The association between preterm delivery and postpartum bleeding in otherwise uncomplicated pregnancies

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Abstract

Objective: The primary aim was to investigate whether preterm delivery was an independent risk factor for blood or blood products transfusion in the intrapartum or postpartum period, considered as a proxy for severe obstetric bleeding.

Material and Methods: Throughout a 9-month-period, 216 uncomplicated singleton deliveries were included in a cross-sectional study after exclusion of severe maternal and fetal morbidity, such as chorioamnionitis, and use of medications including tocolytics. Maternal and neonatal data were evaluated and compared across preterm (between 24 0/7-36 6/7 weeks' gestation) and term (between 37 0/7-41 6/7 weeks' gestation) deliveries. Primary and secondary outcomes were requirement for blood or blood products transfusion until discharge and change in hemoglobin value and hematocrit from baseline to postpartum hour 6, respectively. Logistic regression models were constructed to evaluate the effect of preterm delivery on the primary outcome.

Results: There were 90 (41.7%) preterm deliveries with an overall cesarean section rate of 77.8%. Preterm delivery was not an independent risk factor for the primary outcome, when route of delivery, maternal body-mass index, antenatal steroid administration, and baseline (admission) platelet and leukocyte counts were controlled for [adjusted risk ratio, 2.46; 95% confidence interval (CI), 0.69-8.77; p=0.16]. Subgroup analysis, including cesarean deliveries, revealed a similar result (adjusted risk ratio, 1.65; 95% CI, 0.42-6.48; p=0.47). Secondary outcomes, including decrease in mean or percent values of hemoglobin and hematocrit measurements, were also similar across preterm and term groups, both after vaginal and cesarean delivery (for all comparisons, p>0.05).

Conclusion: Preterm delivery is not independently associated with increased requirement for blood transfusions or decreased hemoglobin and hematocrit values following otherwise uncomplicated vaginal or cesarean delivery of singletons. (J Turk Ger Gynecol Assoc 2022; 23: 177-83)

Keywords: Preterm delivery, postpartum bleeding, cesarean delivery, vaginal delivery

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Introduction

Intrapartum bleeding and postpartum bleeding (PPB) are among most common causes of maternal mortality (1). Intrapartum bleeding is bleeding that occurs during delivery, particularly due to uterine rupture, placenta accreta spectrum and others, whereas PPB refers to hemorrhagic conditions that occur following delivery, such as uterine atony, genital tract injuries, and other causes. Commonly used proxies for PPB include requirement for blood transfusions, development of signs of hypovolemia, or postpartum hematocrit decrease of more than 10% (2). Maternal deaths associated with intrapartum bleeding and PPB can be prevented by providing appropriate medical measures. Therefore, it is important to determine the risk factors for intrapartum bleeding and PPB so that at-risk pregnant women can be delivered under proper supervision, preferably in tertiary settings (3).

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Some risk factors related to intrapartum bleeding and PPB have been identified in previous studies, with cesarean delivery emerging as the main risk factor, with higher morbidity compared to vaginal delivery (4,5). Multiple pregnancy and general anesthesia have been defined as main risk factors for PPB after cesarean delivery (6). Although some other risk factors have been defined (7), prediction of PPB is usually not possible (8).

Recently, an increase in the incidence of intrapartum and postpartum hemorrhage has been noted (9). Risk factors that may cause an increase in the frequency of hemorrhage are being investigated. Increases in postpartum hemorrhage have not been explained by the changing risk profile of women, such as cesarean delivery, women aged 35 years or older, post-term pregnancies, or large-for-gestational age infants (10).

Preterm delivery is commonly defined as delivery before 37 completed weeks of gestation. Maternal infection, adverse neonatal outcomes, and admission to the intensive care unit are more prevalent in early preterm deliveries (11). Considering the risk of PPB in early preterm cesarean deliveries, these risks can be expected to be higher with cesarean section regardless of the uterine incision type. Therefore, management of maternal complications after early preterm deliveries may be important. Recent data also indicate that relatively high preterm birth rates worldwide have not reduced, despite symptomatic treatment (12). It is not known whether this global preterm birth rate of about 11% contributes to an increased incidence of PPB. From a physiological perspective, preterm delivery can be hypothesized to be associated with increased uterine bleeding. The uterine lower segment is not fully formed, and sensitivity to oxytocin receptors may be relatively low in the preterm uterus (13).

Considering these features, we hypothesized that preterm delivery is a risk factor for an increased incidence of intrapartum bleeding and early PPB. To test this hypothesis, we designed a cross-sectional study to compare intrapartum bleeding and PPB in preterm and term pregnancies, stratified by vaginal and cesarean delivery, with the primary outcome defined as requirement for blood or blood products transfusion.

Material and Methods

The study protocol was approved by the Local Ethics Committee of the Süleyman Demirel University (approval number: 157, date: 22.05.2020), and informed consent was obtained from participants prior to inclusion. The study was performed in accordance with the ethical standards described in an appropriate version of the 1975 Declaration of Helsinki, as revised in 2013. Deliveries between 24 0/7 to 41 6/7 weeks' gestation at a single tertiary obstetrics and gynecology unit throughout a 9-month-period (from 1 March 2020 to 30 November 2020) were included in a cross-sectional design study. Gestational age was calculated based on the last menstrual period (LMP) confirmed by the first trimester crown-rump length (CRL), and this had been corrected accordingly if LMP and dating with CRL diverged by more than two days.

Exclusion criteria included: 1) Multiple pregnancy; 2) preeclampsia and its complications including hemolysis, elevated liver enzyme levels, and low platelet levels syndrome; 3) maternal morbidity including thrombophilia, hepatic or renal disease; 4) third trimester bleeding, including a diagnosis of placenta previa or placental abruption; 5) sonographic diagnosis of leiomyoma >1 cm in diameter during pregnancy; 6) acetylsalicylic acid use within seven days before delivery; 7) anticoagulation use within 24 hours before delivery; 8) tocolysis within 12 hours of delivery; 9) complicated deliveries including instrumental vaginal delivery, cervical lacerations, and uterine rupture; 10) non-low transverse uterine incisions, including vertical incisions; and 11) requirement for maternal antibiotic treatment for suspected or confirmed chorioamnionitis.

Preterm labor was diagnosed when progressive cervical dilatation and/or effacement by cervical examination was accompanied by regular uterine contractions evident on external tocodynamometry. Nifedipine was the preferred agent for tocolysis in the study setting, with limited use of indomethacin in selected cases <30 weeks of gestation. Maximum tocolysis duration was 48 hours (acute tocolysis), aiming to delay delivery for fetal lung maturation with antenatal corticosteroids. Nifedipine was administered sublingually or orally using 10 mg capsules (nidicard 10 mg, Koçak İlaç, Tekirdağ, Turkey), 4 doses every 20 minutes initially, followed by 10 mg every 3-4 hours for a total duration of 24-48 hours. Indomethacin (endol 25 mg, Deva Holding, İstanbul) was administered orally as a 50 mg loading dose followed by 25 mg orally every 6 hours for up to 48 hours. Maintenance (>48 hours duration) or combined tocolytic treatment were not attempted.

Intramuscular maternal betamethasone (12 mg every 24 hours) administration was planned for presumptive preterm deliveries <37 weeks of gestation and for planned cesarean deliveries between 37 0/7 to 38 6/7 weeks gestation, depending on the attending physician's discretion. In certain circumstances with possible preterm delivery <32 weeks of gestation, a second betamethasone dose of 12 mg was administered earlier, that is after 8 to 23 hours of the first one.

All women were given 0.2 mg of intramuscular methylergonovine maleate (Metiler ampoule, Adeka, Samsun, Turkey) following delivery of the placenta after either vaginal or cesarean section. Depending on the discretion of the anesthesiologist, intravascular methylergonovine maleate diluted with normal saline solution to a volume of 5 mL was administered over 30-60 seconds during some of the cesarean

section operations only. As an institutional protocol, umbilical cord arterial blood was sampled immediately after birth by the neonatology team, particularly for pH measurements. All postpartum women were started on oxytocin (Synpitan fort, Deva Holding, İstanbul) infusion of 5 to 10 IU in 500 mL normal saline until transfer to inpatient care from the operating room or labor ward.

Postpartum follow-up included evaluation of vital signs, uterine tonus, postpartum vaginal bleeding, and early ambulation with physical examination focused on lower extremities and breasts. All women were encouraged to give exclusive breastfeeding through a baby friendly hospital initiative. At postpartum hour 6, maternal blood was sampled and sent for complete blood count. Lower extremity stockings were used for cesarean and at-risk vaginal deliveries for at least for 48 hours postpartum. Risk assessment for thromboembolic events was carried out in the postpartum period and pharmacological thromboprophylaxis with low-dose, low molecular weight heparin derivatives were initiated >6 hours and >12 hours after vaginal uncomplicated and cesarean delivery, respectively, to at-risk women.

Data retrieval was carried out by one of the researchers (Ü.K.T.). First, mode of delivery (vaginal or abdominal by cesarean section) and preterm or term delivery (defined as delivery between 24 0/7-36 6/7 and 37 0/7-41 6/7 weeks' gestation, respectively) were recorded. Demographic data and obstetric history (gravidity, parity, abortion, previous caesarean delivery, interval between pregnancies) were also retrieved. Maternal body mass index (BMI) at admission to the labor ward was calculated as the ratio of weight (kg) divided by the square of height (m^2). Intrapartum and labor characteristics included gestational age at delivery, route of delivery (vaginal/cesarean), type of anesthesia in the cesarean group, postpartum oxytocin use and cumulative dose, prepartum baseline (at admission to the labor ward) and postpartum (at hour 6) complete blood cell parameters, including hemoglobin value, hematocrit, platelet and leukocyte counts, and transfusion with blood or blood products. Beckman Coulter UniCel DxH 800 Coulter Cellular Analysis System was used to assess blood parameters with mean coefficient of variation of 0.74%, 1.78%, and 1.45% for hemoglobin measurement, platelet count, and leukocyte count, respectively. Birth weight, Apgar scores (at minutes 1, 5, and 10), and cord arterial pH value within 5 minutes after delivery were also recorded.

The primary outcome measure was requirement for blood or blood products transfusion in the intrapartum or postpartum period until discharge, used as a proxy for severe PPB. Secondary outcomes included change in hemoglobin value and hematocrit from baseline to postpartum hour 6.

Statistical analysis

Data were expressed as mean ± standard deviation for continuous data or frequencies (n) with percentages (%) for categorical data. Shapiro-Wilk test was used to test normality of data. Student's t-test or Mann-Whitney U test was used to compare continuous variables, whereas chi-square test and Fisher's exact test were used for comparisons of categorical data. Post-hoc power analyses were performed to evaluate the statistical power of univariate comparisons for the primary outcome measure. To reveal the independent effect of preterm delivery on the primary outcome (i.e., transfusion requirement), logistic regression with a backward stepwise selection approach was used, controlling for parameters with significant differences at univariate comparisons. A p-value less than 0.05 was considered statistically significant in all analyses.

Results

Following exclusions, 216 women were available for analysis. Ninety (41.7%) and 126 (58.3%) of the included women had delivered in the preterm and term period, respectively. Cesarean section rate in the entire group was 77.8% (168/216). Since route of delivery is the main determinant of postpartum blood loss, data from vaginal and cesarean deliveries were evaluated separately. Table 1 shows comparisons of maternal demographic characteristics, and obstetric and neonatal data across preterm and term deliveries, stratified by mode of delivery. Mean maternal age, gravidity, parity, and interpregnancy interval were similar in preterm and term deliveries, irrespective of the route of delivery (Table 1). Mean BMI was higher in term vaginal compared to that of preterm deliveries (p=0.03, Table 1).

As expected, administration of antenatal corticosteroids was more frequent, and mean gestational age at delivery and birth weight were lower for preterm infants, both in vaginal and cesarean deliveries (Table 1). Use of regional anesthesia during cesarean delivery was more frequent (p=0.07) in term (51/97, 52.6%) compared to preterm deliveries (22/71, 31%), probably reflected in lower mean Apgar scores in preterm infants due to the effects of prematurity and general anesthesia (Table 1). No women who delivered vaginally were administered regional anesthesia.

Table 2 details the comparisons of outcome variables in preterm and term pregnancies, stratified by route of delivery. Admission leukocyte counts were higher before preterm deliveries, both by the vaginal (13.43±5.37 $x10^3/\mu L$ versus 10.16±2.88 $x10^3/\mu L$, p=0.009) and abdominal routes of delivery (11.27±4.05 $x10^3/\mu L$ versus 10.09±2.66 $x10^3/\mu L$, p=0.02). Women who delivered preterm had higher admission platelet counts (p=0.04) compared to women delivering at term (Table 1).

Table 1. Comparisons of maternal demographic characteristics, obstetric, and neonatal data across preterm and term deliveries concerning route of delivery

	Cesarean section			Vaginal delivery		
	Preterm (n=71)	**Term (n=97)**	**p**	**Preterm (n=19)**	**Term (n=29)**	**p**
Demographic data						
Maternal age (years)	33.6±6.8	32.2±7.1	0.2	31.6±7.5	31.6±5.1	0.9
Maternal body mass index (kg/m^2)	28.7±3.6	29.5±3.4	0.1	27.4±1.9	29.0±3.0	**0.03**
Gravidity	2.9±1.6	2.7±1.3	0.4	3.0±1.9	2.9±1.8	0.7
Parity	1.1±1.14	1.1±0.9	0.4	0.95±1.0	1.3±1.3	0.3
Previous cesarean section	30/71 (42.3%)	50/97 (51.5%)	0.2	2/19 (10.5%)	-	0.1
Interpregnancy interval (years)	6.7±3.6	6.3±3.1	0.4	5.1±3.7	5.1±2.3	1.0
Obstetric data						
Antenatal corticosteroids (complete course)	36/71 (50.7%)	6/97 (6.2%)	**<0.0001**	13/19 (68.4%)	-	**<0.0001**
Gestational age at delivery (days)	235.4±27.7	268.7±5.6	**<0.0001**	218.8±34.0	273.7±6.2	**<0.0001**
Postpartum oxytocin dose (IU)	5.25±1.18	5.29±0.09	0.8	4.05±1.61	4.14±0.58	0.7
Neonatal data						
Birth weight (g)	2221±842	3122±391	**<0.0001**	1798±995	3294±359	**<0.0001**
Cord blood pH	7.31±0.12	7.33±0.05	0.058	7.26±0.13	7.34±0.05	**0.02**
Apgar score at minute 1	7.50±1.04	7.86±0.47	**0.008**	7.60±0.84	7.83±0.57	0.3
Apgar score at minute 5	8.58±0.91	8.91±0.28	**0.003**	8.89±0.333	8.87±0.62	0.9
Apgar score at minute 10	9.67±0.81	9.95±0.27	**0.006**	10.0	10.0	1.0

Data are expressed as mean ± standard deviations or frequencies and percentages within parentheses. pH: Potential of hydrogen

Table 2. Comparisons of output variables for intrapartum and early postpartum bleeding across preterm and term deliveries concerning route of delivery

	Cesarean section			Vaginal delivery		
	Preterm (n=71)	**Term (n=97)**	**p**	**Preterm (n=19)**	**Term (n=29)**	**p**
Prepartum (admission)						
Hemoglobin (g/dL)	12.09±1.38	12.29±1.41	0.3	11.7±1.55	12.24±1.23	0.1
Hematocrit (%)	36.25±4.27	36.79±4.23	0.4	35.11±4.49	36.58±3.66	0.2
Platelet count (10^3/µL)	222.81±63.37	222.79±67.37	0.9	249.47±87.38	201.82±71.12	**0.04**
Postpartum (at hour 6)						
Hemoglobin (g/dL)	10.66±1.55	10.94±1.64	0.2	10.6±1.71	11.26±1.27	0.1
Hematocrit (%)	31.78±4.49	32.53±4.93	0.3	31.8±5.01	33.52±3.92	0.1
Platelet count (10^3/µL)	206.87±64.64	199.08±65.54	0.4	236.31±73.72	188.1±61.48	**0.01**
Change in blood parameters (postpartum minus prepartum)						
Change in mean hemoglobin (g/dL)	-1.43±1.20	-1.35±1.11	0.6	-1.1±1.15	-0.98±0.75	0.6
Percent change in hemoglobin (%)	-0.11±0.09	-0.11±0.08	0.6	-0.09±0.09	-0.08±0.0	0.6
Change in mean hematocrit	-4.47±3.59	-4.26±3.35	0.7	-3.30±3.56	-3.06±2.54	0.7
Percent change in hematocrit (%)	-0.12±0.09	-0.11±0.09	0.7	-0.09±0.1	-0.08±0.07	0.7
Change in mean platelet count (10^3/µL)	-15.94±28.83	-23.84±28.1	0.07	-13.15±36.34	-13.72±23.21	0.9
Percent change in platelet count (%)	-0.07±0.13	-0.10±0.12	0.08	-0.03±0.13	-0.05±0.10	0.6
Decrease >10% in hematocrit and/or >3 g/dL in hemoglobin	3/71 (4.2%)	3/97 (3.1%)	0.6	1/19 (5.3%)	-	0.3
Requirement for transfusion with blood or blood products	6/71 (8.5%)	4/97 (4.1%)	0.3	1/19 (5.3%)	-	0.3

Data are expressed as mean ± standard deviations or frequencies and percentages within parentheses

The primary outcome measure (requirement for transfusion with blood or blood products) was similar across the preterm and term groups (Table 1). Secondary outcomes, such as decrease in either mean or percent values of hemoglobin and hematocrit measurements following delivery did not significantly differ between the groups (Table 2). Change in platelet counts followed a similar pattern with no significant differences following preterm or term delivery (Table 2).

Post-hoc power analysis revealed 23.1% and 28.0% power in cesarean and vaginal deliveries, respectively, for detecting a significant difference of the primary outcome across preterm and term deliveries at an alpha value of 0.05.

A logistic regression model that included route of delivery, maternal BMI, antenatal steroid administration, and baseline platelet and leukocyte counts as covariates, revealed that preterm delivery was not an independent risk factor (p=0.16) for the outcome variable [adjusted risk ratio, 2.46 and 95% confidence interval (CI), 0.69-8.77]. When cesarean deliveries were evaluated separately (n=168) in an additional logistic regression model with similar parameters to control for the use of regional anesthesia, comparable results were obtained with no significant effect of preterm delivery (p=0.47) on the primary outcome with an adjusted risk ratio of 1.65 (95% CI, 0.42-6.48).

Discussion

The present study showed that, after the effects of possible main risk factors that may cause intrapartum and postpartum hemorrhage were excluded or controlled for, preterm delivery was not a risk factor for increased intrapartum bleeding and early PPB, when requirement for transfusion with blood or blood products until discharge was taken as the proxy. This result persisted when cofactors, such as maternal BMI, antenatal steroid administration, and type of anesthesia were included in regression models. Our data also revealed no significant differences between preterm and term deliveries considering change in hemoglobin and hematocrit values following vaginal or cesarean deliveries, when analyzed separately.

In a population-based cohort study that included over 8.5 million deliveries in the United States, advanced (>35 years) maternal age, multiple pregnancy, leiomyoma, preeclampsia, chorioamnionitis, placenta previa or abruption, cervical laceration, uterine rupture, instrumental vaginal delivery, and cesarean delivery were significant risk factors for PPB (7). In this analysis (7), preterm delivery was not reported as a risk factor, although data on augmentation of labor, type of analgesia or anesthesia, and BMI were lacking. Another study from Tibet with a smaller number of participants (n=4796) revealed similar risk factors, including advanced maternal age, cesarean section, macrosomia, and presence of neonatal asphyxia (14). Gestational age was stratified as <37, 37-40, and >40 weeks of gestation, revealing similar percentages across PPB and non-PPB groups. Interestingly, previous (but not present) preterm birth was found to be associated with a 2.6-fold increased risk of PPB in a logistic regression model. This was explained by possible coexistence of pregnancy complications with preterm deliveries that may lead to endometrial damage and PPB in subsequent pregnancies (14).

Some studies evaluated vaginal and cesarean deliveries, similar to our design. In a study that used regression models for all deliveries and a second one restricted to vaginal deliveries, preterm birth was not associated with PPB (15). A recent case-control study (16), aiming to identify risk factors for relaparotomy due to intra-abdominal hemorrhage following cesarean deliveries, found a significantly higher rate of preterm delivery <37 weeks of gestation among cases. However, this association disappeared in multivariate analysis, leaving other conditions, such as urgent cesarean delivery and surgical difficulties, as independent factors rather than the gestational age (16). Our results generally support these previous data. Therefore, rather than the timing of delivery, other factors seem to be independently associated with PPB.

Mechanisms leading to preterm delivery, premature rupture of membranes, and cervical insufficiency may be associated with prior choriodecidual inflammation (17). Thus, preterm labor can theoretically be prevented with effective treatment of choriodecidual inflammation. Although the presence of maternal infection and findings of chorioamnionitis were excluded in our design, prepartum leukocyte counts in preterm deliveries were higher than that of term pregnancies. An elevated maternal leukocyte count was previously shown to identify patients with intrauterine infection and adverse perinatal outcomes in women with preterm labor and intact membranes (18).

Overall, these findings confirm the relationship between a subclinical intrauterine inflammation and preterm delivery. Mean platelet count was higher before and after preterm vaginal deliveries. This is in line with platelet counts decreasing throughout pregnancy, beginning in the first trimester (19). In a recent study evaluating the trajectories of platelet counts during pregnancy, a decline throughout pregnancy with the nadir occurring on postpartum day 1 was evident (20). Our data also support a relative decrement of platelet counts with advancing gestation. The reason this change was not significant in cesarean deliveries is probably due to earlier mean gestational age at delivery (and therefore timing of blood sampling for platelet count) in the vaginal delivery group (219 versus 235 days).

Cesarean delivery is associated with increased rate of maternal complications including PPB, venous thromboembolism,

amniotic fluid embolism, other surgical morbidities, and anesthesia complications, compared to vaginal delivery (21). There are some conflicting data, however, whether cesarean delivery independently increases the risk of PPB. Although some studies (14,22) found previous cesarean section and emergency cesarean delivery as a risk factor for severe PPB, some epidemiological data found no direct association between cesarean delivery and PPB (23). In our study, none of the women that delivered vaginally at term required transfusions. However, we are not able to comment further on this issue, since our study did not primarily aim to detect differences across vaginal and cesarean deliveries.

Study Limitations

Limitations include a relatively small sample size following numerous exclusions to refine data. We were not able to stratify deliveries considering gestational age, such as early (<34 weeks) or late (34-37 weeks) preterm births due to the limited number of recruited preterm pregnancies. We also did not separately analyze scheduled and emergency cesarean sections. The primary and secondary endpoints provide short-term data, and long-term results, such as complications including placental retention or readmissions, were not evaluated. Similarly, the present analysis did not include postpartum factors, such as breastfeeding, as a covariate. We did not include birth weight, Apgar scores, and umbilical cord blood pH that are probable predictors of postpartum hemorrhage (considering macrosomia and perinatal asphyxia) in the logistic regression models to avoid severe multicollinearity.

Since our results were negative, the calculated post-hoc power was also relatively low, which should not directly be misinterpreted as the trial having inadequate power. Despite these limitations, the present design provides refined data from uncomplicated singleton pregnancies with rigorous exclusion criteria. Another strength was the cross-sectional recruitment of subjects during admission to hospital with longitudinal follow-up until discharge in an observational fashion. The preterm delivery and cesarean section rates were high due to the tertiary setting characteristics of the study site.

Conclusion

Preterm delivery was not an independent predictor of severe intrapartum bleeding and early PPB in uncomplicated pregnancies, when several confounders were excluded and controlled for. Therefore, clinicians can consider other risk factors for PPB in uncomplicated pregnancies, irrespective of gestational age at delivery.

Ethical Committee Approval: *The study protocol was approved by the Local Ethics Committee of the Süleyman Demirel University (approval number: 157, date: 22.05.2020).*

Informed Consent: *Informed consent was obtained.*

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References

1. Ronsmans C, Graham WJ. Lancet Maternal Survival Series steering group. Maternal mortality: who, when, where, and why. Lancet 2006; 368: 1189-200.
2. Committee on Practice Bulletins-Obstetrics. Practice Bulletin No. 183: Postpartum Hemorrhage. Obstet Gynecol 2017; 130: e168-86.
3. Evers AC, Brouwers HA, Hukkelhoven CW, Nikkels PG, Boon J, van Egmond-Linden A, et al. Perinatal mortality and severe morbidity in low and high risk term pregnancies in the Netherlands: prospective cohort study. BMJ 2010; 341: c5639.
4. Sheiner E, Sarid L, Levy A, Seidman DS, Hallak M. Obstetric risk factors and outcome of pregnancies complicated with early postpartum hemorrhage: a population-based study. J Matern Fetal Neonatal Med 2005; 18: 149-54.
5. Bateman BT, Berman MF, Riley LE, Leffert LR. The epidemiology of postpartum hemorrhage in a large, nationwide sample of deliveries. Anesth Analg 2010; 110: 1368-73.
6. Butwick AJ, Ramachandran B, Hegde P, Riley ET, El-Sayed YY, Nelson LM. Risk factors for severe postpartum hemorrhage after cesarean delivery: Case-control studies. Anesth Analg 2017; 125: 523-32.
7. Kramer MS, Berg C, Abenhaim H, Dahhou M, Rouleau J, Mehrabadi A, et al. Incidence, risk factors, and temporal trends in severe postpartum hemorrhage. Am J Obstet Gynecol 2013; 209: 449.e1-7.
8. Prata N, Hamza S, Bell S, Karasek D, Vahidnia F, Holston M. Inability to predict postpartum hemorrhage: insights from Egyptian intervention data. BMC Pregnancy Childbirth 2011; 11: 97.
9. Ford JB, Patterson JA, Seeho SK, Roberts CL. Trends and outcomes of postpartum haemorrhage, 2003-2011. BMC Pregnancy Childbirth 2015; 15: 334.
10. Ford JB, Roberts CL, Simpson JM, Vaughan J, Cameron CA. Increased postpartum hemorrhage rates in Australia. Int J Gynaecol Obstet 2007; 98: 237-43.
11. Reddy UM, Rice MM, Grobman WA, Bailit JL, Wapner RJ, Varner MW, et al. Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Serious maternal complications after early preterm delivery (24-33 weeks' gestation). Am J Obstet Gynecol 2015; 213: 538.e1-9.
12. da Fonseca EB, Damião R, Moreira DA. Preterm birth prevention. Best Pract Res Clin Obstet Gynaecol 2020; 69: 40-9.

13. Tattersall M, Engineer N, Khanjani S, Sooranna SR, Roberts VH, Grigsby PL, et al. Pro-labour myometrial gene expression: are preterm labour and term labour the same? Reproduction 2008; 135: 569-79.
14. Pubu ZM, Bianba ZM, Yang G, CyRen LM, Pubu DJ, Suo Lang KZ, et al. Factors affecting the risk of postpartum hemorrhage in pregnant women in Tibet health facilities. Med Sci Monit 2021; 27: e928568.
15. Ononge S, Mirembe F, Wandabwa J, Campbell OM. Incidence and risk factors for postpartum hemorrhage in Uganda. Reprod Health 2016; 13: 38.
16. Pencole L, Peyronnet V, Mandelbrot L, Lepercq J. Risk factors of relaparotomy for intra-abdominal hemorrhage after cesarean delivery. Eur J Obstet Gynecol Reprod Biol 2021; 260: 118-23.
17. Grigsby PL, Novy MJ, Adams Waldorf KM, Sadowsky DW, Gravett MG. Choriodecidual inflammation: a harbinger of the preterm labor syndrome. Reprod Sci 2010; 17: 85-94.
18. Yoon BH, Yang SH, Jun JK, Park KH, Kim CJ, Romero R. Maternal blood C-reactive protein, white blood cell count, and temperature in preterm labor: a comparison with amniotic fluid white blood cell count. Obstet Gynecol 1996; 87: 231-7.
19. Reese JA, Peck JD, Deschamps DR, McIntosh JJ, Knudtson EJ, Terrell DR, et al. Platelet counts during pregnancy. N Engl J Med 2018; 379: 32-43.
20. Ushida T, Kotani T, Moriyama Y, Imai K, Nakano-Kobayashi T, Kinoshita F, et al. Platelet counts during normal pregnancies and pregnancies complicated with hypertensive disorders. Pregnancy Hypertens 2021; 24: 73-8.
21. Loverro G, Greco P, Vimercati A, Nicolardi V, Varcaccio-Garofalo G, Selvaggi L. Maternal complications associated with cesarean section. J Perinat Med 2001; 29: 322-6.
22. Ekin A, Gezer C, Solmaz U, Taner CE, Dogan A, Ozeren M. Predictors of severity in primary postpartum hemorrhage. Arch Gynecol Obstet 2015; 292: 1247-54.
23. Koroukian SM. Relative risk of postpartum complications in the Ohio Medicaid population: vaginal versus cesarean delivery. Med Care Res Rev 2004; 61: 203-24.