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Evaluation of the Differences in Plasma Fibrinogen Levels Before and After Cesarean Section and its Association with Intra- and Postoperative Bleeding

Maryam Sadat Hosseini[1], Dariush Abtahi[2*], Ardeshir Tajbakhsh[2], Farah Farzaneh[1], Shahram Sayadi[3], Nooshin Amjadi[4], Maral Hosseinzadeh[5]

1. *Department of Obstetrics and Gynecology, Preventative Gynecology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
2. *Department of Anesthesiology, Clinical Research and Development Unit, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
3. *Anesthesia Research Center, Department of Anesthesiology, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
4. *Prevention Gynecology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
5. *Department of Obstetrics and Gynecology, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

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Corresponding Information:
Dariush Abtahi,
Clinical Research and Development Unit, Imam Hossein Hospital, Anesthesiology Department, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Email: drdariushabtahi@yahoo.com

ABSTRACT

Background & Objective: Delayed diagnosis and treatment of postpartum hemorrhage could result in mortality. Today, there is a strong desire to determine the factors affecting postpartum hemorrhage, particularly fibrinogen levels. This study aimed to investigate the role of plasma fibrinogen levels in postpartum hemorrhage and severe postpartum hemorrhage.

Materials & Methods: This cross-sectional study was conducted on 169 term pregnant women who were candidates for an elective Cesarean section. Fibrinogen and other coagulating factors were measured before and at the end of the surgery, and twenty-four hours after surgery. Bleeding volume was also measured during and at the end of the surgery, and twenty-four hours after that. The relationship between coagulation factors and the amount of bleeding was examined using statistical tests.

Results: Mean plasma fibrinogen levels measured before, at the end of, and 24 hours after surgery were 247.65±91.07 mg/dl, 219.4±75.60 mg/dl, and 223.91±65.44 mg/dl, respectively. Sixty-five patients (38.5%) had postpartum hemorrhage (1000-2000mL) and seven patients (4.1%) had severe postpartum hemorrhage (>2000mL). Of the cases with preoperative fibrinogen levels less than 200mg/dl, 72% had postpartum hemorrhage and 14% had the severe form. There was a strong association between the patient's plasma fibrinogen level with PPH and sPPH (P=0.000).

Conclusion: This study showed a strong correlation between plasma fibrinogen levels and postpartum hemorrhage and severe postpartum hemorrhage. In addition, it has been shown that low plasma fibrinogen levels could be a direct prognostic factor for postpartum hemorrhage and severe postpartum hemorrhage. Younger women and preoperative anemia were other strong predictors.

Keywords: Cesarean Section, Fibrinogen, Postpartum Hemorrhage, Anesthesia

Introduction

Postpartum hemorrhage (PPH) is a leading cause of maternal mortality and morbidity **(1-3)**. Although predictable and preventable, PPH is responsible for 19.7% of maternal deaths worldwide. PPH is defined as bleeding greater than 500 ml during normal vaginal delivery or greater than 1000 mL after Cesarean section **(4)**. Primary PPH is defined as bleeding within the first 24 hours after delivery, often caused by uterine atony, pelvic trauma, or abnormal placentation. Secondary PPH is defined as bleeding occurring between 24 hours and six weeks after delivery **(5, 6)**. In the literature, risk factors for PPH are listed as follows: previous PPH, retained placenta, anemia, uterine atony, placenta previa, Cesarean section, and preeclampsia **(7, 8)**.

During pregnancy, hemostatic changes are observed. Procoagulant levels are gradually increased, while anticoagulant levels are reduced or remained unchanged. This hypercoagulable state protects the parturient from massive bleeding **(9)**. The plasma fibrinogen concentration is also higher in pregnant women (400-600 mg/dl) than in non-pregnant women (200-400 mg/dl). At term, the relative time of activated thromboplastin (PTT) is shortened. It should be noted that despite massive bleeding, prothrombin time (PT)

and PTT may remain normal and therefore have limited value in monitoring coagulation status **(6, 10)**. On the other hand, the platelet count may decrease during pregnancy, but the clinical significance of this decrease is unclear **(11)**.

It has been described that fibrinogen plasma levels can anticipate the risk of major bleeding in patients with PPH **(1, 10, 12)**, but it is not yet clear whether the relationship between fibrinogen and PPH is causal or associative. On the other hand, Karlsson et al. have shown that there is no association between pre-delivery fibrinogen levels and the development of PPH **(8)**. Therefore, the present study was conducted to investigate the relationship between preoperative fibrinogen levels and the development of PPH and severe postpartum hemorrhage (sPPH) in the Cesarean section.

Methods

This prospective observational study was conducted on pregnant women scheduled for non-emergency Cesarean section at a tertiary educational and treatment center. After approval by the Iran National Committee for Ethics in Biomedical Research (Code of Ethics: IR.SBMU.RETECH.REC.1397.285) and obtaining the informed consent of the patients, 169 pregnant women having an elective Cesarean section under spinal anesthesia were evaluated in the operating room. Subjects with underlying systemic disease, history of coagulopathy, smoking, substance abuse, or emergency Cesarean section were excluded.

Plasma fibrinogen levels and other coagulation factors such as PT, PTT, INR, platelets, and D-Dimer were measured 24 hours before surgery. Once patients entered the operating room, they underwent standard monitoring (noninvasive blood pressure, electrocardiogram, and pulse oximetry), and operations were performed by senior gynecology residents under the supervision of a specialist. According to our local Obstetric Bleeding Management Protocol, after removal of the placenta, oxytocin infusion was started at a dose of 10 to 40 units in 500mL normal saline at a rate of 60 drops per minute. In cases where bleeding volume exceeded 1500mL, oxytocin was repeated and methylergonovine, misoprostol, and tranexamic acid were used if needed. Bleeding volume during surgery was calculated by measuring the volume of blood collected at suction, counting surgical gases, and examining the patient's drape after surgery. Bleeding measurements were also taken in the recovery room and in the ward. Bleeding of fewer than 1000 ml was defined as normal bleeding, between 1000 and 2000ml was defined as postpartum hemorrhage (PPH), and over 2000ml was defined as severe postpartum hemorrhage (sPPH). Measurement of plasma fibrinogen and other coagulation factor concentrations was also repeated in the recovery room and 24 hours after surgery. Patients' characteristics were compared with Student's *t*-test for the normally distributed quantitative variables and with the Kruskal-Wallis test for the quantitative variables not normally distributed. The distributions of the qualitative variables were compared with the χ^2 test using SPSS software version 17. A non-parametric receiver operating characteristic (ROC) curve and its area under the curve was estimated to evaluate the accuracy of the fibrinogen level for assessing the severity of PPH. MedCalc software was also used to plot the ROC curve.

Results

Of 1343 women who had a Cesarean section during the 18-month survey period, a total of 404 women who met eligibility criteria participated in the study. Of these, 235 were excluded due to incomplete data. The final analysis included 169 women who had undergone Cesarean section. Of the women with major bleeding, 34 received transfusions, and 3 were transferred to the intensive care unit. All patients were discharged from the hospital without complications. The mean age was around 30 years (n=169) and those younger than 19 years had a higher risk of PPH. Most cases of sPPH occurred in the 30-39 years age group (Table 1). The participants' weight, height, and BMI were 77.50±11.06 kg, 162.97±6.41 cm, and 29.16±3.78 kg/m2, respectively. A significant relationship was demonstrated between maternal weight and the probability of PPH (P=0.00) but not for sPPH (P=0.37). There was no significant association between maternal height and risk of PPH (P=0.94). Using Fisher's exact test, it was shown that there is a significant relationship between BMI and the probability of PPH (P=0.002). Among our subjects, only 18 (10.7%) had a normal BMI, 90 (53.3%) were overweight (25<BMI< 29), and 61 (36.1%) were obese (BMI>30). Of seven cases with sPPH, six were obese and one overweight. None of the subjects with normal BMI had excessive bleeding (Table 1).

The relationship between blood group type and education level with bleeding severity was not significant (P=0.068 and P=0.12, respectively). More than 92% of women received prenatal care, and the multivariate regression model showed that those who received prenatal care were 85% less likely to develop sPPH. In addition, 62.7% of patients had a history of Cesarean section and 11.2% had a normal delivery. A multivariate regression model showed no significant difference between the incidence of PPH in mothers with a prior Cesarean section and mothers without a prior birth.

In 39% of cases, there was a history of miscarriage. The most common was a one-time abortion. People with a history of more than three miscarriages were more likely to develop PPH (P=0.045) (Table 1). Twenty-six percent of patients had no history of surgery, and the most common was a one-time surgery (7.33%). Despite this, there was no significant association between the number of previous surgeries and the likelihood of developing PPH (P=0.34). Most

mothers had one or two children, and the regression test showed no significant difference between the number of previous pregnancies and the presence of PPH (*P*=0.06).

Table 1. Maternal characteristics and history

Variables	Items	Normal Bleeding (<1000 mL)	PPH[1] (1000- 2000 mL)	sPPH[2] (>2000 mL)
Age, year	<19	2 (18.2%)	9 (81.8%)	0 (0.0%)
	20-29	34 (54.0%)	28 (44.4%)	1 (1.6%)
	30-39	51 (60.7%)	27 (32.1%)	6 (7.1%)
	>40	10 (90.9%)	1 (9.1%)	0 (0.0%)
BMI[3], kg/m2	18.5 - 24.9	12 (12.4%)	6 (9.2%)	0 (0.0%)
	25 - 29.9	24 (24.7%)	31 (47.7%)	6 (85.7)
	30-39	61 (62.9%)	28 (43.1%)	1 (14.3%)
Parity	0	20 (20.8%)	21 (31.8%)	3 (42.9%)
	1	36 (37.5%)	27 (40.9%)	4 (57.1%)
	2	25 (26.0%)	14 (21.2%)	0 (0.0%)
	>3	15 (15.6%)	4 (6.1%)	0 (0.0%)
Abortion	0	52 (50.5%)	51 (49.5%)	0 (0.0%)
	1	30 (66.7%)	15 (33.3%)	0 (0.0%)
	2	14 (82.4%)	3 (17.6%)	0 (0.0%)
	3	1 (25.0%)	3 (75.0%)	0 (0.0%)

[1]-postpartum hemorrhage, [2]-severe postpartum hemorrhage, [3]-body mass index

The duration of the surgeries ranged from 30 to 120 minutes, averaging about 64.76±18.44 minutes. There was a significant association between the duration of surgery and the likelihood of PPH (*P*=0.000). Despite this, no significant association was found between this factor and sPPH (*P*=0.07).

Of 169 mothers, 156 (92.3%) received prenatal care and these were 85% less likely to develop sPPH. All mothers in PPH received prenatal care. The weight of the newborns was 3130.75±491.72 grams. Fourteen cases (3.8%) were born underweight and one case (0.6%) was born overweight. There was no significant

association between newborns' weight and PPH (*P*=0.102). In our study, the patient's PPH history was based on their reports, and due to the inaccuracy of this method and lack of access to reliable documents, it was not possible to examine this factor.

Bleeding of fewer than 1000 ml was observed in 97 cases (57.4%), between 1000 and 2000 ml in 65 cases (38.5%), and over 2000 ml in seven cases (4.1%). The minimum, maximum, and mean bleeding volumes were 300, 2700, and 941mL, respectively.

Mean hemoglobin concentrations before surgery, in the recovery room, and 24 hours after surgery were 11.36±1.49, 10.90±1.43, and 10.81±1.10g/dl, respectively. According to the definition of maternal anemia in the third trimester of pregnancy with a hemoglobin level less than 11g/dl **(13)**, 33 subjects (19.5%) of our study were anemic. Mean hemoglobin levels were shown based on bleeding volume in Table-2. There is a strong relationship between the presence of preoperative anemia and the likelihood of PPH (*P*=0.000). It was also found that 35.4% of PPH cases and 57.1% of sPPH cases had anemia, while this figure was only 6.2% in those with normal bleeding. Using a multivariate regression model, it was shown that for every gram per deciliter decrease in hemoglobin, the likelihood of PPH and sPPH increased eight-fold and twenty-fold, respectively.

Mean platelet counts before surgery, in the recovery room, and 24 hours after surgery were 200.36±51.18, 196.50±59.28, and 193.70±52.56 thousand per microliter, respectively. Using the definition of third-trimester thrombocytopenia as less than 150,000 platelets per microliter **(14)**, it was shown that 11.2% of the participants in this study had thrombocytopenia before surgery. Mean platelet levels were shown based on bleeding volume in Table 2. There was no statistically significant association between the presence of preoperative thrombocytopenia and the possibility of PPH (*P*=0.963).

The mean prothrombin time (PT) before surgery, in the recovery room, and 24 hours after surgery in these subjects was 12.03±0.92, 11.83±1.05, and 12.22±1.10 seconds, respectively. The mean partial thromboplastin time (PTT) at the same time was 27.10±5.30, 27.01±5.15, and 27.44±5.31 seconds, respectively. Preoperatively, prolonged PT and PTT were observed in 14.3% and 4.1% of patients, respectively. Mean PT and PTT levels were shown based on bleeding volume in Table 2. No significant association was found between PT and long preoperative PTT with PPH (*P*=0.53 and *P*=0.73, respectively).

In our study, 21.9% of the subjects had high serum D-dimer levels. Mean D-dimer levels before surgery, in the recovery room, and 24 hours after surgery were 1158.88±1087.66, 1386.73±1225.81, and 1451.30±1389.46 micrograms per liter, respectively. Mean D-dimer levels were shown based on bleeding volume in Table 2. No correlation was found between D-dimer levels and maternal bleeding (*P*=0.25).

Of 169 pregnant women, 97 (57.4%) cases had normal bleeding, 65 (38.5%) developed PPH, and 7 (4.1%) developed sPPH. The mean plasma fibrinogen levels of all women before surgery, in the recovery room, and 24 hours after surgery were 247.65±91.07 mg/dl, 219.14±75.60mg/dl, and 223.91±65.44 mg/dl, respectively. Mean fibrinogen levels at all times in normal bleeding (<1000 ml), PPH (1000-2000 ml), and sPPH (>2000ml) decreased sequentially (Figure 1) (Table 2). It was shown that 50 cases (29.6%) had less than 200 mg/dL of fibrinogen before surgery. At the end of surgery in the recovery room, the number of low fibrinogen cases had reached 75 (44.4%), but by the end of 24 hours, the number of cases had returned to 58 (34.3%). Patients with normal preoperative fibrinogen levels did not progress to sPPH. In addition, 72% of patients with low fibrinogen levels (<200 mg/dl) had PPH, while 14% of them developed sPPH. Due to the abnormal distribution of all fibrinogen levels, the Kruskal-Wallis test was used to examine the relationship between pre-cesarean fibrinogen levels and PPH, and this relationship was found to be significant (*P*=0.000). In terms of predictability, it was shown that for every milligram per deciliter decrease in fibrinogen levels, the likelihood of PPH and sPPH increased by 2% and 6%, respectively. Sixty percent of the low fibrinogen cases developed PPH while 9.3% developed sPPH. None of the patients with higher fibrinogen levels (>200 mg/dl) had PPH or sPPH. Fisher's exact test showed that the relationship between fibrinogen levels at the end of surgery was significantly associated with the occurrence of PPH and sPPH (*P*=0.000).

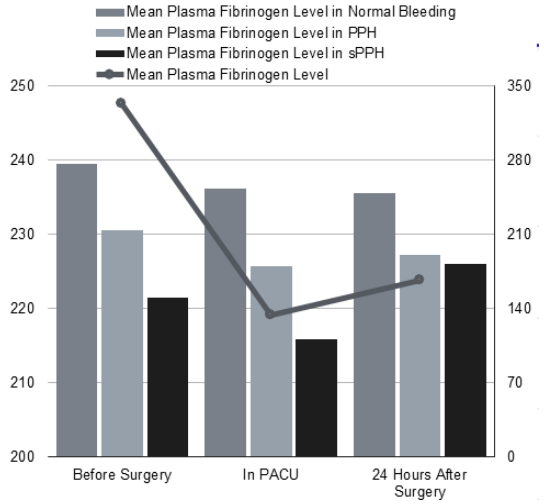

Figure 1. Correlation between plasma fibrinogen level and occurrence of PPH or sPPH. PACU: post-anesthesia unit care

Table 2. Laboratory variables at specific times based on bleeding volume

Variables	Items	Normal Bleeding (<1000 mL)		PPH[1] (1000- 2000 mL)		sPPH[2] (>2000 mL)	
		Mean	SD	Mean	SD	Mean	SD
Hb[3] g/dL	Preoperative	11.89	1.26	10.77	1.51	9.51	0.52
	Recovery room	11.05	1.22	10.62	1.56	11.27	2.37
	24 hours after	10.78	0.95	10.86	1.30	10.70	1.22
PLT[4] microliter	Preoperative	206.31	60.15	190.26	35.82	214.00	16.00
	Recovery room	205.81	67.08	181.53	44.86	209.86	35.75
	24 hours after	202.96	60.69	180.27	37.56	193.43	37.56
D-dimer ng/mL	Preoperative	1294.60	1236.92	1010.30	842.16	698.43	656.29
	Recovery room	1370.79	909.93	1468.39	1607.06	835.43	743.25
	24 hours after	1398.92	805.37	1593.85	1977.83	825.71	827.46
PT[5] seconds	Preoperative	12.03	0.96	11.98	0.88	12.17	0.76
	Recovery room	11.82	0.97	11.80	1.17	12.28	0.65
	24 hours after	12.15	0.88	12.37	1.34	11.65	1.06
PTT[6] seconds	Preoperative	27.17	5.15	27.24	5.70	24.72	2.03
	Recovery room	27.17	5.21	26.64	5.31	28.41	1.5910
	24 hours after	28.04	5.40	26.12	5.08	31.51	1.76
Fibrinogen mg/dL	Preoperative	277.73	103.81	214.21	46.67	150.43	15.52
	Recovery room	253.90	72.67	179.97	49.67	111.71	7.93
	24 hours after	249.53	66.99	191.02	45.78	182.57	41.88

[1]-postpartum hemorrhage, [2]-severe postpartum hemorrhage, [3]-hemoglobin, [4]-platelet, [5]-prothrombin time, [6]-Partial Thromboplastin Time

The sensitivity and specificity of fibrinogen levels for PPH and sPPH results were also examined and the use of the ROC curve to determine a cut-off for fibrinogen showed that levels below 225 mg/dl have a sensitivity of 75.34 and a specificity of 71.87 for predicting PPH, and values below 185 mg/dl have a sensitivity of 85.71 and a specificity of 96.91 for sPPH (Figure 2, 3).

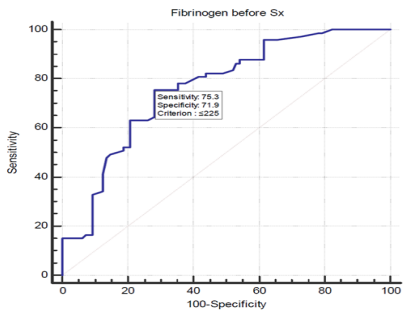

Figure 2. Cut off point for Plasma Fibrinogen Level in PPH

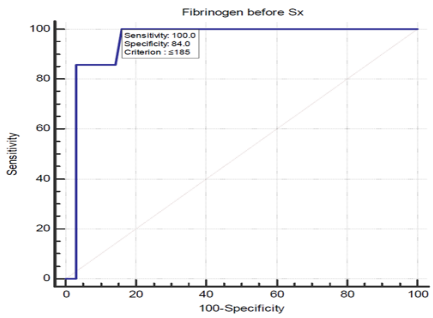

Figure 3. Cut off point for Plasma Fibrinogen Level in sPPH

Discussion

There is always a possibility of severe and unexpected bleeding during a Cesarean section. Because bleeding can be rapid enough to endanger the mother's life, developing predictive factors before surgery can predict severe bleeding and reduce maternal mortality rates. Various studies have suggested many different variables (e.g., coagulation factors, age, weight, and anemia) but failed to demonstrate any correlation or may have encountered much controversy. We examined plasma fibrinogen levels as a predictive tool and to our knowledge, this study is the first in Iran to examine the association between plasma fibrinogen levels and postpartum hemorrhage.

The role of age as a predictor of bleeding has been examined in several studies, with controversial results. Lao et al. showed that advanced maternal age served only as a surrogate factor for PPH due to associated risk factors **(15)**. Freeman et al. showed that being over 45 years of age is an independent risk factor for PPH **(16)**. Cavazos-Rehg et al. investigated the association between maternal age and the risk of labor and birth complications and found an increased risk of PPH only in mothers aged 15 to 19 **(17)**. But these findings are not always supported **(18)**. In our study, 11 (6.5%) mothers were under 19 years old and 11 (6.5%) over 40 years old. Most of the 11 patients under the age of 19 had PPH and this was the highest prevalence among other age groups. With each additional year of life, the probability of belonging to the PPH group decreases by 10%. In other words, bleeding is reduced with age (P=0.000). No sPPH was reported in mothers under 19 years and over 40 years (Table 1). Because of the low incidence of sPPH, specific and larger studies are needed for a better conclusion.

There are conflicting data on maternal weight and body mass index with bleeding severity. Although Charbit, Endo-Kawamura, and Karlsson showed a significant relationship between BMI and PPH, the study by Niepraschk-von Dollen showed no relationship **(1, 7, 8, 18)**. A review article also showed no association between obesity and PPH **(19)**. In the present study, there was a significant relationship between BMI and PPH, and sPPH (P=0.000 and P=0.01, respectively). Logistic regression testing showed that PPH and sPPH increased 20- and 30-fold with each increase in BMI, respectively.

People who received prenatal care visits were 85% less likely to develop sPPH. In the PPH group, all mothers received prenatal care visits. Similar information was not found in other studies. Most cases in our study had a previous Cesarean section. Studies have shown that a previous Cesarean section can increase the risk of postpartum hemorrhage **(7, 20)**. In the present study, none of the previous normal birth cases had sPPH, but no significant correlation was found between the type of birth in previous pregnancies and the severity of bleeding (P=0.09).

Sheldon et al. have suggested previous miscarriages as a risk factor for PPH **(21)**. Although there is insufficient evidence in the literature, our study supports their conclusion. There was a significant correlation between postpartum hemorrhage and more than three miscarriages (P=0.045) (Table 1). Multiparity and grand multiparity can also be considered risk factors. A study in Zambia showed that the optimal parity cut-offs for vaginal births and Cesarean sections were para seven andthree, respectively, and an increase in maternal complications such as PPH **(22)**. Another study showed that high parity was associated with a 17% increased risk of PPH **(23)** and others confirmed the relationship between multiparity and PPH **(24-26)**. There were opposite results in other studies **(1, 12)**. In our study, most mothers had one or two children and there was no significant difference between the number of previous pregnancies and the presence of PPH (P=0.066).

Preoperative anemia is another factor that has been studied. One review article showed a predictive role of maternal anemia in increasing bleeding intensity **(27)**. This result was supported by some authors **(28-31)** and even Frass showed the association between severe anemia and emergency hysterectomy **(32)**. Conflicting results were also reported **(33)**. In our study, 19.5% of the mothers were anemic at the time of admission and there was a significant correlation between the presence of anemia and bleeding volume (P=0.000). The multivariate regression model showed that a decrease of one gram of hemoglobin per deciliter can lead to an eight-fold increase in the incidence of PPH and a twenty-fold increase in the incidence of sPPH. Some studies have shown increased bleeding in maternal thrombocytopenia **(34-36)**, but we cannot demonstrate this relationship. Our results are similar to other studies **(8, 18)** and the association was not significant. A retrospective single-center cohort study conducted in a cohort of 23205 deliveries in a tertiary-level hospital failed to demonstrate the predictive value of thrombocytopenia and severe PPH **(37)**.

Chauleur et al. have shown that blood type O is associated with PPH **(38)**. Although the frequency of blood type O was higher in PPH and sPPH (33.8% and 42.9%, respectively), there was no significant correlation between blood type and bleeding volume in the present study.

Niepraschk-von Dollen et al. reported a correlation between fetal macrosomia (>4000g) as a risk factor for PPH **(18)** and this has been shown in other studies **(39-41)**. As mentioned above, in the present study there was no significant association between neonatal weight and maternal bleeding volume (P=0.102).

It has been suggested that women with a history of PPH are at high risk of PPH **(42)**. Patients' medical histories of their previous PPH were unreliable and we

did not have access to their previous medical records. Therefore, we couldn't evaluate this factor.

A correlation between duration of surgery and PPH or sPPH has been shown. Logistic regression showed that a one-unit increase in operative time increases the probability of being in the PPH category by 4%, which is statistically significant (*P*=0.000). However, no significant correlation was observed in the sPPH group. This correlation may be due to the longer duration of surgery in patients with major bleeding.

Conflicting results are also seen in PT and PTT measurements and the occurrence of PPH. One study showed that activated partial thromboplastin time was less sensitive in predicting blood loss volume and prothrombin time did not correlate with it, importantly activated partial thromboplastin time and prothrombin time remained within normal ranges in most women despite major bleeding **(43)**. Other studies did not show any prediction rules for PT and PTT **(7, 8, 18)**. In the present study, there was no association between preoperative PT and PTT with increased bleeding (*P*=0.129 and *P*=0.255, respectively).

Several studies demonstrated the predictive role of D-dimer and PPH **(7, 44, 45)**. Although 21.9% of the cases had high serum D-dimer levels, no correlation was found between D-dimer levels and maternal bleeding.

The normal plasma concentration of fibrinogen rises to almost 500mg/dl in the third trimester **(46)**. During PPH, fibrinogen levels decrease due to blood loss itself (depletion of coagulation factors) and consumption associated with coagulation activation. Charbit **(1)** and de Lloyd **(43)** showed that low fibrinogen levels before Cesarean section predicted postpartum hemorrhage. Additionally, Cortet suggested that fibrinogen levels below 300mg/dL can predict PPH **(12)**. Other studies support this relationship **(6, 7, 18, 47-49)**. It is not clear whether the relationship between fibrinogen and PPH is causal or associative. On the other hand, Karlsson has shown that there is no association between preoperative fibrinogen levels and the development of PPH **(8)**. In our study, we showed that fibrinogen levels were significantly lower in patients with PPH and sPPH (Table 2) and can be used as a prognostic factor.

We propose that early use of fibrinogen may correct decreased fibrinogen levels and reduce the use of other blood derivatives. It is recommended for fibrinogen infusion when levels fall below 200g/dl **(46)**. In our study, a nonparametric Receiver Operating Characteristic (ROC) curve and its area under the curve (AUC) confirmed the accuracy of fibrinogen levels for assessing PPH and sPPH (AUC=0.762; P<0.0001 for PPH and AUC=0.952; P<0.0001 for sPPH). The ROC curve analysis for fibrinogen (Figure 2) showed that the cut-off point of 225g/dl had the highest power, with a sensitivity of 75% and a specificity of 71% for PPH and that the cut-off point of 185g/dl had the highest power with a sensitivity of 85% and a specificity of 96% for sPPH (Figure 3). Therefore, we suggest that corrective treatment should be initiated immediately if plasma fibrinogen levels are below 225mg/dl.

Our study had two weaknesses in interpreting the results. First, the percentage of PPH in our series is significantly higher than in other studies (42.6% PPH *vs* 2.9% in the Bateman et al. study **(50)**). This high PPH rate in our study is associated with the exclusion of women with vaginal delivery, and this study was conducted at the main referral hospital. Second, the mean pre-delivery plasma fibrinogen levels in all women before surgery were lower than in most previous studies (247.65±91.07 vs 420±120 in the Cortet study **(12)**). This difference may be due to differences in lab kits or genetic differences.

To our knowledge, no study has been conducted to measure fibrinogen levels in pregnant women in Iran, except for a study by Yazdani, which seeks to determine the association of fibrinogen and C-reactive protein with preeclampsia severity. He showed that the mean plasma fibrinogen level measured in mothers over 30 weeks gestation was 360.50±62.35mg/dl. **(51)**. Therefore, it was unfortunately not possible to compare our results with an identical study.

Conclusion

This is the first time in Iran to study the effect of plasma fibrinogen levels on the severity of postpartum hemorrhage and we have shown that this is a predictive factor for PPH and sPPH. We also found that a history of three or more miscarriages, high body mass index, and anemia at the time of admission may increase the risk of postpartum hemorrhage. Paying attention to these factors, which are usually preventable or correctable, can reduce the incidence of this potentially fatal complication. We suggested the measurement of preoperative fibrinogen levels as a predictive tool in all parturient and asked for help from a hematologist in case of severe PPH. Also, thromboelastometry allows the rapid measurement and even near-continuous monitoring of fibrinogen levels.

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Conflict of Interest

Authors declare no conflict of interest.

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Author's Contributions

Dariush Abtahi has conducted the design, execution, and management of the project, including writing and final approval of the manuscript; Ardeshir Tajbakhsh contributed to writing the paper and translation to English and has analyzed and interpreted the data; Shahram Sayadi cooperated on design and writing the manuscript; Maryam Sadat Hosseini cooperated on design and writing the manuscript; Farah Farzaneh cooperated on design and writing the manuscript; Nooshin Amjadi cooperated on design and writing the manuscript; Maral Hosseinzadeh cooperated on design and writing the manuscript.

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