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Effect of severe gestational thrombocytopenia to perinatal outcome

VESNA ELVEĐI GAŠPAROVIĆ • SNJEŽANA GVERIĆ AHMETAŠEVIĆ • PETRANA BELJAN • SNJEŽANA ŠKRABLIN

VESNA ELVEĐI GAŠPAROVIĆ (✉) •
PETRANA BELJAN •
SNJEŽANA ŠKRABLIN
Department of Obstetrics and Gynecology
University Hospital Centre Zagreb, Zagreb
Petrova 13, 10 000 Zagreb
Phone: +38514604728
E-mail: vesnagasparo@gmail.com

SNJEŽANA GVERIĆ AHMETAŠEVIĆ
Department of Obstetrics and Gynaecology
Neonatal Intensive Care Unit
University Hospital Centre Zagreb
Zagreb, Croatia

ABSTRACT

Thrombocytopenia is a common hematologic abnormality during pregnancy. It may be a diagnostic and management problem, and has many causes, some of them specific to pregnancy. We considered all singleton deliveries after 24 weeks of gestation between 2007 and 2012 in our third level centre. Women with a platelet count <100 × 109/L, but who did not suffer from the aforementioned diseases, were considered to have incidental thrombocytopenia. The aim of this study is to investigate the incidences of moderate and severe gestational thrombocytopenia, to determine if the severity of maternal gestational thrombocytopenia affect perinatal outcome and to define if the severity of maternal gestational thrombocytopenia implicates the appearance of neonatal thrombocytopenia.

Key words: gestational thrombocytopenia, neonatal thrombocytopenia

Introduction

Thrombocytopenia, defined as a platelet count of $<150 \times 10^9$/L, is a common hematologic abnormality during pregnancy, with an incidence of 6.6%. (1) When thrombocytopenia is detected during pregnancy, it may be related to a pre-existing underlying disease, such as bone marrow disease, hypersplenism, or congenital platelet disorder. It may also be a sign of complex clinical disorders that are unique to pregnancy, such as preeclampsia and hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome. Furthermore, autoimmune diseases, including systemic lupus erythematosus, antiphospholipid syndrome, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, and immune thrombocytopenia (ITP) may relapse or be first detected during pregnancy. Nevertheless, the most common cause of pregnancy-related thrombocytopenia is gestational thrombocytopenia, which is diagnosed through exclusion when the postpartum platelet count returns to normal and is usually associated with an uneventful pregnancy outcome. Gestational thrombocytopenia (GT) is considered the most prevalent cause of thrombocytopenia in pregnancy and accounts for about 75% of cases of thrombocytopenia during pregnancy. (2) It is defined by a platelet count of no less than 70×10^9/L, especially during the third trimester, and the count returns to normal within 12 weeks of delivery. (3) The etiology is unknown, but is considered to be due to the relative hemodilution in pregnancy, amplified by the capture or destruction of platelets in the placenta. (4) Most existing studies have addressed a specific etiology of thrombocytopenia in pregnant women, but only a few have compared different etiologies, all using a platelet count of 150×10^9/L as the reference value. (5-9) Since it is widely accepted that the prognosis of mild thrombocytopenia (a platelet count above 100,000, generally caused by GT) is acceptable and with no major complications, we focused on moderate to severe thrombocytopenia.

The present study was aimed to investigate the incidence of moderate and severe gestational thrombocytopenia, to determine if the severity of maternal gestational thrombocytopenia affect perinatal outcome and to define if the severity of maternal gestational thrombocytopenia implicates the appearance of neonatal thrombocytopenia.

Materials and methods

We considered all singleton deliveries after 24 weeks of gestation between 2007 and 2012 in our third level centre. Patients were excluded from the study if they suffered from chronic hypertension, diabetes mellitus, liver diseases (acute hepatitis, acute fatty liver, and/or liver cirrhosis), renal diseases and autoimmune disorders such as systemic lupus erythematosus and ITP. Pregnancies complicated with fetal structural or

Table 1. Comparison of maternal characteristics

Variables	Moderate group (n = 63)	Severe group (n = 17)	P
Age (year)	30 (19–44)	29 (21–41)	0.763
Gestational age (week)	39 (33–42)	39 (36–41)	0.345
Platelet count (× 109/L)	82 (51-98)	37 (7-49)	0.001
Primiparity	29 (46.03%)	8 (47.05%)	0.940
Thrombocytopenia in previous pregnancy	2 (3.17%)	3 (17.65%)	0.029
Conception after assisted reproductive technology	2 (3.17%)	2 (11.76%)	0.146
Previous history of abortion	16 (25.40%)	1 (5.88%)	0.081
Previous history of fetal death	1 (1.59%)	1 (5.88%)	0.314
Corticosteroid therapy in this pregnancy	8 (12.70%)	7 (41.18%)	0.008
Transfused with packed platelet cells	1 (1.59%)	2 (11.76%)	0.05

Data are expressed as median or n (%)
Moderate group: platelet count 50-100 $\times 10^9$/L
Severe group: platelet count $<50 \times 10^9$/L

chromosomal anomalies and gestational hypertensive diseases, including preeclampsia, eclampsia, and HELLP syndrome, were also excluded. Women with a platelet count $<100 \times 10^9$/L, but who did not suffer from the aforementioned diseases, were considered to have incidental thrombocytopenia. These individuals were divided into two groups according to the platelet count: Group 1 ("Severe group", severe thrombocytopenia) with a platelet count $<50 \times 10^9$/L and Group 2 ("Moderate group", moderate thrombocytopenia) with a platelet count 50–100 $\times 10^9$/L.

We studied the following perinatal outcomes: type of delivery, placental abruption, severe postpartum bleeding, peripartal hysterectomy, birth weight, fetal death, 1 minute and 5 minute Apgar scores <7, premature delivery, perinatal infection, neonatal thrombocytopenia, admission to the neonatal intensive care unit and neonatal death.

The following maternal characteristics were factors that were evaluated in assessing potential confounding factors in the relationship between maternal platelet count and pregnancy outcome: age of mother, gestational age, parity, method of conception (natural or assisted reproductive technology), previous abortions, thrombocytopenia in previous pregnancies and fetal death in previous pregnancies, use of corticosteroides and transfusions with packed platelet cells. Statistical analysis was performed using SPSS version 20 (SPSS Inc., Chicago, IL, USA). Nominal variables were expressed by count and percentage. Nominal variables were analyzed using Chi-square tests or Fisher's exact test. All measurement variables had nonparametric distribution and were expressed by a median. A p value of <0.05 was considered statistically significant.

Results

There were 80 pregnancies which fulfilled the inclusion criteria for our study for idiopathic (gestational) thrombocytopenia. 67 patients (79%) had a platelet count of 50-100 $\times 10^9$/L, and only 17 (21%) had a platelet count $<50 \times 10^9$/L. Thrombocytopenia in previous pregnancy seems to be an important factor for severe thrombocytopenia in present pregnancy (p=0.029).

We found a significant difference in the need for corticosteroid therapy and packed platelet cells transfusion between the groups; 8 patients (8%) from the Moderate group and 7 patients (41%) from the Severe group received corticosteroid therapy (p=0.008). Two patients from the Severe group (11.76%) and one from the Moderate group (1.59%) were transfused with packed platelet cells during the pregnancy (p=0.05).

We found no difference in severity of maternal thrombocytopenia regarding the method of conception, maternal age, parity, history of previous abortion and fetal death. Two newborns (12%) from mothers with severe thrombocytopenia had neonatal thrombocytopenia, and one of them was admitted to the Neonatal Intensive Care Unit (NICU). Only one newborn from a mother with moderate thrombocytopenia had neonatal thrombocytopenia, what is significantly different (p=0.05). The newborns platelet count returned to normal within seven days without any treatment. A vaginal delivery was carried out in 43 patients (68%) with moderate thrombocytopenia and 9 patients (53%) with severe thrombocytopenia. 20 (32%) patients from the Moderate group and 8 patients (47%) from the Severe group underwent caesarean section due to obstetric indications.

Neonatal bleeding, disseminate intravascular coagulation, severe maternal postpartum bleeding and peripartal hysterectomy did not occur in any of our patients. There were no neonatal deaths.

We found no difference between the groups in Apgar score, perinatal infection and preterm delivery rate. We found no statistically significant difference between the mode of delivery and severity of maternal gestational thrombocytopenia (p=0.240).

Table 2. Maternal, fetal and neonatal outcome

	Moderate group (n =63)	Severe group (n = 17)	P
Postpartum haemorrhage	0	0	1.000
Disseminated intravascular coagulopathy	0	0	1.000
Placental abruption	1 (1.59%)	0	0.601
Caesarean section	20 (31.74%)	8 (47.06%)	0.240
Peripartum hysterectomy	0	0	1.000
Vaginal delivery	43 (68.25%)	9 (52.94%)	0.240
Birth weight (g)	3280 (1820–4480)	3260 (2250–4300)	0.345
Fetal death	0	0	1.000
Preterm delivery	5 (7.94%)	2 (11.76%)	0.620
1-min Apgar score <7	2 (3.17%)	0	0.457
5-min Apgar score <7	0	0	1.000
Admission to NICU	0	1 (5.88%)	0.053
Neonatal thrombocytopenia	1 (1.59%)	2 (11.76%)	0.050
Neonatal death	0	0	1.000

Data are expressed as median or n (%)
Moderate group: platelet count 50-100 $\times$ 10^9/L
Severe group: platelet count <50 $\times$ 10^9/L
NICU, neonatal intensive care unit

We reported one placental abruption in the Moderate group with no serious effects for the mother or the infant.

Discussion

Thrombocytopenia occurring during pregnancy is a common diagnostic and management problem and may have many causes. (10) Platelet counts are within the normal range of 150-450 $\times$ 10^9/L in the vast majority of women during normal pregnancies, however they may be slightly lower, on average, than in healthy, non-pregnant women. (7) The frequency of gestational thrombocytopenia in the largest series of consecutive women admitted for labour and delivery is 5%. (11) In this series, neonatal thrombocytopenia did not occur in infants born to mothers with gestational thrombocytopenia. In our study, cumulative incidence of gestational thrombocytopenia was 0.46% (the incidence rate was 1.83 cases per 1,000 persons per year). Within the group of gestational thrombocytopenia, we found 17 cases (21%) of severe thrombocytopenia, which is about 0.1% of all singleton deliveries in a 5 year period in our hospital, which is similar to Karim et al. who documented incidence of severe thrombocytopenia in less than 0.1%pregnancies. (10) This variance might be due to our exclusion of women with major systemic diseases, as well as those with gestational hypertensive diseases.

In our study, women with thrombocytopenia generally had a higher rate of caesarean delivery than women with a normal platelet count, but with no difference within the study groups (p=0.24) (table 2). Thrombocytopenia is not usually considered an indication of caesarean delivery, and most previous studies have preferred vaginal delivery as long as no other obstetric indications were present.

Nevertheless, clinicians may still be concerned about obstetric complications, such as vaginal hematoma or vaginal wall laceration, which can lead to uncontrolled bleeding when exacerbated by thrombocytopenia. Therefore, when thrombocytopenic women present signs of abnormal labour, clinicians may aggressively suggest a caesarean section, which will increases the incidence. However, our results shows that women who had thrombocytopenia at vaginal delivery, but did not suffer from any other medical diseases, had favourable perinatal outcome.

In one pregnancy complicated with placental abruption we found no disseminated intravascular coagulation or intrauterine fetal death, the mother had a

platelet count of 85 $\times$ 10^9/L. This case suggests that clinicians should exclude occult placental abruption and acute blood loss when investigating the cause of severe thrombocytopenia in women with no major medical disease or gestational hypertensive disorder. However, the risk of postpartum haemorrhage, hysterectomy, disseminated intravascular coagulation, placental abruption, mode of delivery and Apgar score in women with gestational thrombocytopenia was no different when comparing the severity of maternal illness (table 2). Some investigators, such as Parnas et al., observed that patients with moderate to severe thrombocytopenia have higher rates of preterm deliveries (<37 weeks). (11) Our study found no significant difference between preterm delivery rates (p=0.285) (table 2).

One of our objectives was to determine the relationship between severity of gestational thrombocytopenia and neonatal outcome.

Some authors associate thrombocytopenia with adverse neonatal outcome. (1,10,11) We found neonatal thrombocytopenia in 12% of cases in the Severe maternal thrombocytopenia group – a significantly higher rate when compared to the Moderate group (p=0.050) (table 2). The immediate concern is for fetal thrombocytopenia and the resulting risk for intracranial haemorrhage after delivery. A large case series suggests that there is no risk. (12) However, a few smaller case series of selected women with severe thrombocytopenia and their newborns had thrombocytopenia too. Ruggeri's report of 41 pregnancies with gestational thrombocytopenia reported two newborns with mild thrombocytopenia and one with severe thrombocytopenia. (13) Our study confirmed that most cases of severe gestational thrombocytopenia have an uncomplicated course, with no significant maternal or fetal morbidity, even in the extreme situation we had with our patient with a platelet count of 7 $\times$ 10^9/L.

Gestational thrombocytopenia is a benign condition, usually detected incidentally during the third trimester and presents no risk of increased bleeding to the mother. The risk of thrombocytopenia in neonates born to mothers with gestational thrombocytopenia is also considered insignificant. (14-16) Although the etiology of this condition is unknown, many features of gestational thrombocytopenia are similar to those of mild immune thrombocytopenia. Moreover, several observations support the hypothesis that gestational thrombocytopenia may be a mild and transient form of immune thrombocytopenia. (17,18)

There is no consistent correlation between appearance of neonatal thrombocytopenia and the severity of maternal thrombocytopenia. (14,15,16) According to previous studies, the best predictor of neonatal thrombocytopenia is a history of thrombocytopenia in a prior sibling. (17) Our data also shows that thrombocytopenia in a previous pregnancy seems to be an important factor for severe thrombocytopenia in a present pregnancy (p=0.029) (table1). The neonatal platelet count often does not correlate with the maternal platelet count, and treatment of the mother with glucocorticoids does not alter the incidence of fetal thrombocytopenia. (18,19) Our study reported statistically frequent use of glucocorticoids in the Severe group (p=0.008) (table1). Despite this, we found that two newborns from mothers with severe thrombocytopenia had neonatal thrombocytopenia and one of them was admitted to the Neonatal Intensive Care Unit (NICU). Only one newborn from a mother with moderate thrombocytopenia had neonatal thrombocytopenia, what is significantly different (p=0.05)(table2).

According to this study, pregnancies with severe gestational thrombocytopenia do not face an increased risk of intrapartal fetal distress, caesarean section rate, intrauterine fetal death, preterm delivery, low Apgar scores, increased admission rate to the neonatal intensive care unit, intracranial haemorrhage, neonatal death or adverse maternal outcome.

Conclusion

Our results suggest that the appearance of severe gestational thrombocytopenia is more frequent in patients with thrombocytopenia in a previous pregnancy and that the appearance of neonatal thrombocytopenia is more likely from pregnancies with severe maternal gestational thrombocytopenia.

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