



Pre-delivery fibrinogen level is a predictor for severity of placental abruption

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ABSTRACT

Objective: To determine pre-delivery fibrinogen levels in predicting adverse maternal or neonatal outcomes in patients with placental abruption.

Materials and method: We conducted a retrospective study of all women admitted for placental abruption between January 2012 and May 2018. Postpartum hemorrhage (PPH), disseminated intravascular coagulation (DIC), massive blood transfusion and hospitalization in intensive care unit parameters were evaluated for maternal outcomes. For the neonatal outcomes, the 5th minute APGAR score, umbilical artery pH and stillbirth were evaluated.

Results: The mean predelivery fibrinogen levels were 221.3 ± 111.6 mg/dL. In multivariate logistic regression analysis, fibrinogen level was determined as an independent indicator for PPH, red cell concentrate (RCC) and fresh frozen plasma (FFP) transfusion. When fibrinogen levels decreased below 130 mg/dL, the risk of PPH increased and when fibrinogen levels decreased below 100 mg/dL, the risk of overt DIC and also the risk of red cell concentrate and fresh frozen plasma transfusion increased. In terms of the fetal results, there may be adverse neonatal outcomes when fibrinogen levels are below 250 mg/dL.

Conclusion: Predelivery fibrinogen levels are good indicators for predicting adverse maternal outcomes in placental abruption cases. In addition, fibrinogen levels might be a guide for management of placental abruption cases.

Introduction

Placental abruption is a serious obstetric complication during pregnancy and defined as the separation of all or part of the placenta from the implant before delivery. It is one of the most important causes of maternal and perinatal morbidity and mortality and complicates approximately 0.3–1% of pregnancies [1]. Maternal and perinatal risks are related to the severity of placental separation and the risks of both maternal and fetal-neonatal morbidity are higher in severe cases [2]. Maternal complications include disseminated intravascular coagulation (DIC), blood transfusion, hypovolemic shock, hysterectomy and renal failure (2). Disseminated intravascular coagulation develops as a result of the separation of the placenta and tissue factors' traveling into the maternal circulation, resulting in thrombin formation and the activation of the coagulation pathway [3]. Massive postpartum hemorrhage can

progress to situations such as kidney failure and even threaten the life of the mother [4]. The most important point in the treatment of placental abruption is to remove the placenta by performing the delivery as soon as possible and providing a transfusion of the necessary blood products [4]. In this way, DIC and massive hemorrhage can be prevented. The main pathology leading to DIC and massive hemorrhage is the severe depletion of fibrinogen. It is known that the decrease in fibrinogen levels is a more effective indicator than other shock parameters in determining the need for blood transfusion after massive hemorrhage [5]. Therefore, in this study, we aimed to determine the role of fibrinogen levels in predicting adverse maternal and neonatal outcomes, with the hypothesis that predelivery fibrinogen levels may be a good indicator of the severity of placental abruption.

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Materials and methods

The medical records of the patients who were presented with a diagnosis of placental abruption in our clinic between January 2012 and May 2018 were retrospectively reviewed. The study was approved by the local ethics committee and followed the Declaration of Helsinki. Between these dates, the number of births in our clinic was 92137. A diagnosis of placental abruption was made based on the clinical findings (vaginal bleeding accompanying abdominal pain, tetanic uterine contractions, and unreliable non-stress test (NST) and ultrasonographic findings (heterogeneity and thickness increase in the placenta and subchorionic or retroplacental hematoma) or a macroscopic examination of the post-natal placenta, together with the clinical findings. The demographic characteristics of the patients; maternal outcomes, such as concomitant preeclampsia, chronic hypertension, fetal growth restriction, predelivery fibrinogen levels, postpartum hemorrhage (PPH), DIC, transfused blood products, and hospitalization in the intensive care unit; and neonatal outcomes, such as intrauterine fetal death, newborn birth weight, APGAR scores, and umbilical arterial pH parameters, were recorded.

We used MedCalc Statistical Software Version 17.8 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2017) for the statistical analyses. The data are expressed using means and standard deviations or percentages. Receiver operating characteristic (ROC) analysis and area under the curve (AUC) analyses were used to determine the predictive cut-off of predelivery fibrinogen for the maternal outcomes of DIC, PPH, and blood transfusion, as well as for the neonatal outcomes of APGAR score, umbilical artery pH, and stillbirth. A multivariate logistic regression analysis was carried out to analyze the predictive ability of predelivery fibrinogen levels; odds ratios (ORs) and 95% confidence intervals (CI) were reported, and p values of less than 0.05 were considered statistically significant.

Results

The demographic characteristics of 166 patients diagnosed with placental abruption are shown in Table 1. Mean maternal age was 29.3 ± 6.1 years. Mean gestational age at delivery and birthweight were 31.9 ± 4.2 weeks and 1792.2 ± 782.9 gr, respectively. Mean predelivery fibrinogen levels were 221.3 ± 111.6 mg/dL, and the mean transfusion amounts of red cell concentrate (RCC), fresh frozen plasma (FFP) and the fibrinogen concentration were 1.8 ± 2.7, 1.1 ± 2.1 units, and 0.75 ± 1.5 gr, respectively (Table 1). The results regarding the prediction of maternal complications based on fibrinogen levels are shown in Table 2. For the prediction of RCC and FFP transfusions of ≥ 5 units, the AUC (> 0.9) for fibrinogen level (cut-offs of 104 and 100 mg /dL, respectively)

Table1
Characteristics of patients with placental abruption.

	n = 166
Maternal age (years)	29.3 ± 6.1
Gestational age at delivery (weeks)	31.9 ± 4.2
Birthweight (g)	1792.2 ± 782.9
Plasma fibrinogen level (mg/dL)	221.3 ± 111.6
RCC transfusion (units)	1.8 ± 2.7
FFP transfusion (units)	1.1 ± 2.1
Fibrinogen (g)	0.75 ± 1.5
Preeclampsia (n,%)	30 (18.1)
Fetal death on admission (n,%)	76 (45.7)
Fetal death after admission (n,%)	6 (3.6)
Apgar score ≤ 3 at 5 min (n,%)	82 (49.4)
UmbA pH < 7.00 (n,%)	11 (6.6)
Hospital stay (day)	4.43 ± 4.64
Postpartum hemorrhage (n,%)	
Absent	106 (63.9)
Medically managed	50 (30.1)
Surgically managed	10 (6)

RCC, red cell concentrate; UmbA, umbilical artery; FFP, fresh frozen plasma

was high (Table 2). In the multivariate logistic regression analysis, at these cut-of levels, fibrinogen level was found to be an independent predictor of overt DIC (OR=1.07; 95%CI=1.029–1.120, p = 0.001), postpartum hemorrhage (OR=17.2; 95%CI=7.3–40.6, p = 0.000), RCC ≥ 5 units (OR=67.9; 95%CI=8.9–514.4, p = 0.000), and FFP ≥ 5 units transfusion (OR=19.6; 95%CI=7.2–53.3, p = 0.000) (Table 2). In terms of predicting neonatal outcomes based on fibrinogen, for umbilical artery pH < 7.0 (cut-of = 245 mg/dL), an Apgar score of 3 at 5 min (cut-off=254 mg/dL), and stillbirth (cut-of = 254 mg/dL), the AUC values were 0.7, 0.64, and 0.63, respectively. In the multivariate logistic regression analysis, fibrinogen was found to be a good predictor of Apgar scores ≤ 3 at the 5 min and stillbirth.

Discussion

Our aim in this study was to determine the role of predelivery fibrinogen levels in predicting adverse maternal outcomes after placental abruption. We determined that when fibrinogen levels decreased below 130 mg/dL, the risk of PPH increased and that when fibrinogen levels decreased below 100 mg/dL, the risk of overt DIC and also the risk of RCC and FFP transfusion increased. In terms of the fetal results, there may be adverse neonatal outcomes when fibrinogen levels are below 250 mg/dL. Therefore, predelivery fibrinogen levels may be a good predictor of placental abruption severity and adverse maternal and neonatal outcomes.

Placental abruption is defined as the complete or partial separation of the placenta from the implantation area before the delivery of the fetus as a result of bleeding into the decidua basalis. It is a common cause of perinatal mortality and stillbirths during the third trimester [6]. In 1.1% of pregnancy-related deaths in the United States, placental abruption is the direct cause of maternal mortality [7]. The most serious complication seen in placental abruption cases is DIC, and the occurrence of DIC is related to the severity of the placental abruption. In other words, one-third of patients diagnosed with severe placental abruption had DIC. In fact, DIC is a result of the decidual and placentally induced tissue factors entering into the circulation in large amounts, resulting in the depletion of procoagulants and generalized coagulation [8]. As a result, fibrinogen is consumed in large quantities. Therefore, this explains the relationship between the severity of placental abruption and decreased fibrinogen levels, and it has been shown that fibrinogen levels can be used for the prediction of DIC. Making a diagnosis of DIC in time and the rapid initiation of treatment are very important in preventing maternal morbidity and mortality due to DIC [9]. Although many scoring systems have been developed, including laboratory tests such as thrombocyte count, prothrombin time (PT), and D-dimer, it has been shown that fibrinogen levels are more effective in predicting maternal and neonatal outcomes than these tests. Fibrinogen levels are significantly increased in the late stages of pregnancy and range from about 400–650 mg/dL [10]. In women with high basal fibrinogen levels, even though fibrinogen is used after a massive abruption, hemostasis can still be achieved if plasma fibrinogen is sufficient. This may be one of the reasons consumption coagulopathy does not develop, even though fibrinogen consumption is high in some cases of severe abruption.

Although, in cases with severe PPH, many coagulation parameters (INR, fibrinogen, FII and FV, D-dimer, antithrombin, protein C, and soluble fibrin monomer) were found to be significantly different in their prediction of postpartum hemorrhage as compared to cases without severe PPH, it has been shown that fibrinogen levels were the only parameter to predict PPH independently [11]. In addition, it was determined that the decrease in fibrinogen levels is a predictor of the severity of PPH[12]. Moreover, patients with postdelivery fibrinogen levels < 200 mg/dL have a twelve-fold higher risk of severe PPH [13]. In our study, for predelivery fibrinogen levels for PPH, given a cut-off of 131 mg/dL, an OR of 17.2 was found for PPH. Specifically, when predelivery fibrinogen levels are below 131 mg/dL in cases of placental abruption, patients should be followed up more closely in terms of

Table 2

Receiver operating characteristic curve and multivariate logistic regression analysis of fibrinogen predicting maternal outcomes in placental abruption.

Outcomes	Fibrinogen cut-off value (mg/dL)	AUC	Sensitivity	Specificity	Multivariate logistic regression analysis		
					OR	95% CI	p value
PPH	131	0.809	66.7	89.6	17.2	7.3–40.6	0.000
DIC	100	0.961	100	85.6	1.07	1.02–1.12	0.001
RCC transfusion ≥ 5 units	104	0.919	85.7	87.5	67.9	8.9–514.4	0.000
FFP transfusion ≥ 5 units	100	0.949	100	84.4	19.6	7.2–53.3	0.000
Admission to intensive care unit	200	0.867	90.3	71.6	24.5	6.8–88.2	0.000

AUC, area under the curve, CI, confidence interval; DIC, disseminated intravascular coagulation; PPH, postpartum hemorrhage; RCC, red cell concentrate; FFP, fresh frozen plasma; OR, odds ratio.

postpartum hemorrhage, and in case of PPH development, attention should be paid to early and intensive management.

In cases of massive blood loss secondary to placental abruption, the administration of sufficient blood products or fibrinogen concentrate may reduce both the worsening of DIC and the need for hysterectomy [14]. In our study, we determined the fibrinogen cut-off values for 5 units or more for FFP and RCC transfusions, which were 100 and 104 mg/dL, respectively. In cases in which fibrinogen is below these values, due to the necessity of massive transfusions, it is necessary to immediately prepare blood products and replace the appropriate blood products.

This study has certain limitations. First, the study is retrospective. Secondly, due to being single-centered, the selection of subjects was biased. Third, a diagnosis of DIC was made in patients with an overt diagnosis, and the scoring system was not used for the diagnosis of DIC, because D-dimer levels are not routinely evaluated in our clinic.

In conclusion, predelivery fibrinogen level may be a good predictor for severity of placental abruption. In addition, fibrinogen levels might be a guide for management of placental abruption cases. When fibrinogen level is below 130 mg/dL, clinicians should be aware that there is increased risk of PPH, DIC and transfusion of blood products.

Ethical approval

All procedures performed were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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