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Assessing platelet function may reduce platelet transfusion requirements in women in thrombocytopenia undergoing cesarean section

Zhun Xing[1], Yang Li[2], Chang Xu[2], Liqiang Zheng[3], Qiushi Wang[2], Yan Zhao[4]

[1]Department of Anesthesiology, Shengjing Hospital of China Medical University, Shenyang, Liaoning 110801, China;
[2]Department of Blood Transfusion, Shengjing Hospital of China Medical University, Shenyang, Liaoning 110801, China;
[3]School of Medicine, Shanghai Jiaotong University, Shanghai 200240, China;
[4]Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University, Shenyang, Liaoning 110801, China.

Thrombocytopenia is a common comorbidity during pregnancy. A platelet (PLT) count of $<100 \times 10^9$/L is used as the diagnosis for thrombocytopenia. The major adverse effect of thrombocytopenia in the clinical setting is hemorrhage of varying severity.[1] The causes of thrombocytopenia during pregnancy are distinct from those of other diseases. Gestational thrombocytopenia accounts for >75% of thrombocytopenia cases in pregnant women and occurs in 5% to 8% of pregnancies. Other causes of thrombocytopenia include hemolysis, elevated liver enzymes, low platelet count syndrome, autoimmune thrombocytopenic purpura, and other underlying hematologic diseases.[2,3] Most women with thrombocytopenia do not require any specific treatment.[2] For pregnant women whose PLT counts remain low during labor, prophylactic PLT transfusion is used to prevent postpartum hemorrhage. The current guidelines for PLT transfusion in obstetric patients are generally based on following criteria: maintenance of the PLT count $>80 \times 10^9$/L for patients receiving cesarean section under epidural anesthesia and $>50 \times 10^9$/L for women giving natural birth without anesthesia.[4]

Our earlier studies have shown that pregnant women with chronic thrombocytopenia displayed a compensatory enhancement in PLT function.[4] Consequently, we sought to explore the potential of a PLT function assessment and a maximum amplitude (MA) in thromboelastgram (TEG) threshold to avoid unnecessary PLT transfusions. To this end, we retrospectively analyzed the administration of PLT transfusions to pregnant women with a PLT count of $<80 \times 10^9$/L who underwent a cesarean section in our hospital between January 2016 and December 2019. This study is a retrospective survey, without informed consent, and without involving the privacy of pregnant women; this study was approved by the Ethics Committee of Shengjing Hospital of China Medical University (2021ps502k[x1]).

Four hundred and thirty pregnant women with a PLT count of $<80 \times 10^9$/L underwent a cesarean section in Shengjing Hospital between January 2016 and December 2019. Of these, 199 did not receive an apheresis PLT transfusion, and 85 received one apheresis PLT. The enrolled patients were divided into three groups: Group 1 ($n = 147$ cases) included pregnant women who did not receive any transfusions and had no hemorrhagic adverse events; Group 2 ($n = 52$ cases) included pregnant women who did not receive PLT but had hemorrhagic adverse events; and Group 3 ($n = 85$ cases) included pregnant women who received one apheresis PLT.

Specifically, the hemorrhagic adverse events in Group 2 referred to one of the following: (a) postartum hemorrhage (PPH) with blood loss of ≥1000 mL during cesarean; (b) diagnosis of anemia at discharge; and (c) required transfusion of blood components, such as red blood cells, plasma, and cryoprecipitate due to extensive drainage after the cesarean from the beginning of surgery until 72 hours postpartum.

Data on the gestational age, diagnosis, cause of thrombocytopenia, multiple pregnancies, large-for-gestational-age baby, the history of miscarriage, and prognosis of the pregnant women were recorded. The prepartum and

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Zhun Xing and Yang Li contributed equally to this study.

Correspondence to: Dr. Qiushi Wang, Department of Blood Transfusion, Shengjing Hospital of China Medical University, Shenyang, Liaoning 110801, China
E-Mail: wangqs18@vip.126.com;
Dr. Yan Zhao, Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University, Shenyang, Liaoning 110801, China
E-Mail: zhaoy@sj-hospital.org

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postpartum clinical characteristics were recorded, including obstetric complications such as uterine rupture, placenta previa, pernicious placenta previa, placenta accreta, placental abruption, cesarean-scar pregnancy, intrauterine fetal death, and liver disease. The usages units of red blood cells, PLTs, fresh frozen plasma, and cryoprecipitate were recorded for each patient. The time period during which the usage of blood components was analyzed spanned from the beginning of surgery until 72 hours postpartum.

Studies have shown that the value of the TEG MA reflects PLT function.[5,6] Therefore, this study utilized the MA as a parameter of PLT function. The prepartum fibrinogen level, PLT count, and TEG MA before delivery, and the prepartum and postpartum hemoglobin (Hb) levels were analyzed.

Data analysis was conducted using the IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Numerical data that followed a normal distribution were expressed as means ± standard deviations. Pairwise comparisons were conducted using the independent samples *t*-test. Multi-group comparisons were performed using one-way analysis of variance. Qualitative data were expressed as the number of cases and percentages. Intergroup comparisons were conducted using the chi-squared test. The MA threshold was determined using receiver operating characteristic analysis and was defined as the cut-off point at the maximum area under the curve. A P value <0.05 was considered statistically significant.

Compared to Group 3, gestational age in Groups 1 and 2 were shorter, the patients with primary gestational thrombocytopenia were less, but severe preeclampsia, placental abruption, and liver disease were more. This showed that when the pregnant women or the fetus was in an emergency situation, urgent deliveries were needed. The hemorrhage volume, red blood, plasma, and cryoprecipitate-using units were more in Group 2 than Group 1, but they both had no difference when compared to Group 3. For the prepartum coagulation laboratory testing, the fibrinogen level in Group 2 was lower than Groups 1 and 3. The Hb at discharge, PLT, and MA on admission in Group 2 were all lower than Group 1. PLT and MA on admission in Group 2 were both lower than Group 3 [Table 1].

Table 1: Clinical characteristics of pregnant women with thrombocytopenia ($n = 284$).

Items	Group 1 ($n = 147$)	Group 2 ($n = 52$)	Group 3 ($n = 85$)
Baseline characteristics			
Age (years)	28.45 ± 3.24	31.43 ± 3.99	30.63 ± 4.02
Gestational age (weeks)	34.94 ± 3.24*	33.89 ± 3.61*	36.16 ± 3.29
Twin pregnancy (yes/no)	8/139	2/50	1/84
Cause of thrombocytopenia (*n*)			
GP	46†	19†	62
ITP	1	0	2
Severe preeclampsia‡	98†	31†	20
Rheumatism	1	2	1
Hematologic disease	1	0	0
Risk factors for hemorrhage (*n*)			
Uterine rupture	0	1	3
Placenta previa	0	1	4
Pernicious placenta previa	0	0	0
Placenta accreta	0	0	0
Placental abruption	12†	7†	0
Cesarean-scar pregnancy	31	8	18
Intrauterine fetal death	7	4	1
Liver disease	17*	10†	3
Anemia	0†,§	22	23
Prepartum laboratory tests			
Fibrinogen (g/L)	3.95 ± 0.91	3.38 ± 1.21*,†	4.01 ± 0.71
Hb on admission (g/L)	118.01 ± 17.44	109.41 ± 16.98	109.29 ± 22.97
Hb at discharge (g/L)	99.66 ± 16.70	91.34 ± 16.18‡	95.05 ± 15.85
PLTs on admission (100×10^9/L)	58.37 ± 14.99†	50.15 ± 19.99‡	47.63 ± 17.71
MA on admission (mm)	56.93 ± 7.50†	49.40 ± 11.61§	52.50 ± 7.70
Hemorrhage volume and transfusion requirement			
Hemorrhage volume (mL)	211.05 ± 84.46	307.23 ± 328.27‡	229.29 ± 117.89
Red blood cell (U) transfused (*n*)	0	0.80 ± 1.53*,‡	0.39 ± 1.27
Plasma (U)	0	0.83 ± 2.94*,‡	0.14 ± 0.90

Data are presented as *n* or mean ± standard deviation (range). $^{*}P < 0.05$, $^{\dagger}P < 0.01$, compared with Group 3. $^{\ddagger}P < 0.05$, $^{\S}P < 0.01$ compared with Groups 1; including HELLP syndrome. GP: Gestational thrombocytopenia; Hb: Hemoglobin; HELLP: hemolysis, elevated liver enzymes, low platelet count; ITP: Autoimmune thrombocytopenic purpura; PLT: Platelet; MA: Maximum amplitude.

Woiski *et al*[4] recommend that a PLT count $>80 \times 10^9$/L should be maintained during delivery to avoid PPH. The Expert Consensus on the Diagnosis and Treatment of Thrombocytopenia in Adult Critical Care Patients in China proposes that PLT function should be assessed in patients with thrombocytopenia, such as TEG, whole blood PLT aggregometry, and flow cytometry. In recent years, TEG has been increasingly used for the assessment of the coagulation function.[5,6] In our retrospective analysis, there were 199 pregnant women who underwent an emergency cesarean section but did not receive PLT transfusions as a result of supply and time restrictions. No fatal hemorrhage occurred in all 199 pregnant women. However, the Hb of some patients decreased rapidly and would ordinarily have required postoperative transfusion, cry-oprecipitate, or plasma.

Therefore, we divided the 199 pregnant women who did not receive apheresis PLT transfusions into two groups based on adverse outcomes, such as PPH and the need for post-operative blood transfusion, to formulate a function strategy for PLT transfusion. These patients were then compared with the women who received apheresis PLT transfusions. When comparing the two groups (patients that did not require post-operative transfusion and had no adverse events/PPH as Group 1 and the patients who did not receive PLT but had adverse events/PPH as Group 2) of patients who did not receive apheresis PLT transfusions with each other, the two groups showed a statistically different amount of blood loss. Patients in group 2 had a higher transfusion volume of red blood cells compared with Group 3.

The Hb level on admission was not statistically different among the three groups. The fibrinogen level on admission in Group 1 was higher than that in Group 2, and their PLT count and MA were higher than those in Groups 2 and 3. The Hb level at discharge was higher in Group 1 than in Group 2. These findings suggest that despite only including patients whose PLT count was $<80 \times 10^9$/L, pregnant women who did not receive PLT transfusions and had no adverse events showed increases in their fibrinogen levels, PLT counts, and MA compared with the women with adverse events and those who received PLT transfusions. This further underlines the importance of PLT function assessment.

Our results show that the MA may be used to this end. The receiver operating characteristic analysis showed that an MA value of 49.35 mm, at which the sensitivity was 86.2%, the specificity of 52.6% ($P < 0.001$). This suggested that an MA value of 50 mm could be used as a cut-off point. This MA value corresponds to the lower end of the range in a normal population. This MA threshold may, therefore, ensure patient safety while reducing the pressure on PLT supplies. It also reduces transfusion-related adverse events and alloantigen exposure. Furthermore, an MA of 44.65 mm was associated with a specificity of 95.0%. This suggests a greater risk of hemorrhage when the MA is $\leq$45 mm, and PLTs should be prepared in time for these patients.

This observational study analyzed thrombocytopenia in pregnant women at our institution over the past four years. Pregnant women with thrombocytopenia exhibited a compensatory increase in clot strength. The use of a TEG MA threshold of 50 mm to indicate the need for PLT transfusion can be applied to identify pregnant women with thrombocytopenia at risk of PPH. Nonetheless, these results need to be confirmed in larger cohorts.

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Conflicts of interest

None.

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