Pregnancies Complicated by Severe Autoimmune Thrombocytopenic Purpura

Amer Gharaibeh (1)
Tareq Irtaimeh (2)

(1) Amer Gharaibeh, MD, Maternal Medicine Clinic,
King Hussein Medical Center, Amman, Jordan
(2) Tareq Irtaimeh, MD, Department of Obstetrics and Gynecology,
King Hussein Medical Center, Amman, Jordan

Correspondence:
Amer Gharaibeh, MD, Maternal Medicine Clinic,
King Hussein Medical Center, Amman, Jordan
Email: agharaibeh@hotmail.com

ABSTRACT

Objectives: **To assess pregnancy course and perinatal bleeding in women with severe autoimmune thrombocytopenic purpura.**

Material and methods: **We collected data of 38 pregnancies in 24 women, who were on treatment for autoimmune thrombocytopenic purpura early in pregnancy. Indication for treatment was platelets count 50.000/mm^3 or less. We looked for premature rupture of membranes, premature delivery, intrauterine growth restriction and significant blood loss at delivery. Those women were the study group, (group 1). The same variables were looked for in 100 healthy pregnancies taken as control (group 2). Data was compared between the two groups. Information was obtained prospectively from the woman's follow up visits at maternal medicine clinic, King Hussein Medical Center as well as data gathered from women with previous pregnancies complicated by autoimmune thrombocytopenia. Women who had thrombocytopenia secondary to other conditions such as systemic lupus, bone marrow diseases and other causes, were not included in the study.**

Results: **The study group 1 had nine premature ruptures of membranes in 38 pregnancies, whereas only ten women ruptured their membranes out of 100 in control group 2 with an odds ratio 2.9. Four women had significant blood loss at delivery in group 1 and eight women in group 2 which presents marginal increase for group 1 (odds ratio 1.3). No increase in growth restricted babies nor in premature delivery was noticed.**

Conclusion: **Pregnant women with autoimmune thrombocytopenic purpura on treatment, have significant higher risk to rupture their membranes prematurely. No increase in growth restricted babies and premature deliveries. With good care they can deliver safely with minimum hazard of bleeding.**

Key words: **pregnancy, complication, thrombocytopenia, bleeding**

Introduction

Pregnant women with thrombocytopenia are not infrequently met at antenatal clinics (7-10%)(1). Some of them are accidentally discovered during routine blood test. Pregnancy induced thrombocytopenia is the most encountered cause related to pregnancy(2), whereas Idiopathic thrombocytopenic purpura is the most encountered cause that is unrelated to pregnancy(3). Platelets count was found normally lower in pregnancy and decreases as pregnancy advances(4). In one study(5), back in 2001, it was found that platelets function in women with pregnancy induced thrombocytopenia was preserved. A recent study(6) emphasized on the increase in platelets aggregation in pregnant women when compared to non-pregnancy state. Pregnancy course and the complications that may be encountered are attributed to the disease itself or to drugs used to ameliorate the disease. Studies are conducted to minimize the risk of thrombocytopenia on pregnant women and on the developing fetus. Management needs to balance between the hazard of low platelets count and the risk of drugs used on the mother and the fetus. When medication is needed, corticosteroids are first line of treatment(7). It is known for its side effect on blood pressure, glucose tolerance and immunity among others(8). Other immunomodulating drugs are used which are not risk free.

It may be difficult to distinguish between gestational induced thrombocytopenia and ATP when first recognized during pregnancy(9), nevertheless, gestation induced thrombocytopenia is known to have mild disease course. Actual platelets count has to be looked for sometimes when platelets clumps are formed. Tubes with different anticoagulant media are used. Sodium citrate, heparin Ethylenediaminetetraacetic acid tubes are dispatched to the lab, platelets count can be performed manually when suspicion of clumping or agglutination arises(10).

The aim of our study is to look for pregnancy course in women with severe autoimmune thrombocytopenia, in regard to premature rupture of membranes, to fetal body weight at delivery, prematurity and peripartum bleeding.

In our study we followed the course of pregnancies complicated by severe autoimmune thrombocytopenia, which were diagnosed prior to pregnancy, or first discovered during gestation. Severe thrombocytopenia is when platelets count decreases to less than 50,000 x 10^9/L(11).

Methods

24 pregnant women with 38 pregnancies diagnosed with severe autoimmune thrombocytopenic purpura were considered in the study; they were taken as study group and labeled as (group one). Another 100 women with normal course pregnancy and normal platelets count were also included in the study as control group and labeled as (group two). Severe thrombocytopenia is when platelets count decreases to less than 50,000/mm3. They were followed up at maternal medicine clinic, Obstetrics department. Data were obtained prospectively from patients' follow up records and retrospectively of previous pregnancy and post natal visits. All women were on oral steroids; some of them had other immune modulating drugs added. An oral steroid (Prednisolone) was use in a dose of 20 to 60 mg. Azathioprine in doses 50 to 100 mg was added in 4 women. Two women received intravenous immunoglobulin for resistant disease at gestational age 28 for one of them and at 30 weeks for the second patient. The aim of treatment was to keep platelets count at or above 40.000/mm3. Citrate, heparin or ethylene diamine tetra acetic acid tubes were dispatched to the laboratory. Manual count was also requested when suspicion arises. No considerable spontaneous bleeding was met and thus no blood transfusion was considered for any patient before delivery. Minor epistaxis resolved by local hemostatic care. Platelets transfusion was considered only at delivery or before surgery to raise platelets count up to 50.000/mm^3.

The course of pregnancy and bleeding at delivery was studied and compared between the two groups. We looked at premature rupture of membranes, premature delivery, babies small for gestation age and amount of blood loss at delivery.

Premature rupture of membranes was defined as amniotic fluid passage before onset of labour at any gestational age. Deliveries before 37 weeks completed of gestation were taken as premature delivery. Fetal body weight at delivery at or less than the 10th centile was considered small for gestational age. Blood loss was considered significant when hemoglobin concentration decreases by 2gr/dl or more for vaginal delivery and 3gr/dl or more after operative delivery. Caesarean section was conducted for obstetric reasons or as maternal request after counseling the family.

Using MedCalc software, Odds ratio and confidential intervals and p-value were calculated.

Results

38 pregnancies with severe thrombocytopenia were included in the study, all of them were on oral Prednisolone 20 mg and up to 60 mg. Azathioprine was added in a dose of 50 up to 100 mg for 4 women who were resistant to Prednisolone alone. Two cases did not respond to Prednisolone and Azathioprine; they received Intravenous immunoglobulin and 8 women needed platelets transfusion when in labour or before operative delivery.

Nine women in study group ruptured their membranes before the onset of labour (23.6%), four had significant bleeding (10%), five delivered babies at or below the 10th centile (13%), and four had premature deliveries before 37 weeks completed (10%).

In the control group the results were 10 (10%), 8(8%), 12(12%), 11(11%) respectively, (Table 1).

Table 1: Comparison in pregnancy course and peripartum bleeding between groups

Groups	Increased blood loss	SGA 10th percentile	Prematurity 37th week	SRM
Group 1 N=38	4 (10)	5 (13%)	4 (10%)	9 (23.9%)
Group 2 N=100	8 (8%)	12 (12%)	11 (11%)	10 (10%)
OR 95% CI	1.35 0.38 - 4.78	1.1	0.9	2.9 1.03-7.54
P-Value	0.6 n/s	n/s	n/s	0.04

n/s= not significant

Spontaneous rupture of membranes was significantly increased in women with severe thrombocytopenia on treatment than in women with no steroid treatment and normal platelets with an odds ratio of 2.9, (95% CI 1.03-7.53).

There was minimal increase in peripartum bleeding, (OR 1.3, 95% CI 0.3-4.7); it was not statistically significant. No blood replacement was needed.

No difference was found in the rates of premature deliveries or in small for gestation babies between the two groups.

Discussion

Women with thrombocytopenia present a special challenge to obstetricians in the fertility period. Bleeding that may occur during pregnancy and delivery due to obstetric reasons has particular hazard when thrombocytopenia is superimposed. The Obstetrician has to place platelet count at safe levels to ensure maternal health. Drugs used in the aim of achieving this goal may not be risk free. In our study we tried to estimate the hazard of medication used in managing thrombocytopenia in pregnancy.

Prednisolone, a synthetic corticosteroid is the first line and main stay treatment. It was found not to cause major fetal abnormalities (12,13) . Nevertheless the risk of premature rupture of membranes has been recognized by different studies(14). In accordance with those studies, we found that premature rupture of membranes occurred more frequent in thrombocytopenic women on Prednisolone. It is difficult to establish if the increase in premature rupture of membranes is exclusively due to steroids treatment or thrombocytopenia per se presents an independent risk factor.

Blood loss at delivery was marginally increased in women with thrombocytopenia. This emphasises the fact that platelets function is preserved, and the hazard of peripartum bleeding is not immense, particularly when appropriately managed.

Excluding cases with premature rupture of membranes, premature delivery was not increased in our study. This leads to the conclusion that thrombocytopenia is not a direct risk factor for premature delivery.

The risk of small for gestation babies at delivery was not increased also. This highlights the normal fetal growth pattern, normal oxygenation and nutrition.

Conclusion

Our results suggest that pregnant women with severe autoimmune thrombocytopenia on treatment have an increased risk to rupture their membranes prematurely. This may be due to medications used in managing the condition, or due to the disease itself. Risk of bleeding may exist, but with appropriate care and management it is of low risk. Fetal growth and premature deliveries are not more likely in isolation of premature rupture of membranes.

Number of subjects represented a limitation to the study; more studies in larger numbers are needed to verify those results.

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