Original Article

Pregnancy in Women with Idiopathic Thrombocytopaenic Purpura

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Abstract

***Introduction**: Idiopathic thrombocytopaenic purpura (ITP) is a common haematological disorder in young women. The management of ITP in pregnancy is controversial, particularly with regards to the mode of delivery. To date, there is no systematic study of the outcome of these pregnancies in Singapore. **Aim**: To study the outcomes of pregnancies in Asian women with a proven diagnosis of ITP. **Materials and Methods**: Retrospective study of 27 pregnancies in 18 women managed at the Singapore General Hospital from 1 January 1994 to 30 June 2001. **Results**: The mean age of the women was 30 years (range, 20 to 41 years) and the mean parity was 1 (range, 0 to 3). Thrombocytopaenia (platelet count <150 x 10^9/L) occurred in 18 pregnancies (67%). There were 3 first trimester missed abortions (11%), 1 termination of pregnancy (4%), 1 stillbirth (4%) and 22 livebirths (81%) in this series. The mode of delivery was spontaneous vaginal in 14 women (64%), vacuum extraction in 2 women (9%), elective caesarean section in 5 women (23%) and emergency caesarean section in 1 woman (4%). All liveborn neonates were delivered in good condition at term. Neonatal thrombocytopaenia occurred in 4 neonates (18%). Two neonates had cord platelet counts of less than 50 x 10^9/L and 1 required therapy with corticosteroids and intravenous immune globulins. No bleeding complications occurred in any of the neonates. **Conclusion**: Our experience supports the increasingly prevalent practice of managing pregnancies in women with ITP with a conservative approach to investigations and treatment. Caesarean sections should be performed for obstetric indications only, given the rarity of bleeding complications in the offspring of these women and the lack of evidence to support its role in the prevention of neonatal intracranial haemorrhage.*

Ann Acad Med Singapore **2002; 31:276-80**

Key words: Caesarean section, Corticosteroid, Intracranial haemorrhage, Platelet count

Introduction

Idiopathic thrombocytopaenic purpura (ITP) is the most common autoimmune haematological disorder in pregnancy. The pathophysiology of the disease is peripheral destruction of platelets mediated by antiplatelet antibodies.[1] These antibodies readily cross the placenta into the fetal circulation. Hence, neonatal thrombocytopaenia and its attendant risk of haemorrhagic manifestations, particularly intracranial haemorrhage, are potentially serious consequences of the disease.

There are many controversies in the management of these women. Caesarean section has been advocated to prevent fetal intracranial haemorrhage.[2] However, the value of this has been questioned as this intervention has had little effect on the incidence of affected neonates.[3] In addition, the maternal platelet count is a poor predictor of fetal thrombocytopaenia and is not useful in identifying the pregnancies that may be at risk of fetal haemorrhage.[4] Fetal blood sampling via cordocentesis has been used to quantify fetal platelet counts,[5] though even this practice is of doubtful value, given the rarity of poor neonatal outcomes in these women and the inherent risks of this diagnostic procedure.

We present the outcomes of 27 pregnancies in 18 women with proven ITP managed at the Singapore General Hospital over the last 7 years.

Materials and Methods

Case records of all pregnant women seen at our institution with a known diagnosis of ITP before the index pregnancy from 1 January 1994 to 30 June 2001 were reviewed. The diagnosis of ITP was based on thrombocytopaenia (platelet count less than 150 x 10^9/L on more than one occasion), presence of normal or increased megakaryocytes in the bone marrow aspirate and the absence of other causes of thrombocytopaenia such as pregnancy-induced hypertension, systemic lupus erythematosus, disseminated

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intravascular coagulation and drug-induced thrombocytopaenia. Patients with incidental thrombocytopaenia of pregnancy, a condition frequently confused with ITP, were excluded.

The maternal records were studied for demographic data, maternal platelet counts, antenatal treatment with corticosteroids or intravenous immune globulins (IVIG), previous splenectomy, mode of delivery and complications. Neonatal records were reviewed for outcome, cord platelet count, the platelet nadir (the lowest recorded neonatal platelet count) and treatment. Neonatal platelet counts were performed serially for at least the first week of life.

Results

There were 27 pregnancies from 18 women during the study period. The mean age of the women was 30 years (range, 20 to 41 years) and the mean parity was 1 (range, 0 to 3). The women consisted of 11 Chinese, 3 Malays, 3 Indians and 1 Caucasian. These racial proportions are not significantly different from that of the general population of women seen in our unit.

The maternal and fetal characteristics of these pregnancies were studied in relation to the lowest maternal platelet count in the antenatal period. In 18 pregnancies (67%), there was thrombocytopaenia of varying degrees in the antenatal period (platelet count <150 x 10^9/L). In the remaining 9 pregnancies (33 %), there were normal antenatal platelet counts, largely as a result of splenectomies which had been performed prior to the index pregnancy. Details of maternal therapy are shown in Table I.

The mainstay of maternal therapy was corticosteroids and IVIG. Corticosteroids in the form of oral prednisolone were used in doses ranging from 5 to 60 mg/day in a total of 13 women (48%), while IVIG were used in 10 women (37%). The administration of IVIG resulted in a median increase in the platelet count by 74 x 10^9/L (range, 6 to 141 x 10^9/L) within 7 days. The pregnancy outcomes of these women are shown in Table II.

The 3 women, who had missed abortions in the first trimester, underwent evacuation of retained products of conception under general anaesthesia without complications. One patient had a legal termination of pregnancy for social reasons and underwent a laparoscopic sterilisation at the same surgery. Of the 23 pregnancies that progressed to the third trimester, 1 woman had a stillbirth at 32 weeks from abruptio placenta. She was admitted at 31 weeks for non-proteinuric hypertension. Laboratory tests showed normal biochemistry and the blood pressure subsequently normalised while being monitored in the antenatal ward. She was discharged well and scheduled to return 1 week later for a follow-up visit. However, she presented at the Accident and Emergency Department 5 days after discharge following an eclamptic fit. Subsequent investigations confirmed intrauterine death of the fetus. Labour was subsequently induced, resulting in the delivery of a fresh stillbirth which was morphologically normal. Placental abruption was confirmed at delivery. The remaining 22 pregnancies resulted in livebirths at term.

TABLE I: MATERNAL THERAPY

Maternal platelet count (x 10^9 /L)	No. of pregnancies	Corticosteroid therapy	IVIG	Previous splenectomy
>150	9	0	0	5
100 to 150	4	2	0	1
50 to 99	5	2	1	0
<50	9	9	9	1

IVIG: intravenous immune globulins

TABLE II: PREGNANCY OUTCOMES

Outcome	No. of pregnancies (n = 27)
First trimester missed abortion	3 (11%)
Termination of pregnancy	1 (4%)
Stillbirth	1 (4%)
Livebirth	22 (81%)

TABLE III: MODE OF DELIVERY

Mode of delivery	No. of women (n = 22)
Spontaneous vaginal delivery	14 (64%)
Vacuum extraction	2 (9%)
Forceps	0
Elective caesarean section	5 (23%)
Emergency caesarean section	1 (4%)

The mode of delivery of these pregnancies is summarised in Table III. Mode of delivery was determined based on obstetric indications. As a rule, elective caesarean section was not performed for the sole indication of ITP in pregnancy given the lack of evidence to support its role in the prevention of fetal intracranial haemorrhage. The exception was 1 woman who, following a discussion of this and the risks of caesarean section, elected to have one. She delivered an infant who did not have thrombocytopaenia. Of interest was the fact that this woman subsequently had 2 other pregnancies in which she consented to a trial of vaginal delivery. In both these pregnancies, she had spontaneous vaginal deliveries and the neonates had normal platelet counts. The remaining 4 patients had elective caesarean sections for breech presentation, pre-eclampsia, previous caesarean section and a cerebral arteriovenous malformation that was deemed a contraindication to labour and vaginal delivery by her neurologist. One woman had an emergency caesarean section for fetal distress and meconium-stained

liquor in labour, while in the remaining 16 pregnancies, vaginal delivery was achieved.

All 22 neonates were born in good condition. Four neonates had thrombocytopaenia. Details of neonatal outcome and therapy are shown in Table IV. Details of neonatal thrombocytopaenia and complications in this series are compared with those of other recently published studies in Table V.

Discussion

Idiopathic thrombocytopaenic purpura is an autoimmune disorder with its highest frequency in young women in the reproductive years. Consequently, obstetricians and haematologists will occasionally need to manage pregnancies in these women. While management of the pregnant woman with known ITP can be guided by the maternal platelet count, management of the fetus is much more difficult because its platelet count is not readily obtained or predicted. Until fairly recently, the clinical impact of ITP was not well understood and was based on retrospective case reports.[10] The belief that at least some of the babies born to mothers with ITP could be severely thrombocytopaenic and, hence, be at risk for intracranial haemorrhage at the time of delivery led to the practice of caesarean section in an effort to prevent this serious complication.[2] However, the rarity of neonatal thrombocytopaenia in infants of these women and the even rarer occurrence of haemorrhagic complications does not justify this approach.

The diagnosis of ITP in a pregnant woman can be difficult. There is a physiological drop in the platelet count during an uncomplicated pregnancy.[11] Occasionally, this drop is sufficiently pronounced to lead to maternal thrombocytopaenia, a condition called incidental thrombocytopaenia of pregnancy. Unlike ITP, this condition does not warrant treatment as there is no risk of maternal haemorrhage or neonatal thrombocytopaenia. It is for this reason that, in this study, we included only patients with an established diagnosis of ITP prior to the index pregnancy. Our series of 27 women were jointly managed by a team of obstetricians, haematologists and neonatologists. The widespread implications of ITP on mother, unborn fetus and neonate demand that management of these women must take such a multi-disciplinary approach.

In terms of therapy, we managed these pregnancies based on the severity of the maternal ITP. Women with a normal platelet count or only mild thrombocytopaenia were managed with close observation and serial platelet estimations only. When pharmacological therapy was required, we used corticosteroids in the form of prednisolone or intravenous hydrocortisone when oral intake was not possible, for example when a caesarean section had been performed. This has been shown to be safe in pregnancy and potential fetal toxicity, such as adrenal suppression, is unlikely since almost all prednisolone is metabolised by the placenta.[12] High-dose IVIG were used to raise the platelet count particularly when delivery was imminent. This has the advantage of causing a prompt rise in the

TABLE IV: MODE OF DELIVERY AND THERAPY IN THROMBOCYTOPAENIC NEONATES

Maternal platelet count (x 10^9/L)	Mode of delivery	Birthweight (g)	Neonatal cord platelet count (x 10^9/L)	Neonatal platelet nadir (x 10^9/L)	Neonatal therapy (x 10^9/L)
49	SVD	3070	99	26 (day 6)	Nil
5	SVD	2340	32	2 (day 6)	IVIG/Steroids
5	SVD	2800	26	8 (day 4)	Nil
12	Elective LSCS	2675	192	48 (day 8)	Nil

IVIG: intravenous immune globulins; LSCS: lower segment caesarean section; SVD: spontaneous vaginal delivery

TABLE V: NEONATAL THROMBOCYTOPAENIA AND COMPLICATIONS IN WOMEN WITH ITP—COMPARISON WITH OTHER STUDIES

Study	Year of publication	No. of pregnancies	Neonatal cord blood thrombocytopaenia		Caesarean section	Neonatal complications	
			<50 x 10^9/L	<20 x 10^9/L		Minor*	Major**
Garmel et al[5]	1995	39	5	3	7 (18%)	0	0
Christiaens et al[6]	1997	68	10	6	22 (32%)	0	2
Al-Jama et al[7]	1998	28	4	0	10 (36%)	0	1
Ajzenberg et al[8]	1998	63	4	1	19 (30%)	1	0
Valat et al[9]	1998	64	8	2	25 (39%)	0	0
Present study	2002	22	2	0	6 (27%)	0	0

ITP: idiopathic thrombocytopaenic purpura

* Minor complications: petechiae, cephalohaematoma, haematuria, mild gastrointestinal bleeding and umbilical bleeding.

** Major complications: intracranial haemorrhage, severe gastrointestinal bleeding and bloody pericardial effusion.

platelet count. The disadvantages of this treatment lie in its relatively transient effect (typically about 1 month) and its high cost. In addition, there is the small risk of serious complications such as anaphylactic reactions[13] and transmission of hepatitis C[14] as a result of IVIG use. It is worth remembering that, at present, there is no evidence that maternal therapeutic interventions result in a reliable rise in the fetal platelet count.

Pregnancy outcome in this study was generally good. The first trimester pregnancy loss rate of 11% is within the norms described for the general population.[15] Similarly, the only stillbirth in the study was attributable to a placental abruption in a woman with eclampsia and, hence, was unrelated to maternal ITP. The remaining pregnancies progressed to term. Traditionally, mothers with ITP delivered their babies by caesarean section. This strategy was based on 2 assumptions that are now known to be untrue. Firstly, it was thought that maternal ITP carried with it a high risk of neonatal thrombocytopaenia. Analysis of retrospective and prospective data published in the last decade, which included more than 1000 infants born to mothers with ITP, shows that less that 10% of these infants will have a platelet count of less than 50 x 10^9/L.[16] The second assumption was that vaginal delivery carried a greater risk of intracranial haemorrhage to the neonate than caesarean section. Evidence from large studies shows that this is not the case.[2] In addition, operative delivery in these women requires intervention in the form of IVIG and blood and platelet transfusions which ultimately result in longer hospitalisations and increased costs. The caesarean section rate in this series was 27%. With the exception of 1 woman who requested a caesarean section for ITP, the remaining women had obstetric indications for operative delivery. It is notable that 2 women had vacuum extractions without complication. There is evidence to suggest that neonates delivered by vacuum extraction are more likely to sustain cephalohaematomata than those who are delivered by obstetric forceps. This complication may be potentially harmful to a thrombocytopaenic neonate. In these 2 cases, vacuum extraction was still undertaken because, in the assessment of the obstetrician, the delivery could be easily achieved with minimal traction to the fetal scalp. In addition, the 2 women had entirely normal platelet counts antenatally and did not require pharmacological therapy. As we point out later in this discussion, this group of women were unlikely to deliver neonates with thrombocytopaenia. While postpartum haemorrhage is a theoretical risk in ITP, none of the women in this study suffered this complication. There were also no cases of genital tract haematoma or vaginal and perineal lacerations.

The most challenging aspect of managing ITP in pregnancy is the recognition that a small percentage of neonates can have severe thrombocytopaenia. Attempts to predict which infants will be affected using maternal parameters such as the platelet count or the level of maternal platelet-associated immunoglobulin (PAIgG) have been unsuccessful.[17] Invasive techniques, such as cordocentesis which involves the ultrasound-guided aspiration of fetal blood from umbilical vessels in order to establish the fetal platelet count, have been utilised. Unfortunately, there are significant fetal risks with this technique such as fetal distress, fetal bleeding and death. The overall rate of perinatal loss for cordocentesis has been reported[18] as 2.7% and may be even higher in the setting of severe fetal thrombocytopaenia.[19] It would, therefore, be difficult to justify the procedure when the true risk of bleeding in ITP infants is less than 1%.[2] In recognition of this, none of the women in our series were subjected to the procedure. In addition, knowledge of the fetal platelet count would not have significantly altered our management of these women, given the lack of evidence to support the role of maternal therapy or caesarean section in preventing fetal intracranial haemorrhage.

The incidence of neonatal thrombocytopaenia in this study, as evidenced by thrombocytopaenia in either the cord platelet count or subsequent neonatal platelet count, was 18%. While it is true that prediction of the neonatal platelet count from the maternal count is not possible, we note that all 4 thrombocytopaenic neonates were born to mothers whose lowest antenatal platelet count was less than 50 x 10^9/L. Hence, in our experience, the lowest antenatal maternal platelet count may be a useful parameter to identify the group of women who are likely to deliver thrombocytopaenic neonates. The lowest count is likely to be a better indicator of the severity of the underlying maternal disease than the platelet count at delivery, which has usually been elevated from platelet transfusions and IVIG infusions in preparation for the process of labour and delivery. It is recognised that infants born to mothers with ITP will have a fall in their platelet count over the first few days of life following delivery. This platelet nadir is of little significance as it occurs several days after birth whereas it is the actual process of delivery which poses the greatest risk for neonatal intracranial haemorrhage. In this study, the neonatal platelet nadir occurred between day 4 to day 8 in the 4 affected infants. If only neonatal cord platelets were considered, 3 neonates had thrombocytopaenia and only 2 had a cord platelet count of less than 50 x 10^9/L. No bleeding complications, minor or major, occurred in these infants. We also note that all 3 infants who had thrombocytopaenia in their cord platelet counts were delivered vaginally.

The results of this study are comparable with other recently published studies (Table V). The universal finding is that the incidence of severe neonatal thrombocytopaenia and neonatal bleeding complications is remarkably low.

The caesarean section rate in our series compares favourably with other studies.

To summarise, our study showed that:

1. Neonatal intracranial haemorrhage is a rare complication of maternal ITP.
2. Maternal therapy has not been shown to improve neonatal platelet counts.
3. Non-invasive testing is unreliable and invasive fetal tests carry significant risks.
4. Fetal haemorrhage is unrelated to the mode of delivery.

Therefore, we conclude that pregnancy in women with ITP should be managed conservatively and caesarean section should be performed for obstetric indications only. Although the risk of neonatal intracranial haemorrhage is low, we recognise that the catastrophic nature of this complication still demands a cautious approach. A comprehensive discussion with the pregnant woman and her partner and their involvement in the decision-making process, particularly with regards to mode of delivery, is therefore essential.

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