Outcome of Idiopathic Thrombocytopenic Purpura in Pregnancy in King Chulalongkorn Memorial Hospital

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Objective: *To study the maternal and fetal outcome of idiopathic thrombocytopenic purpura (ITP) in pregnancy.*
Material and Method: *The medical records of women who were diagnosed to be idiopathic thrombocytopenic purpura during and before pregnancy from January 1995 to December 2004 were reviewed.*
Results: *There were 33 pregnancies from 29 ITP women as four women had two pregnancies each and one was twins. Nine cases (27.3%) were active ITP, five cases (15.2%) were relapsing ITP and eight cases (24.2%) were inactive ITP. Eleven cases (33.3%) had severe thrombocytopenia during delivery and five neonates (23.8%) had severe thrombocytopenia. There was no statistical correlation between maternal and neonatal platelet concentration (r = -0.0601). None of the mothers and fetuses had serious hemorrhagic complication such as intracranial hemorrhage.*
Conclusion: *There were low hemorrhagic risks in both mothers and infants because of the constant monitoring of multidisciplinary groups of experienced physicians, including obstetricians, hematologists, anesthesiologists and neonatologist.*

Keywords: *Idiopathic thrombocytopenic purpura (ITP), Immune thrombocytopenia, Neonatal thrombocytopenia*

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Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by destruction of circulating antibody-bound platelets by reticuloendothelial system, particularly in the spleen[1-3]. Although adult ITP can present at any age, it tends to occur in women of childbearing age group and does not interfere with pregnancy[1-5]. In the pregnant patient, the antibodies cross the placenta placing the enfant at risk of thrombocytopenia[1]. Thus, treatment of women with ITP during pregnancy is a complex problem, especially to the potential risk of hemorrhage in both mother and fetus during the antenatal and peripartum periods[1-4].

Although several studies have examined the pregnancy outcome of ITP, there are very few available data on the pregnancy outcome of ITP in Thailand. Therefore, the authors retrospectively studied the records of 29 pregnant women with ITP for the clinical courses, diagnosis, treatment, and neonatal outcome.

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Material and Method

Patients were identified by reviewing hospital records for women who delivered at King Chulalongkorn Memorial Hospital from January 1995 to December 2004. The patients with ICD 10 were D69.3 (ITP) and D69.1 (thrombocytopenia). The inclusion criteria were the women who matched the criteria of ITP diagnosis given by the American Society of Hematology 1996[6]. To exclude gestational thrombocytopenia or incidental thrombocytopenia of pregnancy in those women in whom ITP was first discovered during pregnancy, persistent thrombocytopenia after delivery was required[7].

Severity of thrombocytopenia was classified into three groups[8] as below:

- Mild thrombocytopenia: platelet count less than 150,000 to 100,000 per ml.

- Moderate thrombocytopenia: platelet count less than 100,000 to 50,000 per ml.

- Severe thrombocytopenia: platelet count less than 50,000 per ml.

The following information was extracted from the charts for each eligible patient:age, date of diagnosis of ITP, underlying medical conditions, medication, platelet count before and during pregnancy and at delivery, treatments received to raise platelet count during pregnancy or at delivery, gestational age at delivery, type of delivery (vaginal or cesarean section), type of anesthesia, estimated blood loss at delivery, blood products transfused, and complications at delivery and in the postpartum period. Information collected for each infant included platelet count at birth, complications at birth, and treatments received.

Statistical analysis

Data were summarized using the descriptive statistics (mean, standard deviation, range and percentage). The Pearson's correlation was used to study the correlation between the maternal and neonatal platelet count.

Results

During the study interval, 29 women with ITP delivered 34 children in 33 pregnancies. There was one delivery of twins. Twenty-five women (86.2%) delivered on one occasion and four women (13.8%) delivered on two occasions. The mean age of the women at the delivery was 27.7 ± 5.1 (range, 18-36 years). The mean gestational age at delivery was 37.6 ± 2.1 weeks (range, 31-40 weeks). Eighteen women (62%) were known to have ITP before pregnancy and the remaining eleven women (38%) were diagnosed during the index pregnancy.

Disease and maternal status

Among the group (Table 1), there were eight inactive ITP pregnancies (36.4%). All of the patients who were inactive ITP had platelet count of more than 150,000 per ml through out the pregnancy and did not have any medication. Five cases (22.7%) were relapsing ITP after pregnancy. These patients had remission before pregnancy and did not have any medication for at least 6 months before the pregnancy. However, after relapsing ITP they had to take corticosteroids for treatment. One of those patients was splenectomy during cesarean section due to her third relapsing ITP. Nine cases (40.9%) were active ITP and needed corticosteroid for treatment before and throughout pregnancy period. Two of the nine were splenectomy before pregnancy and five required higher dose of prednisolone while pregnant but none of them had serious bleeding complication.

Twenty-four pregnancies (72.7%) required treatment to raise their platelet counts. The decision to treat a woman for thrombocytopenia was made by the attending physician and was based on such factors as platelet count, signs and symptoms of bleeding, and need for invasive interventions. Twenty-one pregnancies were treated with corticosteroids on one or more occasions (one pregnancy was treated with pulse methylprednisolone and two pregnancies were treated with corticosteroids and intravenous immunoglobulin [IVIg]). Duration and dose of therapy depended on patient response, patient ability to tolerate the medication and physician preference.

In the study interval, there was one fetal death in utero at 31 week of gestation with an unknown cause. The fetus had no sign of hemorrhage and anomalies. However, the parents did not give the permission to do postmortem examination.

Delivery

Among the 33 episode of deliveries (Table 2), 11 (33.3%) delivered by vaginal route (1 by forceps extraction), and 22 (66.7%) delivered by cesarean section. Fourteen cases were cesarean delivery due to

Table 1. Clinical status of ITP diagnosed before and during pregnancy

Clinical status of ITP	No. of pregnancies (%)
ITP diagnosed before pregnancy	22 (66.7%)
Inactive ITP	8* (36.4%)
Relapsing ITP	5 (22.7%)
Active ITP	9* (40.9%)
ITP diagnosed during pregnancy (new cases)	11 (33.3%)

* Two patients were splenectomy before pregnancy

Table 2. Route of delivery and maternal platelet status during delivery

Maternal platelet count	Cases (n)	Route of delivery	
		vaginal delivery (n)	Cesarean delivery (n)
normal platelet count	8 (24.3%)	4 (50.0%)	4 (50.0%)
mild thrombocytopenia	3 (9.1%)	1 (33.3%)	2 (66.7%)
moderate thrombocytopenia	11(33.3%)	1+ (9.1%)	10* (90.9%)
severe thrombocytopenia	11 (33.3%)	5 (45.5%)	6 (54.5%)

* One case had splenectomy at the same setting of cesarean section
+ One case was delivered by forceps extraction

obstetric indications, five cases from ITP and three cases from both indications. Splenectomy was done at the same setting as cesarean section in one case with no complication due to the third episode of relapsing ITP. Two fetuses underwent cordocentesis for fetal blood sampling before delivery. There were five cases (45.5%) that had severe thrombocytopenia delivered by vaginal route and six cases (54.5%) delivered by cesarean delivery.

Overall, six women (18.2%) received platelet transfusions during delivery. None of the patients had any serious hemorrhagic complication during antepartum, intrapartum and postpartum although there were four cases who had platelet count less than 20,000/ul during intrapartum period. One patient had minimal bruise at the episiotomy wound however, after supportive treatment the clinical was improved. None of them needed blood transfusion.

Neonatal outcome

None of the neonates had serious hemorrhagic complications such as intracranial hemorrhage. Neonatal platelets were measured in 21 of 33 newborns. Fourteen infants (66.8%) had normal platelet count (> 150,000/ml). One infant (4.7%) had mild thrombocytopenia, one infant (4.7%) had moderate thrombocytopenia and five infants (23.8%) had severe thrombocytopenia. In the severe neonatal thrombocytopenic group, one neonate was treated with intravenous immunoglobulin (IVIg), two neonates were treated with IVIg and platelet transfusion, one neonate was treated with platelet transfusion and one neonate did not received any medication, but the platelet count was rising to normal within 7 days after delivery. There were no statistically correlation between maternal platelet count and neonatal platelet count (r = -0.0601) (Fig. 1)

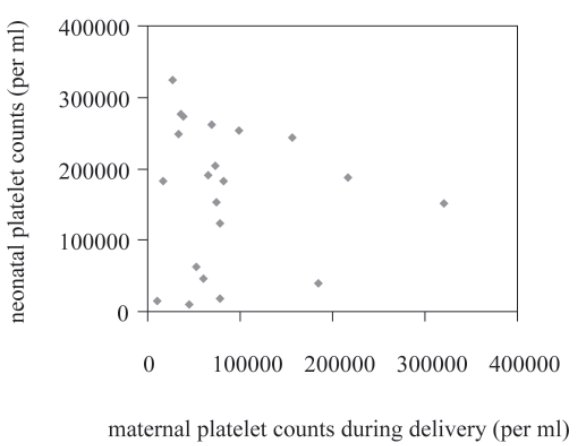

Fig. 1 Correlation of maternal and neonatal platelet counts

Discussion

In our study, the prevalence of ITP was 2-3/10,000 pregnancies and was similar to a previous study[9] that showed the prevalence at 1-5/10,000 pregnancies. ITP were relapsing in five patients (15.2%) during pregnancy and five from nine cases of active ITP (55.6%) needed higher dose of prednisolone during pregnancy. It suggested that pregnancy may aggravate ITP. Although previous studies cannot conclude that pregnancy aggravated ITP, the nadir of maternal platelets was found in the 3rd trimester of pregnancy and hemorrhage risk to both maternal and fetal during delivery[10,11]. The maternal and fetal outcome in this study was similar to previous studies[5,12,13] in which the risk of serious hemorrhagic complications in infants and mothers was low. The good pregnancy outcomes in our series were likely to be the result of the cooperation between obstetricians, hematologists and neonatologists.

The management of ITP during pregnancy was argued for many decades about, 1) when did the doctors need to start medication; 2) which route of

delivery is appropriate, vaginal or cesarean? There is still no conclusion about the appropriate time for the treatment of ITP during pregnancy. The first line drug for treatment of ITP is glucocorticoid. This may cause many maternal complications such as, gestational diabetes mellitus, adrenal insufficiency and infection. Previous studies suggested that asymptomatic patients whose platelet counts were more than 20,000/ul did not require treatment until delivery was imminent and should be carefully monitored[5,6,14]. In our study, three cases that were without medications during antepartum period were closely monitored. One had severe thrombocytopenia (platelets 37,000/ul) the others had moderate thrombocytopenia. One of them had severe thrombocytopenia (platelet count 33,000/ul) during delivery but did not have serious hemorrhagic complications.

Treatment is generally recommended when the platelet count is unacceptably low or when the patient has symptoms, such as petechiae or mucosal bleeding. Many physicians recommend treating the pregnant women with corticosteroids, intravenous immunoglobulin, or both. If a patient does not respond to these interventions, additional treatment such as splenectomy may be necessary. Corticosteroids are cost effective. An initial dose of prednisolone 1 mg/kg is recommended[5,14] and a sequentially tapering toa minimal hemostatic effective dose. IVIg is an appropriate initial treatment for women with platelet counts less than 10,000 per ml in the third trimester or platelet count of 10,000 to 30,000 per ml who are bleeding[6]. Splenectomy should be avoided because of risk of hemorrhage and the difficult to administer during pregnancy. Splenectomy should be performed in second trimester, in women who fail glucocorticoid and IVIg[6,15].

The route of delivery in ITP women was debated for a long time, whether vaginal or cesarean section, to be less risky for both maternal and fetal hemorrhage. Previously, most of these mothers were delivered by cesarean section, however there are no data to support the benefit that cesarean section may lower the risk for thrombocytopenic fetus[5]. There were no clinically significant maternal bleeding[11] and complication in the infants who were born by vaginal route or cesarean deliveries[13]. In our study, 11 cases delivered by vaginal route and 22 cases by cesarean deliveries. None of them had serious maternal and neonatal hemorrhagic complications although five cases who delivered by vaginal route had severe thrombocytopenia (platelet count less than 50,000 per ml). Pregnant women with ITP who had platelet count more than 50,000 per ml were recommended for vaginal delivery[5,6,15]. Some experts extend this level to 30,000-50,000 per ml[16]. In the present study, vaginal delivery was a relatively safe procedure by the experienced obstetrician with the cooperation of hematologists and neonatologist. Cesarean section should be used to deliver in case of obstetric indication or difficult delivery.

Neonatal thrombocytopenia is an important problem because maternal platelet antibody can cross the placenta and induce neonatal thrombocytopenia. Neonatal platelet cannot be reliably predicted by maternal platelet count, maternal platelet antibodies or history of maternal splenectomy from ITP[10-12,16,17]. Fetal blood sampling such as cordocentesis or fetal scalp blood sampling were abandoned because of the risk of neonatal mortality, difficulty to performed, and evidence that neonatal intracranial hemorrhage is quite low (about 1-5%)[14,15]. As in the previous study, there were no serious hemorrhagic complications such as intracranial hemorrhage, although the authors had three infant who had neonatal platelet of less than 20,000. In the present study, there was no statistical correlation between maternal and neonatal platelet and was similar to previous studies[2,5,14,18]. Therefore, maternal platelet count cannot predict neonatal platelet count or neonatal outcomes. However, in women who gave birth more than once during our study, the first infant's platelet count at birth predicted that of the second infant. In other words, mothers with a history of delivering a thrombocytopenic infant were at a greater risk for delivering another thrombocytopenic infant[16,18,19]. In the present study, four cases were sibling. In one case, the first child was born when their mother had severe thrombocytopenia and he had severe neonatal thrombocytopenia (platelet count 10,000 per ml). The second child was delivered at a time when their mother was inactive ITP but he also had severe neonatal thrombocytopenia (platelet counts 40,000). In the second case of sibling, they had normal neonatal platelet while their mother had moderate thrombocytopenia. In the third and fourth cases, one of the siblings was not measured as neonatal for platelet count, thus the predictor cannot be evaluated. Because of the limitation of small sample size in the present study, the predictor of neonatal platelet using history of their siblings should be studied further.

This study was designed to collect retrospectively the data of ITP during pregnancy for 10 years. The long collection period is due to the uncommon hematological disease during pregnancy. Because of its retrospective nature, this study has several limitations. The most significant limitation is that though

efforts were made to obtain complete information, data are not available for all deliveries. However, the strength of this study is the verification of the diagnosis and can exclude other causes of thrombocytopenia. Therefore, this study can obtain the overview of the outcome of ITP in pregnancy. Pregnant women with ITP require monitoring during pregnancy and may require intervention with agents to raise the platelet count. For most women, however, pregnancy is uncomplicated. Even those with severe thrombocytopenia during pregnancy have good outcomes. Fetal loss of approximately 3% continues to occur in ITP and remains, so far, unavoidable.

Conclusion

The current results of our study and other studies about adult ITP confirm the low, serious risk of maternal and neonatal hemorrhage when there is close monitoring of a multidisciplinary group of experienced physicians. Hence, ITP in pregnancy are complicated cases and require the close collaboration of obstetrician, hematologist, anesthesiologist and neonatologist. For the management of the mother and fetus, the collaboration of the specialists is essential. Although the route of delivery of ITP in pregnancy is still controversial, data from our study and other studies suggested that vaginal delivery was safe in non-difficult cases with close monitoring by an experienced physician.

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ผลการตั้งครรภ์ของสตรีตั้งครรภ์ที่เป็นโรค Idiopathic thrombocytopenic purpura ในโรงพยาบาลจุฬาลงกรณ์

สุขฤทัย นิสารัตนพร, นเรศร สุขเจริญ

วัตถุประสงค์: *เพื่อศึกษาผลของการตั้งครรภ์ในมารดาและทารกที่เกิดจากสตรีตั้งครรภ์ที่เป็น idiopathic thrombocytopenic purpura (ITP)*

วัสดุและวิธีการ: *ศึกษาและทบทวนประวัติและเวชระเบียนย้อนหลังของสตรีตั้งครรภ์ที่ป่วยเป็นโรค ITP ตั้งแต่เดือนมกราคม ปี พ.ศ. 2538 ถึงเดือน ธันวาคม ปี พ.ศ. 2547 ที่มาคลอดบุตรในโรงพยาบาลจุฬาลงกรณ์*

ผลการศึกษา: *พบมีการตั้งครรภ์ 33 ครั้งในผู้ป่วย 29 คน ผู้ป่วย 4 ราย ตั้งครรภ์ 2 ครั้งและ 1 รายตั้งครรภ์แฝด มีผู้ป่วย 9 ราย (27.3%) มีปัญหาเกล็ดเลือดต่ำขณะตั้งครรภ์ (active ITP) มีผู้ป่วย 5 ราย (15.2%) มีภาวะเกล็ดเลือดต่ำกลับเป็นซ้ำระหว่างตั้งครรภ์ (relapsing ITP) ในขณะที่ผู้ป่วย 8 ราย (24.2%) มีเกล็ดเลือดปกติตลอดการตั้งครรภ์ (inactive ITP) มีผู้ป่วยที่ได้รับการวินิจฉัยว่ามีเกล็ดเลือดต่ำระดับรุนแรง (severe thrombocytopenia) ระหว่างคลอด 11 ราย (33.3%) พบอุบัติการณ์ของเกล็ดเลือดต่ำ ระดับรุนแรงในเด็กแรกคลอด (neonatal thrombocytopenia) 5 ราย 23.8% และไม่พบความสัมพันธ์ระหว่างระดับเกล็ดเลือดของมารดาก่อนคลอด และระดับเกล็ดเลือดของเด็กแรกคลอด ($r = -0.0601$) ไม่พบปัญหาเลือดออกรุนแรงทั้งในมารดาและทารกแรกคลอด เช่น เลือดออกในสมอง*

สรุป: *พบภาวะเลือดออกรุนแรงในมารดาที่เป็น ITP และทารก ค่อนข้างต่ำ ในกรณีที่ได้รับการติดตามดูแลรักษาอย่างใกล้ชิดจากแพทย์ผู้เชี่ยวชาญ ในสาขาต่างๆ ทั้ง สูติแพทย์ อายุรแพทย์ด้านโลหิตวิทยา กุมารแพทย์ และวิสัญญีแพทย์*