

Outcome Comparison of Pregnancy Termination on 34th and 37th Week of Pregnancy among Patients with Severe Preeclampsia

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Abstract

Background: Severe preeclampsia causes morbidity and mortality of the mother and baby. The purpose of this study was to evaluate patients with severe preeclampsia to determine the best time of pregnancy termination by comparing maternal and baby outcomes in patients with severe preeclampsia who undergo pregnancy termination on 34th weeks and 37th weeks

Methods: The study design was a quantitative study with retrospective cross-sectional design to compare outcomes of mother and baby who met the inclusion criteria. The population in this study were all pregnant women with severe preeclampsia complications treated at the Department of Obstetrics and Gynecology of the Hasan Sadikin Hospital during January 2014 - Desember 2015, as many as 648 women. The instrument was the medical record. The statistical analysis of research data was SPSS for Windows version 17. Data normality test used the Kolmogorov-Smirnov test and Chi Square test to see the significance of differences between the 2 groups.

Results: The study showed differences in outcomes that include maternal HELLP syndrome progression ($p = 0.005$), impending eclampsia ($p = 0.023$), stroke ($p = 0.096$), multiple complications ($p = 0.000$) and eclampsia ($p = 0.005$). There are differences in the RDS infant outcomes ($p = 0.015$), VLBW ($p = 0.005$), LBW ($p = 0.005$), and Apgar score <7 ($p = 0.018$). The difference was statistically significant ($p = <0.05$).

Conclusions: The outcomes of women with severe preeclampsia who performed a 34th week pregnancy termination were better than those with a 37th week termination. The outcome of babies with severe preeclampsia who performed a 34th week pregnancy termination was worse than 37th week termination.

INTRODUCTION

In 2011, severe preeclampsia still contributed as one of the most common causes to maternal mortality, preterm birth, intrauterine growth restriction, and other fetomaternal morbidities. Complications such as HELLP (Hemolysis, Elevated Liver enzyme, Low Platelet count) syndrome, renal disorder, bleeding, pulmonary edema, placental detachment, and stroke may occur, while the infant may suffer from preterm birth, low birth weight, fetal distress, or fetal death.¹ According to the World Health Organization (WHO), hypertension in pregnancy was one of the five major causes of maternal mortalities, with a contribution of 12%. Prevalence of pregnancy hypertension varied worldwide, ranging between 2,6 to 7,3% of overall pregnancies.² In

Asia, the prevalence of hypertension in pregnancy varied, ranging between 0,4 to 8,6% in Thailand, Vietnam, China, and Myanmar; 0,13 to 6,6% in Singapore; and 3,4 to 8,6% in Indonesia.²⁻⁴

Infant mortality rate and complication risks decreased along with estimated gestational weeks between 34 and 42 weeks of gestation, however it rose 6 to 12 times among pregnancies with severe preeclampsia.⁵ Thus, after the diagnoses is established, stabilization and assessment of fetal wellness needs to be done immediately to decide whether delivery has to be assisted straightaway. Delay of delivery for >48 hours is not recommended among patients with severe preeclampsia and gestational age <34 weeks with

unstable conditions, in which delay of delivery is conducted to administer corticosteroid for lung maturation only.⁶⁻⁸ This study aims to reveal the most optimum time and method to assist birth among patients with severe preeclampsia by comparing maternal and fetal outcomes between gestational age of 34 and 37 weeks.

METHOD

This study is a cross-sectional study with retrospective quantitative approach. Data were taken from medical records. Ethical Clearance had been reviewed by Health Research Ethics Committee Universitas Padjadjaran. Confidentiality is maintained during and after the study.

Subject of this study is women with pregnancy in 34th or 37th gestational week with severe preeclampsia during period of January 2014 to December 2015 in the Department of Obstetrics and Gynecology, Dr. Hasan Sadikin General Hospital Bandung. Patients had to fulfill diagnosis criteria of severe eclampsia according to protocol in the Dr. Hasan Sadikin General Hospital Bandung, underwent laboratory examination, and treated by pregnancy termination either with perabdominal or pervaginam methods. Incomplete medical record, patients who had not been administered with magnesium sulfate, and patients who had not completed 4 dosages of corticosteroid were excluded in this study.

All maternal and fetal morbidity and mortality were noted as an outcome. Data acquired were then collected and were analyzed by SPSS version 17 for Windows. Matching were conducted for demographic characteristic such as age, parity, educational status, occupation, ANC visit, and referral status. Chi-square test was used to determine the significance between nominal variables in this study.

RESULTS

As much as 648 pregnant women with severe preeclampsia were administered during period of January 2014 to December 2015, and 172 patients fulfilled the inclusion criteria. Eighty-seven patients with gestational age of 37 weeks were taken from year of 2014, while eighty-seven patients with gestational age of 34 weeks were taken from year of 2015. Patients in the 34 week pregnancy group were most likely to be in productive reproductive age (20-34 years old), while patients in the 37 week pregnancy group were most likely to be in the high risk group (<20 years old and >35 years old). Most of them had educational background of junior or senior high school and most of them were housewives. Most of the subjects were primiparous with

ANC less than 3 times during the pregnancy, while most of the cases were a referral from a satellite hospital in West Java. No sociodemographic character showed significance. Demographic characteristic are listed in table 1.

Table 1

Sociodemographic Characteristic of Subjects

Variables	34 weeks (n=86)		37 weeks (n=86)		P-Value	OR (95% CI)
	F	%	F	%		
1. Age (years old)						
- < 20 yo	6	33,3	12	66,7	0,190	0,6 (0,304-1,290)
- 20-34 yo	57	45,8	47	45,2		
- ≥ 35 yo	23	46	27	54		
2. Educational Background						
- Elementary School	10	50	10	50	0,102	0,4 (0,138-1,643)
- Junior High School	24	41,4	34	58,6		
- Senior High School	44	53,7	38	46,3		
- Diploma Degree	4	100	0	0		
- Bachelor Degree	4	50	4	50		
3. Occupation						
- Housewives	65	46,4	75	53,6	0,141	0,4 (0,204-1,012)
- Civil Worker	5	83,3	1	16,7		
- Blue Collar Worker	13	65	7	35		
- Labor	3	50	3	50		
4. Parity						
- Multigravida	28	43,8	36	56,3	0,26	0,6 (0,360-1,249)
- Primigravida	58	53,7	50	46,3		
5. ANC						
- 4x	10	55,6	8	44,4	0,8	1,2 (0,481-3,425)
- <4	76	49,4	78	51,6		
6. Referral						
- Midwife	7	28	18	72	0,106	1,4 (0,552-3,803)
- Hospital	52	55,3	42	44,7		
- Clinic	3	60	2	40		
- Doctor	4	66,7	2	33,3		
- Government-Owned Health Center (Puskesmas)	8	36,4	14	63,6		
- No Referral	12	57,9	8	42,1		
7. Number of Parity						
- P0	31	47,7	34	52,3	0,538	0,9 (0,275-3,543)
- P1	30	60	20	40		
- P2	15	45,5	18	55,5		
- P3	5	38,5	8	61,5		
- > P3	5	50	5	50		

Notes : χ^2 chi square; significance of p-value < 0,05

Both group showed majority in trombocyte count of >100.000/mm³, while thrombocytopenia with trombocyte count of <100.000/mm³ were more commonly found among patients with gestational age of 34 weeks. The raise of SGOT was more commonly found among patients with gestational age of 34 weeks, while SGPT was more likely to be normal in both groups. Both groups showed high urinary protein level (> +2) and level of LDH > 500, while levels of LDH > were commonly found among patients with gestational age of 34 weeks. It showed that severe preeclampsia among patients with 34 weeks gestational age was more likely to be accompanied with decreasing

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thrombocyte count and rising hepatic enzymes contributing in HELLP syndrome. Thrombocyte count, serum level of SGOT, and serum level of LDG were significant in this study, with p-value of 0,006, 0,043, and 0,01, respectively. Analysis of laboratory parameter can be seen in table 2.

Table 2

Comparison of Patients with Severe Preeclampsia underwent Pregnancy Termination on 34 and 37 gestational weeks according to Laboratory Results

Laboratory Results	34 weeks (n=86)	37 weeks (n=86)	P-Value	OR (95% CI)
- Trombocyte Count				
- <100.000/mm ³	23 (71,8%)	9 (28,2 %)	0,006	3,12 (1,314- 7,231)
- >100.000/mm ³	63 (45%)	77 (55%)		
- SGOT				
- Normal	28 (40,6%)	41 (59,4%)	0,043	0,53 (0,285- 0,983)
- Risen	58 (56,3%)	45 (43,7%)		
- SGPT				
- Normal	68 (47,9%)	72 (52,1%)	0,228	0,613 (0,275- 1,365)
- Risen	18 (60%)	12 (40%)		
- Urinary Protein				
- < +2	9 (45%)	11 (55%)	0,634	0,7 (0,312- 2,033)
- ≥ +2	77 (50,7%)	75 (49,3%)		
- LDH				
- < 500	22 (36,7)	38 (63,3)	0,01	0,4 (0,228- 0,827)
- > 500	64 (37,1)	48 (42,9)		

Notes : χ^2 chi square; significancy of p-value<0,05

Choice of birth between two groups were similar, with caesarean section dominated the method used by the patients. Pervaginam delivery with assistance of forceps were more commonly found among patients with gestational age of 34 weeks. No significancy was found between the choice of birth and gestational age, as seen in table 3.

Table 3

Comparison of Choice of Birth Between Patients with Severe Preeclampsia underwent Pregnancy Termination on 34 and 37 gestational weeks

Choice of Birth	34 weeks (n=86)	37 weeks (n=86)	P-value	OR (95% CI)
- Caesarean section	45 (46,4%)	52 (53,6%)	0,282	0,7 (0,392- 1,314)
- Vaginal Delivery	41 (55%)	34 (45%)		

Notes: χ^2 chi square; significancy of p-value<0,05

Maternal mortalities were more commonly found among patients with gestational age of 37 week. However, no significance was found between maternal outcomes and gestational age, as seen in table 4.

Table 4

Comparison of Maternal Outcome Between Patients with Severe Preeclampsia underwent Pregnancy Termination on 34 and 37 gestational weeks

Outcome	34 weeks (n=86)	37 weeks (n=86)	P- Value	OR (95% CI)
- Survived	81 (50,6%)	79 (49,4%)	0,549	0,697 (0,212- 2,287)
- Died	5 (41,7%)	7 (58,3%)		

Notes : χ^2 chi square; significancy of p-value<0,05

Occurance of progressive HELLP syndrome and eclampsia was more commonly found among patients with gestational age of 34 weeks. Multiple complication, impending eclampsia, stroke, and failure of conservative treatment were also more commonly found among patients with gestational age of 34 weeks. No differences were found among proportion of heart failure and acute renal failure between patients with gestational age of 34 weeks and 37 weeks. Occurance of progressive HELLP syndrome, impending eclampsia, eclampsia, multiple complication, and no complication were significant with p value of 0,005, 0,023, 0,005, 0,000, and 0,000, respectively. Complete comparison was showed in table 5.

Table 5

Comparison of Maternal Complications Between Patients with Severe Preeclampsia underwent Pregnancy Termination on 34 and 37 Gestational Weeks

Complication	34 weeks (n=86)	37 weeks (n=86)	P-Value	OR (95% CI)
- Acute renal failure	4 (50%)	4 (50%)	1,00	1,0 (0,242-4,134)
- Progressive HELLP Syndrome	49 (67,1%)	24 (32,9%)	0,005	3,3 (1,781-6,362)
- Heart Failure	7 (50%)	7 (50%)	1,0	
- Impending eclampsia	9 (90%)	1 (10%)	0,023	9,9 (1,230-80,233)
- Eclampsia	36 (85,7%)	6 (14,3%)	0,005	9,6 (3,774-24,422)
- Stroke	5 (83,3%)	1 (16,7%)	0,096	5,24 (0,600-45,88)
- Failure of Conservative Treatment	2(66,7%)	1 (33,3%)	0,155	2,024 (1,738-2,356)
- No Complication	15(23,4%)	49(76,6%)	0,000	0,16 (0,079-0,322)
- Multiple Complication	33(82,5%)	7(17,5%)	0,000	7,027 (2,895-17,056)

Notes : χ^2 chi square; significancy of p-value<0,05

Most of infants in both groups had a good outcome, with occurrence of stillbirth more commonly found among patients with gestational age of 34 weeks. However, no significance was found between overall infant outcome and gestational age, as seen in table 6.

Table 6

Comparison of Neonatal Outcome Between Patients with Severe Preeclampsia underwent Pregnancy Termination on 34 and 37 gestational weeks

Outcome	34 weeks (n=86)	37 weeks (n=86)	P-Value	OR (95% CI)
- Survived	76 (88,37%)	82 (95,35%)	0,163	2,6 (0,812-8,963)
- Still birth	10 (11,63%)	4 (4,65%)		

Notes : χ^2 chi square; significancy of p-value<0,05

Respiratory distress syndrome was more commonly found among patients with gestational age of 34 weeks and also with low APGAR scores (4-6). Neonates with low birth weight and very low birth weight were more commonly found among patients with gestational age of 34 weeks. Severe preeclampsia patients terminated at gestational age of 34 weeks had bigger proportion of infants with Respiratory Distress Syndrome (RDS), Extreme Low Birth Weight (ELBW), Very Low Birth Weight (VLBW), Low Birth

Weight (LBW), and low 5' APGAR score. Significance was found on RDS, VLBW, LBW, and 5' APGAR score with p-value of 0,015, 0,005, 0,005, and 0,003, respectively.

Complete comparison is showed in table 7.

Table 7

Comparison of Neonatal Complication Between Patients with Severe Preeclampsia underwent Pregnancy Termination on 34 and 37 gestational weeks

Neonatal Complication	34 weeks (n=86)	37 weeks (n=86)	P-Value	OR (95% CI)
Complication				
- RDS	36 (64,3%)	20 (35,7%)	0,015	2,3 (1,230-4,591)
- ELBW	2 (100%)	0 (0%)	0,24	
- VLBW	21 (100%)	0 (0%)	0,005	2,3 (1,947-2,821)
- LBW	65 (86,7%)	10 (14,3%)	0,005	23 (10,333-53,551)
APGAR at 5th Minutes				
- < 7	46 (63%)	27 (37%)	0,003	0,398 (0,214-0,741)
- >7	40 (46,51%)	59 (68,60%)		
Birthweight				
- Normal	4 (5,06%)	75 (94,94%)	0,000	139,7 (42,67-457,8)
- Abnormal	82 (88,17%)	11 (11,83%)		

Notes : χ^2 chi square; significancy of p-value<0,05

DISCUSSION

There was no sociodemographic characteristic showing significance in this study. However, it revealed that severe preeclampsia at 34 weeks of pregnancy was more likely to be found in productive reproduction age (20-34 years old) rather than at 37 weeks. Most patients with 34 weeks of pregnancy had high school educational background, while patients with 37 weeks had junior high school educational background. Most of the subjects in both groups were housewives, primiparous, had a history of Antenatal Care (ANC) less than 4 weeks, and were referred by a hospital in West Java region. It is similar to the study conducted by Cunningham and colleague, Lowe and colleague, Sibai and colleague, and Poon and colleague; they stated that risk factors of severe preeclampsia in both 34 weeks or 37 weeks pregnancy were history of preeclampsia in the family, nulliparity, previous history of preeclampsia, primigravida, age >35 years old or <20 years old, chronic hypertension, renal disease, and multiple pregnancy.^{7,9-11} All sociodemographic characteristic, included age, educational background, occupation, parity, history of ANC, and referral had a p value of > 0,05; thus both groups were homogenous and comparable.

As seen in Table 6, analysis of patient's characteristic with severe preeclampsia adjusted with laboratory examination revealed that several complications occurred. There were differences of HELLP syndrome progressivity, impending eclampsia and eclampsia with p value of 0,005, 0,023, and

0,005 respectively, showing statistical significance between two groups.

According to study conducted by Leeman and colleague in 2015, causes of thrombocytopenia were still undetermined and it was assumed that it was caused by thrombocyte deposition in location of endothelial damage and immunological process.¹² Thrombocytopenia is the most common complication in preeclampsia, however severe thrombocytopenia are rarely found. Thrombocyte count of $<100.000 \text{ cell/mm}^3$ is a marker of severe progression. If delivery was delayed, the level of thrombocyte may drop rapidly. Even if low thrombocyte count is not related with maternal hemorrhagic risk yet, very low thrombocyte count may increase risk of bleeding, and there was no clear evidence proving that infants born from mother with preeclampsia or eclampsia would be suffering from thrombocytopenia; even if the mother suffered from severe thrombocytopenia. On the other hand, maternal mortality rate among women with HELLP syndrome reached a percentage of 1% due to breakage of subcapsular hematomas, bleeding and stroke; and perinatal mortality rate among patients with HELLP syndrome may reach a percentage of 11%.^{9,12}

Autopsy conducted by Sheehan and Lynch showed periportal hemorrhage, ischemic lesion, and fibrin deposition.⁹ Hepatic damage accompanying preeclampsia may be started as mild hepatocellular necrosis with rising serum level of enzyme (aminotransferase activity and lactate dehydrogenase activity) to HELLP syndrome with significantly rising serum level of hepatic enzymes, subcapsular bleeding or hepatic bleeding. It shows symptoms of impending eclampsia and is related with significant maternal mortality and morbidity.¹² Sibai and colleague revealed that complications occurring in severe preeclampsia among women with gestational age of 37 weeks and 34 weeks ranged between 0,6-1,5 %, while patients with HELLP syndrome were met on gestational age of 34 weeks and 37 weeks with a percentage of 2,1% and 4,1%, respectively.⁵ In this study, patients with termination at 34 weeks of gestational age had a bigger proportion of patients suffering from progressive HELLP syndrome and multiple complications compared with patients with termination at 37 weeks of gestational age.

Occurance of eclampsia and impending eclampsia were more commonly found among patients with termination at 34 weeks of gestational age.⁹ The convulsive phase of severe

preeclampsia is a significant cause of maternal mortality with signs and symptoms of headache, visual disturbance, scotoma, and in several cases, retinal ablation.^{13,14} Failure of conservative treatment were also more commonly found among patients with gestational age of 34 weeks, and so were with occurrence of multiple complications which might become a consideration for termination to reduce mortality among patients. In this study, maternal mortality was more commonly found among patients who underwent termination at 37 weeks of gestational age compared with patients who underwent termination at 34 weeks of gestational age. Mortalities might be caused by worsening of progressive complication such as eclampsia, placental detachment, DIC, renal failure, hepatic hematoma, pulmonary edema, ARDS, retinal ablation, miocardial infarct, pancreatitis, or stroke.^{14,15} Complication of heart failure had a similar proportion in both group, as heart failure usually occurred due to coexisting heart diseases.

However, maternal mortalities were more commonly found among groups with pregnancy termination at 37 weeks of gestational age compared with patients with pregnancy termination at 34 weeks of gestational age.

As seen in table 7, there were fetal outcome differences between two groups with RDS, VLBW, LBW, and 5th minute APGAR score with p-value of 0,015; 0,005; 0,018; 0,005, respectively. Infant mortality was also more commonly found in patients with termination at 34 weeks of gestational age. For preterm fetus, termination delay may lead into fetal death. Among fetuses with low birth weight and severe preeclampsia or eclampsia, extrauterine survivability was considered better compared with intrauterine survivability. Intrauterine growth restriction sometimes occurred as manifestation of maternal HELLP syndrome.^{9,12} As adjusted by infant body weight, there were 2 ELBW cases and 21 VLBW cases among group with gestational age of 34 weeks. Multiple complications were seen in as much as 97,1% of subjects in group with termination at 34 weeks, while it only occurred in 2,9% cases in the group with termination at 37 weeks. As progressive HELLP syndrome was frequently met among mother terminated at 34 weeks, the result in this study was in line with a study conducted by Abramovici and colleagues stating that LBW, low APGAR score, and IUFD were more commonly found among patients with severe preeclampsia and HELLP syndrome.

In this study, LBW were more commonly found among the

group with 34th week termination. LBW is an important sign of IUGR and preeclampsia may cause condition of reduced uteroplacental blood and ischemia, as both are important risk factor on IUGR. We might see the similarity on maternal outcomes in this study, on how numbers of complications were higher in the 34th weeks termination group. It may reflect higher degree of severe preeclampsia and leading into worse fetal outcome.

Infant survivability was higher among the group with 37 week termination, as the number of stillbirth was higher on patients with termination at the 34th weeks of gestational age. However, both groups showed higher infant mortality rates compared with a study conducted by Sibai and colleagues.¹⁶ On the other hand, perinatal death might be caused by placental detachment, asphyxia, and extreme prematurity. The WHO stated that low APGAR score and metabolic acidosis may established the diagnosis of asphyxia, as in this study low APGAR score were more commonly found among patients with termination at the 34th week.¹⁷ On the other hand, the results in this study were different compared with a study conducted by Viswanathan and colleagues, regarding that risk of IUFD in the initial 36 weeks was substantially increased; while in this study the proportion of stillbirth was bigger in the group of termination at 34 weeks.¹⁴

However, this study inherits several limitations. This study only uses the minimal sample number since there were numerous exclusion criteria and limited data access. This study also only acquired single-timed data, without considering further disease development of mother and her infant. Further prospective data needed to strengthen this study.

CONCLUSION

Patients with severe preeclampsia who performed termination at 34th weeks of pregnancy were worse compared with those at 37th weeks of pregnancy. Improvements are needed in maternal and fetal monitoring during antepartum and intrapartum care because there are many cases of stillbirth pregnancy termination performed in cases of severe preeclampsia with multiple complications. Implementation of accelerated delivery management as the primary treatment for severe preeclampsia in several cases is needed, aiming to prevent the effects of potential end-organ damage by considering the condition of the fetus after

conservative management, especially in cases that are diagnosed preeclampsia at 34 weeks gestation.

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