

Pregnancy Outcomes in Women with Moyamoya Disease: Experiences at a Single Center in Korea

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Purpose: Moyamoya disease (MMD) occurs predominantly in Korean and Japanese women. The aim of this study was to investigate clinical features and pregnancy outcomes in women with MMD. **Materials and Methods:** We conducted a retrospective chart review of women with MMD who visited our Department of Obstetrics and Gynecology between January 2005 and October 2013. For all study subjects, clinical features, demographic characteristics, and perinatal outcomes were recorded. **Results:** We identified 28 pregnancies in 22 patients who had been diagnosed with MMD. The mean maternal age at delivery was 31.9±3.5 years old. The mean gestational age at delivery was 38.0±0.9 weeks. Among the 28 pregnancies, 25 (92.5%) underwent cesarean section; 19 (76.0%) of them were performed under regional anesthesia and six (24.0%) under general anesthesia. The mean newborn weight was 3233.7±348.2 g. The 5-minute Apgar score in 85% of the newborns was higher than 8, with no other apparent complications. During the puerperal period, transient ischemic attack symptom or seizure occurred in 4 cases, although patients recovered within a few days. **Conclusion:** For pregnant women with MMD, it is important to control blood pressure and prevent hyperventilation during the intrapartum period, and the best methods of delivery and anesthesia should be considered to avoid unfavorable sequelae. Additionally, a multidisciplinary approach (i.e., neurosurgery) is necessary to constantly manage underlying diseases.

Key Words: Moyamoya disease, pregnancy, outcome

INTRODUCTION

Moyamoya disease (MMD) is characterized by angiographic findings of a bilateral steno-occlusion in the terminal internal carotid artery and an abnormal vascular formation of collateral vessels at the base of the brain.¹ Clinical features of this disease vary depending on the age at onset: in children, symptoms include mainly epileptic seizures, motor paralysis, speech impediment, and intelligence decline due to transient ischemic attack (TIA) or cerebral infarction. In adults, headaches and

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consciousness impairments due to cerebral hemorrhage or cerebral ischemia are the major symptoms.²

The frequency of MMD varies across different world regions.³ Nonetheless, the clinical background of MMD in South Korea and in Japan is quite similar.⁴ The age distribution patterns of MMD in Korean patients show two peaks that are nearly identical to those seen in Japanese patients. Notwithstanding, the incidence of adult MMD in South Korea is reportedly 20% higher than that in Japan. A recent study showed that the incidence and prevalence of MMD in Korea were $2.3/10^5$ and $16.1/10^5$ in 2011, respectively,⁵ although these results are higher than those in other studies.

There is no evidence that pregnancy or delivery can increase the risk of intracranial hematoma or cerebrovascular ischemia in women diagnosed with MMD. Nevertheless, physical changes, that is, increased blood flow, increased coagulability tendency, and hyperventilation, during delivery or labor can exacerbate the clinical symptoms of MMD.⁶ Provided that blood pressure and hypocapnia are well managed, pregnancy outcomes have been shown to be good,^{7,8} although there are several reports of patients who experienced ischemic stroke postpartum even when delivery was carefully managed.^{9,10} However, since only a few pregnant women are diagnosed with MMD, no standard obstetrical management protocol has been developed.

Hence, this study aimed to investigate the effects of MMD on pregnancy outcomes and to provide evidence for establishing management protocols through which to ensure safer childbirth in women with MMD.

MATERIALS AND METHODS

We conducted a retrospective review of 28 pregnancies in 22 patients diagnosed with MMD before, during, or after pregnancy between January 2005 and October 2013 at the Department of Obstetrics and Gynecology, Severance Hospital, Yonsei University College of Medicine. The diagnosis of MMD was based on characteristic angiographic findings of bilateral occlusion of the terminal internal carotid arteries and the proximal middle and anterior cerebral arteries, accompanied by extensive formation of collateral vessels. The study protocol was approved by the Institutional Review Board of Severance Hospital.

Maternal age at diagnosis of MMD and at delivery, as well as obstetrical history, clinical symptoms at diagnosis, initial treatment, clinical neurological symptoms before and

after pregnancy, history of pregnancy induced hypertension or preterm labor, gestational age at delivery, method of delivery and anesthesia, and the degree of disability or dependence in the daily activities (modified Rankin Scale) after pregnancy, were investigated. Therapeutic abortion was performed in three cases because pregnancy was detected while subjects were under medication for MMD. These three cases were excluded from this study.

Data are presented as the mean±standard deviation for continuous variables and as numbers and percentages for categorical variables.

RESULTS

We identified 28 pregnancies in 22 patients who had been diagnosed with MMD. Most cases were diagnosed with MMD before childbirth. Only two cases were diagnosed with MMD during the postpartum period of a previous pregnancy.

The mean maternal age at diagnosis was 26.8 ± 4.5 years, and the initial symptoms at diagnosis were TIA in 12 cases, hemorrhagic events in seven cases, and ischemic events in three cases. Twenty-six patients had already been diagnosed with MMD before their first pregnancy, whereas 2 patients were diagnosed postpartum. The mean maternal age at delivery was 31.9 ± 3.5 years. The rates of primiparity (50%) and multiparity (50%) in women with MMD were similar. The mean gestational age at delivery was 38 ± 0.9 weeks. Of the 28 pregnancies, 25 (92.5%) underwent cesarean section; 19 (76.0%) of them were performed under regional anesthesia, including combined epidural anesthesia, and six (24.0%) under general anesthesia. The mean newborn weight was 3233.7 ± 348.2 g, and Apgar scores at 5 minutes for all neonates were above 6. Five-minute Apgar scores in 85% of all neonates were above 8. Most newborns were in good condition, did not present any neonatal complications, and were discharged in a normal state (Table 1).

In this study, there was one case of preterm delivery due to premature rupture of membranes. While there were no cases of hypertensive events during pregnancy, three pregnant women had a history of pregnancy-induced hypertension. During pregnancy and puerperium, five out of 27 cases showed neurologic symptoms, which resolved spontaneously within a few days without any medication or procedure in four of the 5 patients (Table 2). Among the remaining 22

patients, six underwent a surgical procedure including encephalo-duro-arterio-synangiosis (EDAS) or external ventricular drainage (EVD) after being diagnosed with MMD. All patients, excluding one who died, delivered at full term. The final neurologic outcomes were good with a modified Rankin Scale score of 0 in all cases except for one.

DISCUSSION

During the first and second trimester in pregnancy, circulating blood volumes increase by 30–60%. As the circulating blood volume increases and blood coagulation intensifies, pregnancy-induced hypertension occurs, causing blood-brain barrier disruption and vasospasm, which in turn induces neurological deterioration in pregnant women with MMD.¹¹ Therefore, it is thought that preventing cerebral ischemia and cerebral hemorrhage during pregnancy is important in patients with MMD. Although only a few studies have reported the pregnancy outcomes associated with MMD, recent results indicate that pregnant women diagnosed with MMD before pregnancy exhibit a lower incidence of cerebrovascular events than those diagnosed with MMD during pregnancy and puerperium. If a woman is diagnosed with MMD during pregnancy and does not receive appropriate management, the incidence of cerebrovascular events increases and the prognosis is not good. Reportedly, the prognosis of pregnant women was good when blood pressure was strictly controlled, especially when precautions against pregnancy-induced hypertension were exerted.¹² In this study, there were five cases of neurologic symptoms during pregnancy, which were related to TIA symptoms or seizure. Four patients recovered within a few days without the need for medication or surgical procedure, and there

Table 1. Clinical Characteristics and Pregnancy Outcomes among Study Subjects

	Value (n=28)
Patient characteristics	
Maternal age (yrs)	31.9±3.5
Parity	
Primipara	14 (50)
Multipara	14 (50)
Hypertension	0 (0)
History of preeclampsia	2 (7.1)
Period at diagnosis	
Antepartum	0 (0)
Postpartum	2 (7.1)
Before pregnancy	26 (92.9)
Initial clinical symptom at diagnosis	
Transient ischemic attack	12 (54.5)
Hemorrhage	7 (31.8)
Ischemia	3 (13.6)
Pregnancy outcomes	
Pregnancy induced hypertension	0 (0)
Preterm premature rupture of membranes	1 (3.6)
Neurologic event during antepartum	5 (17.9)
Gestational age at delivery (wks)	38.0±0.9
Mode of delivery	
Cesarean section	25 (92.5)
Vaginal delivery	2 (7.4)
Anesthesia	
Regional	19 (76.0)
General	6 (24.0)
Neonatal outcomes	
Birth weight (g)	3233.7±348.2
Apgar score (1 min)	
≤4	1 (3.7)
≥5	26 (96.3)
Apgar score (5 min)	
≤7	4 (14.8)
≥8	23 (85.2)
NICU admission after birth	1 (3.44)

NICU, neonatal intensive care unit.

Values are given as mean±standard deviation or n (%) unless otherwise specified.

Table 2. Summary of Clinical Data from 5 Patients with Neurologic Symptoms due to Moyamoya Disease

Patient no.	Initial clinical symptom at diagnosis	Age, yrs	Parity	Neurologic symptom	Onset time	Treatment	Delivery	Apgar score, 1–5 min	Weight, g	Outcome (mRS)
1	Transient ischemic attack	34	1	Right side weakness	Postpartum 1 month	Conservative	Cesarean	8–9	3680	0
2	Hemorrhage	29	2	Headache	Postpartum 8 months	Conservative	Cesarean	9–10	2960	1
3	Ischemia	37	1	Seizure	IUP at 38 wks	Conservative	Cesarean	6–8	3360	0
4	Hemorrhage	29	0	Both hand numbness, headache	IUP at 13 wks	Conservative	Cesarean	6–8	3480	0
5*	Hemorrhage	30	1	Headache, syncope	IUP at 16 wks	Emergency EVD				

EVD, external ventricular drainage; IUP, intrauterine pregnancy; mRS, modified Rankin Scale.

*The patient was hospitalized with loss of consciousness and died due to intraventricular hemorrhage at the 16th weeks of gestation.

were no further complications. However, one patient died before delivery due to intraventricular hemorrhage at 16th weeks of gestation.

Liu, et al.¹³ reported that four cases of intracranial hemorrhage occurred out of a total of 144 cases of pregnancies among women with hemorrhagic MMD. Three patients had hemorrhages in the third trimester and one in the puerperium. Also, the hemorrhage rate during pregnancy was not significantly higher than that during the non-pregnancy period. It is not clear why intracranial hemorrhage develops during pregnancy in patients with MMD. The rupture of an aneurysm in the circle of Willis or rupture of fragile collateral vessels was found to be the cause of bleeding in women who were not pregnant.¹⁴ However, Liu, et al.¹³ reported that three out of 4 patients were complicated by intracranial hemorrhages in the third trimester without any aneurysm verified by cerebral angiogram. Thus, intracranial hemorrhages in pregnant women with MMD might be related to gestational age. It is, therefore, assumed that increased blood volume, vascular resistance, and hormonal change might play a role in the pathogenesis of intracranial hemorrhage during the third trimester or early postpartum. Thus, careful management of blood pressure and hemodynamic parameters may be necessary during this period.

Several studies have shown that cesarean section is the preferred mode of delivery in women with MMD and should be performed earlier before the estimated date of delivery. Vaginal delivery can induce hypertension, as well as hyperventilation, during the second stage of labor, causing intracranial hemorrhage or cerebral ischemia. Therefore, cesarean section is recommended to prevent this problem. However, cesarean section is associated with rapid circulatory changes due to blood loss perioperatively and is not an unconditionally safe option. Vaginal delivery can be performed using epidural or spinal anesthesia depending on the case and it is not contraindicated. Fukushima, et al.¹⁵ reported vaginal delivery was performed uneventfully in two out of 22 pregnancy cases.

Previously, Takahashi, et al.¹² reported that the incidence of neurological events does not differ between vaginal delivery and cesarean section. According to their survey, administration of epidural anesthesia for painless labor was important to vaginal delivery among patients with MMD. In our study, two cases underwent vaginal delivery without any noticeable event before or after delivery. It is assumed that if hypertension, hypotension, or hyperventilation can be managed well, delivery method will not substantially af-

fect prognosis. However, in case of primipara, the process of vaginal delivery is slow and, if epidural block is not performed successfully, proper symptom management could be challenging, and thus, scheduled cesarean section could be considered as a safer option.

There are various reports on outcomes according to the different types of anesthesia in women with MMD undergoing cesarean section. Strict blood pressure control, prevention of hyperventilation, and maintaining cerebral blood flow are important to avoid unfavorable sequelae. General anesthesia can induce hypertension during intubation or extubation and carries the risk of stomach content aspiration. Under local anesthesia, neurologic symptoms can be monitored, although caution should be exerted against hypotension.¹⁶

This study has a few limitations. First, most patients in this study had normal blood pressure, and delivery was conducted uneventfully. However, 3 patients had a history of pregnancy-induced hypertension, although, in those cases, their first deliveries took place at other hospitals and details regarding their conditions and deliveries were not available. Therefore, data review of our study population could not be perfectly conducted. Second, although Fukushima, et al.¹⁵ reported no significant difference in maternal and neonatal outcomes of a surgical treatment [external carotid artery-internal carotid artery bypass (EC-IC bypass)] group and a non-treatment group, we did not compare treatment groups. In our study, none of the patients underwent an anastomosis procedure, such as EC-IC bypass, although there were four cases of EDAS and three cases of EVD. Nevertheless, we assumed that comparisons between the groups would not be relevant since there were no cases with poor outcomes. Despite these limitations, this is the first study to investigate pregnancy outcomes in women with MMD at a single institute that treats mostly patients in Korea, which has high incidence of MMD.

In conclusion, favorable maternal and perinatal outcomes can be achieved through proper management of pregnant women diagnosed with MMD. Therein, it is important to maintain normal blood pressure and prevent ventilatory disturbance during delivery. When selecting delivery or anesthesia methods, risk factors associated with cerebrovascular events should be examined, as both the cesarean section and vaginal delivery have advantages and disadvantages. Furthermore, interdisciplinary collaboration with a neurosurgeon is essential for managing pregnant women diagnosed with MMD to avoid critical complications.

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