

# ผลลัพธ์ของการรักษาประคับประคองเทียบกับการรักษาแบบเร่งรัดให้คลอด ในสตรีตั้งครรภ์ที่มีภาวะความดันโลหิตสูงชนิดรุนแรง

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Outcome of Expectant and Aggressive management in Pregnancy with severe preeclampsia

## Abstract

**Objective :** To compare maternal and perinatal outcomes in expectant and aggressive management in severe preeclamptic women between 28 to 33 weeks' gestation Methodology : Cross sectional study was conducted in 50 women with severe preeclampsia between 28-33 weeks' gestation who admitted at Maharaj Nakornsrihammarat hospital from January 2011 to October 2014. Cases were divided into two groups, aggressive (n=25) or expectant management (n=25). Aggressive management patients were prepared for delivery, either by cesarean or induction, 48 hours after glucocorticoids therapy. Expectant management patients were managed with bed rest, oral antihypertensives and intensive antenatal fetal testing. I compared maternal and perinatal outcomes in both groups. The data analyzed by t-test and chi-square test.

**Results :** There was no difference between the two groups in mean systolic blood pressure (170 9.7 VS 172 9.4 mmHg), diastolic blood pressure (110 ± 4.2 VS 112 ± 5.4 mmHg) and gestational age (30.7 ± 1.6 VS 30.4 ± 1.5 weeks). The average latency period in the expectant management group was 15.4 days (range 4 to 28 days), which was significant higher than the average of 2.4 days in group 1 (P < 0.001, range 2-3 days). The expectant management group had a significant higher gestational age at delivery (32.9 ± 1.8 VS 30.6 ± 1.7 weeks, P < 0.001) higher birth weight, (1,692 ± 548 VS 1,286 ± 364 gms, P = 0.004), lower incidence of admission to the neonatal intensive care unit (76% VS 92%, p = 0.002). The two groups had similar incidence of abruption placenta (4%). There were no eclampsia, perinatal death or maternal death.

**Conclusion :** Expectant management in severe preeclampsia before 34 weeks' gestation, with close monitoring of mother and fetus in a tertiary-care center with adequate maternal and neonatal facilities reduced neonatal complications there aggressive management.

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**Keywords :** Severe preeclampsia, aggressive management, expectant management, maternal and perinatal outcomes.

## บทคัดย่อ

**วัตถุประสงค์ :** เพื่อเปรียบเทียบผลลัพธ์ของมารดาและทารกในการรักษาสตรีตั้งครรภ์ที่มีภาวะความดันโลหิตสูงชนิดรุนแรงอายุครรภ์ 28-33 สัปดาห์ แบบประคับประคองกับแบบเร่งรัดให้คลอด

**วิธีการศึกษา :** การศึกษาภาคตัดขวางในสตรีตั้งครรภ์ที่มีภาวะความดันโลหิตสูงชนิดรุนแรงอายุครรภ์ 28-33 สัปดาห์ที่เข้ารับการรักษานในโรงพยาบาลมหาวชิราลงกรณศรีธรรมราช ตั้งแต่ มกราคม 2554 ถึง ตุลาคม 2557 จำนวน 50 ราย โดยแบ่งเป็น 2 กลุ่ม กลุ่มละ 25 คน กลุ่มที่ 1 รักษาแบบเดิม คือเร่งรัดให้คลอด ใน 48 ชั่วโมง หลังจากได้รับยา dexamethasone กลุ่มที่ 2 รักษาแบบประคับประคอง โดยได้รับยา dexamethasone นอนพัก ให้ยาลดความดันโลหิต และติดตามดูแลทารกในครรภ์อย่างใกล้ชิดประเมินผลลัพธ์โดยดูผลการรักษาต่อมารดาและทารก เปรียบเทียบกันวิเคราะห์ข้อมูลด้วย t-test และ chi-square test

**ผลการศึกษา :** ข้อมูลพื้นฐานของ 2 กลุ่มไม่แตกต่างกันความดันโลหิต systolic ( $170 \pm 9.7$  กับ  $172 \pm 9.4$  มิลลิเมตรปรอท) ความดันโลหิต diastolic ( $110 \pm 4.2$  กับ  $112 \pm 5.4$  มิลลิเมตรปรอท) อายุครรภ์ ( $30.7 \pm 1.6$  กับ  $30.4 \pm 1.5$  สัปดาห์) ผลลัพธ์การรักษาในกลุ่มเร่งรัดให้คลอดเทียบกับกลุ่มประคับประคองดังนี้ สามารถยุติการตั้งครรภ์ออกไป ( $2.4$  กับ  $15.4$  วัน,  $P < 0.001$ ) อายุครรภ์ขณะคลอด ( $30.6 \pm 1.7$  กับ  $32.9 \pm 1.8$  สัปดาห์,  $P < 0.001$ ) น้ำหนักทารกแรกคลอด ( $1,286 \pm 364$  กับ  $1,692 \pm 548$  กรัม,  $P = 0.004$ ) จำนวนทารกที่เข้ารับการรักษานในหอผู้ป่วยหนักทารกแรกเกิด (ร้อยละ 92 กับ 76,  $P = 0.002$ ) จำนวนวันที่ทารกนอนในหอผู้ป่วยหนักทารกแรกเกิด ( $34.6$  กับ  $20.2$  วัน,  $P < 0.001$ ) ซึ่งแตกต่างกันอย่างมีนัยสำคัญทางสถิติพบภาวะรกลอกตัวก่อนกำหนดกลุ่มละ 1 รายไม่พบ eclampsia, มารดาเสียชีวิตหรือทารกเสียชีวิตทั้ง 2 กลุ่ม

**สรุป :** การดูแลสตรีตั้งครรภ์ที่มีภาวะความดันโลหิตสูงชนิดรุนแรงที่อายุครรภ์ก่อน 34 สัปดาห์ ตามแนวการรักษาแบบประคับประคองร่วมกับการเฝ้าระวังและติดตามดูแลอย่างใกล้ชิดสามารถยุติอายุครรภ์ออกไปได้โดยไม่เพิ่มอันตรายต่อมารดาและทารก ทารกที่คลอดมีภาวะแทรกซ้อนน้อยกว่าเมื่อเทียบกับการรักษาแบบเร่งรัดให้คลอด

**คำห้ส :** ความดันโลหิตสูงรุนแรงขณะตั้งครรภ์, การรักษาแบบเร่งรัดให้คลอด, การรักษาแบบประคับประคอง, ผลลัพธ์ต่อมารดาและทารก

Original Articles

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## Background

The etiology of preeclampsia is unclear<sup>1</sup>. The clinical course of severe preeclampsia is usually characterized by progressive deterioration in both maternal and fetal statuses. The ultimate goals of therapy must always the safety of the mother first and then consideration for optimum perinatal outcomes. Since the only cure for severe preeclampsia is delivery, this desired goal frequently forces the obstetrician to terminate pregnancy in spite of fetal immaturity<sup>2</sup>. Women with severe preeclampsia have more maternal complications and neonatal morbidity than normotensive women at the same gestational age<sup>1,3</sup>. The timing

of delivery in women who develop severe preeclampsia during the preterm period is a very difficult decision for every obstetrician. Usually, neonatal survival is good once a gestational age of 34 weeks has been reached because fetal lung maturity is well developed<sup>3</sup>. In contrast, delivery before 34 weeks' gestation results in more neonatal morbidity, albeit antenatal steroid treatment clearly reduces the incidence of neonatal respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH) and possibly necrotizing enterocolitis (NEC)<sup>4,5</sup>. Protocol for management of severe preeclamptic women is admission, fetal monitoring and lab investigation. Magnesium sulfate

is given as prophylaxis to eclampsia. For pregnancy below gestational age of 34 wks, Dexamethasone is also given to help stimulate fetal lung maturity. Anti-hypertensive agents were given to those with BP  $\geq$  160/110 mmHg. The authors considered terminating pregnancy after 4-6 hr of stabilization with Magnesium sulfate only pregnancy remote from term will be managed conservatively. Expectant management remained undelivered after receiving a full course of corticosteroid therapy, had expectant management to prolong pregnancy. Aggressive management was delivered during or after receiving a full course of corticosteroid therapy (within 48 hr after first dose of dexamethasone). The expectant management with intensive monitoring of maternal and fetal status improved perinatal outcome in patients with severe preeclampsia between 24 and 28 weeks<sup>6</sup>.

## Objective

The purpose of this study was to compare maternal and perinatal outcomes of the aggressive and expectant management of severe preeclampsia between 28 and 33 weeks of gestation.

## Methodology

This was a cross sectional study conducted at obstetric and Gynecology unit in Maharaj Nakorn-sriathammarat Hospital. A total of 50 women who were admitted because of severe preeclampsia between 28-33<sup>+6</sup> weeks' gestation, divided in 2 groups.

Group 1 Aggressive management (n=25)

Retrospectively reviewed cases from January 2011 to December 2012.

Group 2 Expectant management (n=25)

Prospective study from January 2013 to October 2014.

## Inclusion criteria

1. Singleton pregnancy
2. No fetal anomalies
3. No underlying disease (except chronic hypertension)

## In expectant group

- BP. is well control
- NST. Reactive

## Exclusion criteria

1. Abruptio placenta
2. Non reassuring NST, Severe oligohydramnios
3. HELLP syndrome
4. Severe IUGR
5. Twins
6. Placenta previa

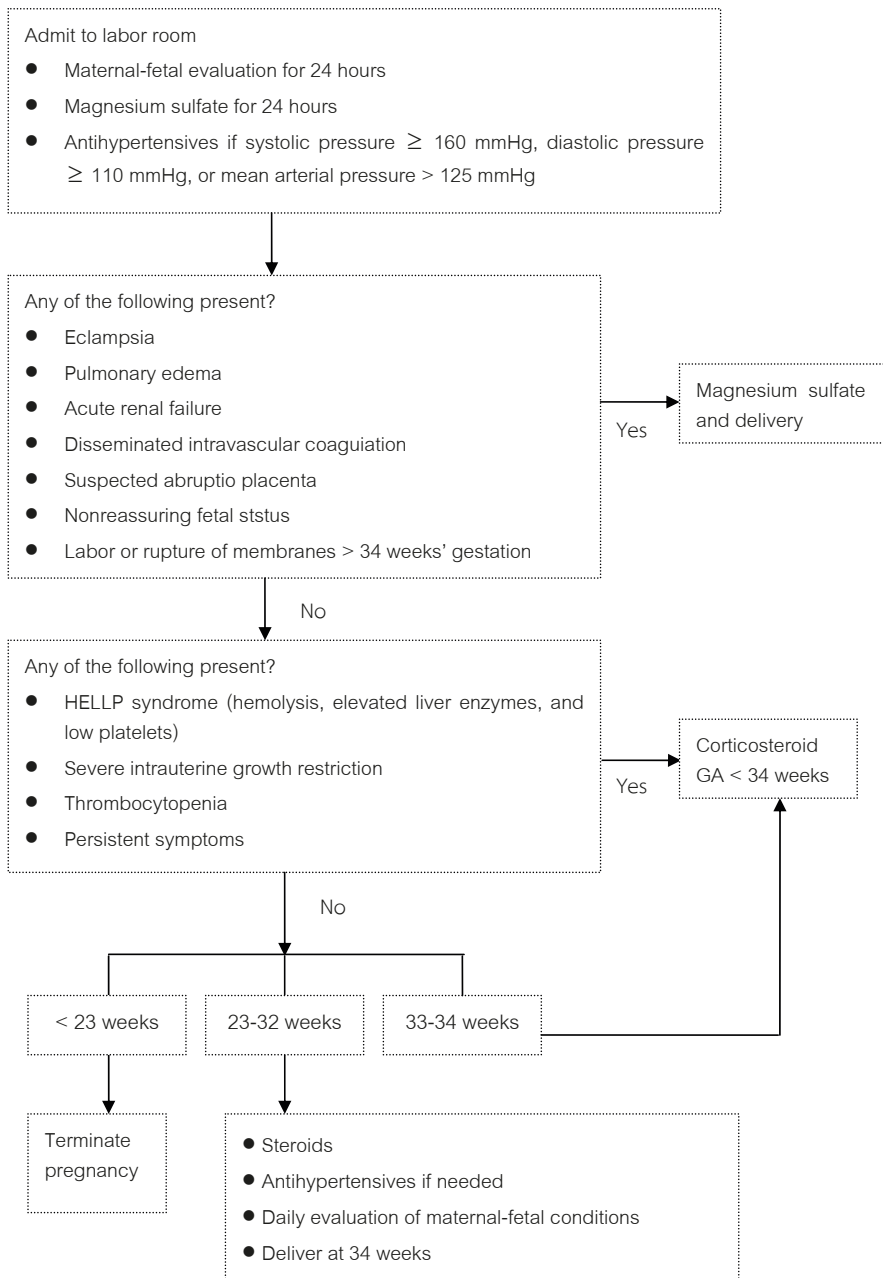
In aggressive management group were retrospective reviewed (search from ICD 10 code O 14.1)

In expectant management group were admitted to the labor room. Management Include bed rest, blood pressure measurement four times daily, maternal weight every other day, and a regular hospital diet. Patients were instructed to report the development of persistent headaches, visual disturbances, epigastric or right upper quadrant pain, uterine contractions, vaginal bleeding or decreased contractions, cramps, vaginal bleeding, or decreased fetal movement. Blood pressure was controlled with nifedipine. The initial dose of nifedipine was 10 mg every 6 hours up to a maximum dose of 120 mg /day (20 mg every 4 hours). The aim of therapy was to keep systolic blood pressures between 150 and 160 mmHg and diastolic blood pressures between 90 and 100 mmHg. Laboratory evaluation included daily determinations of hematocrit, platelet count, uric acid, and liver function tests and semiweekly measurements of 24 hour urinary protein excretion. Maternal indications for delivery were uncontrolled severe hypertension in spite of maximal

doses of nifedipine, new onset of persistent severe headaches with visual symptoms, epigastric pain, vaginal bleeding, preterm labor, rupture of membranes, thrombocytopenia (platelet count  $< 100,000/\text{mm}^3$ ), fetal distress, or attainment of 34 weeks' gestation. Fetal evaluation included daily nonstress test with amniotic fluid index measurement or

biophysical profile and weekly ultrasonography for fetal growth. Fetal indication for delivery included presence of repetitive variable or late decelerations, severe oligohydramnios (largest fluid pocket  $< 2\text{ cm}$  in vertical dimension), or biophysical profile persistently  $\leq 4$ . Cesarean section was performed for obstetric indications only.

### Expectant management



Analysis of data included comparisons of maternal complications, days gained during management, days of maternal hospitalization, and perinatal outcome included mortality, gestational age at delivery, birth weight, neonatal complications and number of days spent in neonatal intensive care nursery. The diagnosis of small for gestational age was made if the birth weight was below the 10<sup>th</sup> percentile according to the growth curves of Brenner et al. Results were expressed as mean  $\pm$  SD. Statistical analysis used the Student t-test, chi-square test.

## Results

The present study population was 50 singleton pregnancies. The demographic and clinical characteristics are presented in Table 1. There was no difference between the two groups in mean systolic blood pressure ( $170 \pm 9.7$  VS  $172. \pm 9.4$  mmHg), diastolic blood pressure ( $110 \pm 4.2$  VS  $112 \pm 5.4$ ) and gestational age ( $30.7 \pm 1.6$  VS  $30.4 \pm 1.5$ ) for the aggressive and expectant management groups.

The average pregnancy prolongation in expectant management group was 15.4 days (range 4 to 28 days), which was significant higher than the

average of 2.4 days in the aggressive management group (  $P < 0.001$ , range 2-3 days). This prolongation of pregnancy was associated with significantly higher gestation age at delivery ( $32.9 \pm 1.8$  VS  $30.6 \pm 1.7$  weeks,  $P < 0.001$ ), higher birth weight ( $1,692 \pm 548$  VS  $1,286 \pm 364$  gms,  $P = 0.004$ ) lower incidence of admission to the neonatal intensive care unit (76% VS 92%,  $P = 0.002$ ) that improvement in neonatal morbidity (respiratory distress syndrome and necrotizing enterocolitis. The one case of abruptio placenta in the aggressive management group was found at cesarean section, whereas the one case in the expectant management group were suspected because of abnormal fetal heart rate testing and vaginal bleeding. There were no cases of eclampsia, pulmonary edema, or disseminated coagulopathy in either group. Indications for delivery in the expectant management group are in Table 3. The maternal indications for delivery were thrombocytopenia (n=1), uncontrolled severe hypertension (n=3), and headache (n=1).

No fetal or neonatal death occurred in either group. The median Apgar score at 1 minute were 5.5 and 7, at 5 minutes were 7.5 and 8. The frequency at 5 minutes of Apgar scores  $< 7$  was 24% and 16%, respectively, for the two groups. (show in table 4)

**Table 1.** Clinical characteristics of study population Aggressive management

	Aggressive management (n=25)	Expectant management (n=25)	P-Value
- Maternal age (Yr)	$28.64 \pm 8.42$	$28.82 \pm 8.53$	0.94
- Nulliparous	10	11	0.95
- Chronic hypertension	1	2	0.50
- Systolic blood pressure (mmHg)	$170 \pm 9.7$	$172 \pm 9.4$	0.94
- Diastolic blood pressure (mmHg)	$110 \pm 4.2$	$112 \pm 5.4$	0.94
- Gestational age (Wks)	$30.7 \pm 1.6$	$30.4 \pm 1.5$	0.95
- GA 28-30 (No.)	11	12	0.96
- GA 31-33 (No.)	14	13	0.96

Table 2. Pregnancy outcome

	Aggressive management (n=25)	Expectant management (n=25)	P-Value
- Gestational age at delivery (Wks)	30.6 $\pm$ 1.7	32.9 $\pm$ 1.8	< 0.001
- Pregnancy prolongation	2.4	15.4	< 0.001
- Cesarean section	23 (92%)	21 (84%)	0.90
- Birth weight (gm)	1,286 $\pm$ 364	1,692 $\pm$ 548	0.004
- Abruptio placenta	1 (4%)	1 (4%)	0
- Postpartum stay (days)	5.3 $\pm$ 2.5	5.1 $\pm$ 1.8	0.96

Table 3. Indications for delivery in the expectant management group

	No	%
- Maternal indications	7	28
- Fetal compromise	4	16
- 34 weeks' gestation	5	20
- Preterm labor, premature rupture of membranes	4	16
- Vaginal bleeding	1	4

Table 4. Neonatal outcomes

	Aggressive management (n=25)	Expectant management (n=25)	P-Value
- Admitted to neonatal intensive care unit	23 (92%)	19 (76%)	0.002
- Days in neonatal intensive care unit	34.6	20.2	< 0.001
- IUGR	5 (20%)	7 (28%)	0.42
- Respiratory distress syndrome	18 (72%)	5 (20%)	0.12
- Sepsis	7 (28%)	5 (20%)	0.35
- Apgar scores 1 min	5.5 $\pm$ 2.9	7 $\pm$ 2.2	0.40
- Apgar scores 5 min	7.5 $\pm$ 2.6	8 $\pm$ 1.8	0.48

## Discussion

Severe preeclampsia between 28 and 33 weeks' gestation is an infrequent complication of pregnancy. Most clinical centers have limited experience in managing such patients. The ultimate goals of any recommended protocol of management must always be safety of the mother first and then delivery of a live mature newborn in optimal condition.

This study, the aggressive management group was retrospective, the expectant management group was cross sectional prospective of severe

preeclampsia between 28 and 33<sup>+6</sup> weeks' gestation. All patients studied had persistent hypertension and proteinuria. I cannot randomize patients with severe preeclampsia. The expectant group were carefully select. First, they were judged suitable for expectant management if they lacked several exclusion criteria, including maternal medical disease (renal disease, diabetes), multifetal gestation, bleeding, severe intrauterine growth retardation and uncontrolled severe hypertension.

I found that it was possible to prolong pregnancy by an average of 15.4 days (range 4 to 28 days) in the expectant management group. This prolongation in pregnancy was associated significant improvement in neonatal morbidity (respiratory distress syndrome and necrotizing enterocolitis) without a significant increase in maternal morbidity compared with the group who had aggressive management. In addition, the expectant management group had a lower incidence of admissions to the neonatal intensive care unit (76% VS 92%,  $P = 0.002$ ) and a lower average number of days spent in that unit (20.2 VS 34.6 days,  $P < 0.001$ )

In recent literature, Bassam et al<sup>7</sup> studied maternal and perinatal outcomes during expectant management of 239 severe preeclampsia women between 24-34 weeks' gestation. They found that perinatal death and neonatal morbidities were significantly higher among those managed at  $< 29$  weeks compared with the other group. There was no maternal death and maternal morbidities were similar between the two groups. Odendaal et al<sup>8</sup> conducted a randomized controlled trial comparing between aggressive and expectant management for 38 patients with severe preeclampsia women between 28-34 week gestation. Expectant management was not associated with an increase in maternal complication but it significantly prolonged the gestational age (mean 7.1 day ;  $p < 0.05$ ), reduced the number of neonates requiring ventilation ( $p < 0.05$ ), and reduced the number of neonatal complications ( $p < 0.05$ ).

In patients with a gestational age of 32 weeks therefore a gain of 2 weeks could be the difference between having an infant admitted to the neonatal intensive care unit or to the well-baby nursery with subsequent discharge home with the mother. These data should be useful in counseling such patients.

When the diagnosis of severe preeclampsia was based primarily on severe hypertension, we

controlled blood pressure aggressively with oral nifedipine (up to 20 mg every 4 hours). The goal was to achieve a systolic blood pressure of 140 to 160 mm Hg and a diastolic blood pressure of 90 to 100 mm Hg. Doses were titrated up ward or downward as needed to keep blood pressures within these ranges.

I found that oral nifedipine was effective in reducing maternal blood pressure in women with severe preeclampsia remote from term. Indeed only three (12%) of treated patients required delivery because of uncontrolled severe hypertension while receiving therapy.

In this study intensive maternal and fetal monitoring were started on admission and performed daily thereafter. I believe that this intensive monitoring was responsible for the absence of fetal deaths, improved neonatal outcome, and infrequent maternal complications. Because of this daily monitoring in the expectant management group<sup>7</sup>, patients were delivered for urgent maternal indications such as severe thrombocytopenia, severe epigastric pain, or uncontrolled severe hypertension. Mode of delivery was based purely on obstetric indications. Early detection of these finding and prompt institution of therapy and delivery were probably responsible for the absence of serious maternal morbidity in this study. In addition, frequent monitoring of the fetal heart rate detected abnormal patterns leading to delivery in four patients (one had abruption placenta). Similar results were reported by Odendaal et al<sup>8</sup>, This findings and those of other<sup>8,9</sup> underscore the need for intensive monitoring if expectant management is instituted in such patients. It also emphasizes the importance of instituting such management only at tertiary care centers with appropriate intensive care facilities.

In summary, the presented data were limited by the retrospective study in aggressive management group and small sample size. Despite this limitation,

I believe that the results of the present study can help obstetricians decide how to apply severe preeclampsia and also be applied as a database for further study, such as for case-control studies, in order to establish the best option of management of severe preeclamptic women. Patients with severe preeclampsia between 28 and 33 weeks' gestation should be referred to a tertiary care center once the diagnosis is made. Expectant management with frequent monitoring of maternal and fetal status is beneficial in a select group of these patients. Such management should be practiced only at a tertiary care center.

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