Perinatal Outcomes in Severe Preeclamptic Women between 24-33^{+6} Weeks' Gestation

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Objective: *The present study was undertaken to determine perinatal and maternal outcomes in severe preeclamptic women between 24 - 33 -week gestation and compare the outcomes between expectant and aggressive management.*
Material and Method: *A retrospective descriptive study of 99 women with severe preeclampsia between 24-33^{+6}-week gestation who delivered at the King Chulalongkorn Memorial Hospital from January 2002 to December 2005 was included. The outcomes were analyzed according to the gestational age at the time of admission (< 28 weeks' and ≥ 28 weeks' gestation) according to expectant compared with aggressive management. Statistical analysis was performed by student t-test and x^2 - test.*
Results: *The perinatal morbidity and mortality were significantly high in the gestational age < 28 weeks group. There were 11 perinatal deaths, 8 in those managed at < 28 weeks and 3 in those managed at 28-29 weeks' gestation ($p < 0.05$). Maternal morbidities were similar among both groups. There was no maternal death.*
Conclusion: *Delivery at remote from term, especially < 2-week gestation, increases neonatal morbidity and mortality in severe preeclamptic women. Expectant management should be done in the tertiary care center with close maternal and fetal monitering.*

Keywords: *Perinatal outcomes, Maternal outcomes, Severe preeclampsia, Expectant management, Aggressive management*

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Pregnancy induced hypertension occurs in approximately 5-8% in the King Chulalongkorn Memorial Hospital [1](KCMH). The etiology of preeclampsia is unclear[2].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 be 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[3]. Women with severe preeclampsia have more maternal complications and neonatal morbidity than normotensive women at the same gestational age[2,4]. 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[4]. 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)[5,6]. In KCMH, protocol for management of severe preeclamptic women is admission, fetal monitoring and lab investigation. Magnesium sulfate is given as

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prophylacxis to eclampsia. For pregnancy below gestational age of 34 wk, Dexamethasone is also given to help stimulate fetal lung maturity. Antihypertensive 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 present study was undertaken to determine perinatal and maternal outcomes in severe preeclamptic women between 24-33^{+6} weeks' gestation according to gestational age and management group in King Chulalongkorn Memorial Hospital (KCMH).

Material and Method

The authors recruited 99 singleton pregnancies from a total number of 132 cases who were admitted because of severe preeclampsia between 24-33^{+6} weeks' gestation and delivered in the King Chulalongkorn Memorial Hospital (KCMH) from January 2002 to December 2005, were retrospectively reviewed. The present study was approved by the ethical committee. The inclusion criteria were GA 24-33^{+6}weeks pregnant women with severe preeclampsia (search from ICD 10 code O14.1), singleton pregnancy without fetal anomalies or hydrop fetalis and no underlying disease (except chronic hypertension). The exclusion criteria were incomplete data charts. Statistical analysis was performed with SPSS version 13 for windows XP. Data are presented as mean, standard deviation (SD) median, range, or percentage, as appropriate. Categorical variables were compaired by x^2-test or Mann Whithey U-test. Continuous variables were analyzed by student *t*- test. A *p*-value < 0.05 was considered significant.

Results

The present study population was 99 singleton pregnancies. The demographic and clinical characteristics are presented in Table 1.

Maternal outcomes: the study population was separated into 2 groups according to gestational age (GA); Group 1: < 28 weeks (n = 22) and Group 2: GA $\geq$ 28-week (n = 77). Expectant management were 7 and 3 cases in group 1 and group 2 respectively. No maternal death was reported in the present study. There were no statistical differences in maternal age, primigravida rate, number of ANC, previous preeclampsia, chronic hypertension, systolic & diastolic blood pressure, proteinuria, oliguria, cerebral or visual disturbances, epigastric pain, impaired liver function, thrombocytopenia, fetal growth restriction and cesarean section rate. There was a highly significant amount of magnesium sulfate ($MgSO_4$) used (35.7 $\pm$ 22.2 vs. 22.8 $\pm$ 20.2; $p < 0.05$) and antihypertensive used (86.4% vs. 53.2%; $p < 0.05$) in gestational age of less than 28 weeks. There was no statistical significance in Dexamethasone usage in both groups (7.1 $\pm$ 9.8 vs. 14.9 $\pm$ 8.6; $p > 0.05$) (Table 2). The two most common maternal complications in both groups were renal insufficiency (18.2%) and antepartum HELLP syndrome (10.1%) (Table 3).

Neonatal outcomes: Group 1 had a lower apgar score at 1 and 5 minutes and significantly higher in the rate of Respiratory distress syndrome(RDS). Intraventricular hemorrhage(IVH), Bronchopulmonary dysplasia (BPD), Necrotizing enterocolitis(NEC), Sepsis, Neonatal intensive care unit (NICU) stay, ventilation used and surfactant used (Table 4). There were 11 perinatal deaths (6 stillbirths and 5 neonatal deaths). The causes of neonatal death were sepsis, pulmonary hemorrhage and acute renal failure. The rates of IUGR were not statistically different between both groups (22.7% vs. 23.4%; $p > 0.05$).

Comparing expectant and aggressive management, the authors found that maternal age, rate of primigravidas, number of ANC, previous preeclampsia rate, chronic hypertension, blood pressure, antihypertensive used and cesarean section rate were not significantly different. Gestational age of expectant management was significantly lower than the aggressive management group (26.9 $\pm$ 2.5 vs. 30.0 $\pm$ 2.4; $p < 0.05$). The rate of IUGR (70%), $MgSO_4$ and Dexamethasone

Table 1. Clinical characteristics of study population (n = 99)

Age (yr)*	30.7 $\pm$ 6.3
Gestational age at admission (wks)□	30 (24-33)
Primigravida (%)	54.5
Previous preeclampsia (%)	14.1
Chronic hypertension (%)	16.2
Cesarean section (%)	88.9
Perinatal death (%)	11.1

Values are expressed as mean $\pm$ SD* and median (range)□
Perinatal death included stillbirths (6) and neonatal deaths (5)

used were highly significant in expectant management (Table 2). Maternal complications were rare and were not different between the two groups (Table 3).

The gestational age at delivery of expectant management was significantly lower than the aggressive management group (27.7 ± 2.4 vs. 30.0 ± 2.4; $p < 0.05$) and NICU stay, endotrachial tube used, surfactant use and neonatal RDS & IVH were highly significant in the expectant management group. Neonatal birth weight in the aggressive group was significantly higher than the expectant group (1317.4 ± 485.8 gm vs. 800.5 ± 139.5 gm; $p < 0.05$). There was no statistical difference in the Apgar score at 1and 5 minutes, IUGR, BPD, NEC, sepsis, death and admission length between both groups (Table 4).

Discussion

In recent literature, Bassam et al[7] 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[8] 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 complications but it significantly prolonged the gestational age (mean 7.1day; $p < 0.05$), reduced the number of neonates requiring ventilation ($p < 0.05$), and reduced the number of neonatal complications ($p < 0.05$). Sibai et al[3] reported the results of conservative management of 60 consecutive patients with severe preeclampsia in the second trimester (18-27 weeks' gestation). Although there was no maternal mortality, the morbidity rate for the 60 patients was very high. Severe maternal complications included abruption placentae (n = 13), eclampsia (n = 10), coagulopathy (n = 5) and renal failure (n = 3). Perinatal outcomes for these pregnancies were exceptionally poor, with 31 of the 60 pregnancies resulting in a

Table 2. Comparison of maternal data from the two gestational age and management group

	Aggressive management	Expectant management	< 28 wks	≥ 28 wks
N	89	10	22	77
Maternal age (yr)*	30.7 ± 6.4	31.2 ± 4.9	30.9 ± 5.6	30.7 ± 6.5
Primigravidas (%)	55.1	50.0	54.5	54.5
GA at admission (wks)□	30.0 ± 2.4□	26.9 ± 2.5	26 (24-27)	31 (28-33)
Number of ANC□	5 (0-10)	4 (3-11)	4 (0-10)	5 (0-11)
Previous preeclampsia (%)	14.6	10.0	22.7	11.7
Chronic hypertension (%)	13.5	40. 0	22.7	14.3
$MgSO_4$ (gm)*	22.4 ± 19.1	4.4 ± 18.4□	35.7 ± 22.2□	22.8 ± 20.2
Dexamethasone (mg)*	14.4 ± 8.9	24.0 ± 0□	7.1 ± 9.8	14.9 ± 8.6
Antihypertensive used (%)	57.3	90.0	86.4 □	53.2
Cesarean sections (%)	89.9	80.0	81.8	90.9
Criteria to diagnosis severe preeclampsia				
- Systolic blood pressure (mmHg)*	174.5 ± 15.9	174.5 ± 10.1	179.7 ± 13.3	173.0 ± 15.7
- Diastolic blood pressure (mmHg)*	111.8 ± 10.4	113.0 ± 9.4	113.4 ± 10.1	111.5 ± 10.3
- Proteinuria (%)	42.7	60.0	54.5	44.2
- Oliguria (%)	3.4	20.0	9.1	3.9
- Cerebral or visual disturbance (%)	47.2	30.0	59.1	41.6
- Pulmonary edema (%)	0	0	0	0
- Epigastric pain (%)	24.7	30.0	31.8	23.4
- Impaired liver function (%)	24.7	20.0	22.7	24.7
- Platelet < 100,000 (%)	12.4	20.0	18.2	11.7
- IUGR (%)	23.6	70.0□	27.3	28.6

Data are presented as mean □ SD* and median (range)□
□ $p < 0.05$

Table 3. Maternal complications according to gestational age and management group

	Aggressive management (n = 89)	Expectant management (n = 10)	< 28 wks (n = 22)	≥ 28 wks (n = 77)
Placental abruption	1.1	0	0	1.3
Eclampsia	2.2	0	0	2.6
Renal insufficiency	20.2	0	13.6	19.5
Intracerebral heamorrhage	1.1	0	0	1.3
HELLP	9.0	20.0	18.2	7.8
Pulmonary edema	3.4	10.0	13.6□	1.3
Coagulopathy	6.7	10.0	13.6	5.2
Hypertensive neuropathy	1.1	0	4.5	0
Rupture hepatic hematoma	0	0	0	0
Death	0	0	0	0

Data are presented as %
□ $p < 0.05$

Table 4. Neonatal outcomes

	Aggressive management (n = 89)	Expectant management (n = 10)	< 28 wks (n = 22)	≥ 28 wks (n = 77)
GA at delivery (wks)□	30.0 ± 2.4□	27.7 ± 2.4	26 (24-28)	31 (28-33)
Apgar 1 min*	5.5 ± 2.9	4.9 ± 3.2	3.0 ± 2.1	6.1 ± 2.7□
Apgar 5 min*	7.6 ± 2.6	6.2 ± 3.3	5.1 ± 2.8	8.1 ± 2.3□
Birth weigh*	1317.4 ± 485.8□	800.5 ± 139.5	744.0 ± 255.5	1414.1 ± 438.3□
NICU (days)*	18.7 ± 24.4	39.6 ± 30.0□	44.0 ± 31.4□	14.2 ± 19.3
Endotracheal tube (%)	34.8	70.0□	81.8□	26.0
Surfactant (%)	16.9	60.0□	59.1□	10.4
Respiratory distress syndrome (%)	32.6	80.0 □	77.3□	26.0
Intraventicular heamorrhage (%)	9.0	40.0□	27.3□	7.8
IUGR (%)	21.3	40.0	22.7	23.4
Bronchopulmonary displasia (%)	11.2	20.0	36.4□	5.2
Necrotizing enterocolitis (%)	13.5	10.0	18.2	11.7
Sepsis (%)	28.1	40.0	59.1□	20.8
Death (%)	10.1	20.0	36.4□	3.9
Admission (days)*	39.2 ± 33.1	67.7 ± 42.4	63.0 ± 45.6□	36.1 ± 29.0

Data are presented as mean ± SD* and median (range)□
□ $p < 0.05$
Death included stillbirths and neonatal death

stillborn infant and 21 resulting in a neonatal death, for a total perinatal mortality rate of 87%.

The present retrospective descriptive study was undertaken to determine perinatal and maternal outcomes in severe preeclamptic women between 24-33^{+6} weeks' gestation and compare the outcomes between expectant and aggressive management in KCMH. When separated into two groups by gestational age; below 28 weeks (n = 22) and at or more than 28 weeks (n = 77). The authors found that the rates of $MgSO_4$ and antihypertensive used were significantly higher in gestational age < 28 weeks. The neonatal outcomes at gestational age < 28 weeks showed a higher incidence of low Apgar score at 1 and 5 minutes, higher surfactant used and perinatal morbidity & mortality rates. These results were because the gestational

age was remote from term and fetal lung immaturity. Maternal complications were similar in the two groups except pulmonary edema which was significantly higher in gestational age < 28 weeks. There were 11 perinatal deaths, 8 in those managed at < 28 weeks and 3 in those managed at 28 -29 weeks' gestation ($p < 0.05$).

There were 89 patients who were aggressively managed and 10 patients who were managed expectantly. Gestational age at delivery was significantly lower in the expectant group than in the aggressive management group (27.7 ± 2.4 vs. 30 ± 2.4; $p < 0.05$). A mean of 6.5 days had been gained to prolong delivery in the expectant group. The rates of chronic hypertension and IUGR were higher in the expectant group, especially IUGR (70% vs. 23.6%; $p < 0.05$). This might be a result from chronic hypertension which effected in decreasing the uteroplacental blood flow. Maternal morbidities were similar and there was no maternal death in both groups.

The need for ventilation, duration of stay in the NICU, rate of surfactant used and duration of hospitalization were significantly higher in the expectant group. Neonatal complication rates were higher in expectant management, especially RDS and IVH, while IUGR, BPD, NEC, sepsis and perinatal death were not statistically different. This result may be due to early gestational age and small population in the expectant group. The causes of neonatal death were RDS, sepsis, acute renal failure and pulmonary hemorrhage.

In summary, the presented data were limited by the retrospective study bias, small sample size and different number of population in both groups. Despite this limitation, the authors 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.

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ผลลัพธ์ของทารก ในสตรีที่มีภาวะความดันโลหิตสูงระหว่างตั้งครรภ์ที่อายุครรภ์ 24-33^{+6} สัปดาห์

สุจิตรา จันทสิงห์, สมชาย ธนวัฒนาเจริญ

วัตถุประสงค์: เพื่อศึกษาผลลัพธ์ของทารก และมารดา ในสตรีที่มีภาวะความดันโลหิตสูงระหว่างตั้งครรภ์ที่คลอดระหว่างอายุครรภ์ 24-33^{+6} สัปดาห์ ในโรงพยาบาลจุฬาลงกรณ์ และศึกษาผลลัพธ์ระหว่างการรักษาแบบ expectant และ aggressive management

วัสดุและวิธีการ: เป็นการศึกษาแบบย้อนหลังโดยการเก็บข้อมูลจากเวชระเบียนผู้ป่วย ในสตรีที่มีภาวะความดันโลหิตสูงระหว่างตั้งครรภ์ที่คลอดระหว่างอายุครรภ์ 24-33^{+6} สัปดาห์ ในโรงพยาบาลจุฬาลงกรณ์ ตั้งแต่เดือนมกราคม พ.ศ. 2545 ถึง ธันวาคม พ.ศ. 2548 จำนวน 99 ราย โดยศึกษาผลลัพธ์ของทารก และมารดาระหว่างอายุครรภ์น้อยกว่า 28 สัปดาห์เปรียบเทียบกับอายุครรภ์มากกว่า 28 สัปดาห์ และระหว่างกลุ่ม expectant managementเปรียบเทียบกับ aggressive management การวิเคราะห์ข้อมูลทางสถิติใช้ student t-test หรือ Mann Whitney U test และ x^2-test

ผลการศึกษา: อัตราทุพพลภาพและอัตราตายของทารกสูงอย่างมีนัยสำคัญในสตรีที่มีอายุครรภ์น้อยกว่า 28 สัปดาห์ พบว่ามีทารกเสียชีวิตจำนวน 11 ราย โดยที่ 8 รายพบในอายุครรภ์น้อยกว่า 28 สัปดาห์ และ 3 รายพบในสตรีที่มีอายุครรภ์ 28-29 สัปดาห์ ($p < 0.05$) อัตราทุพพลภาพและอัตราตายของมารดาไม่แตกต่างกันทั้งสองกลุ่ม ไม่พบการเสียชีวิตของสตรีตั้งครรภ์ที่มีภาวะความดันโลหิตสูง

สรุป: ในสตรีที่มีภาวะความดันโลหิตสูงระหว่างตั้งครรภ์การคลอดก่อนกำหนดโดยเฉพาะอายุครรภ์น้อยกว่า 28 สัปดาห์ เพิ่มอัตราทพุพลภาพและอัตราตายของทารกอย่างมีนัยสำคัญ การรักษาแบบ expectant management ควรทำในสถานพยาบาลระดับตติยภูมิ และต้องดูแลอย่างใกล้ชิดทั้งมารดาและทารกในครรภ์