

## Original Article

## MATERNAL AND NEONATAL OUTCOMES IN PREGNANT WOMEN WITH IMMUNE THROMBOCYTOPENIC PURPURA

Sedigheh Borna MD<sup>\*</sup>, Hajiehe Borna MD<sup>\*\*</sup>, Soghra Khazardoost<sup>\*</sup>

**Background:** The aim of this study was to evaluate the outcome of pregnancies in Iranian women with immune thrombocytopenic purpura (ITP).

**Methods:** In a historical cohort study, maternal and neonatal outcomes were studied in 30 pregnant women with ITP at a hospital in Tehran, from January 1994 through November 2003.

**Results:** Twenty-two cases were diagnosed as ITP before and 8 during pregnancy. Thrombocytopenia (platelet count  $<150 \times 10^9/L$ ) occurred in 22 pregnancies. Eleven (37%) had vaginal delivery and 19 (63%) underwent elective cesarean section. Eight women had severe postpartum hemorrhage. All live-born neonates were delivered in good condition at term. Neonatal thrombocytopenia occurred in 20 (67%) neonates. No bleeding complications occurred in any of the neonates.

**Conclusion:** The outcome of pregnancy in pregnant women with ITP is generally good. Cesarean section should only be performed for obstetric indications. Postpartum hemorrhage is common in these women. Postpartum hemorrhage is unrelated to the mode of delivery. Severe thrombocytopenia and bleeding in the offspring are uncommon.

*Archives of Iranian Medicine, Volume 9, Number 2, 2006: 115 – 118.*

**Keywords:** Immune thrombocytopenic purpura (ITP) • neonatal bleeding • pregnancy

## Introduction

Immune thrombocytopenic purpura (ITP) is the most common cause of significant maternal thrombocytopenia in the first trimester of pregnancy and accounts for approximately one case of thrombocytopenia per 1000 pregnancies and 5% of all cases of pregnancy-associated thrombocytopenia.<sup>1,2</sup>

Although pregnancy is not discouraged in women with preexisting ITP, maternal and fetal complications can occur, and additional monitoring and therapy may be needed. There are many controversies in the management of these women. Cesarean section has been advocated to prevent fetal intracranial hemorrhage.<sup>1, 3, 4</sup> However, its

value is under question, as it was shown that this surgical intervention has little effect on the incidence of affected neonates.<sup>5,6</sup>

In addition, the maternal platelet count is a poor predictor for development of fetal thrombocytopenia and has no value in identifying the pregnancies that may be at risk of fetal hemorrhage.

Since there is no maternal clinical or laboratory characteristics predictive for neonatal thrombocytopenia, the fetal platelet count could be determined either through fetal scalp sampling during labor or by percutaneous umbilical blood sampling (PUBS) prior to delivery. The latter method provides a more reliable estimate, but it is associated with a complication rate of 1%—primarily bleeding and fetal bradycardia.<sup>7-9</sup> We conducted this study to determine the outcome of pregnancy in Iranian women with ITP.

## Patients and Methods

Thirty pregnant women, known cases of ITP, who were admitted to the Department of Obstetrics

**Authors' affiliations:** \*Department of Obstetrics and Gynecology, Tehran University of Medical Sciences, \*\*Department of Pediatrics, Shahed University of Medical Sciences, Tehran, Iran.

**Corresponding author and reprints:** Sedigheh Borna MD, Vali-e-Asr Reproductive Health Research Center, Vali-e-Asr Hospital, Keshavarz Blvd., Tehran 14194, Iran.

Fax: +98-21-88718062, E-mail: s\_borna@hotmail.com.

Accepted for publication: 4 May 2005

and Gynecology of Vali-e-Asr Hospital, Tehran, Iran between 1994 and 2003 along with their neonates ( $n = 30$ ), were included in this study. Medical records of these patients were retrospectively studied for maternal and neonatal outcomes. Collected data were analyzed by the Student's  $t$ -test, using the SPSS software.

Thirty women fulfilled the diagnostic criteria for ITP, established by the American Society of Hematology.

To exclude those with incidental thrombocytopenia or gestational thrombocytopenia of pregnancy in whom the disease was first discovered during pregnancy, the patient was followed to verify the persistent thrombocytopenia after delivery.

Patients with incidental thrombocytopenia of pregnancy, a condition frequently confused with ITP, were excluded. The clinical course, mode of delivery, treatment, maternal complications, and neonatal outcome studied.

Neonatal records were reviewed for outcome, the platelet nadir (the lowest recorded neonatal platelet count) and complications. Neonatal platelet counts were performed serially for at least the first week of life.

## Results

During the study period (9 years), ITP affected at least 30 of 21,452 pregnant women admitted to the hospital. The mean age of women was 28 (range: 18 – 41) years; the mean parity was 1 (range: 0 – 3).

Out of 30 pregnant women with ITP, 22 had a previous diagnosis of ITP; in eight, the diagnosis was made during pregnancy.

The mainstay of maternal therapy was corticosteroids and intravenous administration of immunoglobulin (IV Ig). Oral prednisone was used in 14 (47%) women; IV Ig was used for treatment of 8 (27%) women. In one case, splenectomy had been performed prior to the pregnancy. During pregnancy, five women had spontaneous bruising and epistaxis. One patient had antenatal severe bleeding from placental abruption.

The maternal and fetal characteristics of these pregnancies were studied in relation to the lowest maternal platelet count at the time of delivery. Thrombocytopenia of varying degrees (platelet count  $<150 \times 10^9/L$ ) was observed at the time of delivery in 22 (73%) patients (Table 1).

There were no premature deliveries ( $<37$  weeks of gestation). Of 30 pregnant women, 11 (37%)

**Table 1.** Platelet count of women with ITP at the time of delivery.

Platelet count $\times 10^9/L$	n (%)
$\geq 150$	8 (27)
100 – 150	8 (27)
50 – 99	9 (30)
20 – 49	4 (13)
$<20$	1 (3)
<b>Total</b>	<b>30</b>

had vaginal delivery; 19 (63%) underwent cesarean section of which 8 (42%) were undertaken just for hematologic reasons and 11 for obstetric reasons (Table 2). Five patients with cesarean and 3 with vaginal deliveries had postpartum hemorrhage, severe enough to require blood transfusion. All infants had a normal Apgar score at birth (Apgar score of 7 – 10 at 5 min was considered “normal”). Eight (27%) infants had severe thrombocytopenia (counts  $<50 \times 10^9/L$ ) at birth; two of these thrombocytopenic infants had been delivered vaginally and developed petechiae. None showed any clinical sign of intracranial hemorrhage. All had normal results on cranial ultrasound screening. The lowest platelet count (nadir) occurred at a median of four days after delivery. During the first days of life, 10 (33%) of 30 infants had platelet counts of  $<100 \times 10^9/L$ . Five infants had platelet counts of  $<50 \times 10^9/L$  and one had  $<20 \times 10^9/L$  (Table 3). Two infants required corticosteroid therapy and IV Ig.

## Discussion

The diagnosis of ITP is difficult when it is encountered during pregnancy, since ITP cannot be distinguished with certainty from the incidental thrombocytopenia of pregnancy. Therefore, although history is important, when no prior platelet counts are available and other causes of thrombocytopenia have been excluded. ITP is, therefore, a diagnosis of exclusion. The differential diagnosis comprises all other causes of thrombocytopenia, including drug reactions, sepsis, DIC, (AIDS), myeloproliferative disorder.<sup>8,4,10</sup>

Only measurement of blood pressure, evaluation of liver function, and HIV antibody screening in patients with risk factors for HIV are

**Table 2.** Mode of delivery in 30 women.

Mode of delivery	n (%)
Vaginal	11 (37%)
Elective cesarean section	8 (42%)
Cesarean due to obstetric reasons	11 (21%)

**Table 3.** Infants' platelet count at birth and during the first days of life (n = 30).

Platelet count $\times 10^9/L$	At birth n (%)	After several days n (%)
$\geq 150$	10 (33%)	17 (57%)
100 – 150	5 (17%)	3 (10%)
50 – 99	8 (27%)	5 (17%)
20 – 49	7 (23%)	4 (13%)
<20	0	1 (3%)

considered necessary in the recommendations given by the American Society of Hematology. Management of a pregnant patient with ITP is similar to that of nonpregnant individuals. Due to their efficacy and low cost, many consider corticosteroids as the first line of therapy.<sup>3, 8, 2, 11</sup> Treatment with 1 – 2 mg/kg of prednisone will raise the platelet count in two-thirds of the patients. Nonetheless, relapse is exceedingly common. Moreover, in addition to their usual side effects such as osteoporosis and weight gain, corticosteroids increase the incidence of pregnancy-induced hypertension and exacerbation of gestational diabetes. An alternate to corticosteroids is IV Ig; due to its lower toxicity profile, some experts consider it as the first-line therapy for pregnancy-associated ITP.<sup>2, 12</sup>

High doses (400 mg/kg) of immunoglobulin, given intravenously over five days, result in satisfactory platelet count elevation in two-thirds of patients.

In this study, 14 of 28 patients needed treatment with corticosteroids, because of severe thrombocytopenia and bleeding. No complication of steroids occurred in any of pregnant women. An area of particular concern in the management of pregnant patients with ITP is the fetal platelet count and its implications for the mode of delivery. Due to the transplacental passage of maternal IgG, particularly during the third trimester, the offspring of patients with ITP may also develop thrombocytopenia. Neonatal platelet counts of  $<50 \times 10^9/L$  at delivery occur in 10 – 25% of the offspring of patients with ITP, while counts of  $<20 \times 10^9/L$  occur in 5% of these patients.<sup>7, 13, 14</sup> Pregnancy outcome in this study was generally good. In this study, 23% of offspring of patients with ITP were severely thrombocytopenic. Moreover, there is no reason to believe that maternal treatment can diminish the incidence of fetal thrombocytopenia.<sup>14</sup> Bleeding complications may occur in thrombocytopenic neonates at the time of delivery, though intracranial hemorrhage is rare.<sup>14, 2</sup> In this study, there was no severe bleeding complications

in the thrombocytopenic neonates. These results are similar to the most recent studies reporting low fetal morbidity and mortality associated with maternal ITP. A review of the literature over 20 years included 474 women with ITP.<sup>15</sup> Approximately, 15% of infants were found to have severe thrombocytopenia. The incidence of intracranial hemorrhage among infants with severe thrombocytopenia was 4% after cesarean delivery, as compared with 5% after vaginal delivery. This is statistically significant.

Burrows and Kelton in 1993,<sup>4</sup> reported on their large series of maternal platelet counts collected from all the women admitted over a 6-year period to the Labor and Delivery Wards at McMaster University (n = 15,607), as well as cord blood platelet counts at the time of delivery (15,932 samples). Of 46 women with ITP, four infants were born with severe thrombocytopenia. Three of these four infants were delivered vaginally and one by cesarean section. No infant experienced intracranial hemorrhage.<sup>3, 11</sup> A literature review of 18 studies on maternal ITP involved 601 neonates.<sup>16</sup> Severe thrombocytopenia occurred in 72 (12.0%) of 601 neonates. Intracranial hemorrhage occurred in 6 (1.0%) out of 601 neonates and was unrelated to the mode of delivery. The rate of PUBS was 4.6%.

Since there is no maternal clinical or laboratory characteristics predictive for neonatal thrombocytopenia, the fetal platelet count could be determined either through fetal scalp sampling during labor or by PUBS prior to delivery. Of these, the latter method provides a more reliable estimate, although it is associated with a complication rate, primarily being bleeding and fetal bradycardia (0 – 1%).<sup>14</sup> Since this method would approach or exceed the incidence of severe thrombocytopenia complications in the offspring of patients with ITP, two different approaches for the management of these patients have been proposed. One approach, supported by approximately 60% of perinatologists in the United States, advocates a trial of labor for patients with ITP without prior determination of the fetal platelet count. This approach is based on the belief that severe thrombocytopenia and bleeding in the offspring of these individuals are uncommon and that there is no evidence that the incidence of fetal intracranial hemorrhage is reduced by cesarean section. The second approach involves invasive determination of the fetal platelet count, generally by PUBS, followed by cesarean section if the

platelet count is  $<50 \times 10^9/L$ . None of the women in our series were subjected to PUBS.

In our study, 19 of 30 deliveries were cesarean sections. Eight (42%) of them were performed for hematologic reasons. With the exception of three women who themselves requested cesarean section for ITP, the remaining women had hematologic reasons for the operation. The percentage of cesarean deliveries was far higher than that of other studies. Postpartum hemorrhage is a theoretical complication in patients with ITP. However, eight of the women in our study suffered from this complication.

However, the neonatal platelet nadir occurred several days after delivery and only five infants had a platelet count of  $<50 \times 10^9/L$ .

Regardless of the mode of delivery, cord platelet counts should be obtained from all the neonates born to mothers with ITP at the time of delivery. Moreover, since the platelet count may decline within the first 4 – 5 days after delivery, daily monitoring and institution of appropriate therapy for severe thrombocytopenia, should it develop over this interval, is indicated.<sup>7, 2</sup> In this study, during the first days of life, 10 (33%) of 30 infants had platelet counts of  $<100 \times 10^9/L$ . Five infants had platelet counts of  $<50 \times 10^9/L$  and one had  $<20 \times 10^9/L$  (Table 3). Two infants required corticosteroid therapy and IV Ig. The outcome of pregnancy in those women with ITP was generally good. Cesarean section should be performed only for obstetric indications. Postpartum hemorrhage is common in these women but is unrelated to the mode of delivery. Thrombocytopenia and bleeding are not common among offsprings.

## References

- Gill KK, Kelton JG. Management of idiopathic thrombocytopenic purpura in pregnancy. *Semin Hematol.* 2000; **37**: 275 – 289.
- Burrows RF, Kelton JG. Thrombocytopenia at delivery: a prospective survey of 6,715 deliveries. *Am J Obstet Gynecol.* 1990; **162**: 731 – 734.
- No authors listed. ACOG practice bulletin: thrombocytopenia in pregnancy. Number 6, September 1999. Clinical management guidelines for obstetrician-gynecologists. American College of Obstetricians and Gynecologists. *Int J Gynaecol Obstet.* 1999; **67**: 117 – 128.
- Burrows RF, Kelton JG. Fetal thrombocytopenia and its relation to maternal thrombocytopenia. *N Engl J Med.* 1993; **329**: 1463 – 1466.
- Johnson JR, Samuels P. Review of autoimmune thrombocytopenia: pathogenesis, diagnosis, and management in pregnancy. *Clin Obstet Gynecol.* 1999; **42**: 317 – 326.
- Karim R, Sacher RA. Thrombocytopenia in pregnancy. *Curr Hematol Rep.* 2004; **3**: 128 – 133.
- Lescale KB, Eddleman KA, Cines DB, et al. Antiplatelet antibody testing in thrombocytopenic pregnant women. *Am J Obstet Gynecol.* 1996; **174**: 1014 – 1018.
- Peleg D, Hunter SK. Perinatal management of women with immune thrombocytopenic purpura: survey of United States perinatologists. *Am J Obstet Gynecol.* 1999; **180**: 645 – 649.
- Burrows RF, Kelton JG. Pregnancy in patients with idiopathic thrombocytopenic purpura: assessing the risks for the infant at delivery. *Obstet Gynecol Surv.* 1993; **48**: 781 – 788.
- George JN, el-Harake MA, Raskob GE. Chronic idiopathic thrombocytopenic purpura. *N Engl J Med.* 1994; **331**: 1207 – 1211.
- Sainio S, Joutsen L, Jarvenpaa AL, et al. Idiopathic thrombocytopenic purpura in pregnancy. *Acta Obstet Gynecol Scand.* 1998; **77**: 272 – 277.
- Letsky EA, Greaves M. Guidelines on the investigation and management of thrombocytopenia in pregnancy and neonatal alloimmune thrombocytopenia. Maternal and Neonatal Hemostasis Working Party of the Hemostasis and Thrombosis Task Force of the British Society for Hematology. *Br J Haematol.* 1996; **95**: 21 – 26.
- Payne SD, Resnik R, Moore TR, Hedriana HL, Kelly TF. Maternal characteristics and risk of severe neonatal thrombocytopenia and intracranial hemorrhage in pregnancies complicated by autoimmune thrombocytopenia. *Am J Obstet Gynecol.* 1997; **177**: 149 – 155.
- Lee MS, Kim WC. Intracranial hemorrhage associated with idiopathic thrombocytopenic purpura: report of seven patients and a meta-analysis. *Neurology.* 1998; **50**: 1160 – 1163.
- Cook RL, Miller RC, Katz VL, and Cefalo RC. Immune thrombocytopenic purpura in pregnancy: a reappraisal of management. *Obstet Gynecol.* 1991; **78**: 578 – 583.