Neonatal Outcomes of Pregnancy with Immune Thrombocytopenia

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Abstract Neonates born to mothers with immune thrombocytopenia (ITP) have an increased risk for neonatal thrombocytopenia and hemorrhagic complications. The aim of this study was to determine the maternal and neonatal outcomes of pregnancies with ITP and also to identify risk factors that predicts neonatal thrombocytopenia. We performed a retrospective analysis of 40 pregnancies with ITP and their 40 neonates. Among the 40 neonates, thrombocytopenia (platelet count of less than $150 \times 10^9/L$) was detected in 15 neonates (37.5 %) whom 8 of them had severe thrombocytopenia (platelet count of less than $50 \times 10^9/L$). Ten of the 15 neonates with thrombocytopenia required treatment to increase the platelet counts. There was statistically significant association between neonatal thrombocytopenia and maternal splenectomy history and maternal duration of thrombocytopenia. There was no statistically significant correlation between maternal platelet count and neonatal platelet count. Clinicians should pay special attention in these neonates because of risk for development of neonatal thrombocytopenia. Maternal and neonatal outcomes in patients with idiopathic thrombocytopenic purpura is generally good.

Keywords Immune thrombocytopenia · ITP · Neonatal thrombocytopenia · Newborn

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Introduction

Thrombocytopenia is a common finding in pregnancy and occurs approximately 7–10 % of pregnancies [1]. Overall, about 3–4 % of thrombocytopenia of pregnancies is due to an immune process [2]. Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by low platelet counts and the involvement of platelet autoantibodies. It tends to occur in young women who are especially in the reproductive ages [3]. It is well known that pregnancy affects course of autoimmune disorders [4]. Maternal autoantibodies can transport through the placenta and target platelet membrane glycoproteins. Neonatal platelets are destroyed by these autoantibodies and therefore neonatal thrombocytopenia, which is the major problem associated with maternal ITP, occurs. The incidence of neonatal thrombocytopenia has been reported in previous studies. Both maternal and neonatal thrombocytopenia may be associated with complications such as major hemorrhage or petechial rashes.

It is important to predict neonatal thrombocytopenia because of the risk of major hemorrhagic complications like intracranial hemorrhage (ICH) so that several risk factors have been explored by previous studies.

In this study, we investigated neonates with and without thrombocytopenia born to mothers with ITP and we aimed to determine the maternal and neonatal outcomes and also identify risk factors that predicts neonatal thrombocytopenia.

Materials and Methods

A retrospective chart review was performed for all obstetric patients with ITP who were treated and delivered at Gaziantep University Hospital from January 2011 to

August 2015. Therefore, a total of 40 pregnancies and their infants were eligible for this study.

Maternal ITP had been diagnosed by a hematologist if they met the standard criteria of ITP: isolated thrombocytopenia ($<150 \times 10^9/L$) with normal white and red blood cell counts, normal or increased number of megakaryocytes identified by bone marrow examination, and absence of other known causes such as incidental gestational thrombocytopenia, preeclampsia, HELLP syndrome (hemolysis, elevated liver enzyme levels, low platelets), viral infections or systemic lupus erythematosus etc. The following information was extracted from the medical charts for each patient: age, parity, time of diagnosis, treatment for ITP, platelet count in early pregnancy and at delivery, history of prior splenectomy, bleeding tendency during pregnancy, mode of delivery, gestational age at delivery, neonatal birth weight, APGAR scores, cord artery pH, neonatal platelet count at birth and at nadir, need and nature of postnatal treatment, duration of neonatal thrombocytopenia and occurrence of intracranial or gastrointestinal hemorrhage.

Antenatal need for maternal treatment was assessed by both obstetrician and hematologist. Type and time of delivery was based on only obstetric conditions. Patients were treated with standard ITP treatment regimens, including corticosteroid, intravenous immunoglobulin (IVIG) and if necessary platelet transfusion.

At birth, neonatal platelet counts were performed in blood samples obtained by peripheral venous blood sampling as soon as possible on the first day of life. Normal platelet count was defined as $>150 \times 10^9/L$. Neonatal platelet counts of $100 \times 10^9/L$ – $150 \times 10^9/L$ represent “mild thrombocytopenia”, platelet count of $50 \times 10^9/L$ – $100 \times 10^9/L$ is considered as “moderate thrombocytopenia” and platelet counts of less than $50 \times 10^9/L$ is considered as “severe thrombocytopenia”.

SPSS, version 16.0 (SPSS Inc., Chicago, IL, USA), was used for data analyses. A Chi squared test was used for analysis of qualitative data. The categorical variables between two groups were compared using Fisher’s exact test and Mann–Whitney *U* test for numerical data. Evaluation of correlation between maternal and neonatal platelet count was performed by Pearson correlation test. A *p* value <0.05 was considered statistically significant.

Results

During the study period, 40 women with ITP delivered 40 neonates and all of them enrolled in this study. There was no delivery of twins. Characteristics of pregnant are summarized in Table 1. Maternal platelet count at delivery was $\geq 150 \times 10^9/L$ in 4 pregnancies (10 %), 100 – $150 \times 10^9/L$ in 5 pregnancies (12.5 %),

Table 1 Maternal characteristics (*n* = 40)

Characteristics	Median (range) or number (%)
Maternal age (years)	27.97 (18–41)
Parity, <i>n</i> (%)	
Primiparous	11 (27.5)
Multiparous	29 (72.5)
Diagnosis of ITP, <i>n</i> (%)	
Before pregnancy	22 (55)
During pregnancy	18 (45)
Time since diagnosis (<i>n</i> = 22) (years)	7.7 (2–22)
Prior splenectomy, <i>n</i> (%)	10 (25)
Platelet count	
In early pregnancy ($\times 10^9/L$)	94.5 (9–238)
At delivery ($\times 10^9/L$)	81.8 (28–222)
Bleeding tendency during pregnancy, <i>n</i> (%)	5 (12.5)
Treatment for ITP during pregnancy, <i>n</i> (%)	34 (85)
Only PSL	6 (17.6)
Only IVIG	1 (2.9)
Only platelet transfusion	9 (26.5)
PSL + platelet transfusion	9 (26.5)
IVIG + platelet transfusion	2 (5.9)
PSL + IVIG + platelet transfusion	7 (20.6)
Mode of delivery <i>n</i> (%)	
Vaginal	12 (30)
Cesarean section	28 (70)

100 – $50 \times 10^9/L$ in 20 pregnancies (50 %) and $<50 \times 10^9/L$ in 11 pregnancies (27.5). Only five cases had bleeding tendency during pregnancy and all of them were diagnosed ITP before pregnancy. There was no maternal death.

Of the 40 pregnancies, 34 (85 %) were treated for ITP during pregnancy and only six (15 %) had no treatment. Women in 15 pregnancies were newly started for treatment during pregnancies. The treatment option for one pregnancy was IVIG, for nine pregnancies was platelet transfusion, for six pregnancies was corticosteroid (oral administration of prednisolone-PSL), for two pregnancies were both IVIG and platelet transfusion, for nine pregnancies were both PSL and platelet transfusion and for seven pregnancies all of them were used.

A total of 40 babies were born and all of their APGAR scores were normal and there was no asphyxiated baby. Characteristics of neonates are summarized in Table 2. The comparison of characteristics of neonates with and without thrombocytopenia is shown in Table 3.

Ten neonates (25 %) were treated for thrombocytopenia. Treatment decision was made if neonates had severe thrombocytopenia or clinical findings of thrombocytopenia such as petechial and bleeding. All of them received IVIG at first, after that 7 of them received additional

Table 2 Neonatal characteristics (*n* = 40)

Characteristics	Median (range) or number (%)
Gestational age at birth (weeks)	37.8 (34–40)
Birth weight (grams)	2966 (2150–3920)
APGAR score at 1 min	7.98 (5–9)
APGAR score at 5 min	9.2 (6–10)
Neonatal platelet count at birth ($\times 10^9/L$)	150.5 (6–358)
Neonatal platelet count at birth ($\times 10^9/L$) <i>n</i> (%)	
$\geq 150 \times 10^9/L$	25 (62.5)
$100\text{--}149 \times 10^9/L$	4 (10)
$50\text{--}99 \times 10^9/L$	3 (7.5)
$20\text{--}49 \times 10^9/L$	4 (10)
$<20 \times 10^9/L$	4 (10)
Neonatal platelet count at nadir ($\times 10^9/L$)	147.3 (4–358)
Treatment for neonatal thrombocytopenia <i>n</i> (%)	10 (25)
IVIG	10 (25)
IVIG + PSL	7 (17.5)
IVIG + PSL + platelet transfusion	1 (2.5)
Hemorrhage	1 (2.5)
Need for packed red cell	1 (2.5)
Mortality	1 (2.5)

corticosteroid therapy, and only one of them needed platelet transfusion during therapy (Table 4). IVIG was given as 1 g/kg/day for two consecutive days. Corticosteroid (methylprednisolone) was used at a dosage of 2 mg/kg/day in all neonates. Only one neonate had gastrointestinal system bleeding and needed platelet and packed red cell transfusion, but he died.

Among 15 neonates with thrombocytopenia, 5 neonates did not require any treatment and platelet counts increased spontaneously.

Routine cranial ultrasound examination showed no intracranial hemorrhage in 15 neonates with thrombocytopenia.

Discussion

ITP is an autoimmune disorder caused by autoantibodies against several platelet membrane glycoproteins and results platelet destruction in the reticuloendothelial system. Neonates born to mothers with ITP have risk for thrombocytopenia and its complications.

Thrombocytopenia has been reported in 50.7 % and severe thrombocytopenia has been observed in 29.9 % in neonates with maternal ITP [5]. In an another study, 48 % of neonates born to mothers with ITP had thrombocytopenia at birth [6]. Subbaiah et al. [7] has also reported that 18.5 % of neonates born to mothers with ITP had

severe thrombocytopenia and 3.7 % of them had intracranial hemorrhage. In this retrospective study, thrombocytopenia was seen 37.5 % of neonates and the incidence of mild, moderate and severe thrombocytopenia was 10, 7.5, 20 %, respectively. This findings are similar to those in prior studies [8, 9].

Bayhan et al. [10] has reported administration of medical treatment for neonatal thrombocytopenia in 33 % neonates and there was no treatment related complications. In our study, 10 neonates (25 %) had treatment for thrombocytopenia.

Recent studies have attempted to determine which factors may predict thrombocytopenia in newborns with maternal ITP. Maternal disease severity has been reported as an indicator for predicting neonatal platelet count [11]. In our study, time since diagnosis of ITP and maternal splenectomy history were shown to be risk factors for the development of thrombocytopenia. Valat et al. [12] have also reported an association between the history of maternal splenectomy and neonatal thrombocytopenia. In Koyama's and Hachisuga's retrospective studies, they could not find a positive association between maternal splenectomy and neonatal thrombocytopenia [13, 14]. In their study group there were 127 pregnancies, but only five mother had prior splenectomy, so sample size was small.

Several studies have found poor correlation between maternal and neonatal platelet counts [9–15]. In agreement with these studies, we could not find a correlation between these counts. Maternal platelet count during pregnancy or at the time of delivery was not predictive of the neonatal platelet count at birth.

Our data showed no difference between route of delivery and neonatal thrombocytopenia. In contrast, Kawaguchi showed that a decline of neonatal platelet count after vaginal delivery when compared with cesarean section [16]. Koyama et al. [13] speculate that uterine contractions during vaginal delivery facilitate transplacental transfer of antiplatelet antibodies and this contribute the decline of platelet counts in newborns.

Ozkan et al. [6] showed that maternal age and male gender were risk factors for development of neonatal thrombocytopenia. In our study, there was no significant correlation between those parameters and neonatal thrombocytopenia but in neonatal severe thrombocytopenia group, male gender is a significant risk factor (p 0.027). We found in this study that maternal age is not an important risk factor for neonatal thrombocytopenia. This may result from our small sample size.

Neonatal intracranial hemorrhage associated with maternal ITP has been reported in several studies. Furthermore, intracranial hemorrhage may also develop prenatally [17]. The overall incidence of major hemorrhagic manifestations in this group was reported as approximately

Table 3 Association of risk factors and neonatal thrombocytopenia

Parameter	Neonates with thrombocytopenia ($<150 \times 10^9/L$) (n = 15)	Neonates without thrombocytopenia ($\geq 150 \times 10^9/L$) (n = 25)	p
Maternal age	26.33 (18–35)	28.96 (19–41)	0.066
Time since diagnosis (years)	8.47 (0–22)	1.72 (0–8)	0.001
Multiparity	13 (86.7 %)	16 (64 %)	0.158
Maternal plt count during early pregnancy	79.2 (9–238)	103.68 (9–238)	0.229
Maternal plt count at delivery	87.67 (28–222)	78.24 (30–207)	0.625
Maternal history of treatment	13 (86.7 %)	21 (84 %)	1.000
Maternal history of splenectomy	9 (60 %)	1 (4 %)	<0.001
Maternal PSL therapy	8 (53.3 %)	14 (56 %)	1.000
Maternal plt transfusion	8 (53.3 %)	19 (76 %)	0.175
Maternal IVIG therapy	3 (20 %)	7 (28 %)	0.715
Gestational age (week)	37.33 (34–40)	38.08 (36–40)	0.376
Cesarean delivery	12 (80 %)	16 (64 %)	0.477
Birth weight (g)	3000.67 (2200–3800)	2946.4 (2150–3920)	0.727
Male sex	9 (60 %)	13 (52 %)	0.747

Table 4 Clinical profiles of neonates with thrombocytopenia

n	Sex	GW	BW	Del	Mat plt early	Mat plt del	Neonatal platelet count	Neonatal treatment	Ivlg	PsI	Tx
1	m	38	3000	cs	120	93	21	Yes	+	+	–
2	m	35	2400	cs	100	137	9	Yes	+	–	–
3	f	35	2600	cs	160	29	31	Yes	+	–	+
4	m	38	2930	cs	76	79	10	Yes	+	+	–
5	m	39	3100	cs	21	58	22	Yes	+	+	–
6	m	38	2900	cs	65	78	6	Yes	+	+	–
7	m	36	2950	nvd	9	55	6	Yes	+	+	–
8	f	39	3400	cs	26	40	103	No	–	–	–
9	f	39	3080	nvd	40	28	113	No	–	–	–
10	f	38	3700	cs	70	71	108	No	–	–	–
11	f	39	3500	nvd	73	93	102	No	–	–	–
12	m	34	2250	cs	67	222	61	Yes	+	+	–
13	m	35	2200	cs	80	190	45	Yes	+	+	–
14	f	40	3800	cs	238	70	98	No	–	–	–
15	m	38	3200	cs	56	40	20	Yes	+	–	–

m male, f female, gw gestation week, bw birth weight, del: delivery route, cs cesarean section, nvd normal vaginal delivery, mat plt early early maternal platelet count, mat plt del maternal platelet count at delivery, ivlg intravenous immunoglobuline, psI prednisolone, tx platelet transfusion

1 % of cases [18]. It was also concluded that the risk of ICH estimated at less than 1 % and unlikely to be related by the mode of delivery [19]. For this reason, route of delivery must rely on only obstetrical considerations. There is no evidence that caesarean section is safer for the thrombocytopenic fetus [2]. In our study, no cases had ICH and this finding is also in good agreement with previous studies [3–20] but only one case had fatal gastrointestinal hemorrhage (2.5 %).

Some studies have reported increased incidence of preterm delivery in pregnancies with ITP [21]. In our study, we did not find any increased risk of preterm delivery, mean gestational age was 37.8 weeks.

In pregnant with ITP, therapy is similar with non pregnant. Primary treatment options for maternal ITP are corticosteroids and IVIG [22]. Corticosteroids are considered safe and effective for mother. Prednisolone, is metabolized by the placenta and in high doses have

potential risks for the fetus including premature rupture of membranes and cleft lip anomaly. In our study there was no congenital anomaly.

Our study has several limitations. The first limitation is the retrospective study design. Because of this, we were unable to have information about maternal antiplatelet antibody levels or thrombocytopenia in other siblings and their association with neonatal thrombocytopenia. Also, postnatal platelet count was not repeated for every neonate with a normal platelet count at birth, so the nadir platelet count was assumed to be identical to the platelet count at birth.

In conclusion, management of ITP in pregnancy requires close collaboration between obstetrician, hematologist, anesthetist and neonatologist. Our retrospective study revealed that there is a strong correlation between maternal splenectomy history and neonatal thrombocytopenia. Also, time since maternal diagnosis is associated with neonatal thrombocytopenia. In conclusion, neonatal outcomes with maternal ITP is generally good.

As a result, if a woman with an established diagnosis of ITP wants to become pregnant; should be given pre-pregnancy counseling and risks of worsening ITP, possible need for treatment, hemorrhage and neonatal thrombocytopenia should be discussed with her. Because there is a few reliable risk factors to predict neonatal platelet count, neonatologist should closely follow up each newborn with maternal ITP. Further studies are required to predict neonatal thrombocytopenia in this group.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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