# IS THE INCIDENCE OF LOW BIRTH WEIGHT IN INDONESIA DUE TO PREECLAMPSIA DURING PREGNANCY?: A META-ANALYSIS

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#### **ABSTRACT**

Preeclampsia (PE) is a pregnancy disorder characterized by hypertension, edema, and proteinuria. Preeclampsia remains one of the main causes of maternal death in Indonesia. Preeclampsia can cause stunting of fetal growth because of unbalanced nutrition. Preeclampsia can result in insufficient blood flow to the placenta, reducing the intake of nutrients and oxygen by the fetus, which affects its weight. The long-term impact is that infants may have low birth weights (LBW). This study aimed to determine the estimated combined effect of preeclampsia in pregnant women and the incidence of LBW. This study used a meta-analysis method to analyze articles from Google Scholar using the following criteria: published between 2012 and 2024, full-text availability, case-control or cross-sectional studies, multivariate analysis, and reported odds ratios (OR). Articles were collected using the PRISMA diagram and analyzed using Review Manager 5.4 application with a random-effects analysis model. This study analyzed 36 cross-sectional results (OR 95% CI: 2.16; 1.51–3.08) and 22 case-control results (OR 95% CI: 3.15; 1.76–5.64), showing a significant association between preeclampsia in pregnant women and the incidence of low birth weight in infants (p-value < 0.00001, which is < 0.05). Pregnant women with high levels of preeclampsia were at a higher risk of giving birth to infants with low birth weight (odds ratio [OR 95% CI: 4.66; 1.76–12.31, p-value < 0.00001).

Keywords: hypertension, low birth weight, meta-analysis, preeclampsia, pregnancy, random effect model

# INTRODUCTION

In 2015, the incidence of preeclampsia was seven times higher in developing countries than in developed countries. According to the World Health Organization (WHO), the prevalence in developed countries ranged from 1.3-6%, while in developing countries it ranged from 1.8-18% according to the World Health Organization (WHO). Basic Health Research Results Report 2018, in Indonesia, the incidence of preeclampsia in 2018 was around 3.3%, and the incidence of preeclampsia in Bengkulu Province was 0.8% (Kemenkes RI, 2018). preeclampsia remains a major problem, increasing maternal and infant pain and mortality worldwide. Preeclampsia is related to complications that occur in both the mother and baby. Low-birth-weight infants (LBW) are one of the impacts of mothers with preeclampsia, where the risk increases in severe preeclampsia compared to mild preeclampsia (Sugiantari et al., 2019).

Preeclampsia can cause insufficient blood to enter the placenta, so the intake of nutrients and oxygen to the fetus is reduced, affecting its weight. The long-term impact is that infants experience LBW (Sari, 2021a). Mothers with preeclampsia with a gestational age of less than 34 weeks had a 23% incidence of LBW compared to mothers with a gestational age of more than 34 weeks, by 53% (Faadhillah and Helda, 2020). This is in line with a study conducted by Ukah in 2017, which concluded that 70% of hypertension in pregnancy is a causative factor that affects the growth of the placenta, which causes the birth of an infant with low birth weight (Ukah *et al.*, 2017).

Infants with low birth weight (LBW) have an impact on the incidence of mothers with preeclampsia. Severe preeclampsia is associated with an increased risk of giving birth to infants with LBW compared to mild preeclampsia. According to the *World Health Organization* (WHO), LBW has a birth weight of less than 2500 g (Sugiantari

et al., 2019). According to the WHO Health Organization, the overall incidence of LBW is estimated to reach 15-20%, representing more than 20 million births per year. In 2019, the incidence of LBW in Indonesia was 3.2%. In 2018, in Bengkulu Province, there were 851 infants or 2% of infants with LBW, and in Bengkulu City, there were 2% of infants with LBW (Beyer et al., 2020). In line with research at the Bandung City Hospital showed that there was a relationship between preeclampsia factors and the incidence of LBW, based on the results of statistical tests, a *p-value* of 0.038 with alpha (a) 0.05, where the p-value (0.038) < 0.05 (Maidartati et al., 2019).

The advantages of the meta-analysis are less *subjectivity* and *judgment* like the other 3 methods have been known, the quantitative approach takes a lot of samples so that the results can be more

representative, a combination of various kinds of previous research results, this method focuses on accumulating *impact* from insignificant results so that they can produce something significant, can answer questions about the gap in results from various studies, this research in the field of business meta-analysis makes *good* organizational behavior (Mansyur and Iskandar, 2017). This study aimed to determine the relationship between preeclampsia in pregnant women and the incidence of low birth weight infants using a meta-analysis method.

## **METHODS**

This study was a quantitative study with a meta-analysis design. This research strategy used *PICOTS* based on the maternal *and infant* 

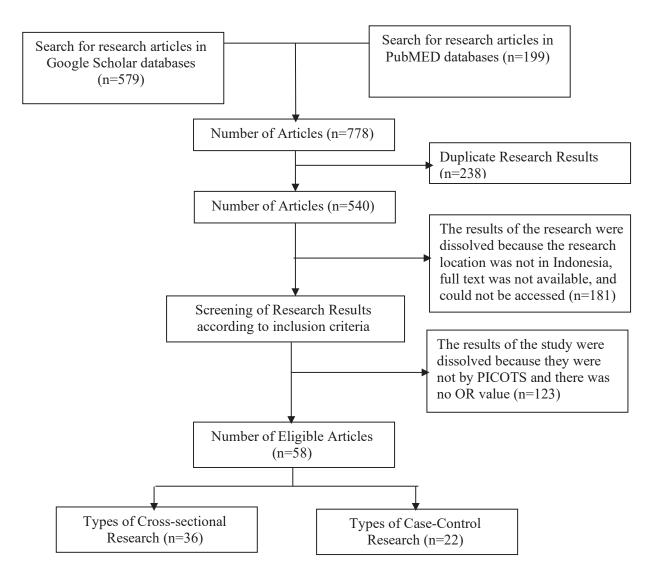


Figure 1. PRISMA Relationship between Preeclampsia in Pregnant Women and the LBW.

population inclusion criteria, preeclampsia intervention in pregnant women, preeclampsia comparators, LBW infant outcomes, publication years 2012 – 2024, studies used a Cross-sectional and a Case-Control Study. Articles published between 2012 and 2024 were included in this study. Articles were obtained from the PubMed and Google Scholar databases. The keywords used to find the article were (Preeclampsi OR Preeclampsia) AND (Ibu Hamil OR Pregnant

Women) OR (Berat Badan Lahir Rendah OR Lowbirth-weight) AND Indonesia.

The process of tracing the research results was performed through a meta-analysis presented in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) chart in Figure 1. In the early stages of identifying the research results, the keywords *preeklampsi OR preeclampsia AND Berat Badan Lahir Rendah OR Low Birth Weight AND Indonesia* were used

Table 1. Prevalence of Preeclampsia and Low Birth Weight (LBW) in Indonesia

Authors	Sample (n)	Prevalence of Preeclampsia	Prevalence of LBW	
(Oktarina et al., 2019a)	78	29.5	23.1	
(Titisari et al., 2019)	118	40.7	79.7	
(Dewi Lieskusumastuti et al., 2022)	460	20.6	6.1	
(Farida and Ifalahma, 2022)	54	72.2	51.9	
(Kusuma et al., 2022)	107	52.3	34.6	
(Sari, 2021b)	3,594	22.2	10.0	
(Yulianti, 2021)	381	32.8	87.1	
(Budiarti et al., 2022)	96	50.0	63.5	
(Lestariningsih et al, 2013)	93	60.2	50.0	
(Kurniasari et al., 2023)	81	48.1	38.3	
(Rahmat et al., 2019)	95	48.1	10.5	
(Anggitasari, 2018)	378	50.0	53.7	
(Risanti and Kusumastuti, 2016)	163	73.6	65.6	
(Wiguna et al., 2023)	72	44.4	30.6	
(Lestari et al., 2015)	185	25.9	89.2	
(Megawati et al., 2023)	355	50.1	60.6	
(Heldawati et al., 2018)	68	50.0	33.8	
(Herlambang et al., 2021)	50	50.0	46.0	
(Hansel Wijaya and Susanto, 2022)	190	19.5	33.7	
(Kumalasari et al., 2018)	47	44.7	61.7	
(Magasida et al., 2024)	100	23.0	43.0	
(Kumalasari et al., 2018)	1,582	27.0	19.6	
(Sinaga, 2022)	229	77.7	21.8	
(Marvika, 2020)	100	16.0	41.0	
(Makbruri, 2015)	1,763	4.8	15.8	
(Saputri et al., 2023)	100	29.0	39.0	
(Hidayat et al., 2023)	104	7.7	44.2	
(Putri Ariyan et al., 2022)	216	51.9	32.9	
(Desi et al., 2024)	150	60.0	79.3	
(Nurul Khairani et al., 2020)	87	17.2	33.3	
(Sukesi et al., 2019)	138	39.9	47.1	
(Gita Tri Wahyuni et al., 2024)	258	26.0	33.3	
(Deviana et al., 2024)	202	13.4	88.6	
(Kusumahati and Sanusi, 2021)	1,582	27.0	19.6	
(Wahyuni et al., 2018)	261	13.0	33.3	
(Sari et al., 2022)	496	7.3	31.9	

in the Google Scholar database, resulting in 2,550 articles. The next step was filtering by eliminating duplicate publications and those that could not be accessed in the full text. In the final process, 36 studies with a cross-sectional design and 22 studies with a case-control design were eligible for the meta-analysis. Data were analyzed using Review Manager (RevMan 5.4) by calculating the differences in outcomes between the Odds Ratio (OR) variables and by estimating the combined effect as well as the variation or heterogeneity across all studies.

# RESULTS AND DISCUSSION

Table 1 shows the distribution of preeclampsia incidence among pregnant women based on 36 research articles with a cross-sectional research design that met the criteria for the meta-analysis. The incidence of preeclampsia among pregnant women ranges from 4.3% to 77.7%, with an average of 36.8%.

Meanwhile, the incidence of preeclampsia in pregnant women in 2015 in developed countries was around 1.3-6%, while in developing countries it ranged from 1.8-18%, according to the World Health Organ (WHO). According to Riskesdas (2018), the incidence of preeclampsia in Indonesia is approximately 3.3% (Kemenkes RI, 2018). The high incidence of preeclampsia in pregnant women is influenced by several factors, including age of pregnant women, Primigravida, and Body Mass Index (BMI). Nursal Research (2017) states that pregnant women aged <20 and >35 years are at risk of developing preeclampsia 4,886 times compared to pregnant women aged between 20 and 35 years (Nursal et al., 2017). Meanwhile, Gustri et al. (2016) stated that the age that can cause preeclampsia is < 20 years and > 35 years because there are structural and functional changes in the body that occur in the peripheral blood vessels that are responsible for changes in blood pressure (Gustri et al., 2016).

Research at RSUD Anutapura Palu City found that primigravida is a risk factor for preeclampsia; in other words, primigravida are 4.654 times more likely to develop preeclampsia than multigravida (Nur and Adhar, 2017). A study conducted at Roemani Muhammadiyah Hospital, Semarang,

found that BMI  $\geq$  25 kg/m2 or obesity affects the incidence of preeclampsia, which can occur due to an increase in adiponectin levels that can suppress the expression of adhesion molecules in vascular endothelial cells and cytokines (Sutrimah *et al.*, 2015). The average incidence of preeclampsia in the pregnant women was 36%. Compared with the incidence in Indonesia, the rate of preeclampsia in pregnant women is relatively high. The high incidence rate can be influenced by the age of mothers aged <20 years or >35 years who are at a higher risk of developing preeclampsia, a gradual increase in blood pressure, proteinuria, and edema during pregnancy, especially in primigravida, and usually occurs in the third trimester until delivery.

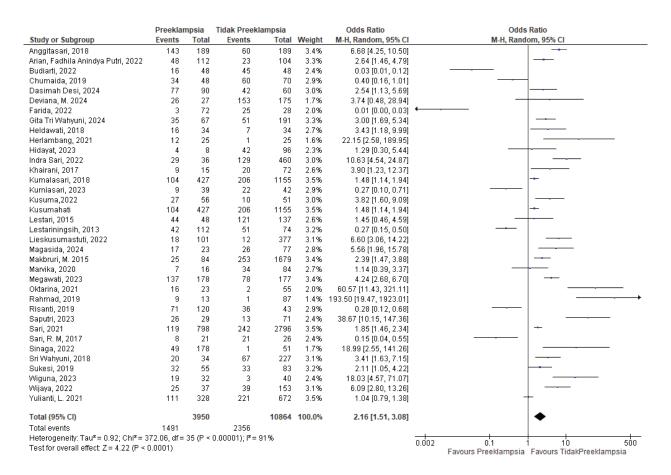
Table 1 shows that, of the 36 research articles with a cross-sectional design, the prevalence of LBW was the lowest at 6.1%, and the highest prevalence of LBW was 89.2%. The incidence of LBW in Indonesia in 2019 was 3.2% (Beyer et al., 2020). The high incidence of LBW in infants is influenced by several factors including maternal age, parity, multiple pregnancies, and preeclampsia. The mother's young age, reproductive organ development, and physiological functions are not optimal. The younger the mother is during pregnancy, the lighter the child will be born. According to research at Arifin Achmad Hospital, Riau Province, mothers aged < 20 and > 35 years are eight times more likely to cause LBW than mothers aged 20-35 years (Triana, 2014). Maternal parity was divided into three categories: primipara (1 child), multipara (2-5 children), and grande multipara (>5 children). Parities 1 and 3 are safe for childbirth. Parity >3 is at risk of giving birth to an LBW baby, whereas parity >5 tends to give birth to an LBW baby. The results of a study at Permata Cibubur-Bekasi Hospital found that mothers who were multipara and grand multipara had a chance of 0.001 compared to mothers who were primipara (Jumhati and Novianti, 2018). Fetal growth in twin pregnancies is prone to inhibition due to excessive uterine tension, the size of the fetus, two placentas, and more amniotic fluid, causing premature birth. In a study at Arifin Achmad Hospital, Riau Province, mothers with multiple pregnancies were 15 times at risk of LBW compared to mothers with single pregnancies (Triana, 2014).

Figure 1 shows the forest plot above shows that the *pooled odds ratio* obtained of the 36 results of cross-sectional research obtained OR (95% CI): 2.16 (1,51-3,08), This suggests that there is a relationship between preeclampsia and the incidence of low birth weight in Indonesia (P-value < 0.00001). Figure 1 also shows the variation between heterogeneous studies, which can be seen from the p-value in the *heterogeneity* test p-value = 0.00001 < 0.05, and the I<sup>2</sup> value of 91% (I<sup>2</sup>>50%); thus, in this analysis, a *random effect model is used*.

Figure 2 shows that the forest plot above shows that the pooled odds ratio obtained from 22 results of the control case research was OR 95% CI: 3.15 (1.76-5.64). This suggests a relationship between preeclampsia and the incidence of low birth weight in Indonesia (p < 0.00001). Figure 2

also shows the variation between heterogeneous studies, which can be seen from the p-value in the *heterogeneity* test p-value = 0.00001 < 0.05, and the I<sup>2</sup> value of 93% (I<sup>2</sup> >50%); thus, in this analysis, a *random effect model is used*.

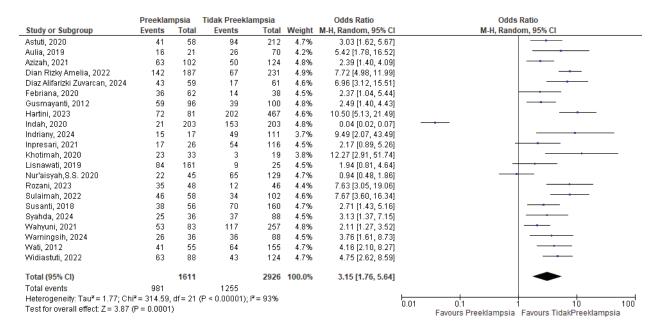
Figure 3 shows the forest plot above shows that the pooled odds ratio obtained from 36 results of the control case research obtained OR (95% CI): 4.66 (1.76-12.31), This suggests that there is a relationship between preeclampsia level and the incidence of low birth weight in Indonesia (p-value < 0.00001), The higher the level of preeclampsia, the greater the risk of LBW. Figure 2 also shows the variation between heterogeneous studies, which can be seen from the p-value in the heterogeneity test p-value = 0.00001 < 0.05, and the I² value of 92% (I² >50%); thus, in this analysis, a random effect model is used.



## Image caption:

- Blue square: Odd Ratio (OR) of each study
- --- CI 95% Odd Ratio (OR)
- Black Diamond: Pooled odds racing.

**Figure 1.** Forest Plot of the Relationship between Preeclampsia in Pregnant Women and LBW with *Cross-sectional Research Design* 



**Figure 2.** Forest Plot of the Relationship between Preeclampsia in Pregnant Women and the LBW with Control Case Research Design

	Preeklampsia	Berat	Preeklampsia	Ringan		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Akib, 2024	17	43	3	24	5.6%	4.58 [1.18, 17.75]	
Dewi Puspita Sari, 2018	42	90	24	80	6.1%	2.04 [1.08, 3.84]	<del></del>
Hanif, 2021	40	85	9	125	6.0%	11.46 [5.14, 25.52]	_ <del></del>
Hartati, 2018	37	98	49	66	6.1%	0.21 [0.11, 0.42]	<del></del>
Khofiyah, 2017	37	69	6	21	5.8%	2.89 [1.00, 8.33]	<del></del>
Martini, 2020	14	17	2	16	5.0%	32.67 [4.71, 226.52]	
Meihartati, 2017	63	90	2	8	5.3%	7.00 [1.33, 36.91]	<del></del>
Muhasidah, 2020	21	26	8	21	5.6%	6.83 [1.83, 25.40]	
Nurliawati, 2015	88	90	2	214	5.0%	4664.00 [646.76, 33633.86]	·
Primadevi, 2022	9	21	7	49	5.7%	4.50 [1.39, 14.61]	<del></del>
Rahmawati,2014	16	23	84	177	5.9%	2.53 [0.99, 6.45]	-
Risnawati, 2018	24	26	4	20	5.1%	48.00 [7.84, 293.72]	
Sari, 2023	18	20	6	15	5.2%	13.50 [2.26, 80.79]	
Sarkiah, 2017	70	160	26	32	5.9%	0.18 [0.07, 0.46]	<del></del> -
Sinaga, 2022	16	47	31	35	5.7%	0.07 [0.02, 0.22]	<del></del>
Sumitro, 2023	12	20	2	16	5.2%	10.50 [1.86, 59.27]	
Suwaibah, 2023	13	17	7	17	5.5%	4.64 [1.06, 20.38]	<del></del>
Wati, 2021	31	40	3	6	5.2%	3.44 [0.59, 20.10]	<del></del>
Total (95% CI)		982		942	100.0%	4.66 [1.76, 12.31]	•
Total events	568		275				
Heterogeneity: Tau <sup>2</sup> = 3.93	3; Chi² = 215.84,	df = 17 (F	P < 0.00001); I <sup>2</sup> =	92%			0.01 0.1 1 10 100
Test for overall effect: Z = 3.10 (P = 0.002)  Test for overall effect: Z = 3.10 (P = 0.002)  Preeklampsia Berat Preeklampsia Ringan							

**Figure 3.** Forest Plot of the Relationship between Preeclampsia Level in Pregnant Women and the LBW with Control Case Research Design

The study's results with a cross-sectional design, the funnel plot in Figure 4 shows that the standard error ranges from 0.2-0.9 on the left-hand plot and the standard error ranges are 0.2 to 1.4 on the right-hand plot. This funnel plot shows a symmetrical distribution of research, with an uneven distribution to the left and right of the centerline, indicating no publication bias. On the results of the study with a control case design, the funnel plot in Figure 5 shows that the standard error ranges from 0.2-0.9 on the left-

hand plot and the standard error ranges are 0.2 to 0.8 on the right-hand plot. This funnel plot shows an asymmetrical distribution of research, with an uneven distribution to the left and right of the centerline, indicating publication bias. This bias may be because only studies showing a link between preeclampsia and low birth weight have been published, whereas studies that did not find such a link were not published.

Preeclampsia is a cause of LBW. This is in line with research conducted by Faadhilah and

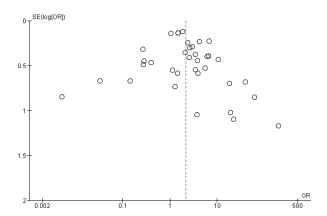


Figure 4. Funnel Plot of the Relationship between Preeclampsia in Pregnant Women and the Incidence of LBW with Cross-sectional Research Design

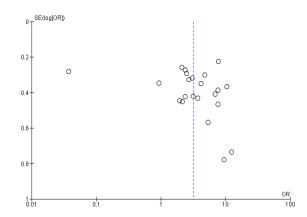


Figure 5. Funnel Plot of the Relationship between Preeclampsia in Pregnant Women and the Incidence of LBW with Case-Control Research Design

Image caption:

SE Standard Error,

o = represents the article, a vertical dotted line

(---) The centerline was used to determine the symmetry of the plot.

Helda (2020), stating that there is a significant relationship between preeclampsia and the incidence of LBW, with p-value = 0.001 (p<0.05). The PR association size was 1.483, with a 95% CI (1.21-1.86). This means that mothers with preeclampsia have a 1,483 risk of having a baby with LBW (Faadhillah and Helda, 2020). The average incidence of LBW infants was 44.70%. Compared to Indonesia, the incidence rate of LBW infants is relatively high. The high incidence rate is also influenced by several factors, including preeclampsia. This occurs because of a decrease in blood flow and nutrients to the placenta owing to impaired placental function. If it lasts for a long time, fetal growth is disrupted, causing the infant to have LBW.

These 36 research articles were combined into a meta-analysis of the relationship between preeclampsia in pregnant women and the incidence of low-birth-weight infants. This study used a Case-control and Cross-sectional study design. Thirteen articles were included in the meta-analysis of the relationship between preeclampsia in pregnant women and the incidence of Low Birth Weight (LBW), 12 did not touch the line of no effect and only one article touched the line of no effect, meaning that there was a significant relationship that showed a significant Odds Ratio

(OR) value. The Odds Ratio was lowest (0.02) to highest (60.57). This is due to the difference in the number of samples and preeclampsia in pregnant women, with the incidence of low-birth-weight infants.

Research conducted by Fitri Nur Indah (2020) at Panembahan Senopati Bantul Hospital, Yogyakarta, obtained the lowest poll odds ratio of 0.02, which stated that there was a meaningful relationship between pregnant women and preeclampsia with the incidence of LBW infants, as evidenced by the p-value of 0.000 < 0.05, and mothers who experienced preeclampsia had a 23.74 times greater risk of giving birth to LBW infants compared to mothers who did not experience preeclampsia (Indah and Utami, 2020). Research conducted at Dr. M. Yunus Hospital, Bengkulu City, obtained a pooled odds ratio of 60.57, which indicated that preeclampsia and the incidence of LBW infants were significantly related, as evidenced by the p-value of 0.000 < 0.05 (Oktarina et al., 2019b).

Pregnant women with preeclampsia experience high blood pressure, which can result in a decrease in acidic substances flowing from the mother to the fetus through the placenta, a decrease in blood flow to the placenta, which results in placental disorders to prevent oxygen intake, and

nutritional intake from the mother to the fetus. Disruption of nutritional intake and oxygen intake for the fetus can result in fetal growth disorders, such that the fetus is born with low body weight. This is in line with the research conducted by Lestariningsih (2019), who found that mothers with preeclampsia are 10.12 times more likely to give birth to an LBW baby than mothers who do not experience preeclampsia (Oktarina et al., 2019b). Research conducted by Inpresari and Pratiwi (2020) in the working area of Jawilan and Petir Health Centers stated that there was no significant relationship between preeclampsia in pregnant women and the incidence of LBW infants. Proven by a p-value of 0.129 > 0.05(Inpresari and Pertiwi, 2021). This meta-analysis showed that there was a publication bias. This happens if the results of the article studied are not published results that are related to the research conducted and are only published or influential.

Using a meta-analysis design, this study has several strengths that contribute to its reliability and generalizability. First, quantitative research allows for an objective analysis of the relationship between preeclampsia in pregnant women and the incidence of low birth weight (LBW) infants. The study utilizes a robust data collection strategy, sourcing articles published between 2012 and 2024 from reputable databases, such as PubMed and Google Scholar. The use of a systematic approach, represented by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram, strengthens the rigor of the research methodology by ensuring transparency in the study selection and data extraction. Additionally, the inclusion of both Cross-sectional and Case-Control studies provided a diverse set of data sources, increasing the comprehensiveness of the findings. The Odds Ratio (OR) used in data analysis enables researchers to estimate the combined effect of studies and assess the strength of the association between preeclampsia and LBW, contributing valuable insights into this relationship.

However, this study had several limitations. One limitation was the heterogeneity of the included studies, which can be a common challenge in meta-analyses when combining studies with varying designs. Despite the rigorous

selection process, the difference in study design (cross-sectional vs. case-control) may introduce inconsistencies in the findings, making it difficult to draw definitive conclusions. This study emphasizes the need for larger, more uniform studies to reduce this heterogeneity, suggesting that variability in sample sizes, methodologies, and population characteristics may have affected the reliability of the results. Furthermore, while the meta-analysis methodology allows for a comprehensive evaluation of the available literature, it is important to note that publication bias may affect the results because studies with statistically significant findings are more likely to be published. Lastly, although this study offers valuable insights for improving pre-eclampsia screening and intervention strategies, the findings might not be fully generalizable to all regions or populations due to the study's focus on data from Indonesia and the specific inclusion criteria used.

# **CONCLUSION**

The incidence of preeclampsia in pregnant women is significantly associated with the incidence of low-birth-weight infants. Efforts are needed to strengthen preeclampsia screening in pregnant women, especially in high-risk groups, and to closely monitor fetal birth weight. Further research with more uniform designs and larger sample sizes is needed to reduce the heterogeneity and clarify the link between preeclampsia and low birth weight. Education and training of medical personnel on the management of preeclampsia and updating clinical guidelines that include prevention strategies and interventions should be prioritized. Collaboration among researchers, practitioners, and policymakers is also important in formulating effective evidence-based policies. Future research should focus on large-scale prospective cohort studies with standardized designs to reduce heterogeneity. Studies with larger and more diverse sample sizes would enhance generalizability and statistical power. Longitudinal studies could explore the long-term outcomes for mothers and infants while investigating the mechanisms linking preeclampsia to low birth weight (LBW), such as placental insufficiency. Research should also examine the effectiveness of early screening and

interventions in high-risk groups. Comparing data across different regions and healthcare settings will help to identify context-specific strategies, and exploring psychosocial and socioeconomic factors could improve maternal and neonatal outcomes.

### **Declaration of Interest Statement**

The authors declare that they have no conflict of interest.

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