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Special Theme Topic:
Stroke During Pregnancy or Delivery

Management of Eclampsia and Stroke During Pregnancy

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Abstract

To establish the etiologies and therapeutic strategies for the treatment of eclampsia and stroke during pregnancy, we performed a questionnaire-based study of stroke during pregnancy in Aichi prefecture (2005–2009). This study revealed the following findings: 66% of deliveries were managed in primary medical institutions, 40% of eclampsia episodes and 31% of strokes occurred at primary medical institutions, and 19% of strokes occurred at home. Home-onset strokes displayed a mortality rate of 40%. Using the results of this questionnaire, we investigated cases of eclampsia and/or stroke during pregnancy and revealed important issues regarding their management. In pregnant women with eclampsia or stroke, accurate antihypertensive and anticonvulsive treatment are necessary. Discriminating between eclampsia and stroke during labor is difficult. However, when facial or arm muscle weakness or a facial deficit is detected, stroke should be strongly suspected. Brain computed tomography can usually detect most cases of hemorrhagic stroke. When a stroke is detected, collaborative treatment with a neurosurgeon should be started as soon as possible. If stroke is suspected at a primary medical institution, rapid maternal transport to an intensive medical institution is necessary. In patients whose blood pressure is greater than 180/120 mmHg, the use of $MgSO_4$ to decrease the risk of convulsions and reduce blood pressure is recommended. These findings might aid the development of therapeutic strategies for pregnant women with eclampsia or stroke.

Key words: eclampsia, stroke, pregnancy

Introduction

Eclampsia and stroke during pregnancy are major causes of maternal and neonatal death in many countries.[3,10,20] Despite the ubiquity of these conditions and their public health impacts, neither their etiologies nor strategies for their treatment have been established. The lack of etiological information about eclampsia and stroke during pregnancy makes it difficult to propose appropriate management strategies for them. Close collaboration with neurosurgeons is necessary to prevent stroke; however, some medical institutions fail to establish good relationships with neurosurgeons, which can affect the prognosis for pregnant women who suffer strokes. In addition, some pregnant women develop hypertension after the onset of labor; however, it is

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difficult to diagnose hypertension during early labor, and overlooked hypertension during labor can result in eclampsia and/or stroke.

We previously performed a questionnaire-based study of eclampsia and stroke during pregnancy involving all of the obstetric institutions in Aichi prefecture. In this study, we used the data obtained during the survey to investigate cases of eclampsia and/or stroke during pregnancy that occurred at the participating institutions. From our findings, we propose therapeutic strategies for stroke during pregnancy.

Materials and Methods

We performed a questionnaire-based study of eclampsia and stroke during pregnancy involving all of the obstetric institutions in Aichi prefecture in 2007 (166 institutions) and 2010 (155 institutions).[14] All of the institutions responded to the survey; i.e., the questionnaire recovery rate was 100%. The questions were designed to obtain detailed information about the cases of eclampsia and stroke during pregnancy experienced by the participating institutions between 2005 and 2009, including the number of cases of each condition; their locations, outcomes, and prognoses; and the treatments employed. Other questions investigated the management of hypertension during labor, how antihypertensive agents should be used, the prevention of labor onset hypertension during routine prenatal follow-up examinations, and collaboration with neurosurgeons. We named this study AICHI DATA. Aichi prefecture accounts for 7% of the Japanese population as well as 7% of annual births in Japan. So AICHI DATA might provide useful etiological data regarding eclampsia and stroke during pregnancy in Japanese mothers.

Results

I. Etiology

Between 2005 and 2009, there were 322,599 deliveries, 126 cases of eclampsia (0.04% of all deliveries), and 26 cases of stroke (0.008% of all deliveries) in Aichi prefecture. The 26 cases of stroke included 8 intracerebral hemorrhages, 5 subarachnoid hemorrhages, 3 moyamoya diseases, 4 intracerebral infarctions, 2 cerebral venous thromboses, 2 posterior reversible leukoencephalopathy syndromes, and 2 others. These rates are similar to those reported previously for other countries.[3,8,10] Forty percent of eclampsia cases and 31% of strokes occurred at primary medical institutions, and 19% of strokes occurred at home. However, 92.8% of eclampsia cases and 100% of strokes were managed at intensive medical institutions. Forty percent of the pregnant women who suffered strokes at home died (Table 1). These findings demonstrate the importance of appropriate diagnosis at primary medical institutions and the establishment of efficient inter-institution transport systems.

The majority of eclampsia episodes occurred during labor (39.7%) or postpartum (43.6%). In 87% of eclampsia cases, brain computed tomography (CT) and/or brain magnetic resonance (MR) imaging was performed for diagnosis. The eclampsia patients all had good outcomes, except for one patient who suffered a second episode of eclampsia (Table 2). The majority of strokes occurred antepartum (34.6%) or postpartum (53.9%) (Table 2). Surgery was performed in 4 of 26 cases. Six of the stroke patients died (2 cerebral hemorrhages, 3 subarachnoid hemorrhages, and 1 cerebral venous thrombosis), and 6 patients suffered further strokes (Table 3).

II. Case 1; eclampsia during labor

A 34-year-old Japanese primigravida woman was admitted to our clinic due to labor onset at 40 weeks gestation. On admission, her blood pressure was 124/80 mmHg. At 7 hours after admission, she suddenly developed hypertonic convulsions, which rendered her unconsciousness, and fetal bradycardia was also detected, which were suggestive of eclampsia. Her blood pressure was elevated to 210/120

Table 1 Eclampsia and stroke during pregnancy in Aichi prefecture from 2005 to 2009

	Total	Intensive institutions	Primary institutions	Home
Delivery	322,599 (100%)	110,997 (34.4%)	211,602 (65.6%)	
Eclampsia (onset)	126 (100%)	75 (59.6%)	50 (39.7%)	1 (0.7%)
Eclampsia (managed)	126 (100%)	117 (92.8%)	9 (7.2%)	
Stroke (onset)	26 (100%)	13 (50.0%)	8 (30.8%)	5 (19.2%)
Stroke (managed)	26 (100%)	26 (100.0%)	0	

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Table 2 Annual characteristics of eclampsia and stroke in Aichi prefecture

	Total	Year				
		2005	2006	2007	2008	2009
Delivery	322,599	63,512	67,311	62,431	65,007	64,338
Eclampsia	126	25	29	22	31	19
Onset						
antepartum	21 (16.7%)	3	4	4	7	3
during labor	50 (39.7%)	12	11	6	12	9
postpartum	55 (43.6%)	10	14	12	12	7
Prognosis						
further episodes (−)	125	24	29	22	31	19
further episodes (+)	1	1	0	0	0	0
death	0	0	0	0	0	0
Stroke	26	2	7	4	4	9
Onset						
antepartum	9 (34.6%)	0	2	1	1	5
during labor	3 (11.5%)	1	1	0	1	0
postpartum	14 (53.9%)	1	4	3	2	4
Prognosis						
further episodes (−)	14	0	4	2	3	5
further episodes (+)	6	2	1	1	0	2
death	6	0	2	1	1	2

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Table 3 Characteristics of stroke during pregnancy (type of stroke)

	Total	Type of stroke						
		CH	SAH	MD	CI	CVT	PRES	Other
Onset institution								
intensive	14	4	2	3	0	2	2	1
primary	7	3	1	0	2	0	0	1
home	5	1	2	0	2	0	0	0
Onset								
antepartum	9	3	2	2	1	0	1	0
during labor	3	2	0	1	0	0	0	0
postpartum	14	3	3	0	3	2	1	2
Prognosis								
further episodes (−)	14	3	2	2	4	0	2	1
further episodes (+)	6	3	0	1	0	1	0	1
death	6	2	3	0	0	1	0	0

Revised with permission from *Hypertension Research in Pregnancy* (1: 40–45, 2013), ©2013, Japan Society for the Study of Hypertension in Pregnancy.[14] CH: cerebral hemorrhage, CI: cerebral infarction, CVT: cerebral venous thrombosis, MD: moyamoya disease, PRES: posterior reversible encephalopathy syndrome, SAH: subarachnoid hemorrhage.

mmHg, and she was immediately transported to intensive medical institution A. She underwent a cesarean section because of the presence of non-reassuring fetal status and hypertension (150/100 mmHg). A live female baby was delivered (weight 2979 g) and displayed Apgar scores of 5 and 8 at 1 and 5 minutes, respectively. At 4 hours after the operation, a second convulsion occurred (133/45 mmHg). The convulsion was stopped by the administration of 5 mg diazepam and 125 mg phenytoin. T_2-weighted and diffusion-weighted MR images obtained at 60 minutes after the second convulsion depicted vasogenic edema in the bilateral putamen and pons (Fig. 1). Her blood pressure

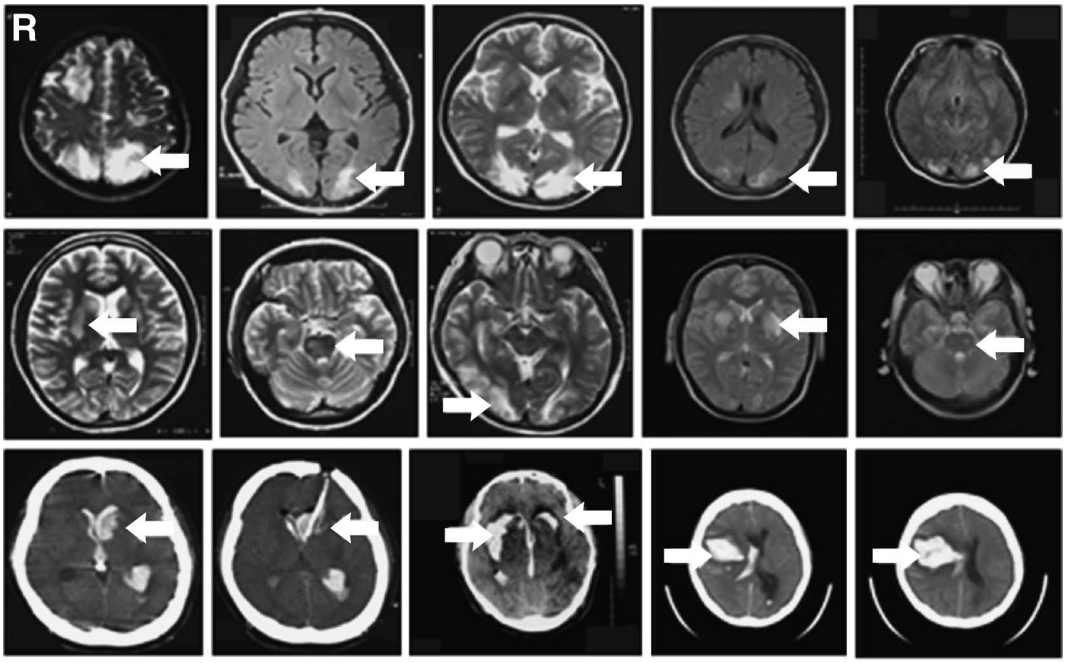

Fig. 1 Computed tomography scans and magnetic resonance images of cases of eclampsia (*upper and middle rows*) and intracerebral hemorrhages (*lower row*). *Arrows* indicate localization of brain edema or hemorrhage. *Upper row*: Brain edema located in the white matter of the occipital lobe in eclamptic cases. *Middle row*: Brain edema located in the putamen, thalamus, and pons in eclamptic cases (leftmost image from Case 1). *Lower row*: Intracerebral hemorrhages (leftmost image from Case 2, and rightmost image from Case 3).

reduced to within the normal range without hypotensor treatment. At 8 days postpartum, the patient and her baby were discharged without any neurological abnormalities.

III. Case 2; intracerebral hemorrhages during labor

A 35-year-old Japanese primigravida woman was moved to hospital B at 35 weeks gestation. Her parents had a history of hypertension. During a routine prenatal examination performed at 35 weeks gestation, her blood pressure and urine protein score on Tes-Tape® (Eli Lilly and Co., Indianapolis, Indiana, USA) were 112/85 mmHg and 3+, respectively, whereas at 36 weeks gestation they were 187/120 mmHg and negative, respectively. She was misdiagnosed with white coat hypertension because she displayed blood pressure values of 130/100 mmHg at home. She was admitted to hospital B due to labor onset at 40 weeks gestation. While her blood pressure was 190/140 mmHg on admission, her blood pressure was not monitored regularly over the following hours. By 11 hours after admission, her blood pressure had increased to 223/139 mmHg, and nicardipine was not effective at reducing her hypertension. An emergent delivery was performed as the patient became drowsy (Japan Coma Scale 100) and developed hypertension (263/176 mmHg). A live male baby was delivered (weight 3174 g) and displayed Apgar scores of 9 and 10 at 1 and 5 minutes, respectively. The patient suddenly developed right hemiparesis during suturing of the perineum, and CT performed at 60 minutes after the delivery detected cerebral hemorrhaging in the left caudate nucleus and ventricular release (Fig. 1). An endoscopic hematoma evacuation was immediately performed. At 57 days postpartum, her condition had improved, and she was moved to a rehabilitation center.

IV. Case 3; intracerebral hemorrhages during pregnancy

A 39-year-old paragravida woman was managed at a primary obstetric institution. At 27 weeks gestation, her blood pressure and urine protein score on Tes-Tape® were 146/80 mmHg and 3+, respectively. Since the following 2 days were holidays, the doctor diagnosed the patient with preeclampsia and advised her to go to an intensive medical institution 3 days later. At 2 days after the consultation, she suddenly developed convulsions, became drowsy (Japan Coma Scale 100), and started vomiting. She was

transported to hospital C, where an emergency care doctor accepted her without the permission of an obstetrician. CT depicted intracerebral hemorrhages in the white matter of the bilateral occipital lobes (Fig. 1). She was transported to university hospital D. By this point, she was unconscious (Japan Coma Scale 200), and her blood pressure had increased to 187/118 mmHg. Her laboratory data (platelets 38000 μ/l, aspartate aminotransferase 685 U/l, alanine aminotransferase 21 U/l, lactate dehydrogenase 3284 U/l, and fibrin degradation products 37 μg/ml) indicated the presence of HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. A neurosurgeon examined her and advised that an emergent cesarean section should be performed. As a result, a live female baby was delivered (weight 810 g) and displayed Apgar scores of 1 and 2 at 1 and 5 minutes, respectively. However, postoperative CT detected massive brain edema and multifocal intracerebral hemorrhages. She died the same day.

V. Blood pressure at onset of eclampsia or intracerebral hemorrhages

We extracted 35 cases of eclampsia or intracerebral hemorrhages during pregnancy in which blood pressure was measured at the time of occurrence from AICHI DATA, Congress of the Japan Society of Obstetrics and Gynecology, and Congress of the Japan Society for the Study of Hypertension in Pregnancy. These cases all occurred between 2006 and 2010. Among the 35 cases, the mean systolic blood pressure (SBP) and diastolic blood pressure at the time of occurrence were 177.3 ± 27.7 mmHg and 106 ± 18.1 mmHg, respectively. All 4 fatal cases involved a SBP of greater than 180 mmHg.[13]

Discussion

I. Pathophysiology of eclampsia

Eclampsia is defined as a seizure that occurs after 20 weeks gestation in the absence of epilepsy and other basic disorders. Although preeclampsia and eclampsia have been extensively investigated from various viewpoints, their effects on cerebral circulation and pathophysiology have not been established. There are two different hypotheses regarding the pathogenesis of eclampsia. One involves cerebral ischemia caused by cerebral arterial vasospasm,[7,22] and the other involves cerebral hyperperfusion due to the breakdown of cerebral circulatory autoregulation.[5,15–17,21,24] Cerebral blood flow autoregulation operates normally within a mean arterial blood pressure range of 60–150 mmHg.[18] If the upper limit is greatly exceeded, hypertensive encephalopathy can occur. We support the latter hypothesis and have previously reported a case of eclampsia combined with cerebral hyperperfusion, which was detected by xenon CT.[17] We have also detected increased cerebral blood flow volume in severely preeclamptic women.[15]

II. Therapeutic strategies for eclampsia and stroke during pregnancy

We used AICHI DATA to investigate cases of eclampsia and/or stroke during pregnancy and revealed several important issues regarding their management. As a result, we suggest the following therapeutic strategies for eclampsia and/or stroke during pregnancy. In pregnant women with eclampsia or stroke, we should give priority to emergent care including performing vital examinations, maintaining respiration, ensuring any required oxygen/intravenous drip infusions are provided, and monitoring fetal heart rate. Accurate antihypertensive and anticonvulsive treatment are also necessary. In cases that occur before delivery, the termination of pregnancy by emergent delivery should be considered.

III. Discriminating between eclampsia and stroke

Discriminating between eclampsia and stroke during labor is difficult. However, a patient's neurological state can be diagnosed using neurological scales including the National Institutes of Health Stroke Scale. Also, when facial or arm muscle weakness or a facial deficit is detected with or without convulsions, stroke should be strongly suspected.[6,9]

Discriminating between eclampsia and stroke can be also done using neuroimaging technologies including CT and MR imaging. In most intensive institutions, CT can be performed 24 hours a day and is available for the diagnosis of intracerebral hemorrhages. MR imaging, including T_2-weighted imaging, fluid-attenuated inversion recovery imaging, diffusion-weighted imaging, and apparent diffusion coefficient mapping, can provide detailed information about brain edema. The main pathophysiology of eclampsia is reversible vasogenic brain edema.[5] Eclamptic brain edema can be localized in various regions including the white matter of the occipital lobe, thalamus, putamen, and pons, as well as combinations of these regions. It is unknown whether eclampsia can lead to cerebral hemorrhaging. Interestingly, both eclampsia and intracerebral hemorrhages tend to affect particular brain regions (Fig. 1). When a stroke is detected, collaborative treatment with a neurosurgeon should be started as soon as possible. Neurological images should be evaluated by specialists including radiologists or neurosur-

geons. If this is not possible, obstetricians should make sure that they do not miss subarachnoid or minute hemorrhages. According to AICHI DATA, 41% of primary medical institutions only transported eclamptic patients after repeated convulsions.[14] If stroke is suspected at a primary medical institution, rapid maternal transport to an intensive medical institution is necessary. In severe preeclampsia and eclampsia, HELLP syndrome might be a frequent complication. The hemolysis, liver dysfunction, and decreased platelet counts encountered in HELLP syndrome can cause disseminated intravascular coagulation and multifocal cerebral hemorrhaging. Indications for the surgical treatment of stroke that take account of the challenges encountered in the obstetrics setting should be developed.

IV. Antihypertensive therapy

In patients whose blood pressure is greater than 160/110 mmHg, the use of $MgSO_4$ to decrease the risk of convulsions and reduce their blood pressure to 140–159/90–109 mmHg should be considered. While the preventative effect of hypotensors on eclampsia has not been established, that of $MgSO_4$ has been confirmed.[19] It is necessary to reduce blood pressure in patients with hypertension of greater than 180/120 mmHg (hypertensive emergencies).[2,4,23] Metildopa, hydralazine, nifedipine, labetalol, and nicardipine can be used as treatments for hypertension during labor. Among them, nicardipine is probably the most commonly used hypotensor. Hydralazine is not suitable for patients with active cerebral hemorrhaging.

According to AICHI DATA, 37% of institutions started using hypotensors when the patient's blood pressure reached 160/110 mmHg, and 30% started using hypotensors when it reached 180/mmHg. Nicardipine and hydralazine were the most frequently used hypotensors. In addition, 19% of institutions used $MgSO_4$ in hypertensive patients without convulsions, 16% used $MgSO_4$ after convulsions occurred, and 59% did not use $MgSO_4$.[14]

AICHI DATA also demonstrated the following findings: 46% of institutions measured blood pressure between hospitalization and delivery in all cases, 32% only measured blood pressure between hospitalization and delivery if the patient's blood pressure on admission was greater than 140/90 mmHg, and 14% allowed supporting medical staff to decide when to take blood pressure measurements. Regarding the criteria for reporting blood pressure data to doctors, 10% of institutions reported all data, 45% only reported blood pressure values of greater than 140/90 mmHg, and 23% left reporting decisions to the supporting medical staff.[14] These findings revealed that the blood pressure measurement strategy during labor was left in the hands of the supporting medical staff in about 20% of institutions. Hypertension during labor can result in eclampsia or stroke. When hypertension occurs, supporting medical staff should report the patient's blood pressure data to a doctor immediately and discuss the necessity of medical intervention.

V. Hypertension during labor

Some pregnant women remain normotensive throughout pregnancy, but then develop hypertension during labor. These patients might be at risk of eclampsia or stroke during labor, which is associated with a poor fetomaternal prognosis. Some previous studies have reported that hypertension that first appears during labor is a physiological change and is associated with good outcomes,[1,25] whereas others have reported that hypertension that first develops during labor represents a late manifestation of preeclampsia that displays similar outcomes to preeclampsia.[11,12] The limited amount of data about blood pressure changes during labor makes it difficult to establish management strategies for hypertension that develops during labor.

To increase the available data regarding blood pressure changes during labor, we examined the cases of 1013 pregnant women who were managed at our clinic without any complications or preeclampsia. The patients were classified into 4 groups: the normotensive group, whose SBP remained below 140 mmHg throughout labor; the mildly hypertensive group, whose maximum SBP during labor ranged from 140/90 mmHg to 160/110 mmHg; the severely hypertensive group, whose maximum SBP during labor ranged from 160/110 mmHg to 180/120 mmHg; and the emergent hypertensive group, whose maximum SBP during labor was greater than 180 mmHg. The normotensive, mildly hypertensive, severely hypertensive, and emergent hypertensive groups contained 761 (75%), 186 (18%), 50 (5%), and 16 patients (2%), respectively.[13] When blood pressure on admission was used to group the 1013 patients, there were 927 (92%) normotensive, 77 (7%) mildly hypertensive, and 9 (1%) severely hypertensive patients. Of the 927 cases who displayed normal blood pressure on admission, 129 (14%), 28 (3%), and 9 (1%) cases demonstrated mild hypertension, severe hypertension, and emergent hypertension between admission and delivery, respectively.

Clinicians should pay attention to the presence of hypertension that first occurs during delivery. In addition, repeated blood pressure measurement is necessary for the successful management of hypertension during labor.

Conclusions

The establishment of appropriate management strategies and collaboration with neurosurgeons might lead to an increased ability to predict pregnancy-associated stroke, and hence, reduce the risk of maternal death. The lack of sufficient etiological data and the absence of a consensus regarding the optimal treatments for eclampsia and stroke make it difficult to establish therapeutic strategies for these conditions. Our study provides important findings regarding the establishment of therapeutic strategies and might be used to revise the associated guidelines.

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Conflicts of Interest Disclosure

The authors have no conflicts of interest to report.

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