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Moderate to severe thrombocytopenia during pregnancy

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Abstract

Objective: The objective was to investigate obstetric risk factors, complications, and outcomes of pregnancies complicated by moderate to severe thrombocytopenia.
Materials and methods: A retrospective case-control study comparing 199 pregnant women with moderate to severe thrombocytopenia (platelet count below 100×10^9/l) with 201 pregnant women without thrombocytopenia, who delivered between January 2003 to April 2004. Stratified analysis, using the Mantel–Haenszel procedure was performed in order to control for confounders.
Results: The main causes of thrombocytopenia were gestational thrombocytopenia (GT) (59.3%), immune thrombocytopenic purpura (ITP) (11.05%), preeclampsia (10.05%), and HELLP (Hemolysis, elevated liver enzymes and low platelet count) syndrome (12.06%). Women with thrombocytopenia were significantly older (30.7 ± 5.9 versus 28.7 ± 5.7; $p = 0.001$) compared with patients without thrombocytopenia, and had higher rates of labor induction (OR = 4.0, 95% CI = 2.2–7.6, $p < 0.001$) and preterm deliveries (OR = 3.5, 95% CI = 1.9–6.5, $p < 0.001$). Even after controlling for labor induction, using the Mantel–Haenszel technique, thrombocytopenia was significantly associated with preterm delivery (weighted OR = 3.14, 95% CI = 1.7–6.0, $p < 0.001$). Higher rates of placental abruption were found in pregnant women with thrombocytopenia (OR = 6.2, 95% CI = 1.7–33.2, $p = 0.001$). In a comparison of perinatal outcomes, higher rates of Apgar scores <7 at 5 min were noted in infants of mothers with thrombocytopenia (OR = 6.3, 95% CI = 1.8–33.8, $p = 0.001$), intrauterine growth restriction (IUGR; OR = 4.6, 95% CI = 1.5–19.1, $p = 0.003$), and stillbirth (65/1000 versus 0 $p < 0.001$). These adverse perinatal outcomes were found in rare causes of thrombocytopenia such as disseminated intravascular coagulation (DIC), familial thrombotic thrombocytopenic purpura (TTP), anti-phospholipid antibodies (APLA) syndrome, and myeloproliferative disease, and not among patients with GT.
Conclusions: Moderate to severe maternal thrombocytopenia points to a higher degree of severity of the primary disease, which increases perinatal complications. However, the adverse outcome is specifically attributed to preeclampsia, HELLP syndrome, and rare causes, while the perinatal outcome of GT and ITP is basically favorable. Special attention should be given to patients with thrombocytopenia due to preeclampsia, HELLP syndrome, and rarer causes during pregnancy.

Keywords: Moderate to severe thrombocytopenia; Pregnancy; Preeclampsia; HELLP; Gestational thrombocytopenia

1. Introduction

Thrombocytopenia is defined as a platelet count below 150×10^9/l, caused by accelerated platelet destruction or decreased production. It is classified as mild with a platelet count of 100–150 $\times 10^9$/l, moderate at 50–100 $\times 10^9$/l, and severe with less than 50×10^9/l [1].

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Thrombocytopenia occurs in approximately 10% of pregnant women [2] and is caused by the conditions described below.

Gestational thrombocytopenia (GT) is considered the most prevalent cause of thrombocytopenia in pregnancy and accounts for about 75% of cases of thrombocytopenia during pregnancy [1]. It is defined by a platelet count of no less than 70×10^9/l, especially during the third trimester, [3] and the count returns to normal within 12 weeks of delivery [1]. The etiology is unknown, but is considered to be the due to the relative hemodilution in pregnancy, amplified by the capture or destruction of platelets in the placenta [4]. GT is considered a minor form of thrombocytopenia in the fetus or newborn, with no risk of hemorrhage to the mother or infant.

Immune thrombocytopenic purpura (ITP) is caused by platelet destruction in the reticular endothelial system, due to platelet auto-antibodies against several platelet membrane glycoprotein complexes. ITP is characterized by a moderate to severe decrease in the platelet count, and constitutes approximately 5% of cases of thrombocytopenia in pregnancy [3,5]. ITP requires monitoring during pregnancy and after delivery, and may require treatment, due to the higher risk of maternal hemorrhage when the platelet count is low. There is a minor risk of thrombocytopenia in the newborn.

Preeclampsia and HELLP (Hemolysis, elevated liver enzymes and low platelet count) syndrome are considered to be the cause of thrombocytopenia in pregnancy in about 21% of cases [6,7]. The maternal platelet count returns to normal within 3–5 days of delivery [3]. HELLP syndrome is a variant of preeclampsia, and is characterized by hemolytic anemia, elevated liver enzymes, and a low platelet count (usually below 100×10^9/l) [1]. It is responsible for maternal deaths (up to 3.0% of HELLP cases may end in maternal mortality) and stillbirth (in up to 20% of cases), especially as a result of placental abruption and preterm delivery [1].

There are additional, rarer causes of thrombocytopenia during pregnancy, including thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), disseminated intravascular coagulation (DIC), systemic lupus erythematosus (SLE), anti-phospholipid antibodies syndrome (APLA), or it may be induced by drugs (such as heparin) [1].

Most existing studies [8–12] 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. Since it is acceptable that the prognosis of mild thrombocytopenia (platelet count above 100,000, generally caused by GT) is good with no major complications, we decided to focus on moderate to severe thrombocytopenia.

The present study was aimed at investigating obstetric risk factors, complications, and outcomes of pregnancies complicated by moderate to severe thrombocytopenia, compared with pregnant women with a normal pregnancy, and to compare the outcomes of different etiologies.

2. Materials and methods

A retrospective case-control study comparing all ($n = 199$) pregnant women with moderate to severe thrombocytopenia with 201 pregnant women without thrombocytopenia, delivered during the same study period, was conducted. Deliveries occurred between 1 January 2003 and 1 April 2004 at the Soroka University Medical Center, which is the sole hospital of the Negev, the southern part of Israel. Out of 17,499 deliveries at the time of the research, moderate to severe thrombocytopenia was observed in 1.14%.

The study population included all pregnant women with moderate to severe thrombocytopenia (platelet count below 100×10^9/l) identified by the computerized hematology laboratory report of the hospital. The control group consisted of consecutive patients without thrombocytopenia and hypertensive disorders delivered during the same period. The clinical details of all women were collected by reviewing their hospital as well as their prenatal records.

The following clinical characteristics were evaluated: maternal age, previous gestations, parity, gestational age, birth weight, and the cause of thrombocytopenia. The following obstetrical risk factors were examined: previous cesarean section (CS), gestational diabetes mellitus, pre-gestational diabetes mellitus, maternal anemia, hydramnios, oligohydramnios, multiple pregnancies (twins/triplets), and intrauterine growth restriction (IUGR). The following pregnancy and labor complications were assessed: blood and platelet transfusions, placental abruption, placenta previa, labor induction, mode of delivery including spontaneous, CS or vacuum delivery (no forceps deliveries occurred during the study period), Apgar scores at 1 and 5 min of less than 7, umbilical cord artery pH less than 7.2, DIC, meconium-stained amniotic fluid, stillbirth, intra-partum fetal death (IPD), and post-partum neonatal death (PPD). The local ethics institutional review broad approved the study.

Statistical analysis was performed using the SPSS package (SPSS, Chicago, IL, USA). Statistical significance was calculated using the χ^2-test, or Fisher's exact test for categorical variables. Student's t-test was used for continuous variables. Stratified analysis, using the Mantel–Haenszel procedure, was performed in order to control for confounders. Odds ratios (OR) and their 95% confidence intervals (CI) were computed. $p < 0.05$ was considered statistically significant.

3. Results

Out of 199 pregnant women with a platelet count below 100×10^9/l, the diagnosis included: 118 women with GT, 22 with ITP, 20 with severe preeclampsia, 24 with HELLP syndrome, 10 with DIC, one with familial TTP, one with APLA syndrome, two due to dilution caused by massive blood transfusions, and one with myeloproliferative disease