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# A retrospective cohort study of hypertension, cardiovascular disease, and metabolic syndrome risk in women with history of preterm and term preeclampsia five years after delivery

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ABSTRACT

*Objectives:* To evaluate maternal hypertension, risk of cardiovascular disease (CVD), and metabolic syndrome five years after delivery in preterm preeclampsia (P-PE), term preeclampsia (T-PE), and normal pregnancy.
*Study design:* This was a retrospective cohort study of women who delivered at Dr. Soetomo Academic Hospital (Indonesia) in 2013 with a diagnosis of PE and were compared with women with normal pregnancies.
*Main outcomes measures:* Blood pressure, National Cholesterol Education Program Adult Treatment Panel III criteria for metabolic syndrome (NCE-ATP III), and Framingham Risk Score (FRS).
*Results:* In this study, 92 women participated. They were divided into the P-PE (27), T-PE (35), and control groups (30). Women with a history of PE, P-PE, or T-PE had higher blood pressure five years after delivery than those in the control group ($p < 0.05$). Systolic blood pressure (SBP) >140 mmHg was seen in 66.7% of P-PE and 25.7% of T-PE, while 55.6% of P-PE and 34.3% of T-PE had diastolic blood pressure (DBP) >90 mmHg ($p < 0.05$). Women with P-PE had the highest risk of developing hypertension (Relative risk (RR): 20; 95% Confidence interval [CI]: 2.85–139.92). Women with history of P-PE (RR: 1.85; 95% CI: 0.77–4.41), T-PE (RR: 1.28; 95% CI: 0.51–3.19), and total PE (RR: 1.53; 95% CI: 0.68–3.43) had an increased risk of positive NECP-ATP III five years after delivery. Women with history of P-PE (RR: 5.17; 95% CI: 0.26–103.22; $p = 0.282$) and T-PE (RR: 6.03; 95% CI: 0.32–112.22; $p = 0.228$) are at a greater risk of having an FRS >10% compared to the control group ($p = 0.04$).
*Conclusions:* History of PE, P-PE, and T-PE increased the risk of hypertension and CVD five years after delivery. The results also showed a tendency toward an increased risk of metabolic syndrome in women with a previous history of PE and P-PE.

## 1. Introduction

Preeclampsia (PE) is a major obstetrics issue, particularly in underdeveloped nations, where it is a leading cause of maternal mortality (10%–15%)[1]. According to 74 scientific studies on PE across 40 countries, 1.4%–4.6% of pregnancies are affected by pre-eclampsia[2]. PE and eclampsia were the leading causes of maternal death at Dr. Soetomo General Academic Hospital in Surabaya in 2010[3,4]. In 2014, the incidence of PE at Dr. Soetomo General Academic Hospital in Surabaya, Indonesia increased from 27.88% to 32.48%. A 2016 multicenter retrospective study of seven tertiary care hospitals in Indonesia reported that the prevalence of hypertension during pregnancy was 22.1% in a

*Abbreviations:* CI, Confidence Interval; CHAMPS, The Cardiovascular Health After Mother Placental Syndromes; CVD, Cardiovascular Disease; DBP, Diastolic Blood Pressure; DM, Diabetes Mellitus; FBG, Fasting Blood Glucose; FRS, Framingham Risk Score; HDL, High-density Lipoprotein; LDL, Low-density Lipoprotein; MAP, Mean Arterial Pressure; NCE-ATP III, National Cholesterol Education Program Adult Treatment Panel III; OR, Odd Ratio; PE, Preeclampsia; P-PE, Preterm Preeclampsia; RR, Relative Risk; SBP, Systolic Blood Pressure; SGA, Small for Gestational Age; TC, Total Cholesterol; TG, Triglyceride; T-PE, Term Preeclampsia.

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total of 17,771 deliveries. Among those, 54% were classified as having late-onset preeclampsia and 46% as having early onset preeclampsia. Maternal and perinatal mortality rates were 2% and 12%, respectively. Dr. Soetomo Academic Hospital saw a high incidence of severe complicated preeclampsia as it is the only tertiary referral hospital in East Java [5].

PE causes substantial morbidity and mortality in the mother and fetus or infant owing to multisystem organ dysfunction[6,7]. PE is divided into two categories based on delivery timing: preterm PE (P-PE) was diagnosed if PE led to delivery before 37 weeks; term PE (T-PE) was diagnosed if PE led to delivery ≥37 weeks[8–10]. P-PE and T-PE are hypothesized to result from distinct etiology [11–13]. P-PE occurs during the first trimester of pregnancy and is associated with immunological and inflammatory responses during implantation. This process involves release of several growth factors and cytokines. P-PE is characterized by shallow trophoblast invasion and suboptimal vascular remodeling, resulting in placental hypoperfusion. This results in the release of reactive chemicals that enter the bloodstream and damage the endothelium, which is essential for maintaining the balance between vasodilation and vasoconstriction via nitric oxide synthesis. In contrast, T-PE is primarily caused by maternal vascular and chronic inflammatory maladaptation, ultimately resulting in preeclampsia[11]. This distinction affects clinical presentation, severity, and prognosis of P-PE compared to those of T-PE. Christensen et al. demonstrated that the gestational age at the onset of preeclampsia is negatively associated with markers of subclinical atherosclerosis, including carotid plaque presence, carotid intima-media thickness, aortic pulse wave velocity, and heart rate augmentation index, 12 years after delivery. After delivery, women with P-PE had worse atherosclerotic characteristics than women with T-PE[12]. In an Australian national cohort study, hypertension in pregnancy, especially early onset hypertension, was associated with a higher risk of cardiovascular disease (CVD) than late-onset hypertension, which was enhanced by smoking[13].

PE is an issue because of its association with mortality and short-term morbidity, and its role in long-term morbidities such as chronic hypertension, CVD, cerebrovascular illness, and metabolic syndrome[14–16]. Indonesia has a much higher incidence of female metabolic syndrome than European countries. Sigit et al. reported that the prevalence of metabolic syndrome was 46% in Indonesian women and 24% in Dutch women[17]. Compared with women without a history of PE in pregnancy, women with a history of PE in pregnancy have a higher incidence of metabolic syndrome. Obesity, hypertension, insulin resistance, high fasting blood sugar levels, dyslipidemia, and microalbuminuria are the risk factors for CVD. PE can increase the likelihood of developing metabolic syndrome, which may be the primary cause of development of CVD. In a *meta*-analysis encompassing 55,695 patients, PE was found to significantly increase the risk of metabolic syndrome (Crude odds ratios [OR] = 2.93; 95% confidence interval [CI] = 1.92–4.47 and Adjusted OR = 1.62; 95% CI = 1.25–2.08)[18]. PE shares similar risk factors and pathophysiological problems with arterial-coronary illnesses, including insulin resistance. Framingham Risk Score (FRS) can be used to predict the probability of developing CVD 10 years after PE. A previous study found that the risk of developing CVD was 4.52 times higher in women with a history of PE compared with women with no history of PE[19]. Metabolic syndrome refers to a group of disorders that increase the risk of various diseases[20]. Most studies have indicated that women with preeclampsia have an increased risk of developing metabolic syndrome after birthing, indicating its role in the pathophysiology of diseases, ranging from preeclampsia to long-term CVD. Metabolic syndrome was diagnosed using the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III)[21].

To date, no Indonesian studies have linked the onset of PE to the risk of chronic hypertension, CVD, or metabolic syndrome. This study was conducted to determine the risk of maternal hypertension, CVD disorders, and metabolic syndrome five years after delivery in women with severe preeclampsia (P-PE and T-PE) compared with normal pregnancy using clinical and laboratory measurements, FRS[21], and NCEP-ATP III criteria[22].

## 2. Methods

This retrospective cohort study was conducted at Dr. Sutomo General Academic Hospital, Surabaya, Indonesia from January 2018 to December 2018 and was approved by the hospital ethics committee. This study consisted of women with or without PE (during pregnancy and delivery) who delivered in the hospital five years prior to 2018 (Jan 2013 to Dec 2013). Purposive sampling was used to select these criteria. Women with a normal pregnancy, no signs or symptoms of PE during pregnancy and delivery, and a term birth in 2013 comprised the control group. The other groups consisted of women with PE during pregnancy who delivered in 2013. The PE groups were separated based on delivery timing into P-PE (delivered at <37 weeks) and T-PE (delivered at ≥37 weeks) groups. Patients with obesity, chronic hypertension, congenital cardiac disease, diabetes mellitus, autoimmune disease, or rheumatism before or during pregnancy were excluded.

Primary outcomes were hypertension, metabolic syndrome, and CVD risk. We also measured maternal serum markers of metabolic syndrome: high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride (TG), total cholesterol (TC), and fasting blood glucose (FBG) levels. The diagnosis of hypertension during pregnancy, P-PE, and T-PE was based on the International Society for the Study of Hypertension in Pregnancy (ISSHP) definition[23,24]. Hypertension was defined as systolic blood pressure (SBP) >140 mmHg and/or diastolic blood pressure (DBP) >90 mmHg, based on the average of at least two measurements[24]. Metabolic syndrome was diagnosed according to the NCEP-ATP III criteria[25]. According to the NCEP-ATP III definition, metabolic syndrome occurs when three or more of the following five conditions are met: waist circumference >35 in, blood pressure >130/85 mmHg, fasting TG levels >150 mg/dl, fasting HDL cholesterol (HDLC) levels <50 mg/dl, and FBG level >100 mg/dl[25]. Additionally, we measured the birth weight percentile, percentile <10, and percentile <5 using the INTERGROWTH calculator to evaluate neonatal outcomes[26].

The FRS was used to assess the risk of CVD. Six coronary risk factors, namely, age, sex, TC, HDLC, SBP, and smoking behavior, were used to produce the FRS. The calculation thresholds for FRS were: TC <160, 160–199, 200–239, 240–279, and ≥280 mg/dL; SBP <120, 120–129, 130–139, 140–159, and ≥160 mmHg; HDLC <40, 40–49, 50–59, and ≥60 mg/dL. Total points were used to determine the 10-year risk in percentage terms (1 point = 6%, 2 points = 8%, 3 points = 10%, 4 points = 12%, 5 points = 16%, 6 points = 20%, 7 points = 25%, and 10 points or more >30%). The percentage of absolute CVD risk over a 10-year period was categorized as low risk (10%), intermediate risk (10%–20%), and high risk (>20%)[27].

Patients were selected from the database of medical records at Dr. Soetomo Academic Hospital between January 2016 and December 2016 based on the inclusion and exclusion criteria. The researchers contacted the participants and informed them about the study. Patients who agreed to participate signed an informed consent form. The researcher then performed a clinical assessment and collected blood samples. Blood pressure was measured using a standardized method: women in a seated position with their feet flat on the floor, correct cuff size, Korotkoff V for DBP, and an automated device[28]. Blood pressure was measured twice in each arm with a 15-minute interval between measurements. Blood pressure was determined by averaging two readings. Subsequently, body weight (kg), height (cm), and waist circumference (cm) were measured. Waist circumference was measured using a flexible measuring tape. The tape measure was wrapped around the broadest section of the abdomen across the belly button and measured while the woman exhaled. Three milliliters of blood were collected to determine the serum levels of blood TG; fasting blood sugar; and total, LDL, and HDL cholesterol (mg/dL). All measurements were performed using automated laboratory procedures.

Statistical analyses were performed using the SPSS 25. Data are initially presented using descriptive statistics, followed by a test of normality distribution. We analyzed the statistical differences in categorical data using the chi-square test (normally distributed data) or Fisher's exact test (abnormally distributed data). For the numerical data, we measured the differences using either the *t*-test or Mann–Whitney *U* test, depending on the normality distribution of the numerical data. The relative risk was measured for categorical data for each parameter.

## 3. Results

From the evaluated medical records of 452 preeclamptic pregnancies, only 62 patients met the selection criteria, including 27 with P-PE and 35 with T-PE (Fig. 1). Of the 452 patients, 256 were excluded because of chronic hypertension (60), Diabetes Mellitus (DM) (65), obesity (105), heart disease (15), and autoimmune disease (15). Thirty women with normotensive pregnancies who delivered term-delivered infants were included in the control group. The maternal history and background characteristics of the groups are shown in Table 1. Maternal age was higher in the T-PE group than in the P-PE and control groups. The P-PE group had a higher incidence of maternal complications (55.55% vs. 14.28%), cesarean delivery (74.1% vs. 57.1%), and perinatal death (29.6% vs. 8.2%). In addition, the gestational age at delivery was lower in the P-PE group than that in the T-PE and control groups. Birth weight, birth weight percentile, percentile <10, and percentile <5 were consistently lower in the P-PE than in the T-PE and control groups ($p < 0.05$) (Table 1). Table 2 compares the clinical and laboratory examinations of the PE, P-PE, and T-PE groups with those of the control group. Five years after delivery, 66.7%, 27.5 %, and 3.3% of women in the P-PE, T-PE, and control groups, respectively, had hypertension.

Both the clinical and laboratory results were significantly different between the PE and control groups (Table 2). Mean SBP and DBP (87.95 ±16.71 vs 66.53±11.41 mmHg), Mean Arterial Pressure (MAP) (105.9 ±16.71 vs 66.53±11.41 mmHg), waist circumference (88.74±10.90 vs 83.46±2.09 cm), TC (224.46±101.66 vs 175.47±46.97 mg/dL), LDL (120.74±70.08 vs 83.7±36.29 mg/dL), TG (263.68±230.42 vs 154.43 ±47.35 mg/dL), and FBG (107.45±64.01 vs 84.3±21.98 mg/dL) of the PE group were significantly higher compared to those of the control group ($p < 0.05$). However, the mean HDL of the PE group was lower compared to the control group (51.61±13.57 vs 60.83±3.42 mg/dl; $p <$

**Table 1**
Maternal History and Background Characteristics.

| | Control (n = 30) | Preterm PE (n = 27) | Term PE (n = 35) | *p* |
|---|---|---|---|---|
| Maternal Ages (years old) | 33.1±6.05 | 36.93±6.65 | 39.31±6.16 | **0.001**[a] |
| Nullipara [n (%)] | 19 (63.3) | 14 (51.9) | 21 (60) | 0.666[b] |
| BMI (kg/m$^2$) | 25.84+2.64 | 27.94+2.87 | 25.48+3.09 | **0.003**[a] |
| SBP during pregnancy (mmHg) | 111.67±5.76 | 145±30.41 | 131.80 ±23.74 | **0.000**[a] |
| DBP during pregnancy (mmHg) | 70.67±9.07 | 90±16.41 | 84±15.75 | **0.000**[a] |
| Complications [n (%)] | 0 | 15 (55.55) | 5 (14.28) | 0.051[b] |
| Acute Kidney Injury [n (%)] | 0 | 2 (7.41) | 0 | – |
| HELLP Syndrome [n (%)] | 0 | 1 (3.70) | 2 (5.71) | – |
| Eclampsia [n (%)] | 0 | 2 (7.41) | 1 (2.85) | – |
| Acute Pulmonary Edema [n (%)] | 0 | 0 | 2 (5.71) | – |
| Multiple complications [n (%)] | 0 | 4 (14.81) | 0 | – |
| GA at delivery (weeks) | 38.63±1.40 | 32.04±2.19 | 37.77±2.00 | **0.000**[a] |
| Cesarean delivery [n (%)] | 10 (33.3) | 20 (74.1) | 20 (57.1) | **0.008**[b] |
| Birth weight (g) | 2950 ±366.72 | 1695±445.97 | 3002.94 ±557.31 | **0.000**[a] |
| Birthweight percentile | 41.32±21.78 | 28.51±24.87 | 55.54±30.15 | **0.001**[a] |
| Birthweight percentile < 10n (%) | 0 | 9 (33.3) | 2 (5.7) | **0.000**[b] |
| Birthweight percentile < 5n (%) | 0 | 4 (14.8) | 1 (2.9) | **0.033**[b] |
| Perinatal death [n (%)] | 0 | 8 (29.6) | 3 (8.6) | **0.002**[b] |

[a] One Way ANOVA.
[b] Chi-square test.

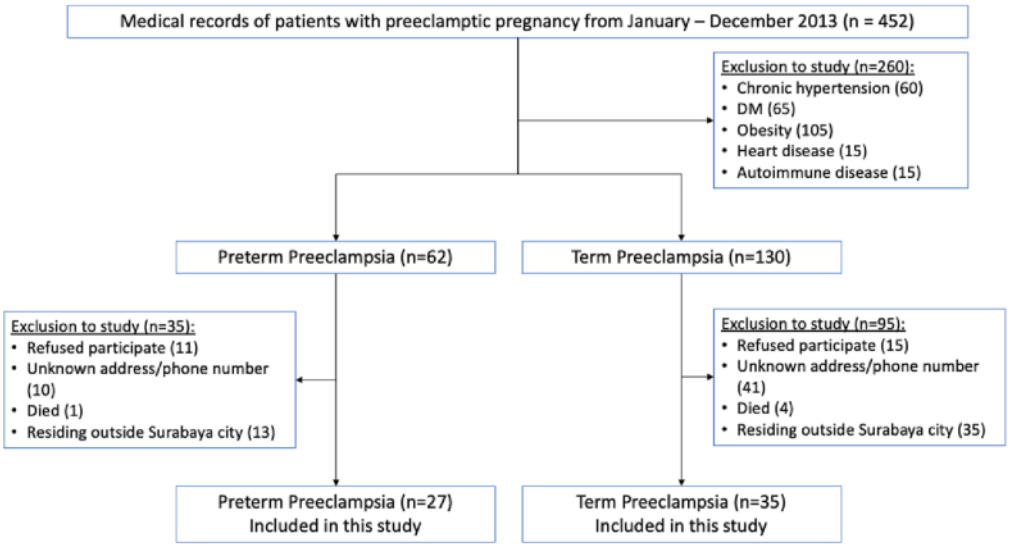


**Fig. 1.** Algorithm Patients Recruitment.

**Table 2**
Comparison of Clinical and Laboratory Examination of Preterm PE, Term PE, and PE (total) Compared with Control.

| | PE (total) (N = 62) | Preterm PE (N = 27) | Term PE (N = 35) | Control (N = 30) | PE (total) vs control | Preterm PE vs Control | Term PE vs Control |
|---|---|---|---|---|---|---|---|
| SBP (mm Hg) | 141.90±24.02 | 154.96±23.48 | 131.83±19.34 | 115.60±14.25 | **p < 0.01** | **p < 0.01** | **p < 0.01** |
| DBP (mm Hg) | 87.95±16.71 | 96.00±16.163 | 81.7±14.49 | 66.53±11.41 | **p < 0.01** | **p < 0.01** | **p < 0.01** |
| MAP (mmHg) | 105.90±18.21 | 115.58+16.99 | 98.42+15.37 | 82.80+11.65 | **p < 0.01** | **p < 0.01** | **p < 0.01** |
| Waist Circumferential (cm) | 88.74±10.90 | 93.14+11.89 | 85.34+8.81 | 83.46+12.09 | **P = 0.03** | **p < 0.01** | p = 0.76 |
| HDL (mg/dL) | 51.61±13.57 | 51.74+16.58 | 51.51+10.96 | 60.83+13.42 | **p < 0.01** | **p = 0.03** | **p = 0.01** |
| LDL (mg/dL) | 120.74±70.08 | 140.70+64.23 | 105.34+71.39 | 83.70+36.29 | **p < 0.01** | **p < 0.01** | p = 0.31 |
| Triglycerides (mg/dL) | 263.68±230.42 | 331.00+281.254 | 211.74+168.513 | 154.43+47.354 | **P = 0.01** | **p < 0.01** | p = 0.43 |
| Total cholesterol level (mg/dL) | 224.46±101.66 | 257.30+104.63 | 199.17+93.03 | 175.47+46.97 | **P = 0.02** | **p < 0.01** | p = 0.50 |
| Fasting Blood sugar (mg/dL) | 107.45±64.01 | 104.81+37.88 | 109.48+79.01 | 84.30+21.98 | **P = 0.01** | p = 0.33 | p = 0.15 |

0.05). P-PE had higher levels of SBP (154.96±23.48 vs 115.6±14.25), DBP (96±16.16 vs 66.53±11.41), MAP (115.58±16.99 vs 82.8±11.65), LDL (140.7±64.23 vs 83.7±36.29), TG (331±281.254 vs 154.43 ±47.35), and TC (257.3±104.63 vs 175.47±46.97), a larger waist circumference (93.14±11.89 vs 83.46±12.09), and lower HDL levels (51.74±16.58 vs 60.83±13.42) compared to the control group ($p < 0.05$). SBP (131.83±19.34 vs 115.6±14.25), DBP (81.7±14.49 vs 66.53 ±11.41), MAP (98.42±15.37 vs 82.80±11.65), and HDL levels (51.51 ±10.96 vs 60.83±13.42) differ significantly between the T-PE group and the control group. P-PE was strongly associated with increased SBP, DBP, MAP, LDL, TG, and TC levels and a larger waist circumference compared with T-PE ($p < 0.05$) (Table 2).

Table 3 shows the NCEP-ATP III classification in all groups at five years after delivery. Positive NCEP-ATP III criteria were found in 37%, 25.7 %, and 20% of the P-PE, T-PE, and control groups, respectively. Women with history of P-PE (Relative Risk (RR): 1.85; 95% CI: 0.77–4.41), T-PE (RR: 1.28; 95% CI: 0.51–3.19), and total PE (RR: 1.53; 95% CI: 0.68–3.43) increase the risk of positive NECP-ATP III five years after delivery (Table 3). FRS analysis showed that most participants were in the low-risk classification: control group (100%), P-PE (92.6%), and T-PE (91.4%) (Table 4). The P-PE group (7.4%) was classified as having a high-risk FRS, while the T-PE group (8.6%) had an intermediate-risk FRS. Our findings revealed that women with P-PE or T-PE are at a greater risk of having an intermediate- or high-risk FRS (>10%) than the control group (p = 0.04) (Table 4). However, there was no significant difference in the FRS between total PE and control group ($p = 0.278$) (Table 4). We also measured the relative risk of FRS >10% (intermediate-high risk) in P-PE vs control (RR: 5.17; 95% CI: 0.26–103.22; $p = 0.282$), T-PE vs control (RR: 6.03; 95% CI: 0.32–112.22; $p = 0.228$), and total PE vs control (RR: 5.41; 95% CI: 0.31–94.79; $p = 0.25$).

Additionally, outcomes between total PE and control groups were compared. The incidence of abnormal SBP (43.5% vs. 3.3%), DBP (43.5% vs. 3.3%), and LDL >100 mg/dL (53.2% vs. 26.7%) was substantially higher among women with a history of PE ($p < 0.05$) than in women without a history of PE (Table 5). Excessive waist circumference, HDL, TG, and FBG levels did not differ significantly between the groups ($p > 0.05$) (Table 5). PE, P-PE, and T-PE increased the risk of high blood pressure, waist circumference, and metabolic syndrome serum markers

**Table 3**
NCEP-ATP III Among Women Five Years After Delivery.

| | Control | Preterm PE | Term PE | *p* |
|---|---|---|---|---|
| Positive | 6 (20%) | 10 (37%) | 9 (25.7%) | 0.342[a] |
| Negative | 24 (80%) | 17 (63%) | 26 74.3%) | |
| | Control | Total PE | | *P* |
| Positive | 6 (20%) | 19 (30%) | | 0.282[a] |
| Negative | 24 (80%) | 43 (70%) | | |

[a] Chi-square test.

**Table 4**
Framingham Risk Score Classification in Women Five Years After Delivery.

| | Control (n = 30) | Preterm PE (n = 27) | Term PE (n = 35) | *p* |
|---|---|---|---|---|
| Low Risk (<10%) | 30 (100%) | 25 (92.6%) | 32 (91.4%) | **0.04***[a] |
| Intermediate Risk (10–20%) | 0 | 0 | 3 (8.6%) | |
| High Risk (>20%) | 0 | 2 (7.4%) | 0 | |
| | Control (n = 30) | Total PE (n = 62) | | *p* |
| Low Risk (<10%) | 30 (100%) | 57 (91.9%) | | 0.278[a] |
| Intermediate Risk (10–20%) | 0 | 3 (4.8%) | | |
| High Risk (>20%) | 0 | 2 (3.3%) | | |

[a] Chi-square test.

**Table 5**
Blood Pressure and Metabolic Syndrome Markers in Control vs PE Group.

| | Control (n = 30) | PE (n = 62) | P value | RR (95% CI) |
|---|---|---|---|---|
| Systolic blood pressure > 140 mmHg | 1 (3.30%) | 27 (43.5%) | < **0.01***[a] | 13.08 (1.86–91.62) |
| Diastolic Blood Pressure >90 mm Hg | 1 (3.30%) | 27 (43.5%) | < **0.01***[a] | 13.06 (1.86–91.82) |
| Waist Circumference >88 cm | 10 (33.3%) | 28 (45.2%) | 0.28[a] | 1.35 (0.76–2.40) |
| LDL >100 mg/dL | 8 (26.7%) | 33 (53.2%) | **0.01***[a] | 1.99 (1.05–3.78) |
| HDL <50 mg/dL | 7 (23.3%) | 28 (45.2%) | 0.06[a] | 1.93 (0.95–3.91) |
| Triglycerides >150 mg/dL | 16 (53.3%) | 40 (64.5 %) | 0.30[a] | 1.21 (0.82–1.77) |
| Fasting blood sugar >125 mg/dL | 2 (6.7 %) | 13 (21.0%) | 0.08[a] | 3.14 (075–13.05) |

[a] Chi-square test.

five years after disease development (Table 6). The P-PE group has the highest risk of developing high blood pressure, with a risk for SBP >140 mmHg (RR: 20.00; 95% CI: 2.85–139.92) and DBP >90 mmHg (RR: 16.67; 95% CI: 2.35–117.92). P-PE also has a higher risk for LDL (>100 mg/dL) compared to the control group (RR: 2.78; 95% CI: 1.47–5.24). Meanwhile women with T-PE were at a higher risk to develop high SBP (RR: 7.71; 95% CI: 1.03–57.43) and DBP (RR: 10.26; 95% CI: 1.41–74.56) (Table 6).

## 4. Discussion

This is the first study from Indonesia to investigate the risk of CVD and metabolic syndrome following preeclamptic pregnancy based on delivery timing (P-PE or T-PE). After postpartum haemmorhage, PE is the second leading cause of maternal death in Indonesia [29]. In Indonesia, the maternal mortality rate is 305 per 100.000 live births

**Table 6**
Risk of Abnormal Systolic and Diastolic Blood Pressure, Waist Circumference, Triglyceride, LDL, HDL, and Fasting Blood Glucose in the Preterm PE, Term PE, and Control Groups.

| | SBP <140 mmHg | SBP >140 mmHg | *p* | RR (95% CI) |
|---|---|---|---|---|
| Control subject | 29/30 (96.70%) | 1/30(3.30%) | | 1 |
| Preterm PE | 9/27 (33.3%) | 18/27 (66.7%) | **<0.01** | 20.00 (2.85–139.92) |
| Term PE | 26/25(74.3%) | 9/25(25.7%) | **0.01** | 7.71 (1.03–57.43) |
| | DBP <90 mmHg | DBP >90 mmHg | | |
| Control subject | 29/30 (96.70%) | 1/30(3.30%) | | 1 |
| Preterm PE | 12/27(44.4%) | 15/27 (55.6%) | **<0.01** | 16.67 (2.35–117.88) |
| Term PE | 23/35 (67.7%) | 12/35 (34.3%) | **<0.01** | 10.26 (1.41–74.56) |
| | Waist circumferential <88 cm | Waist circumferential >88 cm | | |
| Control subject | 20/30(66.7%) | 10/30 (33.3%) | | 1 |
| Preterm PE | 12/27 (44.4%) | 15/27 (55.6%) | 0.09 | 1.66 (0.90–3.06) |
| Term PE | 22/35 (44.4%) | 13/35 (55.6%) | 0.75 | 1.11 (0.57–2.16) |
| | LDL <100 mg/dL | LDL >100 mg/dL | | |
| Control subject | 22/30 (73.3%) | 8/30 (26.7%) | | 1 |
| Preterm PE | 7/27 (25.9%) | 20/27 (74.1%) | <0.01 | 2.78 (1.47–5.24) |
| Term PE | 22/35 (62.8%) | 13/35 (37.2%) | 0.37 | 1.39 (0.67–2.9) |
| | HDL >50 mg/dL | HDL <50 mg/dL | | |
| Control subject | 23/30(76.7%) | 7/30 (23.3%) | | 1 |
| Preterm PE | 15/27 (55.6%) | 12/27 (44.4%) | 0.09 | 0.72 (0.49–1.07) |
| Term PE | 19/35 (54.3%) | 16/35 (45.7%) | 0.05 | 0.70 (0.49–1.01) |
| | Triglycerides <150 mg/dL | Triglycerides >150 mg/dL | | |
| Control subject | 14/30 (46.7 %) | 16/30 (53.3%) | | |
| Preterm PE | 7/27 (25.9%) | 20/27 (74.1%) | 0.10 | 1.38 (0.92–2.07) |
| Term PE | 15/35 (42.9%) | 20/35 (57.1%) | 0.75 | 1.07 (0.68–1.66) |
| | Fasting blood sugar <125 mg/dL | Fasting blood sugar >125 mg/dL | | |
| Control subject | 28/30 (93.3 %) | 2/30 (6.7 %) | | 1 |
| Preterm PE | 20/27 (74.1 %) | 7/27 (25.9 %) | 0.07 | 3.88 (0.88–17.13) |
| Term PE | 29/35 (82.9 %) | 6/35 (17.1 %) | 0.22 | 2.57 (0.56–11.80) |

[5,29]. We discovered that after five years women with a history of PE had higher blood pressure than women with no history of PE. A history of PE increased the risk of SBP >140/90 mmHg (RR: 13.08) and DBP >90 mmHg (RR: 13.06) compared to non-PE pregnancies. Moreover, P-PE was associated with a greater risk of developing hypertension (higher SBP, DBP, and MAP) five years after occurrence than T-PE. The risk of developing an SBP ≥140 mmHg (RR: 20 vs. 7.71) and a DBP ≥90 mmHg (RR: 16.67 vs 10.26) was higher in the P-PE group than in the T-PE group. Numerous studies reveal that PE increases the chance of developing CVD, metabolic syndrome, and hypertension by more than threefold (RR: 3.7; 95% CI: 2.50–5.05) after 14.1 years [30–33]. In one study, 50% of the women with a history of PE had chronic hypertension, and the highest blood pressure levels were reported in patients with early onset PE[34,35]. Increases in blood pressure tend to be related to alterations in lipid profile and metabolic syndrome characteristics, which are significantly distinct from those in PE-free women. The Cardiovascular Health After Mother Placental Syndromes (CHAMPS) Study found that women with PE had a 12-fold higher risk of developing CVD and metabolic syndrome than women without PE[31]. Lipid profile, waist circumference, and blood sugar levels all affect the risk of developing atherosclerosis in the blood vessels. Theoretically, atherosclerosis begins when LDL interacts with macrophage chemoattractant proteins to activate them, thereby promoting monocyte development. This reaction results in endothelial damage and formation of atherosclerotic plaques. As a result, an imbalance in nitric oxide levels increases blood pressure and mean arterial pressure[32,33]. This study implies that severe PE is associated with an increase in cardio-metabolic risk at 5 years post-delivery.

Based on marker abnormalities (waist circumference, LDL, HDL, TG, TC, and FBG), this study found that women with a history of PE and P-PE had a greater chance of developing metabolic syndrome than women without a history of PE. Compared to women with normal pregnancies, those with a history of PE had a higher prevalence of LDL levels >100 mg/dL. Metabolic syndrome, characterized by alterations in lipid profile, FBG level, and waist circumference, increases the risk of type II diabetes, coronary heart disease (CHD), and stroke[32]. According to two *meta*-analyses, women with a history of PE had a three-fold increased risk of developing hypertension and a two-fold increased risk of developing stroke and ischemic heart disease later in life[35]. Contrary to previous findings, none of the patients in this study were diagnosed with type II diabetes, CHD, or stroke five years after PE. This is likely due to the gradual progression from metabolic changes to disease occurrence. In addition, our results indicate an upward tendency in metabolic syndrome markers, which may eventually manifest as the previously mentioned diseases later in life[3335].

Similar to previous studies [36–42], the sample data were divided into P-PE and T-PE to evaluate whether PE type influenced chronic hypertension, metabolic syndrome, and CVD. This study demonstrated that P-PE had a greater impact on metabolic syndrome markers (lipid profiles and waist circumference) than T-PE. The P-PE group had a higher average abnormal waist circumference and LDL, HDL, TG, TC, and FBG levels than the control group. In contrast, women with T-PE only had abnormal HDL levels compared to women without PE. In a study of 718 women with a history of preeclampsia, Veerbeek et al. found that lipid profiles and fasting blood sugar levels were significantly different between early onset PE, late-onset PE, and gestational hypertension. Early onset PE had the worst profile compared to the other two conditions[43]. In a cohort analysis of 1102 women with a history of PE, the incidence of postpartum metabolic syndrome was more strongly related to P-PE combined with small for gestational age (SGA) than to T-PE or P-PE without SGA. Both the timing of PE and fetal growth restriction influence the likelihood of developing metabolic syndrome following a preeclamptic pregnancy[10,44].

This study revealed that women with a history of PE, either P-PE or T-PE, had a substantially increased risk of CVD (based on FRS). In accordance with similar finidngs, our results demonstrated the significance of PE in the development of heart disease. In a *meta*-analysis involving >6 million women and 258 thousand women with a history of PE, PE was associated with a four-fold increase in the future incidence of heart failure and a two-fold increase in the risk of coronary heart disease, stroke, and CVD-related death[36]. In addition, we discovered that patients with P-PE had higher FRS than those with T-PE. This is consistent with the findings of a *meta*-analysis that included >3.5 million women, which demonstrated that CVD risk is dependent on

certain pregnancy factors, such as the timing of PE. Women with P-PE have a noticeably increased risk of CVD compared with women with T-PE (RR: 7.71, 95% CI: 4.40–13.52 vs RR: 2.16, 95% CI: 1.86–2.52)[37].

In addition, although not statistically significant, women with a history of PE tended to have a higher risk of metabolic syndrome based on NCEP-ATP III criteria. Both FRS and metabolic syndrome can predict the risk of CVD and diabetes, with FRS being more predictive of CVD [44]. Our study found that women with a history of PE, P-PE, or T-PE had significantly lower HDLC levels. HDL is a lipoprotein marker that has the greatest impact on the value of cardiovascular events relative to other lipoprotein variables. Low HDL levels increase the incidence of cardiovascular events by 1.34 times (95% CI: 1.24–1.44)[45].

The incidence of hypertension, metabolic syndrome, and cardiovascular risk later in life was higher among women with P-PE than among those with T-PE[46]. However, the exact explanation for these findings remains controversial. Some researchers have argued that PE can cause sustained damage to the vascular endothelium after delivery [47]. The endothelial damage sustained in P-PE is likely to be more severe and persistent than that in T-PE. Additionally, P-PE and T-PE exhibited distinct vascular adaptations. Patients with P-PE had a higher total vascular resistance than those with T-PE[48]. Increased vascular resistance leads to vascular dysfunction and ultimately to hypertension, which increases the risk of CVD[43].

In this study, the majority of women with a history of PE were still of reproductive age five years after delivery, necessitating health treatment and monitoring. Interventions are advantageous for women with a history of PE[49]. Our findings can be used to prevent CVDs and other metabolic disorders in cases of P-PE. Short- and long-term preventive interventions must include routine screening for CVD risk factors and other metabolic syndrome, as well as ongoing maintenance of a healthy lifestyle[43,46,50]. The American College of Obstetricians and Gynecologists recommends that all women affected by hypertension during pregnancy have initial contact with an obstetric care provider within three weeks postpartum, followed by a comprehensive postpartum visit within 12 weeks postpartum and annual cardiovascular follow-up thereafter[51]. The American Heart Association advises cardiovascular follow-up after HDP, but does not specify a period[52]. For all women with HDP, Kavia et al. proposed a regimen based on follow-up during the first two weeks postpartum and 6–12 weeks postpartum, with specialty follow-up for persistent hypertension, proteinuria, or hyperglycemia at delivery discharge, and annually thereafter[53]. Modifying lifestyle habits is essential to lower the long-term risk of CVD in women with a history of PE. FIGO's postpartum guidelines for women with pregnancy-related cardiovascular risk markers include breastfeeding and lifestyle changes such as a healthy diet and adequate physical activity[54,55].

## 5. Conclusion

This study revealed that women with a history of PE, P-PE, or T-PE were more likely to develop hypertension and CVD five years after childbirth. Although this study did not identify individuals with metabolic syndrome (such as diabetes), abnormal biomarker results implied that women with a history of PE had an increased risk of developing metabolic syndrome later in life. The long-term risk of hypertension, CVD, and metabolic syndrome is greatest in P-PE. To reduce these risks, it is essential to regularly examine maternal health and promote healthy lifestyles in women with a history of PE.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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