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## OBSTETRICS

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# Pregnancy Outcomes amongst Normotensive and Severe Preeclampsia with or without Underlying Chronic Hypertension Pregnancy

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### ABSTRACT

**Objectives:** To compare maternal and neonatal outcomes in singleton pregnant women with severe preeclampsia with or without underlying chronic hypertension, and singleton pregnant women with normal blood pressure.

**Materials and Methods:** In a retrospective study, 200 pregnant women with severe preeclampsia, with or without underlying chronic hypertension, were compared to 200 pregnant women with normal blood pressure between January 1<sup>st</sup>, 2011 and December 31<sup>st</sup>, 2012. The demographic characteristics, mode of delivery, complications and outcomes of pregnancy were analyzed.

**Main outcome measures:** Maternal morbidities of acute renal failure, pulmonary edema, neurological complication, HELLP syndrome, coagulopathy, placenta abruption and postpartum hemorrhage were evaluated. Neonatal morbidities were also measured.

**Results:** Maternal outcomes for the 200 women with severe preeclampsia compared to women with normal blood pressure demonstrated significantly increased rates of acute renal failure (4.0% VS 0%,  $p<0.001$ ), pulmonary edema (2.0% VS 0%,  $p=0.044$ ), neurologic complications (5.0% VS 0%,  $p<0.001$ ), and cesarean section (57.5% VS 41.5%,  $p=0.023$ ). Likewise, there was a significant increase in Neonatal outcomes, including preterm birth (45.0% VS 17%,  $p=0.011$ ), low birth weight (47.0% VS 14%,  $p<0.001$ ), rate of neonatal resuscitation (19.0% VS 10%,  $p=0.011$ ), and stillbirth (3.5% VS 1%,  $p=0.092$ ).

**Conclusion:** Maternal outcomes including acute renal failure, pulmonary edema, neurological complications and cesarean section rates were significantly worse in the study group. Neonatal outcomes consisting of rate of preterm birth, low birth weight, neonatal resuscitation and stillbirth were also worse in the study group.

**Keywords:** severe preeclampsia, maternal outcomes, neonatal outcomes

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## ผลการตั้งครรภ์ในมารดาความดันโลหิตปกติ และครรภ์เป็นพิษรุนแรง ที่มีหรือไม่มีความดันโลหิตสูง เป็นโรคประจำตัว

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**วัตถุประสงค์:** เพื่อเปรียบเทียบผลกระทบบและภาวะแทรกซ้อนต่อมารดาและทารกจากการตั้งครรภ์เดี่ยว และมีภาวะครรภ์เป็นพิษรุนแรงที่มี หรือไม่มีโรคประจำตัวเป็นความดันโลหิตสูง เทียบกับหญิงตั้งครรภ์ที่มีความดันโลหิตปกติ

**วัสดุและวิธีการ:** การศึกษาแบบย้อนหลังเปรียบเทียบระหว่างหญิงตั้งครรภ์ 200 คน ที่มีภาวะครรภ์เป็นพิษรุนแรงที่มีหรือไม่มีโรคประจำตัวเป็นความดันโลหิตสูง กับหญิงตั้งครรภ์ 200 คนที่มีความดันโลหิตปกติที่มาคลอดระหว่าง 1 มกราคม พ.ศ.2554 ถึง 31 ธันวาคม พ.ศ.2555 โดยศึกษาภาวะแทรกซ้อนมารดา ได้แก่ ภาวะไตวายเฉียบพลัน ปอดบวม น้ำ ภาวะแทรกซ้อนทางระบบประสาท กลุ่มอาการ HELLP การแข็งตัวของเลือดผิดปกติ รกลอกตัวก่อนกำหนด ภาวะตกเลือดหลังคลอด รวมถึงศึกษาภาวะแทรกซ้อนของทารก

**ผลการศึกษา:** ภาวะแทรกซ้อนของมารดาที่มีภาวะครรภ์เป็นพิษรุนแรงเมื่อเทียบกับหญิงตั้งครรภ์ที่มีความดันโลหิตปกติ พบสูงกว่าอย่างมีนัยสำคัญ ได้แก่ ภาวะไตวายเฉียบพลัน (4.0%, 0%,  $p<0.001$ ) ภาวะปอดบวม น้ำ (2.0%, 0%,  $p=0.044$ ) ภาวะแทรกซ้อนทางระบบประสาท (5.0%, 0%,  $p<0.001$ ) และการผ่าตัดคลอด (57.5%, 41.5%,  $p=0.023$ ) ในขณะเดียวกันทารกที่คลอดจากมารดาที่มีภาวะครรภ์เป็นพิษรุนแรงมีภาวะแทรกซ้อนมากกว่าทารกที่คลอดจากมารดาที่มีความดันโลหิตปกติ ได้แก่ การคลอดก่อนกำหนด (45.0%, 17%,  $p=0.011$ ) น้ำหนักตัวน้อย (47.0%, 14%,  $p<0.001$ ) อัตราการช่วยกู้ชีพทารกแรกเกิด (19.0%, 10%,  $p=0.011$ ) และทารกตายคลอด (3.5%, 1%,  $p=0.092$ )

**สรุป:** ภาวะแทรกซ้อน ได้แก่ ภาวะไตวายเฉียบพลัน ภาวะปอดบวม น้ำ ภาวะแทรกซ้อนทางระบบประสาท การผ่าตัดคลอดพบสูงกว่าในกลุ่มที่มีครรภ์เป็นพิษรุนแรง ภาวะแทรกซ้อนของทารก ได้แก่ การคลอดก่อนกำหนด น้ำหนักตัวน้อย อัตราการช่วยกู้ชีพทารกแรกเกิด และทารกตายคลอดพบสูงกว่าในกลุ่มที่ทำการศึกษาเช่นกัน

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## Introduction

Preeclampsia is a common complication in pregnancy. The prevalence of severe preeclampsia is 3.3% in developing countries<sup>(1)</sup>. The hospital in this study is a tertiary referral center with an incidence rate of severe preeclampsia of 2.96%. Severe preeclampsia is associated with high maternal and neonatal morbidity; the incidence of acute renal failure was 3.13%, postpartum hemorrhage 12.5%<sup>(2)</sup>, pulmonary edema 5%, placenta abruption 2%<sup>(3)</sup>. The neonates who were born from mothers with severe preeclampsia are mostly preterm infants and had complications such as low birth weight 27.9%<sup>(4)</sup>, fetal growth restriction 25.2%, APGAR score < 7 at 5 minutes 7.1%<sup>(5)</sup>, required resuscitation 40.75%, neonatal intensive care unit admission 25.9% and neonatal death 3.7%<sup>(2)</sup>.

To date, few studies have reported maternal and neonatal outcomes of severe preeclampsia in Thailand. The purpose of this present study is to compare maternal and neonatal outcomes between normotensive and severe preeclampsia with or without underlying chronic hypertension in singleton pregnant woman.

## Materials and Methods

The present study was a retrospective study and was performed at a tertiary care center in Pitsanulok, Thailand. This study was approved by the hospital's Ethics committee. Two hundred women, who were diagnosed with severe preeclampsia with or without underlying chronic hypertension and delivered in this hospital during the period from January 2011 to December 2012, were enrolled into the study group. Two hundred women with normotensive blood pressure, who delivered after each study case as a ratio 1:1, were enrolled into the control group. The medical records were reviewed. Exclusion criteria included incomplete medical records and multifetal gestation.

The definition of severe preeclampsia and preeclampsia superimposed on chronic hypertension were according to Pregnancy Hypertension in Williams Obstetrics<sup>(6)</sup>. Severe preeclampsia was diagnosed as the presence of hypertension, blood pressure  $\geq 140/90$  mmHg after 20 wk of gestational age and urine protein 24 hour  $\geq 300$  mg/day or urine dipstick  $\geq 1+$

and the presence of at least one of the following:

- Diastolic blood pressure  $\geq 110$  mmHg
- Systolic blood pressure  $\geq 160$  mmHg
- Proteinuria  $\geq 3+$
- Headache
- Visual disturbances
- Upper abdominal pain
- Convulsion (eclampsia)
- Oliguria
- Serum creatinine elevation ( $\geq 1.2$  mg/dL)
- Thrombocytopenia (platelet  $< 100,000/\mu\text{L}$ )
- Marked elevate serum transaminase
- Fetal growth restriction
- Pulmonary edema

The data was collected on maternal characteristics which composed of age, gravidity, body mass index (BMI) and underlying disease. Maternal complications were composed of acute renal failure, pulmonary edema, neurological complication, HELLP syndrome, coagulopathy, placenta abruption, postpartum hemorrhage, death and mode of delivery. Data on neonatal outcomes collected include gestational age at birth, birth weight, preterm birth, low birth weight, APGAR score at 1 minute < 7, APGAR score at 5 minute < 7, neonatal resuscitation and stillbirth.

Acute renal failure was defined as serum creatinine  $\geq 1.2$  mg/dL. Woman who had signs and symptoms of pulmonary congestion were diagnosed with pulmonary edema. Hemolysis, thrombocytopenia and elevated serum liver transaminase level is referred to as HELLP syndrome. Coagulopathy was defined as prolonged prothrombin time and activated partial thromboplastin time. Placenta abruption means premature separation of the placenta. Postpartum hemorrhage has been defined as blood loss  $\geq 500$  mL of normal labor or  $\geq 1,000$  mL of cesarean section. Preterm birth was defined as birth before 37 weeks of gestation, low birth weight was defined as birth weight < 2,500 g, and stillbirth was defined as absence of signs of life at or after birth.

All data was analyzed by independent t-tests for continuous variables, chi-square, and Fisher's exact test for discrete variables. A p-value < 0.05 was considered statistically significant.

## Results

The two hundred pregnant women in the study group were composed of one hundred and eighty seven women with severe preeclampsia, and thirteen pregnant women with preeclampsia superimposed on chronic hypertension. All were treated with magnesium sulfate. The control group was two hundred normotensive pregnant women. Demographic characteristics of the study group and the control group are shown in Table

1.

Maternal complications are shown in Table 2. Acute renal failure, pulmonary edema and neurological complications (eclampsia) were shown to be significantly higher in pregnant women with severe preeclampsia. The incidence of postpartum hemorrhage was not different between the two groups, and there was no incidence of maternal death in both groups.

**Table 1.** Demographic characteristics in severe preeclampsia and pregnant women with normal blood pressure.

Characteristics	Study group (n=200)	Control group (n=200)	P
Maternal age (yr)	28.31 ± 7.65	25.88 ± 7.32	0.001
≤ 19 yr	30 (15.0%)	50 (25.0%)	0.025
20-34 yr	119 (59.5%)	123 (61.5%)	0.797
≥ 35 yr	51 (25.5%)	27 (13.5%)	0.007
Gravidity			0.226
1	80 (40.0%)	92 (46.0%)	
≥ 2	120 (60.0%)	108 (54.0%)	
BMI (kg/m <sup>2</sup> )	29.87 ± 6.19	26.92 ± 4.42	<0.001
Underlying disease			1.000
All medical underlying	13 (6.5%)	13 (6.5%)	0.177
DM	4 (2.0%)	1 (0.5%)	0.317
SLE	1 (0.5%)	0 (0%)	0.317
Anti-phospholipid syndrome	1 (0.5%)	0 (0%)	0.251
Other	7 (3.5%)	13 (6.5%)	0.249

**Table 2.** maternal adverse outcomes.

Complication	Study group (n=200)	Control group (n=200)	P	Odds ratio	95% CI
Acute renal failure	8 (4.0%)	0	0.004	N/A	N/A
Pulmonary edema	4 (2.0%)	0	0.044	N/A	N/A
Neurological complication	10 (5%)	0	0.001	N/A	N/A
HELLP syndrome	2 (1.0%)	0	0.156	N/A	N/A
Coagulopathy	3 (1.5%)	0	0.082	N/A	N/A
Placenta abruption	2 (1.0%)	1 (0.5%)	0.562	2.012	0.104 – 119.163
Postpartum hemorrhage	12 (6.0%)	12 (6.0%)	1.000	1.000	0.399 – 2.502

\* N/A = not available

Pregnant women with severe preeclampsia with or without underlying chronic hypertension have a higher cesarean section rate (57.5%), compared with the control group (41.5%) (Table 3.). In the hospital for this study, severe preeclampsia is not the absolute indication for cesarean section. In addition, the indication for cesarean section in this study is described

in Table 4. The fetal indication for cesarean section was composed of thick meconium stain amniotic fluid, fetal distress, placenta abruption and intrauterine growth restriction. The maternal indication for cesarean was composed of uncontrolled blood pressure, eclampsia and pulmonary edema.

**Table 3.** Presented mode of delivery.

Mode of delivery	Study group (n=200)	Control group (n=200)	P
Normal delivery	70 (35.0%)	109 (54.5%)	0.004
Breech assisting	2 (1.0%)	0	N/A
Vaginal operative delivery	13 (6.5%)	8 (4.0%)	0.275
Cesarean section	115 (57.5%)	83 (41.5%)	0.023

\*N/A = not available

**Table 4.** Indication of cesarean section.

Indication	Study group (case)	Control group (case)
Unfavorable cervix	45	0
CPD	29	39
Previous uterine scar	18	23
Malpresentation	7	13
Fetal indication	10	8
Maternal indication	6	0
Total cesarean section	115 (57.5%)	83 (41.5%)

\* N/A = not available

Neonates who were delivered from mothers with severe preeclampsia with or without underlying chronic hypertension, have an average gestational age at birth less than neonates who were born from mothers with normal blood pressure (361/7 weeks VS 381/7 weeks). Incidences of preterm births were higher in the patient

group (45.0% VS 17.0%,  $p=0.11$ ). Incidences of low birth weight (birth weight 1,500-2,499 gm, 34.5% VS 12.0%), very low birth weight (birth weight 1,000-1,499 gm, 6.5% VS 1.5%), extremely low birth weight (birth weight < 1,000 gm, 6.0% VS 0.5%) were higher. Other neonatal outcomes are shown in Table 5.

**Table 5.** Neonatal outcomes

Complication	study group (n=200)	Control group (n=200)	P
Gestational age at birth (day)	253.0 ± 24.6	266.8 ± 16.7	< 0.001
Birth weight (gm)	2507 ± 840	2952 ± 577	< 0.001
Low birth weight	94 (47.0%)	28 (14.0%)	< 0.001
1,500-2,499 gm	69 (34.5%)	24 (12.0%)	< 0.001
1,000-1,499 gm	13 (6.5%)	3 (1.5%)	0.012
< 1,000 gm	12 (6.0%)	1 (0.5%)	0.002
Apgar score			
At 1 min < 7	31 (15.5%)	16 (8.0%)	0.020
At 5 min < 7	10 (5.0%)	8 (4.0%)	0.630
Neonatal resuscitation	38 (19.0%)	20 (10.0%)	0.011
Stillbirth	7 (3.5%)	2 (1.0%)	0.092

## Discussion

Severe preeclampsia is an important cause of poor obstetrics outcomes. After use of magnesium sulfate to prevent eclampsia about 60 years ago, there was an improvement in the outcomes of women with severe preeclampsia<sup>(7)</sup>, but there was still a high maternal and neonatal morbidity<sup>(2)</sup>. Women with severe preeclampsia have a morbidity rate of 3.9%<sup>(8)</sup>. The present study found that advanced maternal age (age ≥ 35 years) had an influence on severe preeclampsia, but previous studies in Khon Kaen Hospital, Thailand, and other countries in Southeast Asia (KK Woman's and Children's Hospital in Singapore) showed that maternal age were not an influence<sup>(3, 9)</sup>. Primigravida versus multigravida was shown to have no effect on the disease, similar to previous studies<sup>(2, 9-11)</sup>. Obesity is one of the significant factors of severe preeclampsia<sup>(12)</sup>. In this study, the patient group had a higher body weight than the control group at the time of delivery. But we cannot explore pre - pregnancy weight and total weight gain during pregnancy due to limited data on the medical records. Women with a previous underlying medical condition had a significant increase in the incidence of severe preeclampsia, but it had an influence on 13 cases (6.5%) of preeclampsia superimposed on chronic hypertension.

Maternal complications in women with severe preeclampsia were higher than in women with normal

blood pressure. The incidence of acute renal failure in this study was 4.0%. It was shown to be significantly different between the patient and control group, while the incidence rate in previous studies was about 3.1 – 3.6%<sup>(2,11)</sup> but did not show a significant difference. Kumar et al.,<sup>(13)</sup> reported the incidence of pulmonary edema as 1.9%, similar to this study which was 2.0%. 10 cases with neurological complications were eclampsia, and the incidence was not different from the previous study<sup>(5)</sup>. The cesarean section rate of women with severe preeclampsia in Thailand was 47.9 – 82.8%<sup>(9,13,15)</sup>, and our center had a cesarean section rate of 57.5%.

This study showed a significant incidence of preterm birth and low birth weight in neonates who were delivered from women with severe preeclampsia. APGAR score at 1 minute was low (< 7) in the patient group, but there was no difference in the APGAR score at 5 minutes. Because of the study hospital's guidelines, there is a pediatrics team on standby in the labor room or operative room, ready for resuscitation of a newborn from a mother who was treated with magnesium sulfate. This protocol may have an effect on improving the APGAR score in newborns.

This was a retrospective study, which has limitations in addition to incomplete medical records. This study was done in a tertiary referral center, which may present a higher incidence of severe preeclampsia

than in the normal Thai population.

In conclusion, this study showed that severe preeclampsia has high adverse maternal and neonatal outcomes. The identification of pregnant women, who carried a risk of the preeclampsia syndrome, should be given information, started on a prevention program, and monitored closely, followed by early detection and subsequent treatment of preeclampsia, to reduce maternal and neonatal morbidity.

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