

The deviated management of preeclampsia with severe features at Maharat Nakhon Ratchasima Hospital

Siraya Kitiyodom, M.D.*

Penwimon Srithong, M.D.*

Abstract:

Objectives: To study the prevalence and causes of deviated management of preeclampsia with severe features and to study the complications of preeclampsia with severe features at Maharat Nakhon Ratchasima Hospital (MNRH). **Patients and Methods:** This retrospective descriptive study collected data from referral letters and medical records of preeclampsia with severe features and eclampsia at MNRH diagnosed and treated between 1 December 2014 and 31 October 2015. The standard management guidelines include antihypertensive treatment, MgSO₄ for convulsion prevention, termination of pregnancy; and prevention of complication. The patients were categorized into 2 groups whether there was deviated management or not. The data of two groups were expressed as percentage and compared using the Chi-Square test and if p-value was < 0.05, it would be considered statistically significant. **Results:** Among 186 patients with diagnosis of preeclampsia with severe features and eclampsia, deviated management was found in 154 patients (81.7 %). The top-three common deviated managements were the subtherapeutic level of MgSO₄ before delivery (61.2 %), delayed increment of MgSO₄ despite subtherapeutic level (50.7 %) and delayed laboratory test results (46.1 %). In deviated management group, 84.4 % had BMI ≥25 kg/m² that were significantly more than those of the usual management group. However, the pregnancy outcomes and complications among two groups were not different. **Conclusion:** The deviated management was found in more than 80 % of preeclampsia with severe features and eclampsia at MNRH but no serious sequelae were seen. **Keywords:** Preeclampsia; Eclampsia; Magnesium sulfate; Serum magnesium; Body mass index

*Department of Obstetrics and Gynecology, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima 30000

บทคัดย่อ: ความคลาดเคลื่อนในการรักษาภาวะครรภ์เป็นพิษแบบรุนแรงในโรงพยาบาลมหาราชนครราชสีมา
สิริยา กิติโยดม, พ.บ.*, เพ็ญวิมล ศรีทอง, พ.บ.*

*กลุ่มงานสูติ-นรีเวชกรรม โรงพยาบาลมหาราชนครราชสีมา จ.นครราชสีมา 30000

เวชสารโรงพยาบาลมหาราชนครราชสีมา 2561; 40: 153-61.

วัตถุประสงค์: ศึกษาความชุกและสาเหตุความคลาดเคลื่อนในการดูแลรักษาภาวะครรภ์เป็นพิษแบบรุนแรง และศึกษาภาวะแทรกซ้อนจากครรภ์เป็นพิษแบบรุนแรง ในโรงพยาบาลมหาราชนครราชสีมา **ผู้ป่วยและวิธีการ:** การวิจัยเชิงพรรณนา โดยเก็บข้อมูลจากหนังสือส่งตัวและเวชระเบียนย้อนหลังในสตรีที่มีครรภ์เป็นพิษ แบบรุนแรง และภาวะชกจากครรภ์เป็นพิษ ในโรงพยาบาลมหาราชนครราชสีมา ระหว่าง 1 ธันวาคม 2557 ถึง 31 ตุลาคม 2558 แนวทางมาตรฐานในการดูแลครรภ์เป็นพิษ ได้แก่การให้ยาลดความดันโลหิตสูง แมกนีเซียมซัลเฟต กันชัก ยุติการตั้งครรภ์ และป้องกันภาวะแทรกซ้อน แบ่งประชากรเป็น 2 กลุ่ม คือ กลุ่มที่มีกับไม่มีความคลาดเคลื่อนในการรักษา เปรียบเทียบข้อมูลประชากรสองกลุ่ม รายงานเป็นร้อยละ และทดสอบด้วย Chi-Square test จะถือว่ามีความสำคัญทางสถิติเมื่อ P-value < 0.05 **ผลการศึกษา:** มีภาวะครรภ์เป็นพิษแบบรุนแรง และภาวะชกจากครรภ์เป็นพิษทั้งหมด 186 คน มีความคลาดเคลื่อนในการรักษา 154 คน (ร้อยละ 81.7) ความคลาดเคลื่อนมากที่สุด 3 อันดับแรกคือ แมกนีเซียมในเลือดต่ำกว่ามาตรฐาน ก่อนคลอดร้อยละ 61.2 การไม่เพิ่มระดับแมกนีเซียมที่ยังต่ำกว่ามาตรฐานร้อยละ 50.7 และ ผลทางห้องปฏิบัติการล่าช้าร้อยละ 46.1 และในกลุ่มที่มีความคลาดเคลื่อนในการรักษา มีผู้ที่มีดัชนีมวลกาย ≥ 25 กก/ม² ถึงร้อยละ 84.4 ซึ่งมากกว่ากลุ่มที่ไม่มีมีความคลาดเคลื่อนอย่างมีความสำคัญทางสถิติ แต่ผลการตั้งครรภ์และภาวะแทรกซ้อนระหว่างสองกลุ่มไม่ต่างกัน **สรุป:** พบความคลาดเคลื่อนในการดูแลรักษาภาวะครรภ์เป็นพิษแบบรุนแรง และภาวะชกจากครรภ์เป็นพิษในโรงพยาบาลมหาราชนครราชสีมา มากกว่า ร้อยละ 80 แต่ไม่พบภาวะแทรกซ้อนแบบ รุนแรงจากความคลาดเคลื่อนในการรักษา

คำสำคัญ: ครรภ์เป็นพิษ; ภาวะชกจากครรภ์เป็นพิษ; แมกนีเซียมซัลเฟต; ระดับแมกนีเซียมในเลือด; ดัชนีมวลกาย

Introduction

Gestational hypertension and preeclampsia are the complications that could be found in 10 % of all pregnancies⁽¹⁾. Particularly, preeclampsia with severe features is one of the three leading causes of death among pregnant women⁽²⁾. Preeclampsia is considered to be a severe condition with multiple organs involvement, e.g., thrombocytopenia, renal dysfunction, hepatocellular necrosis, placental abruption, pulmonary edema, central nervous system involvement (cerebral hemorrhage, seizure) and death.

Diagnostic criteria for preeclampsia with

severe features include systolic blood pressure ≥ 160 mmHg and/or diastolic blood pressure ≥ 110 mmHg and/or cerebral symptoms (headache, blurred vision), epigastrium pain, pulmonary edema, or abnormal laboratory results, e.g., kidney function test (creatinine > 1.1 mg/dL or 2 folds higher than normal value without the presence of any other disease), the platelets count $< 100,000/\mu\text{L}$ and a development of eclampsia (in the absence of any other causes). The proteinuria can be either positive or negative. The level of proteinuria is ≥ 300 mg in a 24-hour urine or the protein/creatinine ratio at one time of urination is higher than 0.3⁽¹⁾.

The principles of the management for preeclampsia with severe features include antihypertensive treatment, the prevention of eclampsia, and the termination of pregnancy. Currently, MgSO_4 is used as the preventive medication for eclampsia.

During 2012-2013, among 734 cases with preeclampsia with severe features at Maharat Nakhon Ratchasima Hospital (MNRH), 31 had eclampsia, 1 was dead due to intracranial hemorrhage and 14 developed eclampsia during the course of MgSO_4 therapy while their serum magnesium was found to be subtherapeutic level⁽⁴⁾. This led to the revision of the guideline for the administration of MgSO_4 therapy in MNRH⁽⁵⁻⁷⁾. According to the new guideline, the dose of MgSO_4 would be adjusted continuously in accordance with BMI and the renal function. If the therapeutic level of magnesium was not achieved, the rate of MgSO_4 infusion would be increased until it reached the therapeutic level. After the implementation of this new guideline, no pregnant women were found to develop eclampsia after receiving MgSO_4 therapy although some pregnant women were still found to have subtherapeutic level of serum magnesium. Besides this, some other deviated managements were also detected, e.g., the delayed diagnosis and delayed referrals from community hospitals, the delayed laboratory test results, the delayed adjustment of MgSO_4 dose despite subtherapeutic level and delayed antihypertensive drugs for systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg⁽¹⁾.

We aimed to review the prevalence and causes of deviated management of preeclampsia with severe features and eclampsia at MNRH. Hopefully the findings would improve the treatment guideline to reduce complications and deaths among cases of preeclampsia with severe features.

Patients and Methods

The study collected data retrospectively from referral letters from community hospitals and the medical records of patients with preeclampsia with severe features and eclampsia at MNRH during 1 December 2014 to 31 October 2015. From 211 cases, 25 were excluded because of incomplete data, only 186 were enrolled. The standard management guidelines for these cases included the antihypertensive treatment, MgSO_4 to prevent eclampsia and termination of pregnancy. The initial dose of MgSO_4 was 4-6 g intravenously and it would be given continuously thereafter by adjusting the dose in accordance with BMI and the renal function. For cases with BMI ≥ 25 kg/m² and abnormal renal function (Cr > 1.1 mg%), MgSO_4 would be infused continuously at the rate of 1 g/hr and if the BMI ≥ 25 kg/m², the rate would be increased to 2 g/hr. The level of magnesium would be monitored every 4 hours to keep the therapeutic level of 4.8-8.4 mg/dL. If the serum magnesium level did not reach the therapeutic level, the rate of MgSO_4 infusion would be increased until the therapeutic level was reached. The patients would be observed for an overdose of MgSO_4 (>8.4 mg/dL) clinically characterized by the respiratory rate slower than 14 times/minute, the absence of patella reflex and urine output less than 25 ml/hr. MgSO_4 infusion would be continued until 24 hours after delivery. Antihypertensive drugs would be given when the systolic blood pressure was ≥ 160 mmHg and/or diastolic blood pressure ≥ 110 mmHg or when the blood pressure was persistent with systolic blood pressure ≥ 150 mmHg or diastolic blood pressure ≥ 110 mmHg (and still high after the blood pressure was taken at least 2 times consecutively with an interval of 4-6 hours⁽¹⁾.

The diagnosis of preeclampsia with severe features was based on the new diagnostic criteria defined by The New ACOG Task Force⁽¹⁾. For the blood test, the standard time interval from the initiation of blood drawn to the time of the test result reported was defined as 90 minutes. If longer than 90 minutes, it was considered as delayed. After MgSO₄ was discontinued, the symptoms of eclampsia that would be continuously observed until 72 hours after

delivery included headache, blurred vision and epigastrium pain. The blood pressure would also be monitored and antihypertensive drugs would be given for the persistent hypertension.

Data would be analyzed statistically by using the software program Stata/SE 11.1 Chi-Square test. The findings were considered as statistically significant when P value was < 0.05.

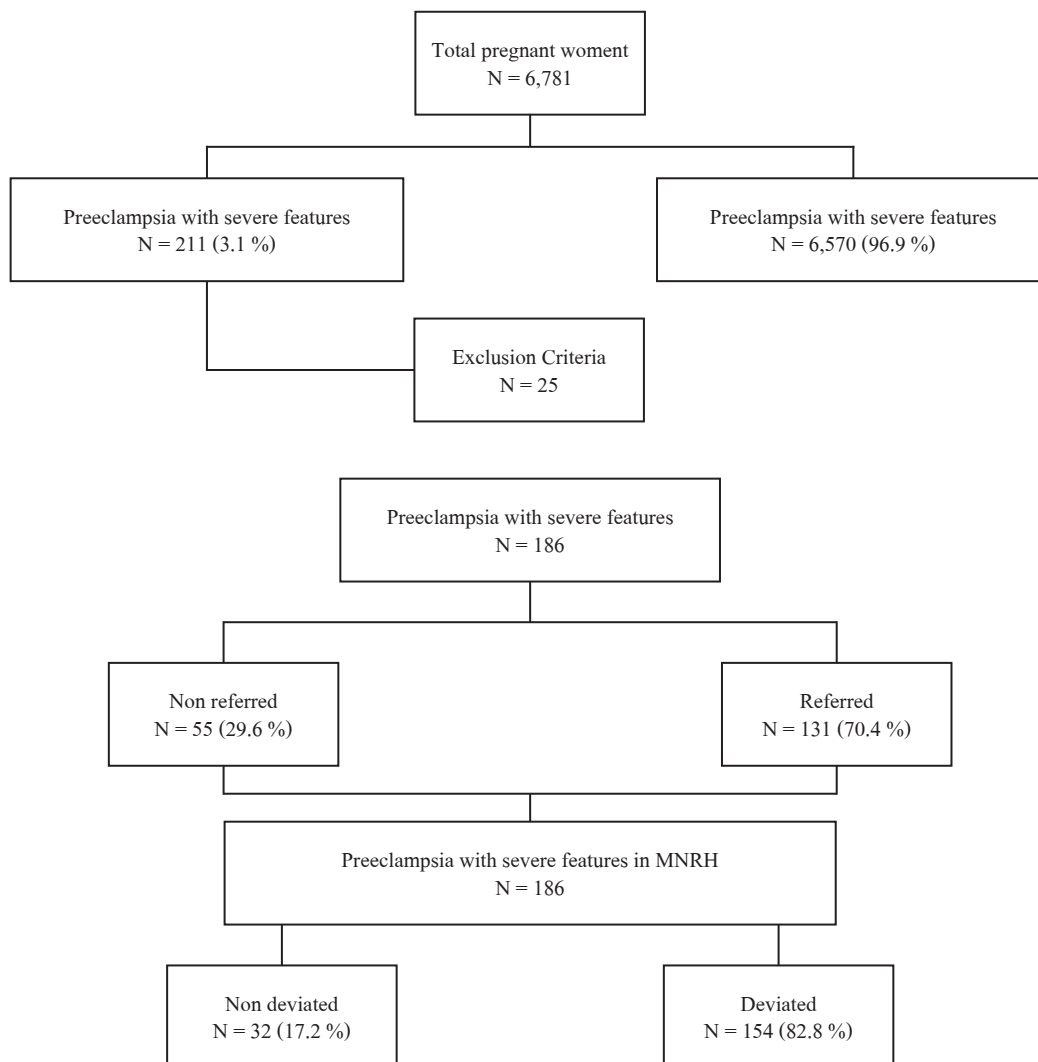


Figure 1

Results

The total pregnant women treated at MNRH during the study period were 6,781. Of these, 211 were diagnosed as having preeclampsia with severe features; 25 were excluded due to incomplete data; only 186 enrolled in the study. If the traditional diagnostic criteria⁽⁷⁾ had been used, the number of patients would have become 124 only (66.7 %). Of all 186, 131 (70.4 %) were referred from other hospitals. Some of them received deviated management. The two most common deviated managements outside MNRH were a delayed diagnosis and the non-standard treatment prior to the referral. (Figure 1)

Among 186 patients with preeclampsia with severe features, only 32 cases (17.2 %) had standard management whereas 154 cases (82.8 %) had deviated management. With regard to demographic data (shown in Table 1), age group, parity, gestational age, number of fetus, and number of ANC attendance were not different between both groups. However, the BMI of these two groups were significantly different, viz., the number of patients whose BMI ≥ 25 kg/m² in the deviated management group was 130 (84.4 %), compared with those of 21 (65.6 %) in the other group, (p=0.023).

Table 1 Baseline demographic characteristics

Characteristics	No deviate (N) (%)	Deviated (N) (%)	P value
Age (years)			0.376
<20	8 (25.0)	23 (14.9)	
20 - <35	19 (59.4)	103 (6.9)	
≥ 35	5 (15.6)	28 (18.2)	
Gravida			0.080
Primigravida	21 (65.6)	73 (47.4)	
Multipara	11 (34.4)	81 (52.6)	
Gestational age (weeks)			0.162
<34	12 (37.5)	37 (24.0)	
34-<37	10 (31.3)	43 (27.9)	
≥ 37 -42	10 (31.3)	74 (48.1)	
BMI (kg/m ²)			0.023*
<25	11 (34.4)	24 (15.6)	
≥ 25	21 (65.6)	130 (84.4)	
Number of fetus			1.000
Singleton	31 (96.9)	149 (96.8)	
Twin	1 (3.1)	5 (3.3)	
Number of ANC			0.791
0	3 (9.4)	10 (6.5)	
1-4	3 (9.4)	14 (9.1)	
≥ 5	26 (81.3)	130 (84.4)	

BMI = Body mass index, ANC = Antenatal care

*Statistical significance

The top-three common deviations of management were the subtherapeutic level of magnesium before delivery 93 cases (61.2 %), delayed adjustment of MgSO₄ dose despite the subtherapeutic level 77 cases (50.7 %), and delayed laboratory test results 70 cases (46.1 %). Moreover, 39 cases (25.7 %) received continuous infusion of MgSO₄ with inappropriate dose for their BMI: 36 cases (23.7 %) had BMI ≥25 kg/m² and 33 (21.7 %) had subtherapeutic level of magnesium after delivery. In this study, none had inappropriate loading of MgSO₄. (Table 2)

Pregnancy outcomes including the asphyxia component of APGAR score at the 1st and 5th minutes, the emergence of HELLP syndrome, postpartum hemorrhage, eclampsia and death between two groups were not different. The route of delivery for most cases was Cesarean section.

Five cases developed eclampsia and one of them died. The deceased one was referred from a community hospital. Preeclampsia was diagnosed after the delivery and rapidly progressed to the ec-

lampsia before the initiation of MgSO₄ therapy. She developed HELLP syndrome and died of cerebral hemorrhage. The other four had convulsion before admission. And after receiving the treatment, they did not have any episode of eclampsia again.

Discussion

Preeclampsia is the most severe complication of pregnancy and is one of the three leading causes of death among pregnant women⁽²⁾. However, this condition is preventable and its severity can be reduced by preventing eclampsia⁽³⁾. This study followed the new diagnostic criteria of The New ACOG Task Force⁽¹⁾ which could diagnose preeclampsia more sensitively than the traditional criteria⁽⁸⁾. This is consistent with the finding of Sibai in 2009⁽⁹⁾ who found the diagnosis of preeclampsia could be based on its signs and symptoms alone, no need of hypertension or proteinuria. The new diagnostic criteria will extend the prevention and treatment of this condition and help reducing its complications as well.

Table 2 The deviation of management of pre-eclampsia with severe features at Maharat Nakhon Ratchasima

Hospital	
Sub therapeutic level of MgSO ₄ before delivery	93 (61.2 %)
Delayed adjustment of MgSO ₄ despite the sub therapeutic level	77 (50.7 %)
Delayed laboratory report (> 90 min)	70 (46.1 %)
Not proper maintenance dose of MgSO ₄	39 (25.7 %)
BMI ≥25	36 (23.7 %)
BMI <25	3 (2.0 %)
Sub therapeutic level of MgSO ₄ after delivery	33 (21.7 %)
Delayed antihypertensive drugs	25 (16.4 %)
Improper adjustment of MgSO ₄ after delivery	11 (7.2 %)
Delayed detection of warning sign of preeclampsia with severe feature	4 (2.6 %)
MgSO ₄ level overdose	3 (2 %)
Improper loading dose of MgSO ₄	0 (0 %)

BMI = Body mass index

Table 3 Outcomes of management pre-eclampsia severe feature in MNRH

Outcomes	Non deviated N=32 (%)	Deviated N=154 (%)	P value
Route of delivery			0.93
Vagina	5 (15.6)	26 (16.9)	
Vacuum	2 (6.3)	15 (9.7)	
Breech assistant	0 (0.0)	1 (0.7)	
Cesarean section	25 (78.1)	111 (72.1)	
Cesarean section with subtotal hysterectomy	0 (0.0)	1 (0.7)	
Birth weight			0.093
ELBW (<1,000 g)	2 (6.5)	10 (6.5)	
VLBW (1,000-1,499 g)	7 (22.6)	11 (7.2)	
LBW (1,500-2,499 g)	9 (29.0)	55 (36.0)	
NBW (2,500-3,999 g)	13 (41.9)	77 (50.3)	
Birth asphyxia at 1 min	5 (15.6)	13 (8.4)	0.203
Birth asphyxia at 5 min	3 (9.3)	8 (5.2)	0.405
HELLP syndrome	1 (3.1)	7 (4.6)	1.000
Postpartum hemorrhage	0 (0.0)	12 (7.8)	0.226
Eclampsia	0 (0.0)	4 (2.6)	1.000
Death	0 (0.0)	1 (0.6)	1.000

ELBW = Extremely low birth weight

VLBW = Very low birth weight

LBW = Low birth weight

NBW = normal birth weight

HELLP syndrome = Hemolysis, Elevated Liver enzyme, Low Platelet

Cases of preeclampsia were predominantly referred from outside more than came directly to MNRH and some already received the deviated management from outside including the delayed diagnosis and the non-standard treatment. This is consistent with the study of Sibai in 1988⁽¹⁰⁾ which investigated the errors in the diagnosis and treatment of preeclampsia in USA and found that there were some confusions about definitions, the procedures of blood pressure taking, and the diagnostic procedures of preeclampsia, resulting in a need to have a clear treatment guideline in place. Due to these reasons, an approach has been initiated to use the clinical practice guidelines as the

basis for giving treatment. Community hospitals and other hospitals have been provided with relevant knowledge so they can make the diagnosis within a short time and can provide a standard treatment.

The management of preeclampsia in MNRH was mostly found to be deviated, viz. cases whose BMI ≥ 25 kg/m² in the group of deviated management mainly had subtherapeutic level of magnesium, in both the antepartum and postpartum periods however no complications were found from such deviation. This is consistent with the study of Dayicioglu⁽¹¹⁾ which found that among 194 cases of preeclampsia with severe features who received an initial dose of

MgSO₄ as 4.5 g, followed by 1.8 g/hr, the cases with heavier body weights would have a higher chance of treatment failure because the level of serum magnesium below therapeutic level was more common among them. Similarly Kitiyodom compared between the rate of 2 g/hr and 1 g/hr of continuous MgSO₄ infusion into the cases of preeclampsia with severe features with overweight and found that the level of magnesium was closer to the therapeutic level in the former than in the latter, both before and after delivery but neither magnesium overdose (above therapeutic level) nor convulsion was found in both groups⁽⁷⁾. Charoenvidhya also found the serum magnesium was closer to therapeutic level in 2 g/hr than in 1 g/hr infusion in cases of preeclampsia with severe features in prospective study⁽¹²⁾. Jaisamut⁽⁵⁾ at MNRH found that pregnant women with greater BMI had a higher tendency to have serum magnesium below the therapeutic level although they never developed eclampsia.

One patient died in our study. Her preeclampsia with severe features was diagnosed after the delivery. She had high blood pressure with epigastrium pain, developed HELLP syndrome and finally died of intracranial hemorrhage. This was consistent with the study of Khan⁽¹³⁾ who found that two common causes of death among eclampsia patients were the intracranial hemorrhage (40%) and pulmonary edema (21%).

Ghulmiyyah⁽¹³⁾ found that preeclampsia was one of the three major causes of death among pregnant women. During the past 50 years, the incidence of convulsion, the mortality rate, and complications have decreased significantly in developed countries. On the contrary, all of these are still high in developing countries due to the ineffectiveness and insufficiency of antenatal care attendance and the antenatal care provision, the improper treatments as well as improv-

er referral and the lack of availability of hospitals resulting in a delayed diagnosis. All of these are consistent with the findings of this study. Therefore, there should be a clear clinical guideline for the management of preeclampsia for healthcare workers to enhance their efficiency for providing maternal and child care.

The limitation of this research was to retrospectively collect data and there might be a selection bias due to incomplete data.

Conclusion

Over 80 % of the management for preeclampsia with severe features was deviated in MNRH. The top-three common deviations were the subtherapeutic level of magnesium before delivery, delayed adjustment of MgSO₄ dose despite the subtherapeutic level and delayed laboratory test results. But severe sequelae from such deviations were not found. The new diagnostic criteria were more sensitive screening for preeclampsia with severe features. In the future, the clinical practice guidelines for the management of preeclampsia will be adapted for better standard and less deviation of management.

Reference

1. American College of Obstetricians and Gynecologists: Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol* 2013; 122: 1122-31.
2. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY, et al. Hypertensive disorders in pregnancy. In: *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014; 728.
3. ราชวิทยาลัยสูตินรีแพทย์แห่งประเทศไทย. RCOG Clinical Practice Guideline Management of Pre-

- eclampsia and Eclampsia; สิงหาคม 2558: 60-76.
4. Kitiyodom S. Eclampsia in Maharat Nakhon Ratchasima Hospital. *Med J Srisaket Surin Buriram Hospitals* 2014; 29: 129-38.
 5. Boonyongchaisawad R. Association between maternal body mass index and subtherapeutic serum magnesium level in severe preeclampsia at Maharat Nakhon Ratchasima Hospital. *Thai J Obstet Gynaecol* 2559; 24: 145-52.
 6. Jaisamut P. Effect of maternal body mass index on serum magnesium level given for severe preeclampsia at Maharat Nakhon Ratchasima Hospital. *Thai J Obstet Gynecol* 2560; 25: 159-66.
 7. Kitiyodom S. Comparison of the level of magnesium during maintenance between 2 gram and 1 gram per hour infusion in overweight mothers with preeclampsia. *J Med Assoc Thai* 2016; 99 suppl 7: S133-7.
 8. ACOG. Committee on Practice Bulletins-Obstetrics. Diagnosis and management of preeclampsia and eclampsia. *Obstet Gynecol.* 2001; 98: 159-67.
 9. Sibai BM, Stella CL. Diagnosis and management of atypical preeclampsia-eclampsia. *Am J Obstet Gynecol* 2009; 200: 481.e1-7.
 10. Sabai BM. Pitfalls in diagnosis and management of preeclampsia. *Am J Obstet Gynecol* 1988; 159: 1-5.
 11. Dayicioglu V, Sahinoglu Z, Kol E, Kucukbas M. The use of standard dose of magnesium sulfate in prophylaxis of eclamptic seizures: do body mass index alterations have any effect on success? *Hypertens Pregnancy* 2003; 22: 257-65.
 12. Charoenvidhya D, Manotaya S. Magnesium sulfate maintenance infusion in women with preeclampsia: a randomized comparison between 2 gram per hour and 1 gram per hour. *J Med Assoc Thai* 2013; 96: 395-8
 13. Khan A, Ghosh A, Banerjee PK, Kumar T. Analysis of the causes of maternal death in eclampsia, *Int Org Sci Res J Dental Med Sci* 2014; 13: 7-10.
 14. Ghulmiyyah L, Sibai BM. Maternal mortality from preeclampsia/eclampsia. *Semin Perinatol* 2012; 36: 56-9.