN METODE**

This study is a retrospective descriptive study conducted at South Tangerang City Hospital with a population of pregnant women diagnosed with hypertension (pre-eclampsia) in a certain period. Samples were taken using the total sampling method or purposive sampling based on inclusion and exclusion criteria.

The inclusion criteria in this study included pregnant women undergoing treatment at South Tangerang City Hospital who had been diagnosed with pre-eclampsia. In addition, patients included in the study must have complete and clear medical record data to ensure the accuracy of the information analyzed. Another criterion is patients who use antihypertensive drugs as part of the medical therapy they are undergoing.

The exclusion criteria in this study were applied to eliminate subjects who did not meet the inclusion criteria or had factors that could interfere with the validity of the data. Patients excluded were those whose medical record data were not accompanied by laboratory results, so that the required clinical information was incomplete. In addition, pregnant women who were not

undergoing antihypertensive treatment were also excluded from the study, because the use of antihypertensive drugs is an important variable in the analysis carried out. Independent variables include demographic characteristics (maternal age, gestational age, history of comorbidities, parity), clinical profile (proteinuria, blood pressure), and use of antihypertensive drugs. Dependent variables are the profile and clinical characteristics of hypertension (pre-eclampsia) in pregnant women.

## RESULT

### Characteristics of Respondents

**Table 1** Characteristics of Respondents

| Characteristics<br>(Unit)  | Variables                          | (F) | P (%) |
|----------------------------|------------------------------------|-----|-------|
| Maternal Age<br>(Years)    | 17–25                              | 15  | 19,7  |
|                            | 26–35                              | 31  | 40,8  |
|                            | 36–45                              | 30  | 39,5  |
| Gestational Age<br>(Weeks) | 0–12 (First Trimester)             | 0   | 0     |
|                            | 13–28 (Second Trimester)           | 14  | 18,4  |
|                            | 29–42 (Third Trimester)            | 62  | 81,6  |
| Comorbidities              | None                               | 36  | 47,4  |
|                            | Present                            | 40  | 52,6  |
| Parity                     | Primigravida (First pregnancy)     | 20  | 26,3  |
|                            | Multigravida (2nd–4th pregnancy)   | 48  | 63,2  |
|                            | Grandmultigravida (≥5 pregnancies) | 8   | 10,5  |

F: Frequency, P: Percentage

### Patient Clinical Profile Based on Laboratory Examination

Analysis of the patient's clinical profile is carried out to detect the presence of other organ dysfunction that may occur. Some of the examinations carried out are urine dipstick and blood pressure.

#### a. Urine dipstick examination

Urine dipstick examination aims to determine the level of protein in urine using a dipstick measuring instrument.

**Table 2** Urine Dipstick Examination

| Characteristics | Variables  | RV      | (F) | P (%) |
|-----------------|------------|---------|-----|-------|
| Proteinuria     | Positive 1 | 0.3–0.5 | 31  | 40,8  |
|                 | Positive 2 | 0.5–2   | 32  | 42,1  |
|                 | Positive 3 | >2      | 13  | 17,1  |

RV: Reference value (grams/24 hours)

#### b. Blood pressure

Blood pressure examination aims to assess the severity of hypertension in pregnant women and detect possible complications of pre-eclampsia<sup>28</sup>

Routine blood pressure monitoring is very important to assess the effectiveness of antihypertensive therapy and prevent the risk of further complications, such as organ dysfunction, impaired blood flow to the placenta, and the risk of eclampsia, which can endanger the mother and fetus<sup>29</sup>.

**Table 3** Blood Pressure Examination

| Characteristic | Category | Reference Value              | Observed Range                 | F (%)      | Mean    |
|----------------|----------|------------------------------|--------------------------------|------------|---------|
| Platelet Count | Low      | <150 ×10 <sup>3</sup> /μL    | (82–137) ×10 <sup>3</sup> /μL  | 4 (5.3%)   | 106.75  |
|                | Normal   | 150–440 ×10 <sup>3</sup> /μL | (152–426) ×10 <sup>3</sup> /μL | 69 (90.8%) | 277.1   |
|                | High     | >440 ×10 <sup>3</sup> /μL    | (460–487) ×10 <sup>3</sup> /μL | 3 (3.9%)   | 472.67  |
| Creatinine     | Low      | <0.51 mg/dL                  | (0.45–0.47) mg/dL              | 2 (2.6%)   | 0.46    |
|                | Normal   | 0.51–0.95 mg/dL              | 0.51–0.95 mg/dL                | 63 (82.9%) | 0.69    |
|                | High     | >0.95 mg/dL                  | 1.02–3.07 mg/dL                | 11 (14.5%) | 1.42    |
| Blood Pressure | MP       | 140/90–159/109 mmHg          | 141/79–159/108 mmHg            | 30 (39.5%) | 149/95  |
|                | SP       | ≥160/110 mmHg                | 142/78–197/141 mmHg            | 46 (60.5%) | 170/110 |

MP: Mild pre-eclampsia

SP: Severe Pre-eclampsia

## Use of Antihypertensive Drugs

### a. Antihypertensive Drugs Mild Preeclampsia

**Table 4** Use of Antihypertensive Drugs for Mild Preeclampsia

| Therapy Type             | Drug Name                               | F (%)      |
|--------------------------|-----------------------------------------|------------|
| Monotherapy              | Methyldopa 250 mg                       | 7 (23.4%)  |
|                          | Nifedipine 10 mg                        | 13 (43.3%) |
|                          | Amlodipine 10 mg                        | 1 (3.3%)   |
| Combination<br>(2 drugs) | Methyldopa 250 mg<br>+ Nifedipine 10 mg | 8 (26.7%)  |
|                          | Methyldopa 250 mg<br>+ Bisoprolol 5 mg  | 1 (3.3%)   |

### b. Antihypertensive Drugs for Severe Preeclampsia

**Table 5** Use of Antihypertensive Drugs for Severe Preeclampsia

| Jenis Terapi        | Nama Obat                                                     | F(%)      |
|---------------------|---------------------------------------------------------------|-----------|
| Monoterapi          | Methyldopa 250 mg                                             | 9 (19,5%) |
|                     | Nifedipine 10 mg                                              | 13(28,7%) |
|                     | Amlodipine 10 mg                                              | 1(2,1%)   |
| Kombinasi<br>2 obat | Methyldopa 250 mg<br>+ Nifedipine 10 mg                       | 10(21,7%) |
|                     | Methyldopa 250 mg<br>+ Nifedipine 30 mg                       | 7(15,2%)  |
|                     | Methyldopa 250 mg<br>+ Amlodipine 5 mg                        | 2(4,3%)   |
|                     | Nifedipine 10 mg<br>+ Amlodipine 5 mg                         | 2(4,3%)   |
| Kombinasi<br>3 obat | Methyldopa 250 mg<br>+ Nifedipine 10 mg<br>+ Amlodipine 5 mg  | 1(2,1%)   |
|                     | Methyldopa 250 mg<br>+ ifedipine 10 mg<br>+ Bisoprolol 2,5 mg | 1(2,1%)   |

## DISCUSSION

Based on **Table 4**, of the 76 pregnant women with preeclampsia, the majority were in the age range of 26–35 years (early adulthood), which was 31 patients (40.8%). Although the age of 26–35 years is often considered a relatively safe gestational age, external factors such as work, stress, and psychological disorders still play a role in increasing the risk of preeclampsia. However, early adulthood is also a productive period, where preventive efforts can be applied to reduce the risk of preeclampsia<sup>14</sup>. The results of this study are in line with the findings of<sup>30</sup>, which reported that the 26–35 age group had the highest prevalence of preeclampsia (55.6%) among the 20 patients studied.

Recent studies have examined the relationship between maternal age and the risk of preeclampsia. While one study found

the highest prevalence of preeclampsia in women aged 31–35 years<sup>31</sup>, others reported higher incidence in women aged 18–26 and 35–42 years<sup>32</sup>. Research on first pregnancies in young women identified age below 20 years as a significant risk factor, with the highest prevalence between 16 and 25 years<sup>33</sup>. Among patients with preeclampsia, maternal age <25 years was associated with an increased risk of preterm birth, low birth weight, and small for gestational age, especially in cases that occurred earlier. For women ≥35 years with preeclampsia that occurred earlier, there was an increased risk of preterm birth before 28 weeks<sup>34</sup>.

One of the main risk factors for preeclampsia is stress, which can trigger negative biological mechanisms in the body. Hypothalamic activation due to stress causes the release of high levels of adrenaline, noradrenaline, and cortisol hormones. Increased cortisol levels can suppress the immune system, increasing the risk of various diseases, including preeclampsia<sup>35</sup>.

**Table 4** also shows that the majority of preeclampsia patients are at 29–42 weeks of gestation or the third trimester, with a total of 62 patients (81.6%). As gestational age increases, maternal weight tends to increase, which can worsen the risk factors for preeclampsia, especially if accompanied by limited physical activity and an unhealthy lifestyle<sup>30</sup>. This finding is in accordance with research<sup>35</sup>, which reported that 98% of preeclampsia cases occurred in the third trimester of pregnancy. In addition, 52.6% of preeclampsia patients in this study had comorbidities, with a total of 40 patients. Comorbidities, especially chronic hypertension and diabetes mellitus, substantially increase the risk of preeclampsia<sup>36</sup>. Pregnant women with hypertension have a 2.149 times greater risk of experiencing preeclampsia, while pregnant women with diabetes mellitus have a 6.682 times higher risk<sup>36</sup>. Other identified risk factors include multiple pregnancies, obesity, birth spacing, and history of antenatal care<sup>37</sup>. The majority of preeclampsia cases occur in women under 20 years or over 35 years of age, with low parity (≤2), and risky pregnancy spacing (<2 years)<sup>38</sup>. A history of hypertension before pregnancy is also a major risk factor, with a 21-fold increased risk of preeclampsia compared to pregnant women without a history of hypertension<sup>12</sup>. Uncontrolled hypertension can worsen pregnancy conditions and increase the likelihood of complications in subsequent pregnancies.

Table 4.1 also shows that the majority of pre-eclampsia patients are pregnant women with parity 2 to 4 (multigravida), as many as 48 patients (63.2%). The etiology of hypertension in pregnancy can be influenced by various factors, including genetic factors, stress, unhealthy diet, multiple pregnancies, kidney disease, and obesity<sup>36,8</sup>. Mothers with multiparous status (having given birth two to five times) are more susceptible to hypertension in pregnancy due to greater risk factors<sup>39</sup>. Parities that are at high risk for pregnancy complications include pregnancies that occur less than three months after the last delivery, pregnancies with a duration of more than five consecutive pregnancies, and mothers who have not been pregnant for more than eight years after the last pregnancy<sup>9</sup>. Maternal mortality data shows that the safest parity status is parity 2 and 3, while parity 1 and parity>3 have a higher risk of maternal death. This is due to the continuous stretching of the uterus in each pregnancy, which can increase the risk of complications in pregnancy, childbirth, and the postpartum period<sup>40</sup>. If pregnancy occurs repeatedly without sufficient rest, it



is feared that there will be weakness in the uterus, which can increase the risk of obstetric disorders <sup>741</sup>. This finding is in accordance with Hidana's 2019 study, which reported that preeclampsia occurs more often in multigravida pregnant women, with a prevalence of 71.5% <sup>41</sup>.

The results of the study showed that the majority of pregnant women with preeclampsia had positive proteinuria, 2, namely 32 patients (42.1%) (**Table 4.2**). Preeclampsia is a serious pregnancy complication characterised by the appearance of hypertension and proteinuria after 20 weeks of gestation <sup>42</sup>. Nutritional factors play an important role in modulating the risk of this condition. A healthy diet rich in vegetables, fruits, and whole grains has been shown to be associated with a reduced risk of preeclampsia. In contrast, a Western-style diet actually increases the susceptibility <sup>43</sup>. In addition, hyperlipidemia, especially hypertriglyceridemia, has been identified as one of the main risk factors, so routine examination of lipid profiles during pregnancy is very relevant <sup>44</sup>. Obesity is also associated with an increased risk of preeclampsia, thought to be through the mechanism of impaired placental development and disruption of metabolic homeostasis <sup>45</sup>. Fatty acid profile analysis in women with preeclampsia showed increased palmitoleic acid levels, while higher omega-3 levels have a potential protective effect <sup>42</sup>. These results suggest a complex interaction between diet, lipid metabolism, and inflammation in the pathogenesis of preeclampsia, highlighting the importance of nutritional intervention and metabolic monitoring as preventive strategies during pregnancy. High dietary salt intake during pregnancy is associated with decreased nitric oxide-mediated endothelium-dependent vasodilation and increased oxidative stress, potentially affecting maternal vascular health <sup>46</sup>. Similarly, excessive maternal saturated fat consumption may negatively impact offspring renal health through renal programming mechanisms <sup>47</sup>. In preeclampsia, podocyte damage plays a key role in the development of proteinuria, which is associated with VEGF and free nitric oxide deficiencies, increased endothelin-1, and oxidative stress (Zieli, 2020). This condition can lead to long-term renal complications, including a higher risk of end-stage renal disease and focal segmental glomerulosclerosis <sup>48</sup>. The pathophysiology of preeclampsia involves abnormal placentation, impaired angiogenesis, and endothelial dysfunction, resulting in acute kidney injury and an increased risk of chronic kidney disease and cardiovascular disease throughout life <sup>49</sup>.

Based on Table 4.3, the majority of pregnant women with preeclampsia, the majority have normal platelet levels, namely 69 patients (90.8%). Thrombocytopenia, or a decrease in the number of platelets below 150,000/ $\mu$ l of blood, is one of the blood disorders that can occur during pregnancy, with a prevalence of around 7 to 10 cases per 100 pregnancies. A decrease in the number of platelets during normal pregnancy can be caused by hemodilution, increased consumption of platelets in peripheral tissues, and increased platelet aggregation due to higher thromboxane levels <sup>50</sup>.

Gestational thrombocytopenia affects 12% of pregnancies, with platelet counts decreasing more significantly in affected women compared to controls <sup>51</sup>. Hyperhomocysteinemia has been associated with various pregnancy complications, including PE and fetal growth restriction <sup>52</sup>. The results of this study indicate that although preeclampsia can affect various hematological

parameters, most patients in this study did not experience significant disturbances in platelet levels, which may be due to physiological compensation factors during pregnancy. In addition, based on Table 4.3, the majority of pregnant women with preeclampsia had normal creatinine levels, which were 63 patients (82.9%). Creatinine is a metabolic product of creatine and phosphocreatine, which is synthesised in the liver, pancreas, and kidneys <sup>53</sup>. Urea and creatinine levels in the blood are important indicators in assessing the balance between kidney production and excretion <sup>54</sup>. When kidney function decreases, urea and creatinine levels in the blood will increase, indicating impaired renal filtration <sup>55</sup>. **Table 4.3** also shows that the majority of patients experienced severe preeclampsia, which was 46 patients (60.5%). One of the factors causing the high number of severe preeclampsia cases is the low awareness among pregnant women of the need to carry out routine antenatal checks <sup>56</sup>. Patients with mild preeclampsia are often unaware that they have the condition because there are no significant symptoms, so that preeclampsia develops into a more severe form due to late detection and treatment <sup>57</sup>. Severe preeclampsia is characterised by organ complications, such as headaches, visual disturbances, oliguria, pain in the upper abdomen, and pulmonary edema <sup>56</sup>. The risk of preeclampsia tends to increase in the third trimester of pregnancy, along with increased maternal organ metabolism and placental activity in distributing nutrients to the fetus <sup>57</sup>. The older the gestational age, the higher the possibility of the mother experiencing preeclampsia <sup>58</sup>.

Based on **Tables 4.4** and **4.5**, the data show that of the 76 pregnant women with preeclampsia, the majority of patients with mild preeclampsia and severe preeclampsia received nifedipine 10 mg monotherapy, 13 patients (43.3%) and 13 patients (28.7%), respectively. Nifedipine has emerged as an antihypertensive and tocolytic agent that is widely used during pregnancy, especially for preeclampsia and preterm labour management <sup>59</sup>, the results showed that nifedipine is effective in prolonging pregnancy and controlling blood pressure in severe preeclampsia <sup>60</sup>. The mechanism of action of nifedipine focuses more on vasodilation of blood vessels without disrupting uteroplacental blood flow, so it is relatively safe for the mother and fetus. It does not cause abnormalities in the fetal heart <sup>61</sup>. The results of this study are in line with a study reporting that Nifedipine was the most frequently prescribed antihypertensive drug (81.4%) for pregnant women with hypertensive disorders in a Ghanaian hospital study, which reported a prevalence of this disorder of 12.5% <sup>62</sup>. In addition, based on Table 4.4, the results show that the combination of two drugs, namely methyldopa 250 mg and nifedipine 10 mg, was used by the majority of patients with mild preeclampsia, as many as 8 patients (26.7%) and severe preeclampsia as many as 10 patients (21.7%). This combination therapy has been shown to be effective in treating preeclampsia from mild to severe stages and can prevent further complications such as eclampsia. The use of combination therapy is an option when monotherapy does not provide an optimal response to lowering blood pressure <sup>59</sup>. Overall, nifedipine appears to be a safe and effective option for treating hypertensive disorders and preterm labour during pregnancy, with minimal maternal and neonatal side effects <sup>60</sup>.

Furthermore, based on Table 4.5, the use of a combination of three drugs in patients with severe preeclampsia, namely

methyldopa 250 mg + nifedipine 10 mg + amlodipine 5 mg and methyldopa 250 mg + nifedipine 10 mg + bisoprolol 2.5 mg, was found in 1 patient (2.1%) each. Triple drug combination therapy is used if monotherapy and a combination of two drugs do not provide optimal results in controlling blood pressure<sup>63</sup>. However, beta-blockers such as metoprolol and bisoprolol, although well tolerated, can increase the risk of small for gestational age babies<sup>64</sup>. Several studies have reported that bisoprolol can cross the placenta and cause bradycardia and hypoglycemia in the fetus<sup>64</sup>. In addition, bisoprolol can also be excreted through breast milk, so its use in breastfeeding mothers requires special attention<sup>65</sup>.

The results of this study indicate that the selection of antihypertensive therapy in pregnant women with preeclampsia needs to be adjusted to the severity of the condition and consider the safety for the mother and fetus. Nifedipine monotherapy is still the main choice, while a combination of two or three drugs is applied if the response to single therapy is not optimal.

## CONCLUSION AND PERSPECTIVES

The results of this study indicate that the majority of pregnant women with pre-eclampsia are in the age range of 26–35 years and in the third trimester of pregnancy, which is a high-risk period due to increased stress, physiological changes, and limited physical activity. The main risk factors for pre-eclampsia include stress that triggers the release of the hormone cortisol, the presence of comorbidities, a history of hypertension before pregnancy, and multiparous status. In addition, a diet high in fat and salt contributes to an increased risk of pre-eclampsia through impaired kidney and vascular function.

The majority of pre-eclampsia patients in this study experienced positive proteinuria 2, with platelet and creatinine levels that were generally still within normal limits. However, most patients experienced severe pre-eclampsia due to a lack of awareness to carry out routine antenatal checks.

In terms of therapy, nifedipine monotherapy is the main choice in the treatment of mild to severe pre-eclampsia, while a combination of two or three drugs is used in cases with blood pressure that is more difficult to control. The selection of antihypertensive therapy needs to consider the severity of pre-eclampsia and safety for the mother and fetus. Preventive efforts such as stress management, healthy diet, and regular pregnancy check-ups are very important to reduce the incidence of pre-eclampsia and its complications.

## DECLARATION OF COMPETING INTEREST

The authors declare no competing financial interest.

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