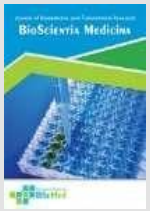
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Preeclampsia Risk in Bali, Indonesia: The Role of Maternal Body Mass Index (BMI) and Gestational Weight Gain (GWG)

I Gede Wara Nugraha[1*], Rini Martina Siallagan[2]

[1]Puri Bunda Hospital, Denpasar, Indonesia

[2]Department of Clinical Nutrition, Puri Bunda Hospital, Denpasar, Indonesia

ARTICLE INFO

Keywords:
Body mass index
Gestational weight gain
Maternal health
Preeclampsia
Pregnancy complications

***Corresponding author:**
I Gede Wara Nugraha

E-mail address:
igedewaranugraha@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v9i1.1164

A B S T R A C T

Background: Preeclampsia, a hypertensive disorder of pregnancy, significantly contributes to maternal and infant mortality and morbidity globally, including in Indonesia. Pre-pregnancy obesity and excessive gestational weight gain (GWG) are established risk factors for preeclampsia. This study investigated the association between pre-pregnancy body mass index (BMI) and GWG with the incidence of preeclampsia in Bali, Indonesia. **Methods:** A case-control study was conducted at a Maternal Hospital in Bali, Indonesia, from May 2023 to May 2024. The study included 429 pregnant women: 143 with preeclampsia (cases) and 286 without (controls). Data were collected from medical records. BMI was categorized using Asia-Pacific criteria, and GWG was assessed based on the 2009 Institute of Medicine (IOM) guidelines. Logistic regression analysis was performed to determine the associations, adjusting for maternal age, education, and occupation. **Results:** Obesity class II (BMI ≥ 30 kg/m²) and obesity class I (BMI 25.0-29.9 kg/m²) were significantly associated with an increased risk of preeclampsia, with adjusted odds ratios (AOR) of 2.90 (95% CI: 1.19-7.08) and 2.78 (95% CI: 1.60-4.81), respectively, compared to women with normal weight. Excessive GWG was also significantly associated with preeclampsia (AOR 2.53; 95% CI: 1.48-4.33) compared to adequate GWG. **Conclusion:** Maternal obesity and excessive GWG are significant risk factors for preeclampsia in Bali, Indonesia. These findings underscore the importance of pre-pregnancy counseling and interventions to manage weight and promote healthy GWG to reduce the burden of preeclampsia.

1. Introduction

Preeclampsia, a pregnancy-specific hypertensive disorder typically characterized by new-onset hypertension and proteinuria after 20 weeks of gestation, remains a leading cause of maternal and perinatal morbidity and mortality worldwide. It is a complex multisystem disorder that affects various organs, including the cardiovascular, renal, hepatic, and neurological systems. The clinical presentation of preeclampsia can range from mild to severe, with potentially life-threatening complications such as eclampsia (seizures), HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets), stroke, and multi-organ failure. The global prevalence of preeclampsia is estimated to be between 2% and 8% of all pregnancies, with significant variations across regions and populations. The incidence is higher in low- and middle-income countries, where access to quality antenatal care and timely interventions may be limited. In Indonesia, preeclampsia contributes substantially to maternal mortality, accounting for a significant proportion of pregnancy-related deaths. The Indonesian Ministry of Health reported that hypertensive disorders in pregnancy, including preeclampsia, were the leading cause of maternal mortality in 2023, highlighting the urgent need to address this public health challenge.[1-3]

The etiology of preeclampsia is complex and multifactorial, involving an interplay of genetic, immunological, and environmental factors. While the exact mechanisms remain incompletely understood, it is widely recognized that abnormal placentation plays a crucial role in the pathogenesis of preeclampsia. In normal pregnancies, the placenta undergoes extensive remodeling of the maternal spiral arteries, ensuring adequate blood flow and nutrient supply to the developing fetus. However, in preeclampsia, this process is disrupted, leading to shallow trophoblast invasion and inadequate placental perfusion. This results in placental ischemia and the release of various factors into the maternal circulation, including anti-angiogenic factors, inflammatory cytokines, and reactive oxygen species, which contribute to systemic endothelial dysfunction, vasoconstriction, and the clinical manifestations of preeclampsia. While the underlying causes of abnormal placentation in preeclampsia are still under investigation, several risk factors have been identified that increase the likelihood of developing the condition. These risk factors can be broadly categorized into maternal, fetal, and placental factors. Maternal factors include advanced maternal age, nulliparity, history of preeclampsia in previous pregnancies, family history of preeclampsia, chronic hypertension, diabetes mellitus, renal disease, and autoimmune disorders. Fetal factors include multiple gestations and fetal growth restriction. Placental factors include placental abruption and placenta previa.[4-6]

In addition to these established risk factors, modifiable lifestyle factors such as pre-pregnancy obesity and excessive gestational weight gain (GWG) have been consistently recognized as significant contributors to the development of preeclampsia. Obesity, defined as a body mass index (BMI) of 30 kg/m² or higher, is a growing public health concern globally, and its prevalence is increasing in Indonesia. Obesity is associated with various metabolic and cardiovascular disturbances, including insulin resistance, dyslipidemia, chronic inflammation, and endothelial dysfunction, which can predispose women to preeclampsia. Adipose tissue, particularly visceral fat, is an active endocrine organ that secretes various hormones, cytokines, and adipokines, which can influence systemic inflammation and vascular function. In obese individuals, the increased production of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), can contribute to a state of chronic low-grade inflammation, which is implicated in the pathogenesis of preeclampsia. Furthermore, obesity is associated with impaired insulin signaling and altered lipid metabolism, which can further exacerbate endothelial dysfunction and vascular complications.[7-9]

Gestational weight gain (GWG) refers to the total weight gained during pregnancy, reflecting the growth and development of the fetus, placenta, amniotic fluid, maternal blood volume, and uterine tissue. While adequate GWG is essential for a healthy pregnancy, excessive GWG, exceeding the recommended ranges, can lead to adverse maternal and fetal outcomes, including preeclampsia. The Institute of Medicine (IOM) has provided guidelines for appropriate GWG based on pre-pregnancy BMI. These guidelines aim to optimize maternal and fetal health by promoting healthy weight gain within safe limits. Excessive GWG can contribute to the development of preeclampsia through several mechanisms. It can exacerbate insulin resistance, leading to hyperinsulinemia and compensatory hyperglycemia, which can promote oxidative stress and inflammation. Additionally, excessive GWG can increase the workload on the cardiovascular system, leading to elevated blood pressure and an increased risk of endothelial dysfunction. Furthermore, excessive GWG can contribute to the accumulation of visceral fat, which, as mentioned earlier, is a major source of pro-inflammatory cytokines and other factors that can promote the development of preeclampsia.[10-12]

In Indonesia, the prevalence of preeclampsia and its associated risk factors, including obesity and excessive GWG, vary across regions and populations. Bali, a province in Indonesia known for its unique

cultural heritage and rapid economic development, has a relatively high prevalence of preeclampsia, highlighting the need for further investigation into the contributing factors in this specific population. The increasing prevalence of obesity and lifestyle changes associated with modernization may be contributing to the burden of preeclampsia in Bali.[13-15] This study aimed to investigate the association between pre-pregnancy BMI and GWG with the incidence of preeclampsia in Bali, Indonesia. Understanding these associations can inform targeted interventions and strategies to prevent preeclampsia and improve maternal and child health outcomes in this region.

2. Methods

This study employed a case-control design, a retrospective observational approach well-suited to investigating the association between potential risk factors and a specific outcome, in this case, preeclampsia. Case-control studies are particularly valuable when studying relatively rare conditions or outcomes, as they allow for the efficient recruitment of a sufficient number of cases for comparison with a control group. This design is also advantageous when examining multiple exposures or risk factors simultaneously, as it allows for the collection of detailed information on various potential contributors to the outcome of interest. The study was conducted at a leading Maternal Hospital in Bali, Indonesia, a tertiary referral center for obstetric care in the region. This hospital serves a diverse population, representing a wide range of socioeconomic backgrounds and geographic locations across Bali. The selection of this hospital as the study site ensured access to a large and heterogeneous patient population, enhancing the generalizability of the study findings to the broader population of pregnant women in Bali.

The study population consisted of all pregnant women who delivered at the Maternal Hospital in Bali, Indonesia, during the study period from May 2023 to May 2024. This comprehensive inclusion criterion ensured that the study sample was representative of the overall obstetric population at the hospital, minimizing the potential for selection bias. Cases were meticulously defined as women who met the diagnostic criteria for preeclampsia according to the International Society for the Study of Hypertension in Pregnancy (ISSHP) criteria. These criteria require the presence of new-onset hypertension, defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, after 20 weeks of gestation, accompanied by proteinuria, defined as ≥300 mg/24 hours or a protein/creatinine ratio ≥0.3. The use of standardized and internationally recognized diagnostic criteria ensured the accurate identification of cases and minimized the potential for misclassification bias. Controls were carefully selected from among women who delivered during the same period but did not experience preeclampsia or any other hypertensive disorders of pregnancy. The selection of controls was performed using a systematic random sampling technique, ensuring that every eligible woman had an equal chance of being included in the control group. This approach minimized the potential for selection bias and ensured that the control group was representative of the overall population of pregnant women without preeclampsia at the hospital. The final study sample comprised 429 women, consisting of 143 cases and 286 controls. This sample size was carefully determined based on a power calculation, taking into account the prevalence of preeclampsia in Bali, the expected effect size of the association between BMI, GWG, and preeclampsia, and the desired level of statistical power. The power calculation ensured that the study had sufficient statistical power to detect meaningful associations between the exposures of interest and the outcome, minimizing the risk of type II error (failing to detect a true association).

Data were collected retrospectively from medical records using a standardized data collection form. This form was meticulously developed based on a comprehensive review of the literature and expert consultation, ensuring that it captured all relevant information pertaining to the study objectives. The use of a standardized form ensured consistency in data

collection across all participants, minimizing the potential for information bias. The following information was systematically extracted from the medical records; Sociodemographic characteristics: Age, education level, occupation, parity, and history of preeclampsia. These variables were chosen based on their potential to confound or modify the association between BMI, GWG, and preeclampsia; Anthropometric measurements: Pre-pregnancy weight and height (to calculate BMI) and weight at the first antenatal visit. These measurements were carefully recorded by trained healthcare professionals using standardized protocols and calibrated equipment, ensuring accuracy and reliability; Clinical data: Gestational age at delivery, blood pressure readings, and presence of proteinuria. These data were obtained from routine clinical assessments and laboratory investigations conducted during antenatal care and delivery, providing objective measures of the key diagnostic criteria for preeclampsia.

BMI was calculated as weight (kg) divided by height squared (m^2) and categorized according to the Asia-Pacific guidelines. These guidelines provide specific BMI cut-off points for different weight categories that are tailored to the Asian population, taking into account their unique body composition and health risks associated with different BMI levels. The use of Asia-Pacific guidelines ensured that the BMI classification was appropriate for the study population and minimized the potential for misclassification bias. The following BMI categories were used; Underweight: BMI < 18.5 kg/m^2; Normal weight: BMI 18.5 - 22.9 kg/m^2; Overweight: BMI 23.0 - 24.9 kg/m^2; Obesity Class I: BMI 25.0 - 29.9 kg/m^2; Obesity Class II: BMI ≥ 30 kg/m^2.

GWG was meticulously calculated by subtracting the pre-pregnancy weight from the weight at the first antenatal visit. This approach provided an accurate measure of the total weight gained during pregnancy, reflecting the cumulative impact of various factors, including fetal growth, placental development, and maternal physiological changes. The adequacy of GWG was carefully assessed based on the 2009 IOM guidelines. These guidelines provide specific recommendations for total GWG based on pre-pregnancy BMI, taking into account the physiological needs of both the mother and the developing fetus. The IOM guidelines are widely recognized as the standard for assessing GWG and have been validated in various populations, ensuring the reliability and validity of the GWG assessment in this study.

Descriptive statistics were employed to summarize the characteristics of the study participants, providing a comprehensive overview of the study population. Continuous variables, such as age and BMI, were presented as means and standard deviations, measures of central tendency and variability, respectively. Categorical variables, such as education level and occupation, were presented as frequencies and percentages, indicating the number and proportion of participants in each category. Logistic regression analysis, a powerful statistical technique for analyzing binary outcomes, was performed to examine the association between pre-pregnancy BMI, GWG, and the risk of preeclampsia. This method allowed for the estimation of odds ratios (ORs) and their corresponding 95% confidence intervals (CIs), providing a measure of the strength and precision of the association between the exposures of interest and the outcome. The logistic regression model was carefully adjusted for potential confounders, including maternal age, education level, and occupation. Confounding occurs when a third variable is associated with both the exposure and the outcome, potentially distorting the true relationship between them. By adjusting for these potential confounders, the analysis aimed to isolate the independent effects of BMI and GWG on the risk of preeclampsia, providing a more accurate estimate of their true association. All statistical analyses were rigorously conducted using SPSS version 27 (IBM Corp., Armonk, NY, USA), a widely used statistical software package. A p-value of less than 0.05 was considered statistically significant, indicating that the observed association was unlikely to have occurred by chance alone.

3. Results

Table 1 presents the characteristics of the 429 participants in the study, categorized by those who developed preeclampsia (PE) and those who did not (Non-PE). The average age of participants was slightly higher in the PE group (29.2 years) compared to the Non-PE group (28.1 years). This difference was statistically significant (p=0.102), suggesting a potential association between age and preeclampsia risk. While the majority of women in both groups were under 35, a larger proportion of women with PE were 35 years or older (18.2% vs. 12.2%). There was a significant association between education level and preeclampsia (p=0.002). Women with lower education levels were more likely to develop preeclampsia (67.8% in the PE group vs. 52.4% in the Non-PE group). A slightly higher proportion of housewives experienced preeclampsia compared to employed women (12.6% vs. 8.4%), but this difference was not statistically significant (p=0.093). There was a very strong association between pre-pregnancy BMI and preeclampsia (p<0.001). The proportion of women with obesity (BMI ≥ 25.0) was significantly higher in the PE group (60.2%) compared to the Non-PE group (20.6%). Specifically, women with obesity class II (BMI ≥ 30) had the highest risk of preeclampsia (12.6% in the PE group vs. 3.8% in the Non-PE group). Gestational weight gain also showed a very strong association with preeclampsia (p<0.001). The majority of women who developed preeclampsia had excessive GWG (74.1%) compared to those who did not (37.8%).

Table 1. The participant characteristics.

Variables	**PE (n = 143)**	**Non-PE (n = 286)**	**p-value**
	Cases (%)	Controls (%)	
Age			0.102
<35 years old	117 (81.8%)	251 (87.8%)	
≥35 years old	26 (18.2%)	35 (12.2%)	
Education			0.002
High	46 (32.2%)	136 (47.6%)	
Low	97 (67.8%)	150 (52.4%)	
Occupation			0.093
Employed	125 (87.4%)	232 (81.1%)	
Housewife	18 (12.6%)	54 (18.9%)	
BMI			<0.001
<18.5	2 (1.4%)	18 (6.3%)	
18.5-22.9	43 (30.1%)	145 (50.7%)	
22.9-24.9	12 (8.4%)	64 (22.4%)	
25.0-29.9	68 (47.6%)	48 (16.8%)	
≥30.0	18 (12.6%)	11 (3.8%)	
GWG			<0.001
Inadequate	6 (4.2%)	68 (23.8%)	
Adequate	31 (21.7%)	110 (38.5%)	
Excessive	106 (74.1%)	108 (37.8%)	

Table 2 presents the results of the logistic regression analysis, examining how pre-pregnancy BMI and gestational weight gain (GWG) relate to the risk of preeclampsia. BMI and Preeclampsia Risk Model 1 (unadjusted) shows the crude association between BMI categories and preeclampsia risk without considering other factors (like age, education, etc.). It suggests that women with higher BMI have a greater risk of preeclampsia. For example, women with obesity class I (BMI 25.0-29.9) had almost 5 times the odds of developing preeclampsia compared to women with normal weight (OR 4.77, 95% CI: 2.89-7.89). Model 2 (adjusted) is more important, as it adjusts for potential confounders (age, education, occupation). It shows the independent effect of BMI on preeclampsia risk. The association between higher BMI and preeclampsia remains strong. Obesity class I and II still significantly increase the risk (OR 2.78, 95% CI: 1.60-4.81 and OR 2.90, 95% CI: 1.19-7.08, respectively). Interestingly, being underweight (BMI <18.5) did not show a significant association with preeclampsia risk in either model. GWG and Preeclampsia Risk Model 1 (unadjusted) similar to BMI, the unadjusted model suggests a strong link between excessive GWG and preeclampsia. Women with excessive GWG had over 3 times the odds of developing preeclampsia compared to those with adequate GWG (OR 3.48, 95% CI: 2.15-5.63). Model 2 (adjusted) even after adjusting for other factors, excessive GWG remained a significant predictor of preeclampsia (OR 2.53, 95% CI: 1.48-4.33). Inadequate GWG did not show a statistically significant association with preeclampsia risk in either model.

Table 2. Association between BMI, GWG, and preeclampsia.

Exposure	**PE**	**Non-PE**	**Model 1**	**p-value**	**Model 2**	**p-value**
	(n = 143)	(n = 286)				
BMI				<0.001		<0.001
<18.5	2 (1.4%)	18 (6.3%)	0.37 (0.08-1.67)		0.66 (0.14-3.13)	
18.5-22.9	43 (30.1%)	145 (50.7%)	ref		ref	
22.9-24.9	12 (8.4%)	64 (22.4%)	0.63 (0.31-1.27)		0.52 (0.24-1.09)	
25.0-29.9	68 (47.6%)	48 (16.8%)	4.77 (2.89-7.89)		2.78 (1.60-4.81)	
≥30.0	18 (12.6%)	11 (3.8%)	5.51 (2.42-12.57)		2.90 (1.19-7.08)	
GWG				<0.001		<0.001
Inadequate	6 (4.2%)	68 (23.8%)	0.31 (0.12-0.79)		0.35 (0.13-0.91)	
Adequate	31 (21.7%)	110 (38.5%)	ref		ref	
Excessive	106 (74.1%)	108 (37.8%)	3.48 (2.15-5.63)		2.53 (1.48-4.33)	

4. Discussion

Our study revealed a robust association between pre-pregnancy obesity and an increased risk of preeclampsia. Women with obesity class II (BMI ≥ 30 kg/m²) exhibited a nearly three-fold increase in the odds of developing preeclampsia compared to women with normal weight, even after adjusting for potential confounders such as age, education, and occupation. Similarly, women with obesity class I (BMI 25.0-29.9 kg/m²) also experienced a significantly elevated risk. These findings are consistent with numerous studies conducted across diverse populations, underscoring the global impact of obesity on preeclampsia risk. The underlying mechanisms linking obesity to preeclampsia are indeed multifaceted and complex, involving a complex interplay of metabolic, hormonal,

and inflammatory pathways. Adipose tissue, particularly visceral fat, is not merely a storage depot for excess energy but also functions as an active endocrine organ, secreting a variety of hormones, cytokines, and adipokines that can profoundly influence systemic inflammation and metabolic homeostasis. In obesity, the expanded adipose tissue mass leads to an overproduction of pro-inflammatory mediators, including TNF-α, IL-6, and C-reactive protein (CRP), creating a state of chronic low-grade inflammation. Endothelial Dysfunction and Vascular Inflammation pro-inflammatory cytokines can directly impair endothelial function, a critical regulator of vascular tone and permeability. Endothelial dysfunction, a hallmark of preeclampsia, is characterized by reduced nitric oxide bioavailability, increased production of reactive oxygen species, and enhanced expression of adhesion molecules. These changes promote vasoconstriction, platelet aggregation, and leukocyte adhesion, leading to vascular inflammation and impaired placental perfusion. The inflammatory milieu associated with obesity can also disrupt the delicate balance of angiogenic and anti-angiogenic factors, crucial for proper placental development. Imbalances in these factors can lead to abnormal placentation, characterized by shallow trophoblast invasion and inadequate spiral artery remodeling, further compromising placental perfusion and contributing to the clinical manifestations of preeclampsia. Obesity is strongly associated with insulin resistance, a condition in which cells fail to respond adequately to insulin, the hormone responsible for regulating glucose uptake and metabolism. This impaired insulin signaling leads to elevated blood glucose levels and compensatory hyperinsulinemia, a state of excessive insulin secretion in an attempt to overcome insulin resistance. Insulin resistance and hyperinsulinemia can exacerbate oxidative stress and inflammation, both of which are implicated in the pathogenesis of preeclampsia. Hyperglycemia can promote the formation of advanced glycation end products (AGEs), which can bind to their receptors (RAGE) on endothelial cells and immune cells, triggering the release of pro-inflammatory cytokines and reactive oxygen species. Elevated insulin levels can also stimulate the sympathetic nervous system, leading to increased blood pressure and vasoconstriction, further contributing to the development of preeclampsia. The sympathetic nervous system plays a crucial role in regulating vascular tone and blood pressure, and its overactivation can exacerbate the vascular dysfunction associated with preeclampsia. Obesity can profoundly disrupt lipid metabolism, leading to dyslipidemia, a condition characterized by elevated levels of triglycerides and low-density lipoprotein (LDL) cholesterol and decreased levels of high-density lipoprotein (HDL) cholesterol. These alterations in lipid profiles can contribute to the development of preeclampsia through several mechanisms. Oxidized LDL cholesterol, a modified form of LDL that is particularly prone to oxidation, can trigger the release of pro-inflammatory cytokines and chemokines, further exacerbating vascular inflammation and endothelial dysfunction. Oxidized LDL can also impair nitric oxide production and promote platelet aggregation, contributing to vasoconstriction and reduced placental perfusion. Oxidative stress, an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses, can damage cellular components, including lipids, proteins, and DNA, contributing to the pathogenesis of preeclampsia. Obesity can exacerbate oxidative stress by increasing ROS production and impairing antioxidant defenses, further promoting endothelial dysfunction and vascular inflammation. Adipose tissue secretes a variety of adipokines, including leptin and adiponectin, which can influence insulin sensitivity, inflammation, and vascular function. Obesity can disrupt the balance of these adipokines, leading to increased leptin levels and decreased adiponectin levels, further contributing to the development of preeclampsia. Leptin, a hormone that regulates appetite and energy expenditure, can also promote inflammation and endothelial dysfunction. Elevated

leptin levels in obesity can contribute to the chronic low-grade inflammation associated with preeclampsia. Adiponectin, an anti-inflammatory and insulin-sensitizing adipokine, is typically decreased in obesity, further contributing to the risk of preeclampsia. Adiponectin can improve insulin sensitivity, reduce inflammation, and enhance endothelial function, and its deficiency in obesity can exacerbate the metabolic and vascular disturbances associated with preeclampsia. Obesity can impair placental function, leading to inadequate nutrient and oxygen delivery to the developing fetus. This can trigger the release of placental factors into the maternal circulation, including anti-angiogenic factors, inflammatory cytokines, and reactive oxygen species, which contribute to systemic endothelial dysfunction, vasoconstriction, and the clinical manifestations of preeclampsia. The placenta plays a crucial role in regulating maternal blood pressure and vascular function through the production of various hormones and signaling molecules. Obesity can disrupt these delicate mechanisms, leading to impaired placental signaling and increased risk of preeclampsia. Obesity can also contribute to placental hypoxia, a condition of reduced oxygen supply to the placenta, which can further exacerbate oxidative stress and inflammation, contributing to the pathogenesis of preeclampsia. Endothelial dysfunction, a hallmark of preeclampsia, is characterized by impaired vasodilation, increased vascular permeability, and enhanced leukocyte adhesion. These changes can lead to vasoconstriction, reduced placental perfusion, and the clinical manifestations of preeclampsia. Obesity can contribute to endothelial dysfunction through various mechanisms, including inflammation, oxidative stress, insulin resistance, and dyslipidemia. These factors can act synergistically to impair endothelial function and promote the development of preeclampsia. While obesity is a significant risk factor for preeclampsia, it is important to acknowledge that genetic and epigenetic factors also play a role. Certain genetic variations may predispose individuals to both obesity and preeclampsia, while epigenetic modifications can alter gene expression and contribute to the development of both conditions. The interaction between genetic, epigenetic, and environmental factors, including obesity, is likely to contribute to the complex pathogenesis of preeclampsia. Obesity can interact with genetic predispositions to amplify the risk of preeclampsia, highlighting the importance of considering both genetic and environmental factors in the prevention and management of this condition. Emerging evidence suggests that the gut microbiome, the community of microorganisms residing in the human gut, may also play a role in the development of preeclampsia. Obesity can alter the composition and function of the gut microbiome, leading to increased intestinal permeability and the translocation of bacterial products into the circulation. Inflammation and Immune Responses bacterial products, such as lipopolysaccharide (LPS), can trigger inflammation and immune responses, potentially contributing to the pathogenesis of preeclampsia. LPS can activate toll-like receptors (TLRs) on immune cells, leading to the release of pro-inflammatory cytokines and chemokines, which can promote endothelial dysfunction and vascular inflammation.[16-20]

Excessive gestational weight gain (GWG), exceeding the recommended ranges based on pre-pregnancy BMI, emerged as another significant risk factor for preeclampsia in our study. Women with excessive GWG had a more than two-fold increase in the odds of developing preeclampsia compared to women with adequate GWG, independent of their pre-pregnancy BMI. This finding underscores the importance of managing weight gain during pregnancy, even in women who begin their pregnancy with a healthy weight. Excessive gestational weight gain (GWG) during pregnancy is more than just a number on the scale. It represents a complex interplay of metabolic, inflammatory, and vascular changes that can significantly increase the risk of preeclampsia, a serious hypertensive disorder that threatens both mother and baby. While appropriate weight gain is essential for a healthy pregnancy, exceeding the

recommended ranges can disrupt this delicate balance and set the stage for preeclampsia. Imagine your body's cells as locked rooms, and insulin as the key that unlocks them to allow glucose, the body's primary energy source, to enter. In insulin resistance, these locks become rusty, and the key struggles to open them. This leads to a buildup of glucose in the bloodstream and a compensatory overproduction of insulin, a condition known as hyperinsulinemia. Excessive GWG can worsen this "rusty lock" phenomenon, further impairing glucose metabolism and contributing to a cascade of metabolic disturbances that promote oxidative stress, inflammation, and endothelial dysfunction, all key players in the development of preeclampsia. As insulin resistance worsens, the body's ability to regulate blood sugar levels deteriorates, leading to impaired glucose tolerance. In some cases, this can progress to gestational diabetes mellitus (GDM), a form of diabetes that develops during pregnancy. GDM is a well-established risk factor for preeclampsia, and its development in the context of excessive GWG can further amplify the metabolic imbalances that contribute to the disease. Excessive GWG can also disrupt the delicate balance of fats in the bloodstream, leading to dyslipidemia, characterized by elevated levels of triglycerides and "bad" cholesterol (LDL) and decreased levels of "good" cholesterol (HDL). This imbalance can fuel oxidative stress, a harmful process in which reactive oxygen species damage cells and tissues, further contributing to the inflammatory and vascular dysfunction that underlies preeclampsia. Excessive GWG leads to the expansion of adipose tissue, particularly the visceral fat that surrounds internal organs. This fat tissue is not just a passive storage depot but an active endocrine organ that releases a variety of signaling molecules, including pro-inflammatory cytokines. As fat tissue expands, it pumps out more of these inflammatory messengers, creating a chronic state of low-grade inflammation that can set the stage for preeclampsia. Excessive GWG can also activate immune cells, such as macrophages and neutrophils, which are the body's first line of defense against infection and injury. However, in the context of excessive weight gain, these immune cells can become overzealous, releasing a flood of pro-inflammatory cytokines and chemokines that further damage blood vessels and contribute to the vascular dysfunction characteristic of preeclampsia. The placenta, the lifeline between mother and baby, is not immune to the inflammatory effects of excessive GWG. This vital organ plays a crucial role in regulating maternal immune responses and ensuring a healthy pregnancy. However, excessive weight gain can trigger placental inflammation, disrupting these delicate mechanisms and contributing to systemic inflammation and endothelial dysfunction, both of which increase the risk of preeclampsia. Imagine your heart as a pump working tirelessly to circulate blood throughout your body. Excessive GWG adds to this workload, forcing the heart to pump harder and faster to accommodate the increased blood volume and metabolic demands of the growing fetus and maternal tissues. This can lead to elevated blood pressure and increased cardiac output, straining the cardiovascular system and increasing the risk of preeclampsia. The endothelium, the inner lining of blood vessels, plays a crucial role in regulating blood flow and vascular tone. Excessive GWG can damage this delicate lining, leading to endothelial dysfunction, characterized by impaired vasodilation (widening of blood vessels) and increased vasoconstriction (narrowing of blood vessels). This can further compromise blood flow to the placenta, contributing to the clinical manifestations of preeclampsia. Excessive GWG can also disrupt fluid balance, leading to fluid retention and edema, or swelling, particularly in the legs and ankles. This excess fluid can further increase blood pressure and strain the cardiovascular system, exacerbating the risk of preeclampsia. Excessive GWG often leads to the accumulation of visceral fat, the type of fat that surrounds internal organs. This fat is not just an inert storage depot but a metabolically active endocrine organ that releases a variety of signaling molecules, including adipokines, which can influence insulin

sensitivity, inflammation, and vascular function. Excessive GWG can disrupt the delicate balance of these adipokines, leading to increased levels of leptin, a hormone that promotes inflammation and endothelial dysfunction, and decreased levels of adiponectin, an anti-inflammatory and insulin-sensitizing adipokine. This imbalance further contributes to the metabolic and vascular disturbances that underlie preeclampsia. The placenta, the lifeline between mother and baby, is responsible for delivering nutrients and oxygen to the developing fetus and removing waste products. Excessive GWG can impair placental growth and function, compromising this vital exchange and potentially hindering fetal growth and development. Excessive GWG can also increase the risk of placental abruption, a serious condition in which the placenta separates from the uterine wall prematurely. This can deprive the fetus of oxygen and nutrients, leading to severe complications, including preeclampsia. While adequate weight gain is essential for fetal growth, excessive GWG can lead to fetal overgrowth and macrosomia, a condition in which the baby is significantly larger than average. This can complicate labor and delivery, increasing the risk of birth injuries and maternal complications, including preeclampsia.[21-24]

The findings of this study resonate far beyond the confines of our research setting, carrying significant implications for clinical practice and public health interventions aimed at reducing the burden of preeclampsia in Bali, Indonesia, and globally. Preeclampsia, with its potential for devastating maternal and fetal complications, demands a comprehensive and proactive approach that spans the continuum of care, from pre-pregnancy counseling to postpartum surveillance. Pre-pregnancy counseling provides a valuable opportunity to lay the foundation for a healthy pregnancy. It's a time to assess risk factors, address modifiable lifestyle behaviors, and empower women to make informed choices that can optimize their health and that of their future children. For women who are overweight or obese, pre-pregnancy counseling should emphasize the importance of achieving a healthy weight before conception. This can be achieved through a combination of dietary modifications and increased physical activity, tailored to the individual's needs and preferences. Culturally sensitive dietary recommendations, incorporating traditional foods and culinary practices, can enhance adherence and promote sustainable lifestyle changes. Registered dietitians or nutritionists can provide personalized guidance on healthy eating habits, emphasizing the importance of a balanced diet rich in fruits, vegetables, whole grains, and lean protein. They can also help women identify and address potential nutritional deficiencies, such as iron or folate deficiency, which can increase the risk of preeclampsia. Regular physical activity is crucial for maintaining a healthy weight and improving cardiovascular health. Pre-pregnancy counseling should encourage women to engage in at least 150 minutes of moderate-intensity aerobic activity per week, spread throughout the week. Activities can be tailored to the individual's fitness level and preferences, ranging from brisk walking and swimming to dancing and yoga. It's essential to recognize that socioeconomic factors can significantly influence access to healthy food and opportunities for physical activity. Pre-pregnancy counseling should address these barriers and connect women with resources that can support their efforts to achieve a healthy lifestyle. Antenatal care provides ongoing monitoring and support throughout pregnancy, allowing for the early detection and management of potential complications, including preeclampsia. Healthcare providers should closely monitor GWG throughout pregnancy, providing personalized guidance to ensure that women are gaining weight within the recommended ranges based on their pre-pregnancy BMI. Regular weight checks and individualized counseling can help women stay on track and address any concerns or challenges they may face. Nutritional counseling should continue throughout pregnancy, adapting to the changing

needs of the mother and baby. Education on healthy eating habits can empower women to make informed choices and manage their weight gain effectively. Women should be encouraged to maintain regular physical activity throughout pregnancy, tailored to their fitness level and stage of pregnancy. Moderate-intensity aerobic activity and strength training can help improve cardiovascular health, manage weight gain, and reduce the risk of preeclampsia. Regular blood pressure monitoring and urine testing for proteinuria are essential components of antenatal care. These tests can help detect early signs of preeclampsia, allowing for timely intervention and management. Women identified as high-risk for preeclampsia, including those with obesity or excessive GWG, should receive increased surveillance and closer monitoring. This may include more frequent antenatal visits, additional blood pressure checks, and more comprehensive assessments of maternal and fetal well-being. Early detection and prompt management of preeclampsia are crucial to prevent severe complications such as eclampsia (seizures), HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets), and preterm birth. Healthcare providers should be vigilant in recognizing the signs and symptoms of preeclampsia, which may include elevated blood pressure, proteinuria, headache, visual disturbances, and abdominal pain. In women diagnosed with preeclampsia, timely interventions are essential to manage the condition and prevent severe complications. Antihypertensive Medications to lower blood pressure and reduce the risk of stroke and other cardiovascular complications. Magnesium Sulfate to prevent seizures and protect against eclampsia. Corticosteroids to promote fetal lung maturity in cases of preterm delivery. Delivery in severe cases or when the fetus is at risk, delivery may be necessary, even if the pregnancy is preterm. The postpartum period is a critical time for monitoring and managing potential complications of preeclampsia. Women with a history of preeclampsia should continue to have their blood pressure monitored regularly in the postpartum period. Postpartum education and counseling should address the long-term health implications of preeclampsia, including the increased risk of cardiovascular disease and other chronic conditions. Women should be encouraged to adopt healthy lifestyle habits, including maintaining a healthy weight, engaging in regular physical activity, and following a balanced diet, to reduce their risk of future complications. Public health interventions play a crucial role in addressing the burden of preeclampsia at the population level. Community-based programs can promote healthy lifestyle choices, provide education on preeclampsia prevention and management, and improve access to antenatal care. Health promotion campaigns can raise awareness of preeclampsia risk factors and encourage women to seek pre-pregnancy counseling and early antenatal care. Policy initiatives can support healthy lifestyle choices, improve access to healthcare, and promote early detection and management of preeclampsia.[25-29]

5. Conclusion

This study has underscored the significant association between maternal obesity, excessive gestational weight gain (GWG), and the heightened risk of preeclampsia in the Balinese population. These findings strongly advocate for comprehensive pre-pregnancy counseling and consistent antenatal monitoring. The focus should be on promoting healthy weight management and ensuring GWG stays within recommended guidelines. Healthcare professionals must be vigilant in early detection and management of preeclampsia to mitigate severe complications for both mother and child. By addressing these modifiable risk factors, we can strive to reduce the incidence of preeclampsia and improve maternal and child health outcomes in Bali and potentially contribute valuable insights to global strategies for managing this prevalent condition.

6. References

1. World Health Organization. Recommendation on calcium supplementation before

pregnancy for the prevention of pre-eclampsia and its complications. Geneva. 2020.
2. Ministry of Health of the Republic of Indonesia. Indonesia's health profile in 2023. Jakarta. 2024.
3. Chang K-J, Seow K-M, Chen K-H. Preeclampsia: recent advances in predicting, preventing, and managing the maternal and fetal life-threatening condition. Int J Environ Res Public Health. 2023; 20(4): 2994.
4. Fox R, Jamie K, Leeson P, Aye CYL, Lewandowski AJ. Preeclampsia: risk factors, diagnosis, management, and the cardiovascular impact on the offspring. J Clin Med. 2019; 8: 1625.
5. Jung E, Romero R, Yeo L, Gomez-Lopez N, Chaemsaithong P, Jaovisidha A, et al. The etiology of preeclampsia. Am J Obstet Gynecol. 2022; 226(2): S844-S866.
6. Olson KN, Redman LM, Sones JL. Obesity “complements” preeclampsia. Physiol Genomics. 2019; 51: 73–76.
7. Monaco-Brown M, Lawrence DA. Obesity and maternal-placental-fetal immunology and health. Front Pediatr. 2022; 20.
8. Jiménez-Osorio AS, Carreón-Torres E, Correa-Solís E, Ángel-García J, Arias-Rico J, Jiménez-Garza O, et al. Inflammation and oxidative stress induced by obesity, gestational diabetes, and preeclampsia in pregnancy: role of high-density lipoproteins as vectors for bioactive compounds. Antioxidants. 2023; 12: 1894.
9. Kutchi I, Chellammal P, Akila A. Maternal obesity and pregnancy outcome: in perspective of new Asian Indian guidelines. J Obstet Gynecol India. 2020; 70: 138–44.
10. Staff AC. The two-stage placental model of preeclampsia: an update. J Reprod Immunol. 2019; 134-135: 1-10.
11. Wainstock T, Sergienko R, Sheiner E. Who is at risk for preeclampsia? risk factors for developing initial preeclampsia in a subsequent pregnancy. 2020. J Clin Med. 2020; 9: 1103.
12. Rimboeck J, Gruber M, Weigl M, Huber P, Lunz D, Petermichl W. Obesity correlates with chronic inflammation of the innate immune system in preeclampsia and HELLP syndrome during pregnancy. Biomedicines. 2023; 11: 2851.
13. Langley-Evans SC, Pearce J, Ellis S. Overweight, obesity and excessive weight gain in pregnancy as risk factors for adverse pregnancy outcomes: a narrative review. J Hum Nutr Diet. 2022; 35: 250–64.
14. Kelly AC, Powell TL, Jansson T. Placental function in maternal obesity. Clin Sci (Lond). 2020; 134(8): 961–84.
15. Alston MC, Redman LM, Sones JL. An overview of obesity, cholesterol, and systemic inflammation in preeclampsia. Nutrients. 2022; 14: 2087.
16. Ulhaq RA, Anis W, Fatmaningrum W, Akbar MIA. Association between pre-pregnancy body mass index and gestational weight gain and the risk of preeclampsia: a systematic review and meta-analysis. Asian Pac J Reprod. 2021; 10(1): 1-10.
17. Zhang S, Qiu X, Qin J, Song X, Liu Y, Wei J, et al. Effects of maternal pre-pregnancy BMI and gestational weight gain on the development of preeclampsia and its phenotypes: a prospective cohort study in China. J Clin Med. 2022; 11: 5521.
18. Yaktine AL, Rasmussen KM, Eds. Weight gain during pregnancy: reexamining the Guidelines National Research Council. Institute of Medicine. Board on Children, Youth, and Families. Food and Nutrition Board. Committee to Reexamine IOM Pregnancy Weight Guidelines. National Academies Press: Washington, DC, USA. 2009.
19. Abramova M, Churnosova M, Efremova O, Aristova I, Reshetnikov E, Polonikov A, et al.

Effects of pre-pregnancy overweight/obesity on the pattern of association of hypertension susceptibility genes with preeclampsia. Life. 2022; 12: 2018.

20. Robillard P-Y, Dekker G, Scioscia M, Bonsante F, Iacobelli S, Boukerrou M, et al. Increased BMI has a linear association with late onset preeclampsia: a population-based study. PLoS One. 2019; 14(10): e0223888.
21. Gong X, Li J, Jiang Y, Yuan P, Chen L, Yang Y, et al. Risk of preeclampsia by gestational weight gain in women with varied prepregnancy BMI: a retrospective cohort study. Front Endocrinol. 2022; 13: 967102.
22. Lewandowska M, Wieckowska B, Sajdak S, Lubinski J. Pre-pregnancy obesity vs. other risk factors in probability models of preeclampsia and gestational hypertension. Nutrients. 2020; 12: 2681.
23. Song W, Zhang Z, Zheng W, Gao L, Liang S, Cheng D, et al. Patterns of gestational weight gain among women with obesity and its correlation with hypertensive disorders of pregnancy in Chinese women. Matern Child Nutr. 2023; 19: e13416.
24. Ogunwole SM, Mwinnyaa G, Wang X, Hong X, Henderson J, Bennett WL. Preeclampsia across pregnancies and associated risk factors: findings from a high- risk us birth cohort. J Am Heart Assoc. 2021; 10: e019612.
25. Yang Y, Ray IL, Zhu J, Zhang J, Hua J, Reilly M. Preeclampsia prevalence, risk factors, and pregnancy outcomes in Sweden and China. JAMA Network Open. 2021; 4(5): e218401.
26. Lewandowska M, Wieckowska B, Sajdak S. Pre-pregnancy obesity, excessive gestational weight gain, and the risk of pregnancy-induced hypertension and gestational diabetes mellitus. J Clin Med. 2020; 9: 1980.
27. Zheng W, Huang W, Zhang L, Tian Z, Yan Q, Wang T, et al. Suggested gestational weight gain for Chinese women and comparison with institute of medicine criteria: a large population-based study. Obes Facts. 2021; 14: 1–9.
28. Abraham T, Romani AMP. The relationship between obesity and pre-eclampsia: incidental risks and identification of potential biomarkers for pre-eclampsia. Cells. 2022; 11: 1548.
29. Mayrink J, Souza RT, Feitosa FE, Filho EAR, Leite DF. Incidence and risk factors for preeclampsia in a cohort of healthy nulliparous pregnant women: a nested case-control study. Sci Rep. 2019; 9: 9517.