

Retrospective analysis of maternal and fetal outcomes in pregnant women with chronic immune thrombocytopenic purpura

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Abstract

Objective: In the present study, we investigated the demographic, clinical, laboratory, birth information, treatment method and maternal-fetal outcomes of pregnant patients who were diagnosed with chronic immune thrombocytopenic purpura.

Methods: Hospital records of 24 women with the diagnosis of chronic immune thrombocytopenic purpura and their 26 pregnancies in the obstetrics department were retrospectively analyzed.

Results: All the patients had immune thrombocytopenic purpura diagnosed before pregnancy. The mean age of the cases was 29.50 ± 7.03 years (17-42), mean parity was 2.88 ± 2.86 (0-10), mean gestational age was 36.00 ± 3.40 weeks (27-39), respectively. The cases were admitted to our clinic with causes including the beginning of birth pains (65%), preterm labor (15%), premature rupture of membranes (4%), mort fetus (4%), headache (4%), abruptio placentae (4%), gestational hypertension (4%) and intrauterine growth restriction (4%). Although 15 (57.6%) patients were treated prednisolone during pregnancy, others did not receive any treatment. The mean platelet counts of patients before and after delivery were $62,226 \pm 38.04/\text{mm}^3$ and $70,061 \pm 22.93/\text{mm}^3$, respectively. Ten cases (40%) with the mean platelet counts $28,240/\text{mm}^3$ received treatments containing platelet apheresis, fresh frozen plasma, random platelets or combined treatments in order to increase the platelet count. Eleven cases (42%) were born vaginally and 15 (58%) by cesarean. The birth with cesarean section was performed according to obstetric causes in fourteen cases (93%). None of the patients experienced postpartum complications. The mean platelet count of newborn babies was $201,521 \pm 95.46/\text{mm}^3$ (range, 35,900-446,000) and none of them experienced hemorrhagic complication.

Conclusion: Although women with immune thrombocytopenic purpura carry the risk in pregnancy, birth and after birth, maternal and fetal outcomes are better than expected by appropriate treatment. Decision regarding the form of birth can be made according to obstetric causes in these patients.

Key words: Pregnancy, immune, thrombocytopenic purpura, newborn.

Kronik immün trombositopenik purpuralı gebelerde maternal ve fetal sonuçlarının retrospektif analizi

Amaç: Bu çalışmada kronik immün trombositopenik purpura tanılı gebe olgulara ait demografik, klinik, laboratuvar, doğum bilgileri, tedavi yönetimi ve maternal-fetal sonuçlar araştırıldı.

Yöntem: Obstetri kliniğinde doğum için yatırılan kronik immün trombositopenik purpura tanılı 24 gebe kadının 26 gebeliğine ait dosyaları retrospektif olarak analiz edildi.

Bulgular: Tüm hastalarda immün trombositopenik purpura tanısı gebelikten önce mevcuttu. Olguların ortalama yaşı 29.50 ± 7.03 yıl (17-42), ortalama paritesi 2.88 ± 2.86 (0-10), ortalama gestasyonel haftaları 36.00 ± 3.40 (27-39 hafta) idi. Olgular, kliniğimize doğum ağrılarının başlaması (%65), preterm eylem (%15), erken membran rüptürü (%4), mort fetus (%4), dekolman plasenta (%4), gestasyonel hipertansiyon (%4), intrauterin gelişme kısıtlılığını (%4) içeren sebeplerle yatırıldı. Onbeş olgunun (%57.6) gebeliği boyunca prednizolon tedavisi almasına rağmen diğerlerinin herhangi bir tedavi almadığı saptandı. Olguların doğum öncesi ortalama trombosit sayısı $62,226 \pm 38.04/\text{mm}^3$, doğum sonrası $70,061 \pm 22.93/\text{mm}^3$ idi. Ortalama trombosit sayısı $28,240/\text{mm}^3$ olan 10 (%40) olgu trombosit sayısını arttırmak amacıyla trombosit aferezi, taze donmuş plazma, random platelet veya birleşik tedaviler aldı. Olguların 11'i (%42) vajinal, 15'i (%58) sezaryen ile doğurtuldu. Sezaryen ile doğum 14 olguda (%93) obstetrik nedenlere göre yapıldı. Hastaların hiçbirinde postpartum erken dönemde bir komplikasyon ortaya çıkmadığı gözlemlendi. Yenidoğan bebeklere ait ortalama trombosit sayısı $201,521 \pm 95.46/\text{mm}^3$ ($35,900-446,000/\text{mm}^3$) idi ve hiçbirinde hemorajik komplikasyon olmadığının tespit edildi.

Sonuç: Kronik immün trombositopenik purpuralı kadınlar, gebelik, doğum ve doğum sonrasında risk taşımakla birlikte iyi bir tedavi yönetimiyle maternal ve fetal sonuçlar beklenenden daha iyi olmaktadır. Bu hastalarda doğum şeklinin kararı obstetrik nedenlere göre alınabilir.

Anahtar sözcükler: Gebelik, immün, trombositopenik purpura, yenidoğan.

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Introduction

Thrombocytopenia defined as platelet count in blood less than $150,000/\text{mm}^3$ is seen about 6-10% of all pregnancies.^[1] It is most frequently seen as temporary thrombocytopenia of pregnancy. However, it also may appear due to various reasons such as severe preeclampsia and HELLP syndrome, disseminated intravascular coagulopathy, thrombotic thrombocytopenic purpura, immune thrombocytopenic purpura (ITP), myeloproliferative diseases and aplastic anemia.^[2] ITP is a rare reason for thrombocytopenia in pregnancy. While its incidence at pregnancy is 0.14%, it is responsible for 3% of thrombocytopenias during delivery.^[3] Chronic type of ITP is more widespread among adults while it has two clinical forms as acute and chronic. Chronic ITP has a quiet beginning and chronic progress without any viral or bacterial infection beforehand. While it generally cause skin and mucosa bleedings, it is the most fearful intracranial bleeding case.^[4] It is important to do differential diagnosis of other diseases by ITP in terms of both treatment management and the diversity of maternal and fetal outcomes.^[5] There are few studies related with ITP which is rarely seen as the reason for thrombocytopenia during pregnancy, therefore there are no certain rules for its treatment.

In this study, we aimed to present our experiences related with maternal demographic, clinical, laboratory, birth information and newborn outcomes for cases followed up during perinatal period.

Methods

Information of 24 out of 26 pregnant with chronic ITP diagnosis who were hospitalized for delivery in the Clinic of Obstetrics and Gynecology Department of Dicle University in between January 1st, 2007 and November 1st, 2011 was analyzed retrospectively. Approval was received from the Ethics Committee of Medical Faculty of Dicle University. Our both cases were the pregnant who delivered twice intermittently in our clinic. Thrombocytopenia cases who were hospitalized due to pregnancy and thrombocytopenia diagnosis with no definitive diagnosis were excluded from the study. Information of the cases was collected by analyzing their files in the archive of Medical Faculty of Dicle University. The cases were evaluated in terms of age, parity, gestational week, undergone splenectomy history, referral symptoms, biochemical

and full blood values, spot urine results, prenatal and post-transfusion (for those who underwent transfusion) and postnatal platelet counts, delivery types, cesarean indications and newborn outcomes.

The cases were categorized under 4 groups according to thrombocytopenia status as $<20,000/\text{mm}^3$, $20,000-50,000/\text{mm}^3$, $50,000-100,000/\text{mm}^3$ and $>100,000/\text{mm}^3$, and newborn platelet counts among the groups were evaluated.

For statistics, SPSS (statistical package for social sciences) for Windows 11.5, Epi info and Excel software were used. Non-parametric descriptive tests were used since most of the data did not have normal distribution. Non-parametric Mann-Whitney U test and Kruskal Wallis H test were used in order to compare prenatal mean maternal platelet count with newborn platelet count in 4 groups established according to platelet count, splenectomy status and prednisolone medication during pregnancy. Results were accepted as statistically significant when they were within 95% confidence interval and $p<0.05$.

Results

Mean age of the cases was 29.50 ± 7.03 year (17-42), mean parity was 2.88 ± 2.86 (0-10), and mean gestational week was 36.00 ± 3.40 week (27-39). Four cases had undergone splenectomy history. It was found that four of our cases had complaints about mild nosebleed during their pregnancies before they were hospitalized in our clinic and that others cases did not have any complaint. Seventeen of cases (65%) were hospitalized in our clinic as their delivery pains began without any obstetric complication. Reasons of hospitalization of the cases were shown in **Table 1**. As a treatment, it was found that 15 of the cases (57.6%) had prednisolone during pregnancy and others had no treatment.

Table 1. Diagnosis for hospitalization of cases (%).

Delivery pains	65
Premature labor	15
Early membrane rupture	4
Ablatio placentae	4
Intrauterine mort fetus	4
Intrauterine growth restriction (IUGR)	4
Gestational Hypertension	4
Total	100

While the mean platelet count of all cases was $62,226 \pm 38.04/\text{mm}^3$ before delivery, it was found as $70,061 \pm 22.93/\text{mm}^3$ after the delivery. Transfusion treatment was applied to 10 cases (40%) who had mean platelet count as $28,240/\text{mm}^3$ before delivery in order to increase platelet count. One case was applied fresh frozen plasma (TDP), one case was applied random platelet (RP), 4 cases were applied platelet apheresis (TA), 3 cases were applied TA and TDP and one case was applied TA and RP. The mean platelet counts of cases who had and did not have transfusion before delivery, after transfusion and after delivery are shown in **Table 2**.

It was seen that 11 of the cases (42%) had vaginal delivery while 15 of them (58%) had cesarean delivery. Indications of cesarean were found as previous cesarean history in 7 cases, abruptio placentae in one case, non-progressive labor in one case, fetal distress in 4 cases, breech presentation in one case and chronic immune thrombocytopenic purpura in one case. In all cases, no complication was seen in intrapartum and postpartum period.

Of newborn babies, mean height was 47.03 ± 5.16 cm (30-53 cm), mean weight was $2,821.92 \pm 753.99$ g (800-3,940 g), mean 1st minute Apgar score was 4.88 ± 2.06 (0-9), and mean 5th minute Apgar score was 7.15 ± 2.25 (0-10). Platelet count was found in 19 of newborns and it was averagely $201,521 \pm 95.46/\text{mm}^3$ ($35,900$ - $446,000/\text{mm}^3$). No complication was observed in postpartum period. A stillbirth was seen in only one case due to intrauterine mort fetus and the baby of a case who had cesarean due to abruptio placentae died in newborn intense care due to excessive prematurity.

No significant difference was found when prenatal platelet count and newborn mean platelet counts are

compared in terms of prednisolone treatment and splenectomy status. In all four groups established according to platelet count, no significant difference was found in terms of newborn platelet counts (**Table 3**).

Discussion

ITP is rarely the reason of thrombocytopenia during pregnancy.^[6] It is an autoimmune disease appeared by skin, mucosa and organ bleedings as the result of destruction of auto-antibodies and thrombocytes developed against thrombocytes, and mostly against glycoprotein IIb/IIIb which is a fibrinogen receptor.^[7] Although there is no certain rules for treatment and perinatal outcomes of ITP at pregnancy, some treatment types are suggested based on case series published in the literature. In the studies of Territo et al.^[8] and Murray and Harris,^[9] it is suggested to patients with ITP to avoid pregnancy due to maternal and fetal bleedings, case series and compilations published later showed that ITP has milder effects on newborns and mothers.^[10-13] In this study where we presented our experiences from 24 out of 26 cases with chronic ITP diagnosis, maternal and fetal outcomes were quite good. This showed us that maternal and fetal outcomes are not so scary at perinatal period in pregnant with ITP when facilities required for transfusion are available.

Clinical characteristics of ITP during pregnancy is similar with women who are not pregnant, and they may vary from asymptomatic situation to bruises on skin, mucosal bleeding, petechia and serious bleedings according to the level of thrombocytopenia. Most of our cases are asymptomatic (85%), and only four of them (15%) had nose bleedings during their pregnancies.

Table 2. Mean platelet counts before delivery, after transfusion and after delivery in cases who receive maternal transfusion treatment and in cases who do not.

	N (26)	Platelet count before delivery	Platelet count after transfusion	Platelet count after delivery
Those who receive treatment				
Fresh frozen plasma (TDP)	1	33,400/ mm^3	105,000/ mm^3	100,000/ mm^3
Random platelet (RP)	1	48,400/ mm^3	65,000/ mm^3	65,000/ mm^3
Platelet apheresis (TA)	4	35,175/ mm^3	101,525/ mm^3	67,475/ mm^3
TA and TDP	3	16,500/ mm^3	799,66/ mm^3	46,066/ mm^3
TA and RP	1	10,400/ mm^3	61,000/ mm^3	62,100/ mm^3
Those who do not receive treatment	16	83,468/ mm^3	–	74,150/ mm^3

Table 3. Comparison of prenatal mean platelet count and newborn mean platelet count according to prednisolone treatment, splenectomy status and platelet count of cases.

	Platelet count before delivery (/mm ³ ±SD)	p	Newborn platelet count (/mm ³ ±SD)	p
Prednisolone treatment				
Available	57,366±45.30	0.392	180,290±74.34	0.462
N/A	68,854±25.70		225,111±114.45	
Splenectomy				
Available	45,650±31.59	0.320	211,333±122.27	1
N/A	65,240±38.96		199,681±94.45	
Platelet (10³/mm³) and case count				
<20 (6)	14,433±4.50	0.001	156,250±49.74	0.191
20-50 (3)	38,466±8.60		301,000±69.29	
50-100 (14)	72,778±14.89		212,100±102.36	
>100 (3)	132,330±25.92		160,300±107.99	

1/3 of pregnant women with ITP are diagnosed during pregnancy while 2/3 of them are diagnosed before pregnancy.^[14] Its diagnosis during pregnancy is difficult especially in cases who do not give any finding and who have mild thrombocytopenia; because this can be confused with temporary thrombocytopenia which develops mostly in 2nd and 3rd trimester and is characterized with mild thrombocytopenia.^[15] Besides, antibody tests used for ITP diagnosis are insufficient. Non-existence of a significant difference between both groups in the study of Boehlen et al.^[16] where they researched thrombocyte auto-antibodies in thrombocytopenic and non-thrombocytopenic pregnant women supports this opinion. Since the diagnoses of all patients in our study were made by a hematologist before pregnancy, it was seen that all of our cases really had chronic ITP and therefore differential diagnosis could not be made.

The purpose of treatment in cases with ITP is to prevent bleedings and treatment approach during pregnancy is similar with those who are not pregnant. It is suggested that platelet count should be over 20,000/mm³ in patients who do not have and delivery indication, over 50,000/mm³ for vaginal delivery and over 80,000/mm³ for cesarean.^[17]

For medical treatment, intravenous immunoglobulin (IVIg) which has similar effects, oral corticosteroids or both are used and splenectomy is applied in cases who do not respond to treatment. Excess weight gaining, triggering gestational diabetes, increase in bone loss, hypertension and fetal congenital anomaly risks may appear due to corticosteroid treatment at preg-

nancy. Therefore, IVIg treatment may be preferred instead of corticosteroid treatment.^[17] Webert et al.^[18] emphasized in their studies where retrospective analysis was performed for 92 pregnant women with ITP that 68.9% of cases did not need treatment while Won et al.^[19] reported that they applied treatment on 61.3% of cases in order to increase platelet count. In our study, prednisolone treatment was applied to 15 cases (57.6%). In 2 (13%) of the patients who received prednisolone, early membrane rupture and in utero fetal death developed as an obstetric complication while no congenital anomaly was observed in newborns after delivery. Non-existence of congenital anomaly made us to think that prednisolone treatment may be preferred in cases with ITP. It was learnt that four of our cases underwent splenectomy operation before pregnancy. No significant difference was seen between cases who received prednisolone treatment and who did not, and cases who underwent splenectomy and who did not in terms of platelet count before delivery.

As haemorrhagic complication was suspected in newborn, cesarean was being preferred in pregnant women with ITP as a delivery type.^[9] Later, it was suggested that vaginal delivery might be preferred by determining fetal platelet count by cordocentesis just before delivery.^[20] However, due to potential complications of this invasive process like abortion, and less rate of serious thrombocytopenia in fetus according to observations made up to this period, it is preferred today to take cesarean indications according to obstetric reasons.^[21] In our study, 15 cases were delivered by cesare-

an. Except 1 case which had cesarean with chronic ITP diagnosis, all cesarean decisions were made due to obstetric reasons. Non-existence of complication and serious thrombocytopenia in the babies of cases who had both vaginal and cesarean deliveries made us to think that it is not inconvenient to consider obstetric reasons when determining delivery type.

Although it is considered in pregnant women with ITP that anti-thrombocyte antibodies pass through placenta and cause thrombocytopenia in fetus, the major mechanism is not understood well; because, the relationship between the severity of newborn thrombocytopenia and the severity of maternal thrombocytopenia, level of maternal antibodies and whether mother is splenectomy or not could not be detected.^[22] However, it was found that there is a relation with thrombocytopenia of previous baby.^[23] In this study, prednisolone treatment undergone by mother, splenectomy status and maternal platelet count were considered and newborn platelet counts were compared; however, no significant difference was detected. Outcomes show that these criteria are not effective on newborn platelet count.

Recent studies publishing the results of newborns of cases with ITP have revealed that effects of ITP on newborn are not as serious as expected. Webert et al.^[18] reported in their studies that in 71.6% of 109 newborns from 92 pregnant women had more than 150,000/mm³ platelet count and it was lower than 20,000/mm³ only in 5.5% of babies. In the study where Won et al.^[19] published the results of newborns of pregnant women with ITP, no complication developed in 28 of 31 babies, in utero mort fetalis developed due to an unknown reason in 2 pregnant women and one baby died due to prematurity when the baby was delivered at 27th gestational week due to hemorrhagic complication of mother. In our study, platelet counts of 19 newborns were obtained. Platelet count was found as more than 150,000/mm³ except four newborns, of whom had 35,900; 82,000; 93,000 and 119,000/mm³ platelet count. No complication was observed in 24 of the newborns. One of the other two babies was mort fetalis and other one is the baby who was delivered by cesarean due to abruption placenta diagnosis and died only at 27th gestational week due to prematurity. In these babies, no hemorrhagic complication was seen.

There were some restrictions in our study. One of them was the lack of detailed information about side effects due to chronic ITP beginning from the pregnancies up to delivery. Because these cases were

referred to our hospital for delivery since we are reference hospital in our region. Another restriction was that we were unable to access platelet counts of all newborns through their files.

Conclusion

ITP is a hematologic disease that appears before or during pregnancy and complicates pregnancy. Carrying out close follow-up and appropriate treatment during and after delivery and keeping platelet count above 50,000/mm³ before delivery prevents maternal and fetal complications. Though ITP during pregnancy has risks, maternal and fetal outcomes are quite good. Decision of delivery type may be made according to obstetric reasons.

Conflicts of Interest: No conflicts declared.

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