



# Incidence of Preeclampsia during the Third Trimester and Its Impact on Low Birth Weight Infants

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## ABSTRACT

Indonesia is one of the developing countries that occupy the third position in ASEAN and second in the South East Asian Nation Regional Organization region with the largest Maternal Mortality Rate and perinatal. All maternal deaths were 99% occurred in developing countries, one of which was Indonesia. In terms of maternal health, newborns, and nutrition in developed and developing countries, birth weight is known as an important and reliable indicator for the survival of neonates and infants. Moreover, pre-eclampsia serves as one of the factors that contribute to the occurrence of Low Birth Weight (LBW). This condition is a pregnancy-specific syndrome characterized by hypertension and proteinuria, due to reduced organ perfusion as a result of vasospasm and endothelial activation. Furthermore, the elevated blood pressure in this disorder causes a decrease in uteroplacental perfusion. These further decreases blood circulation to the fetus and results in a lack of oxygen and nutrients as well as stunted fetal growth, which manifests as LBW. The mutual existence of several pre-eclampsia and LBW incidence cannot be denied. However, the presence of pre-eclampsia in the mother may not always be the cause of LBW, despite the association between these two factors. Preterm gestation, multiple pregnancy, and antepartum hemorrhage are also among the risk factors that might contribute to this condition. journal selection method is conducted by researchers by looking from various sources such as PubMed / NCBI, google scholar, science direct by entering the initial keyword sedentary, which is then followed by other keywords namely Hypertension in pregnancy, preeclampsia, birth weight, third trimester, maternal mortality rate and perinatal mortality rate. The purpose is to review and broadening insights into relationships and factors that affect low birth weight by predicting the possibility of preeclampsia as well as efforts to prevent low birth weight babies. The result of this review is mothers who suffered from preeclampsia/eclampsia during their pregnancy had a 4,164 times higher risk of having babies with LBW and 70% of hypertension in pregnancy affects placental growth, resulting in babies born with LBW due to fetal growth retardation. Conclusion based on a literature review, a relationship between the incidence of preeclampsia in the third trimester and the birth weight of the baby was observed.

**Keywords:** *Hypertension in Pregnancy; Preeclampsia; Low Birth Weight; Maternal Mortality Rate*

## 1. INTRODUCTION

Indonesia is a developing country with the highest maternal and perinatal mortality rate, ranking third in ASEAN and second in the Southeast Asian Nation Regional Organization. These maternal and infant mortality rates can be used to assess the degree of health in a country. Therefore, several programs, such as Maternal and Child Health (MCH) are used to improve health status, reduce mortality, and disease occurrence in mothers and children [1].

Maternal Mortality Rate (MMR) is a parameter, which can be used to evaluate the health status of a country. In 2012, the World Health Organization (WHO)

estimated that approximately 800 women died daily from complications related to pregnancy, childbirth, and postpartum globally. Furthermore, 99% of this incidence occurred in developing countries, including Indonesia [2]. In 80% of the cases, the main complications were caused directly by maternal death while 20% were indirect [3]. These direct causes include bleeding, sepsis, hypertension in pregnancy, obstructed labor, high-risk complications, and other factors. In addition, preeclampsia and eclampsia are types of hypertensive events in pregnancy that have serious consequences on both the woman and the fetus in their womb [4].

Preeclampsia is a type of hypertension that occurs during pregnancy, with blood pressure and proteinuria

levels above 140/90 mmHg at 20 weeks of gestation, and 300 mg/24 hours, respectively [5]. This condition also causes approximately 15–20% of maternal deaths globally and is a major contributor to the occurrence of fetal mortality and morbidity [1]. Risk factors, such as age, parity, previous preeclampsia, family history of preeclampsia, twin pregnancy, previous medical histories, including diabetes, chronic hypertension, autoimmune disease, distance pregnancy, and other factors, influence this condition [7].

Furthermore, preeclampsia is divided into early-onset and late-onset. Late-onset preeclampsia (gestational age at or more than 34 weeks) is associated with good fetal development without any signs of disturbances. Meanwhile, the early-onset form (pregnancy age < 34 weeks) is accompanied by abnormal trophoblast invasion in the spiral arteries resulting in symptoms of impaired fetal development [8]. The third trimester during pregnancy occurs between the 29-40th week and the occurrence of preeclampsia during this period is characterized by the presence of hypertension, with proteinuria, and/or organic symptoms affecting birth weight [9]. In addition, the size of a baby one hour after birth is known as the birth weight. The goal of this weighing process is to determine if the baby's birth weight is normal, low, or high [10]. This procedure is also related to study on the long-term health effects of LBW or Macromosia (Excessive Birth Weight) [12].

According to the WHO, birth weight is a significant and reliable parameter for the survival of neonates and infants. This variable is the leading cause of perinatal and neonatal mortality in developed and developing countries and can be seen from the aspect of maternal health, newborn, and nutrition. Various factors, including maternal, fetal, and placental variables result in LBW babies [2]. Preeclampsia can also cause high rates of maternal morbidity and mortality [1].

Some discrepancies regarding preeclampsia in pregnancy and the baby's birth weight still exist. Study at Undata Hospital Palu presented a correlation between preeclampsia in pregnancy and LBW. This finding was due to the fact that this condition can result in Intrauterine Growth Retardation (IUGR), leading to LBW babies.[34] Meanwhile, according to RSUP DR. M. Djamil Padang, these factors are not significantly related. Furthermore, due to the different pathogenesis of the two onsets, only the early-onset problems can result in delayed developmental barriers.[42] Early-onset preeclampsia is associated with placental abnormalities while late-onset is correlated minimally or not at all due to an increased uterine artery resistance, which is not noticeable in the fetus. Impaired uteroplacental perfusion due to placental abnormalities causes fetal development delays during pregnancy, resulting in LBW for gestational age (KMK). Therefore, this study discusses the relationship between third-trimester preeclampsia and birth weight. The results

are expected to provide pregnant women with information regarding pregnancy care and increase their understanding of the association between the incidence of preeclampsia in third-trimester pregnant women and LBW.

## 2. DEFINITION OF PREECLAMPSIA

Preeclampsia is a phenomenon that develops as a result of pregnancy and includes hypertension, proteinuria, edema, and in some cases, organ system diseases. This condition usually occurs at the inception of the third trimester [8].

### 2.1. Risk Factor

Immunological maladaptation, genetic predisposition, and media-vascular aspects are estimated to influence this condition [13].

### 2.2. Classification of Hypertension in Pregnancy

1. Preeclampsia-eclampsia
2. Chronic hypertension
3. Chronic hypertension with superimposed preeclampsia
4. Gestational hypertension

### 2.3. Classification of Preeclampsia

The classification of preeclampsia is divided into three, including mild preeclampsia, severe preeclampsia, and eclampsia [8]

### 2.4. Pathophysiology

The placenta receives blood supply from the uteroplacental arteries, which are formed by the invasion of interstitial evacuation and endovascular trophoblasts into the spiral arteriole walls. These changes result in low resistance, low pressure, and high flow in the uteroplacental artery. During a normal pregnancy, the trophoblast induces the transition of blood vessels from the intervillous space to the original spiral arterioles. The first stage of this change involves the inversion of the decidual portion in the spiral arterioles from endovascular trophoblast evacuation and the myometrial portion in the first and second trimester, respectively [14]. Furthermore, the placentation process in preeclampsia is abnormal because not all spiral arteries receive proper invasion from the trophoblast cells [14].

In pregnancies associated with preeclampsia, the maternal vascular placentation response is incompetent. The decidual portion of the uteroplacental artery usually contains the vessel transitions, while the myometrial portion of the spiral arteriole typically exhibits

musculoelastic specifications, making it highly responsive to hormonal influences.

## 2.5. Signs and symptoms

The first type of preeclampsia symptoms is based on the clinical picture, which is characterized by excessive weight gain. Meanwhile, the second is predicated on subjective symptoms, such as frontal lobe headaches, epigastric pain, and visual disturbances [14].

## 2.6. Diagnosis of Preeclampsia and Pregnancy Hypertension

Hypertension, commonly known as high blood pressure, is a condition in which the blood pressure rises above the normal value of 120/80 mmHg. This condition can be declared in a person with blood pressure above 140/90 mmHg, however, a value less than 130/85 mmHg can be considered as normal (usually the limit includes adults over the age of 18 years) [15].

Currently, the diagnosis of preeclampsia is clarified if hypertension occurs after 20 weeks of gestation, followed by 1 worsening symptom, such as greater than 300 mg/24 hours proteinuria or dipstick >1, serum creatinine >1.1 mg/dl, pulmonary edema, more than 2x increased work on liver function, platelets <100,000/mm<sup>3</sup>, the occurrence of headaches, visual impairment, and epigastric pain [11].

## 2.7. Diagnosis of Preeclampsia

A condition cannot be directly diagnosed as preeclampsia if only hypertension is detected, the presence of specific organ disorders must also be observed. Several preeclampsia cases have been confirmed by the presence of protein in the urine. Also, other signs can verify the diagnosis of this disorder, including thrombocytopenia with platelets <100,000/microliter, renal impairment with serum creatinine > 1.1 mg/dL, or an increase of this value in the absence of other renal abnormalities. Conversely, liver disorders can also be observed if there is a 2-fold increase in the transaminase concentrations and pain in the epigastric area/right upper region of the abdomen. Other symptoms for pulmonary edema and neurological signs, such as stroke, headache, and visual disturbances, can also be identified. This occurrence may impair fetal development, which is a symptom of uteroplacental circulation complications, such as oligohydramnios, Fetal Growth Restriction (FGR), or Absent or Reversed-End Diastolic Velocity (ARDV) [15].

## 2.8. Complications

Preeclampsia complications are either maternal or fetal. Furthermore, uterine atony, HELLP syndrome, and kidney failure are some of the complications experienced

by the mother [12]. Meanwhile, neonatal asphyxia, inhibition of infant development, and intrauterine hypoxia are observed in the fetus/infant.

## 2.9. Management

Preeclampsia can be managed both actively and conservatively. The active component (Magnesium sulfate) can be used medicinally and terminated while the conservative can be observed and evaluated. In addition, the magnesium sulfate is discontinued when the mother shows signs of mild preeclampsia within 24 hours. This condition is considered a medical treatment failure if there is no improvement after 24 hours and must be terminated. Also, patients may be discharged if the preeclampsia symptoms become mild [9],[10].

## 2.10. Prevention

The general terminology for the 'prevention' of preeclampsia is divided into primary, secondary, and tertiary [15].

## 2.11. Birth Weight

Birth weight is a growth parameter, which depicts the nutritional status obtained by the fetus while in the womb and is measured from childhood to adulthood. Furthermore, a baby born with a weight <2500 grams is considered to have LBW, regardless of the gestation period [16].

## 2.12. Definition

The birth weight of a baby is defined as the measurement obtained on a scale, 1 hour after birth. The process of weighing is essential to discover if the baby's birth weight is normal or low. In addition, the total weight of <2500 grams in a newborn is referred to as LBW [17].

## 2.13. Prevalence

Ministry of Health state that the prevalence of LBW in Indonesia has gradually decreased over the last 7 years from 2007 (11.5%) to 2013 (10.2%). Meanwhile, East Java Province experienced an increase from 2.79% in 2010 to 3.32% in 2013. This condition is known as the leading cause of neonatal mortality in this province, accounting for 38.03% of the cases based on the data from Public Health Office of East Java Province on 2013. Also, babies born with LBW are at risk of suffering from mortality and morbidity during their development. The incidence of having LBW babies is typically higher during the first pregnancy/primigravida. In addition, adolescent primigravida (<20 years) are at a higher risk of developing preeclampsia in Nigeria [16].

LBW and premature babies are the leading causes of neonatal mortality, accounting for 30.3% of the cases.

IDHS in 2012 stated that this disorder also has the highest risk of death in comparison with normal birth weight, particularly during the perinatal period [18].

### **2.14. Factors affecting birth weight**

LBW is influenced by a combination of maternal, fetal, and environmental aspects. The maternal variable includes parity, gestational spacing, maternal age, and nutritional status. Experiencing multiple pregnancies and abnormalities in the fetus are examples of the fetal aspect. Meanwhile, the environmental aspects include the availability of health facilities, poor lifestyle, and economic conditions [17].

### **2.15. The relationship between preeclampsia and birth weight**

Severe cases of preeclampsia and eclampsia may exacerbate the pathology in certain body parts and organs due to vasospasm and ischemia. Furthermore, hypertension in pregnant women may increase the stimulation of various endogenous substances (e.g prostaglandins and thromboxane), which may result in vasospasm and platelet aggregation. The further accumulation of thrombus and bleeding can also affect the central nervous system with symptoms, such as headache, local nerve deficits, and seizures. In addition, renal necrosis may decrease glomerular filtration rate and proteinuria while liver damage from hepatocellular necrosis may result in epigastric pain and elevated liver function tests. Decreased intravascular volume, increased cardiac output, and peripheral vascular resistance are all cardiovascular manifestations. Also, increased microangiopathic hemolysis may result in anemia and thrombocytopenia. Placental infarction and obstruction may further cause a delay in fetal development (IUGF), with LBW as one of the symptoms [8].

## **3. METHOD**

Journal searches are conducted by researchers by looking from various sources such as PubMed/NCBI, google scholar, science direct by entering the initial keyword sedentary, which is then followed by other keywords namely Hypertension in pregnancy, preeclampsia, birth weight, third trimester, maternal mortality rate and perinatal mortality rate. Displayed about 136,000 results (0.08 seconds) and taken as many as 10 international journals for review

## **4. RESULT AND DISCUSSION**

A prospective cohort study was used by Ukah et al., [6] to examine the documentation sheet obtained from the Canadian Institutes of Health Research (CIHR). Consequently, it was concluded that 70% of hypertension in pregnancy affects placental growth, resulting in babies

born with LBW due to fetal growth retardation [6] Also, Ernawati et al. [7] conducted study on the health of children born to mothers who had preeclampsia. This was a population-based correlative prospective cohort study performed in 2014 at the Jagir Health Center, with a sample of 37 pregnant women. Accordingly, this report stated that infants born with LBW are twice at risk of experiencing several diseases, such as cerebral palsy, respiratory, metabolic, and endocrine disorders [7].

Furthermore, Johan et al., [19] showed that preeclampsia had a relationship with LBW, where a significant value of ( $p$ ) = 0.01 indicated that mothers with preeclampsia were five times more likely to have babies with LBW. An analytical method and a cross-sectional design were used to conduct this study.[19] Kumalasari et al. [30] also stated that preeclampsia is a risk factor for LBW with an event rate of 24.4% in all deliveries at the General Hospital Dr. Mohammad Hoesin Palembang, South Sumatra Province. This study was conducted using a cross-sectional design with an analytical survey method and 1582 medical records from a population that fulfilled the inclusion criteria. The results of bivariate ( $p=0.005$ ) and multivariate ( $p=0.010$ ) tests showed a significant relationship between preeclampsia and LBW events. This is relevant to Kurniawati's study, which detected a significant relationship between preeclampsia and LBW births, with the risk of LBW birth being 3.25 times higher than in non-preeclampsia patients [30].

According to study by Wati et al. [22], mothers who suffered from preeclampsia/eclampsia during their pregnancy had a 4,164 times higher risk of having babies with LBW [22]. Through a consecutive sampling method, this analytical and case-control study was conducted using the medical record data of 210 mothers. Meanwhile, Srinivas et al. [26], who employed a case-control study demonstrated that women with preeclampsia had a 2.7 times higher risk of having a developmentally retarded fetus (IUGR) than those without preeclampsia. [26]. Fatemeh et al., also showed a significant correlation between preeclampsia and the condition of retarded fetal development in a case-control study, which was conducted with analytical method descriptions in Iran [28]. Study of Mallisa et al. [34], which was performed with an analytic observational method and a case-control approach using medical record data of 184 infants, also revealed that there was a relationship between preeclampsia and LBW infants with a  $p$ -value = 0.003 and a weak relationship strength of 0.215. Moreover, preeclampsia is a risk factor that is 2.48 times more likely to cause the emergence of LBW than non-preeclampsia [34].

Another study by Wahyuni et al. [35], which examined the medical record data of 90 mothers through the chi-square crosstab test, also indicated that there was a significant relationship between severe preeclampsia and LBW [35]. These findings are relevant to this theory

because preeclampsia results in vasoconstriction, which causes a decrease in blood flow and reduces the supply of oxygen and nutrients to the fetus. This phenomenon can lead to IUGR and result in LBW babies [34]. Study by Mallisa et al. [36], which involved the use of a case-control study design, also discovered an odds ratio (OR) of 2.48. This result suggests that OR >1 or preeclampsia is a risk factor with a 2.48 times greater chance of causing LBW than non-preeclampsia because the former is an aspect of LBW occurrence [34]. Furthermore, Bacak stated that preeclampsia increases the risk of IUGR and LBW due to the decreased uteroplacental blood flow [36].

## 5. CONCLUSION

Based on a literature review, a relationship between the incidence of preeclampsia in the third trimester and the birth weight of the baby was observed. Furthermore, preeclampsia in uteroplacental circulation and Hb-O<sub>2</sub> levels causes a decrease in the blood flow to the placenta and hence a disruption or decrease in the supply of nutrients and oxygen. This occurrence can result in the production of oxidative stress in the placenta, increased uterine tone, and sensitivity to stimuli. Therefore, the fetus in the womb will be deprived of nutrients and water, resulting in LBW.

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