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Article

ARTICLE

Fibrinogen plasma concentration before delivery is not associated with postpartum haemorrhage: a prospective observational study

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Abstract

Background: Low plasma fibrinogen concentration has been linked to postpartum haemorrhage. The primary aim of this study was to assess whether fibrinogen concentration at admission before labour is associated with severe postpartum haemorrhage. Secondary aims were to describe fibrinogen concentration before and after labour and to identify predictors for severe postpartum haemorrhage.

Methods: 1951 healthy women were included in a prospective observational study. Fibrinogen concentration was determined at admission to the labour ward and in a subgroup of women (n=80) also after the placenta was delivered. Bleeding volume postpartum was estimated by weighing surgical sponges and pads and by measuring collected blood. Predictors for severe postpartum haemorrhage (>1000 ml) were identified with bivariate and multivariate regression analyses.

Results: Mean fibrinogen concentration was 5.3 (SD 0.8) g litre^{-1}. Median estimated blood loss was 450 (range 70–4400) ml and 250 (12.8%) women bled >1000 ml. Fibrinogen concentration was not correlated with postpartum haemorrhage in the entire cohort (r_s=0.003, P=0.90) or in any subgroup. Fibrinogen concentration was not associated with bleeding >1000 ml (odds ratio 1.01 (CI 95% 0.85–1.19), P=0.93) and did not differ significantly before and after delivery. Oxytocin stimulation, instrumental delivery, Caesarean section and exploration of uterus were identified as independent predictors of haemorrhage >1000 ml.

Conclusions: Fibrinogen plasma concentration at admission before labour does not predict severe postpartum haemorrhage in a general obstetric population. Fibrinogen concentration does not decrease significantly during normal labour. Excessive postpartum bleeding is mainly as a result of obstetric complications.

Key words: delivery; fibrinogen; obstetric labor complications; postpartum hemorrhage

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Editors' key points

- This large, prospective, observational study shows that endogenous fibrinogen plasma concentration at admission just before labour does not predict severe postpartum haemorrhage(PPH) in a general obstetric population.
- Fibrinogen concentration is not reduced after delivery in the absence of severe PPH.
- This study also shows that oxytocin stimulation, instrumental delivery, Caesarean section and exploration of uterus increased the risk of severe PPH.

Postpartum haemorrhage (PPH) is a common cause of obstetric morbidity and mortality. Although mortality from PPH has declined in developed countries, PPH is now the most common cause of severe morbidity during labour and the most common obstetric cause of intensive care admission.[1 2] Uterine atony, placental retention, Caesarean section, lacerations, premature separation of the placenta and placenta previa increase the risk of severe PPH.[3–5] Coagulopathies reportedly occur in about 1% of all cases of PPH.[3] Peripartum coagulopathies can be caused by congenital bleeding disorders, secondary to obstetric complications, the bleeding *per se*, and haemodilution as a result of crystalloid and colloid infusions.[3 6]

Fibrinogen is a key factor in haemostasis.[7] Three studies have reported that a low fibrinogen concentration after the onset of bleeding is associated with a higher risk of severe PPH.[8–10] However, it is unclear if the reduced fibrinogen concentration after the onset of PPH is a result of low endogenous fibrinogen concentration present already before labour or if low fibrinogen concentration is a result of consumption, bleeding and/or haemodilution.

We know of no previous study that prospectively analysed the association between endogenous fibrinogen plasma concentration just before labour and postpartum bleeding volume. We therefore evaluated if there is an association between fibrinogen concentration at admission to the labour ward and PPH severity. Secondary aims were to describe fibrinogen concentration before and after labour and to identify predictors for severe PPH.

Methods

Participants

Two thousand women were recruited at five maternity units in Västra Götaland, Sweden from June 2013 to March 2014. Women were asked to participate when they arrived at the labour ward. There were no exclusion criteria. Participant's characteristics are presented in Table 1.

The final study group consisted of 1951 women after exclusion of 49 women without documented social security number, for whom data from the electronic patient records could not be obtained. Fibrinogen results were lacking because of haemolysis (n=23), coagulated sample (n=7) and missing data (n=78). Therefore, final analyses of fibrinogen concentration and its associations with postpartum bleeding included 1843 women. Eighty of the women at one of the maternity units were included in a substudy where a second blood sample was collected immediately after the placenta was delivered. There was no specific inclusion or exclusion criteria in this subgroup.

The Regional Ethical Review Board in Gothenburg, Sweden approved the study. Written informed consent was obtained from all participants.

Study procedures

After women arrived at the labour ward, blood was collected in tubes containing 0.13 M citrate either from direct venipuncture or from intravenous cannulae. The blood samples were centrifuged at 2000 g at room temperature for 20 min. Plasma was frozen at −70°C until analysed. Fibrinogen concentration in plasma was analysed in batches with the Clauss method (STA® Fibrinogen 5, Diagnostica Stago, Asnières sur Seine, France) on a STA-R Evolution instrument (Diagnostica Stago). The non-pregnant reference range is 2.0–4.5 g litre^{-1}. Estimated blood loss (EBL) at delivery and postpartum were determined by the responsible midwife by weighing surgical sponges and pads and by measuring collected blood.

Patient characteristics (age, body mass index, parity, gestational week at delivery, epidural analgesia, diagnosis and bleeding at delivery) were obtained from electronic patient records (Obstetrix, Siemens AB, Healthcare Sector, Upplands Väsby, Sweden). Severe postpartum haemorrhage was defined as EBL >1000 ml.[4 11] Predefined subgroups included women with different age, body mass index, parity, gestational weeks, fibrinogen concentrations, preeclampsia, induction of labour, use of oxytocin stimulation, epidural analgesia, Caesarean section and women undergoing uterus exploration (Table 2).

Table 1 Patient characteristics and outcome variables. Data are shown as mean (SD)/median (range) or number (n) and (%). Subgroup with two samples *vs* the remaining group: *P<0.01, **P<0.001

Characteristic	All women, n=1951	Women with fibrinogen samples before and after delivery, n=80
Age, years	30.6 (5.0)	31.3 (5.3)
BMI, kg m^{-2}	24.9 (4.7)	23.1 (3.4)**
Parity 0, n	948 (48.6%)	49 (61.2%)
1, n	529 (27.1%)	21 (26.2%)
2, n	199 (10.2%)	7 (8.8%)
3, n	53 (2.7%)	1 (1.2%)
≥4, n	26 (1.3%)	0 (0%)
Missing data, n	196 (10.0%)	2 (2.5%)
Gestational week at delivery	40.1 (27.7–43.3)	40.3 (34.4–42.3)
Fibrinogen, g litre^{-1}	5.34 (0.83) 5.30 (2.90–8.80)	5.34 (0.82) 5.30 (2.90–8.80)
Preeclampsia, n	60 (3.1%)	0 (0%)
Spontaneous labour, n	1530 (78.4%)	73 (91.2%)
Induction of labour, n	417 (21.4%)	7 (8.8%)*
Missing data, n	4 (0.2%)	0 (0%)
Oxytocin stimulation, n	1082 (55.6%)	39 (51.3%)
Epidural analgesia, n	864 (44.4%)	42 (52.5%)
Vaginal delivery, n	1605 (82.3%)	67 (83.8%)
Instrumental delivery, n	136 (7.0%)	8 (10.0%)
Caesarean delivery, n	206 (10.6%)	5 (6.2%)
Missing data, n	4 (0.2%)	0 (0%)
Postpartum exploration, n	93 (4.8%)	3 (3.8%)
Estimated blood loss, ml	450 (70–4400)	450 (150–2180)