

## Preventing the Incidence of Severe Preeclampsia by Maintaining an Ideal Body Weight During Pregnancy

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### Abstract

Preeclampsia is a pregnancy-specific disease potentially leading to complications, morbidity, and mortality. In general, obesity may cause preeclampsia through several common mechanisms. This study aimed to examine the association between obesity and the incidence of severe preeclampsia (SP) at Dr. Dradjat Prawiranegara General Hospital, Serang, Indonesia. A retrospective cohort design was used and the sample comprised of 168 parturients (84 SP and 84 non-SP subjects). Sample selection was consecutively conducted from June to November 2023, while data were analyzed using the Chi-Square test and multivariable analysis with multiple logistic regression. There was a statistically significant relationship between nutritional status and obesity in participants with SP history ( $p < 0.05$ ). Obese women had a 2.96 times higher risk of developing SP compared to non-obese. Additionally, the study found that multigravidas ( $\geq G2$ ) had a 2.19 times higher risk of suffering from SP compared to primigravidas (G1) ( $p = 0.019$ ). Furthermore, women who only completed  $\leq$  junior high school education had a 2.14 times higher risk of suffering from SP compared to those who completed  $\geq$  high school ( $p = 0.060$ ). In conclusion, women in delivery who suffered from obesity have a 2.68 times greater risk of suffering SP than non-obese, as evident from both bivariable and multivariable analyses.

**Keywords:** Body mass index, obesity, parity, severe preeclampsia, uteroplacental insufficiency

### Introduction

Hypertension is a common condition affecting 10% of pregnancies worldwide, including 3-5% of all pregnancies that experience preeclampsia complications.<sup>1</sup> In general, preeclampsia is one pregnancy-specific disease that causes complications, morbidity, and mortality,<sup>2</sup> usually during  $\geq 20$  weeks of gestation age.<sup>3</sup> It is characterized by hypertension, extremities edema, and proteinuria.<sup>4</sup> The various serious complications, include severe preeclampsia (SP), which is defined as preeclampsia with systolic  $\geq 160$  mm Hg or diastolic  $\geq 110$  mm Hg at least 4 hours apart on the 2 occasions. Other complications include liver or renal dysfunction, thrombocytopenia, pulmonary

edema, and central nervous system disorders.<sup>2</sup> It also significantly contributes to fetal-related complications associated with prematurity, fetal distress, growth restriction, intrauterine fetal death (IUFD), as well as increased mortality rates.<sup>3</sup>

According to the World Health Organization (WHO), SP occurs in  $\pm 2$ -10% of pregnancies worldwide, with 1.8-16.7% of the incidents in developing countries, and 0.4% in developed countries.<sup>5</sup> Obesity is considered one of the risk factors and the association can be explained through several common mechanisms.<sup>6,7</sup> Furthermore, SP, similar to obesity, is related to an increased risk of maternal cardiovascular diseases.<sup>1,4</sup>

Obesity, according to the WHO is defined as an abnormal or excessive fat accumulation that poses a harmful health risk,<sup>8</sup> indicated by body mass index (BMI) of 30 or greater.<sup>9</sup> It is a global public health issue with high rates in both developed and developing countries. About one-third of U.S. adults suffer from obesity,<sup>4</sup> and in 2022,

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WHO reported the obesity pandemic in Europe as one implication of the COVID-19 pandemic, with 60% of European citizens being reportedly overweight or obese.<sup>10</sup> Furthermore, obesity is related to various comorbidities, including SP during pregnancy,<sup>4</sup> diabetes, and cardiovascular disease.<sup>8</sup> Nutritional risk factor differentiation plays a role in the SP provenance. Excessive weight gain during pregnancy or pre-pregnancy, related to insulin resistance, hyperinsulinism, and maternal systemic inflammation, is proposed as one of the pathophysiologies that leads to endothelial dysfunction, hypertension, proteinuria, thrombotic and multi-organ failure.<sup>4</sup>

Modest weight reduction  $\geq 5\text{--}10\%$ , can improve health status outcomes. Many people struggle to maintain weight loss, although strategies such as increased frequency of consultation can improve the success of body weight reduction.<sup>8</sup> Given the strong association between obesity and preeclampsia, this study aimed to evaluate the impact of obesity on the incidence of severe preeclampsia.

## Methods

This was a retrospective cohort study conducted to examine the impact of obesity in both SP and non-SP subjects at Dr. Dradjat Prawiranegara General Hospital Serang, Banten, Indonesia from June to November 2023. The population comprised all parturients who registered at Dr. Dradjat Prawiranegara General Hospital, for six months in 2023. Inclusion criteria for SP subjects include parturients who suffered from SP both in early-onset and late-onset SP, maternal age 18–35 years old,  $\geq 24$  weeks gestational age, singleton fetus, all types of labor either spontaneously or terminated pregnancy, presence of body weight data before pregnancy in medical register data/books/pregnancies notebooks. Meanwhile, inclusion criteria for non-SP subjects include parturients with normal delivery, maternal age 18–35 years old,  $\geq 24$  weeks gestational age, singleton fetus, all types of labor either spontaneously or terminated pregnancies, presence of body weight data before pregnancy or in the first-trimester in medical register data/books/pregnancy notebooks.

Exclusion criteria were maternal age  $< 18$  or  $> 35$  years old,  $< 24$  weeks gestational age, multiple fetuses, and maternal pregnancy with complications, such as Diabetes Mellitus (DM), systemic diseases, or chronic hypertension. Dropout criteria include incomplete data, and

having no available body weight data before pregnancy in medical register data/book/pregnancy notebooks.

The sample size was calculated based on the Lemeshow formula. Consequently, the sample size was 74 for SP subjects and 74 non-SP subjects, each added with 10 subjects to anticipate dropout. Therefore, the total number of samples consecutively selected for both groups was 168.

The data used comprised both primary and secondary, collected through patients medical records or anamnesis according to the sample criteria. The instrument used in this study was the checklist, while the collected data were analyzed descriptively and analytically. Data analysis used the Chi-Square test and multivariable analysis with multiple logistic regression. This study received approval from the Health Research Ethics Committee, Polytechnic of the Health Ministry of Health of the Republic of Indonesia Tanjungkarang, Bandar Lampung, Indonesia (No. 355/KEPK-TJK/V/2023).

## Results

This study examined the impact of obesity on SP among 84 delivery women with SP and 84 non-SP women. Other variables studied apart from obesity were BMI, maternal and gestational age, as well as parity, education, and occupation, with the complete results presented in Table 1. Table 1 shows that most of the subjects had maternal age  $< 30$  years, with a lower proportion in SP subjects vs non-SP (60.7% vs. 66.7%). Gestational age was mostly in the normal range between 37–42 weeks, and lower in the SP vs non-SP subjects (76.2% vs 84.5%). A significant proportion had parity status found in multigravidas vs primigravidas, with higher value in the SP vs non-SP subjects (64.3% vs 54.2%). In terms of education, the subjects mostly graduated from high school, with a lower proportion in SP vs non-SP (73.8% vs 79.8%). Regarding occupation, the majority were unemployed (housewives), with a higher proportion in SP vs non-SP subjects (100% vs 92.9%). Late-onset was higher than early-onset (76.2% vs 23.8%) and a significant proportion had protein ++ level (58.3%). Based on the results, characteristics that showed a relationship with SP incidence were parity ( $p=0.013$ ) and occupation ( $p=0.028$ ).

Delivery women who suffered SP consist of 20 subjects (23.8%) in the early-onset category and 64 (76.2%) in the late-onset. The relationship

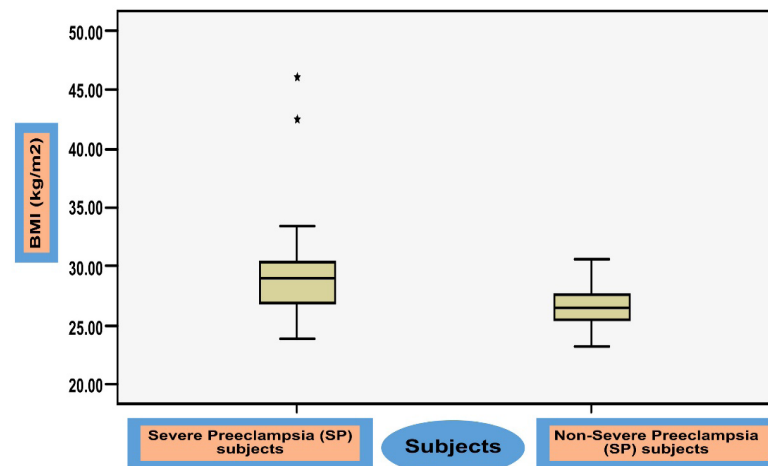
**Table 1 Characteristics of Severe Preeclampsia and Non-Severe Preeclampsia Subjects**

Characteristics	Severe Preeclampsia (SP) (n=84)	Non Severe Preeclampsia (n=84)	p-value
Maternal age (year)			
18–29	51 (60.7%)	56 (66.7%)	
30–35	33 (39.3%)	28 (33.3%)	
Average (SD)	27.3 (5.2)	26.0 (5.1)	
Gestation Age (week) :			
<37	20 (23.8%)	13 (15.5%)	0.422
37–42	64 (76.2%)	71 (84.5%)	
Average (SD)	37.4 (3.7)	38.3 (2.2)	
Parity:			
G1	30 (35.7%)	46 (54.8%)	0.174
≥G2	54 (64.3%)	38 (45.2%)	
Education :			
≤Primary High School	22 (26.2%)	14 (16.7%)	0.013
High School	62 (73.8%)	67 (79.8%)	
Academic/University	0	3 (3.6%)	
Occupation:			
Working	0	6 (7.1%)	0.083
Unemployed/Housewife	84 (100%)	78 (92.9%)	
Category of SP			
Early-onset SP	20 (23.8%)	-	0.028**
Late-onset SP	64 (76.2%)	-	
Protein :			
+1	26 (31.0%)	-	
+2	49 (58.3%)	-	
+3	9 (10.7%)	-	

**Table 2 Relationship between Nutritional Status with Severe Preeclampsia Incidence**

Nutritional Status (BMI, kg/m <sup>2</sup> )	Group		p-value	OR (95% CI)
	SP Subjects (n=84)	Non-SP Subjects (n = 84)		
18.5–<23	1 (1.2%)	0	0.008	-
23.0–<25	4 (4.8%)	13 (15.5%)		
25.0–<30	55 (65.5%)	61 (72.6%)		
≥30	24 (28.6%)	10 (11.9%)	<0.001**	1.0
Average (SD)	29.06 (3.56)	26.88 (1.97)		2.93 (0.90-9.52)
Median	28.89	26.52		7.80 (2.04-29.84)
Range	21.08-46.02	23.23-31.87	0.007	2.96 (1.31-6.67)
≥30 (obesity)	24 (28.6%)	10 (11.9%)		
<30 (non obesity)	60 (71.4%)	74 (88.1%)		

Note: Chi-square test; \*\* Mann-Whitney test; OR (95% CI): Odds Ratio and 95% Confidence Interval



**Figure 1 Comparison of Body Mass Index (BMI) between Delivery Women with Severe and Non-Severe Preeclampsia**

between nutritional status and obesity with SP history was not statistically significant ( $p > 0.05$ ).

Obesity showed a statistically significant relationship with delivery women who suffered SP incidence ( $p < 0.05$ ). The risk of developing SP was 2.96 times greater among delivery women with obesity.

Multivariable analysis between obesity and characteristics of SP was analyzed by multiple logistic regression. The calculation comprised variables that had  $p$ -values  $p < 0.25$  from bivariable results namely parity, education, gestational age, occupation, and obesity. Calculation results with backward methods obtained a significant final model as shown in Table 4.

Multivariable logistic regression (Table 4) showed that multigravidas ( $\geq G2$ ) had a 2.19-fold higher risk of SP compared to primigravidas ( $p = 0.019$ ), and women with  $\leq$  junior high school education had a 2.14-fold higher risk compared to those with higher education, although this was marginally significant ( $p = 0.060$ ). Obesity remained a significant independent risk factor, with a 2.68-fold higher risk of SP compared to non-obese women ( $p = 0.021$ ).

## Discussion

This study found that multigravida women

**Table 3 Description of Nutritional Status in Severe Preeclampsia Case**

Nutritional Status (BMI, kg/m <sup>2</sup> )	Severe Preeclampsia Category		p-value
	Early-onset SP (n=20)	Late-onset SP (n=64)	
18.5–<23	0	1 (1.6%)	0.097
23.0–<25	3 (15.0%)	1 (1.6%)	
25.0–<30	12 (60.0%)	43 (67.2%)	
$\geq 30$	5 (25.0%)	19 (29.7%)	
$\geq 30$ (obesity)	5 (25.0%)	19 (29.7%)	0.685
<30 (non obesity)	15 (75.0%)	45 (70.3%)	

Note: \*) Chi-Square Test

**Table 4 Multiple Logistic Regression Analysis of Various Factors Associated with Severe Preeclampsia Incidence among Delivery Women (Final Model)**

Variable	Coefficient B	SE (B)	p-value	OR <sub>adj</sub> (CI 95%)
Parity ( $\geq$ G2)	0.784	0.333	0.019	2.19 (1.14–4.20)
Education (Primary High school)	0.763	0.406	0.060	2.14 (0.97–4.75)
Obesity	0.985	0.425	0.021	2.68 (1.16–6.16)

Note: OR Adj (CI 95%): Odds Ratio Adjusted and 95% Confident Interval

and unemployed/housewives had significantly higher risks of severe preeclampsia (SP), along with obesity as an independent predictor). This study produced results different from the theory stating that SP mostly occurs in primigravida, due to the maternal first exposure to fetal trophoblast. The parity status found in multigravida vs primigravida was higher in the SP subjects vs non-SP (64.3% v.s. 54.2%). Similar results were found in other studies conducted at Dr. M. Soewandhie Hospital, Dr. Soetomo, and Haji Hospital, as well as some community health centers in Surabaya, Indonesia, on early detection score of SP risk. One of the significant factors of SP risks is a history of multigravida, which is usually present as hypertension worsened by pregnancy. SP is generally found among multigravida mothers who have experienced vascular diseases including DM, chronic hypertension, or systematic diseases, which also may occur due to high parity. The incidence, according to the parity, mostly occurs in multigravida (64.5%) and primigravida (35.5%). Furthermore, a significant correlation was found between the parity and the SP incidence (OR=2.464). Multigravida mothers have a two-time higher risk of suffering from SP than primigravida.<sup>11</sup>

The results also showed that the majority of the subjects were unemployed (housewives), with a higher proportion in SP vs non-SP (100% vs 92.9% with  $p=0.028$ ). Similar results were found in a previous population-based study in Canadian hospitals (except Quebec) on the incidence and risk factors for SP, elevated liver enzymes, hemolysis, and low platelet count syndrome, as well as eclampsia at preterm and term gestation. It was a retrospective, population-based cohort study of all women with a singleton delivery from 2012 to 2016 ( $n=1,078,323$ ). The results showed that the rates of SP ( $n=2533$ ), regardless of gestational age and socioeconomic status were inversely associated.<sup>2</sup>

Table 2 shows that delivery women who

suffered SP consisted of 20 subjects (23.8%) in the early-onset SP category and 64 (76.2%) in the late-onset. The relationship between nutritional status and obesity with SP history was not statistically significant ( $p>0.05$ ). The result is similar to the theory stating that dietary intake of proper foods and nutrients can prevent and reduce the risk of SP, while also improving the outcomes. Excessive body weight gain is associated with SP risk, which is usually related to fluid retention. High dietary fibers such as fruits, and vegetables, can reduce the risk, while adherence to Western diet styles may increase the risk. Other nutrients, that may improve hypertension, such as sodium or salt, have little to no effect on the risk. In this case, there is a possibility that each person has individual differences in the dietary intake of foods and nutrients.<sup>12</sup> Based on the results, obesity had a statistically significant relationship ( $p<0.05$ ) with SP. Delivery women with obesity had a 2.96 times greater risk of developing SP compared to normal.

This study produced results similar to the theory stating that obesity during pregnancy is directly related to obstetric complications including SP<sup>13</sup> as well as a mediation analysis conducted in Paris, France, on maternal obesity and SP among immigrant women. Pre-pregnancy obesity mediates the association between maternal place of birth and SP in the PreCARE cohort among pregnant women ( $n=9,579$ ). About 95 women (0.99%) suffered SP, including 47.6% non-European immigrants, 16.3% born in Sub-Saharan Africa, and 12.6% obese (BMI  $\geq 30$  kg/m<sup>2</sup>). Women suffering from SP were higher in Sub-Saharan Africa ( $p=0.023$ ) and among the obese population ( $p=0.048$ ). Sub-Saharan African women had more risk of SP vs European-born women (aOR 2.53, 95% CI 1.39–4.58) and the obesity-mediated indirect effect was 18% of the total risk (aOR 1.18, 95% CI 1.03–1.35). In conclusion, Sub-Saharan African immigrant women have a two-fold higher risk of developing



SP than European-born women, one-fifth of which is mediated by pre-pregnancy obesity.<sup>14</sup>

Another study on SP prevalence and pregnancy outcomes in Sweden and China reported obesity as a significant risk factor. The condition was found as a stronger risk factor in China than in Sweden with (OR 5.12; 95% CI, 3.82–6.86 vs OR, 3.49; 95% CI, 3.31–3.67).<sup>15</sup>

Based on the results in Tables 3 and 4, the multivariable analysis between obesity and characteristics of SP were analyzed using multiple logistic regression. The calculation comprised variables that had p-values  $p < 0.25$  from bivariable results namely parity, education, gestational age, occupation, and obesity.

Delivery women who were multigravidas ( $\geq G2$ ) had a 2.19 times greater risk of suffering SP compared to primigravidas (G1) with a p-value of 0.019. Similar results were found in a previous study conducted in Surabaya, Indonesia, on early detection score of SP risk. The incidence, according to the parity, mostly occurs in multigravida (64.5%) and primigravida (35.5%). This shows that there is a significant correlation between parity and SP incidence in pregnant women with (OR=2.464). In other words, multigravidas has twice a greater risk of suffering SP than primigravidas.<sup>11</sup>

This study showed that women who graduated from primary high school had a 2.14 times greater risk of suffering SP compared to those who graduated from  $\geq$ high school, with  $p = 0.060$  (Table 4). Similar results were obtained in a previous study conducted in Pakistan on SP incidence as well as maternal and neonatal outcomes with associated risk factors. The prospective study examined 142 patients with gestational hypertension and SP during two years. The results showed 8.67% cases of gestational hypertension and 3% of SP. Most of the preeclamptic women were in lower socioeconomic levels (44.4%) and had low educational levels (81.1%). The incidence of SP is related to good nutrition and proper diet, awareness, as well as low economic status.<sup>5</sup>

Another study in Turkey examined the effect of an education and counseling program on maternal neonatal outcomes in pregnant women at risk of SP. It was a randomized controlled trial design study and was conducted among 132 pregnant women attending an antenatal clinic for routine care. The results found a significant correlation between healthy lifestyle behaviors related to education and counseling with SP ( $p < 0.008$ ). Patient education and counseling can prevent nearly half of the most harmful

outcomes<sup>16</sup> as shown in Table 4.

SP, defined as preeclampsia with systolic  $\geq 160$  mmHg or diastolic  $\geq 110$  mmHg, commonly develops after 20 weeks of pregnancy. It is evidenced by maternal organ or uteroplacental insufficiency, including renal or liver dysfunction, pulmonary edema, thrombocytopenia, and disturbances of the central nervous system.<sup>1</sup>

<sup>2</sup> Furthermore, the WHO defines obesity as an abnormal or excessive fat accumulation that can increase health risk,<sup>8</sup> indicated by BMI of 30 or greater.<sup>9, 17</sup> Pre-pregnancy BMI can be classified based on body weight into several categories namely underweight (BMI  $< 18.5$  kg/m<sup>2</sup>), normal weight (BMI 18.5–24.9 kg/m<sup>2</sup>), obesity (BMI 25–29.9 kg/m<sup>2</sup>), and obese classes I, II, III (BMI  $> 30$  kg/m<sup>2</sup>). Although both are pregnancy high-risk factors, women who suffer obesity have statistically significantly higher complications than underweight women.<sup>17</sup> The adjusted risk of suffering SP is two times higher for overweight women (BMI of 26 kg/m<sup>2</sup>), and almost three times for obese women (BMI of 30 kg/m<sup>2</sup>).<sup>4</sup>

The results are based on the pathophysiology that SP has complexity and is not clearly understood yet. It is associated with abnormal placentation, systemic inflammation, and oxidative stress. Appropriate remodeling failure of the spiral arteries causes abnormal placentation, placental blood circulation resistance, and hypo-perfusion of the placenta. SP causes chronic placental ischemia, decreases blood circulation to the developing fetus, fetal hypoxia, and harmful adverse outcomes.<sup>1</sup> Pathological results are often present before the clinical onset, while endothelial and vascular abnormalities are responsible for the characteristic vasoconstriction.<sup>4</sup>

Nutritional risk factor differences such as deficiency of protein, calcium, essential fatty acids, and vitamins, have been shown to play a role in the SP provenance. In addition, excessive weight gain during pregnancy or a pre-pregnancy state of obesity and overweight, related to insulin resistance, hyperinsulinism, and maternal systemic inflammation, are proposed as one of the pathophysiology that leads to endothelial dysfunction, hypertension, proteinuria, thrombotic and multi-organ failure. These conditions increase future risk of cardiovascular disease as well as maternal mortality and morbidity.<sup>4</sup>

By carrying out early assessment of health risks, as well as providing support, motivation, prompt knowledge, and treatment tools, health practitioners can assist patients to achieve

optimal weight loss and health status.<sup>8</sup> Expert nutritionist advice is required throughout the pregnancy period. Current recommendations include restricting calories up to 1200 kcal/day, routine walking or physical exercise in the third trimester, and administering 150 mg aspirin to all women with BMI >35 kg/m<sup>2</sup>.<sup>17</sup>

In conclusion, multigravida status, low education, and obesity were identified as significant risk factors for SP. These findings underscore the importance of early risk stratification, patient education, and weight management interventions before and during pregnancy to reduce the burden of SP and its complications.

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