



Letter to the Editors-In-Chief

Risk factors and obstetric outcomes in pregnancies complicated by pelvic vein thrombosis, and in the subsequent pregnancy



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Dear Editors-in-Chief,

Pelvic vein thrombosis has a much higher incidence during pregnancy compared to the incidence in the non-pregnant population [1]. This single-centre, retrospective study aims to examine risk factors, as well as obstetric and foetal outcomes, in women with antepartum pelvic vein thrombosis and their high-risk subsequent pregnancies [2], and evaluate the efficacy and safety of anticoagulant treatment and thromboprophylaxis as determined by the guidelines issued by the Swedish Society for Obstetrics and Gynaecology [3].

1. Patients and methods

The patients were identified through the Thrombosis registry, which was started in 2000 at the Obstetrics Department of the Karolinska University Hospital. The study was approved by the local Ethics Committee and the patients had given their written consent prior to inclusion. Of the 49 patients who were diagnosed with pelvic vein thrombosis during pregnancy and were followed up and treated with low molecular weight heparin (LMWH) at this department during the years 2000–2014, 39 were eligible for inclusion (cohort 1; four patients were excluded because the thrombosis could not be verified as located in the pelvic veins, one was excluded due to termination of pregnancy and five because they were treated or delivered at other hospitals). Of the 39 women included in cohort 1, 23 had at least one pregnancy during the follow-up period (2002–2015) and were included even in the study for subsequent pregnancies (cohort 2).

According to the guidelines issued by the Swedish Society for Obstetrics and Gynaecology, the initial therapeutic dose of LMWH for women suffering antenatal thrombosis is based on maternal weight (125 IU/kg dalteparin twice daily) and is followed up and adjusted by measuring trough (0.3–0.4 IU/ml) and peak (0.6–1.3 IU/ml) levels of anti-factor Xa. The initial dosage is administered for at least one month followed by high-dose prophylactic treatment for the remainder of the pregnancy and continued at least 6 weeks postpartum. Treatment with LMWH is usually reduced by half during labour but not completely

interrupted. Patients with a history of thrombosis are treated with thromboprophylaxis during subsequent pregnancies, receiving normal dose thromboprophylaxis (start dose 5000 IU dalteparin administered once daily) or high dose thromboprophylaxis (start dose 5000 IU dalteparin administered twice daily and adjusted to maintain a trough level of anti-factor Xa 0.1–0.2 IU/ml), depending on the presence of additional risk factors. Thromboprophylaxis is discontinued 24 h prior to estimated delivery [3].

The control group was comprised of women who gave birth in the Stockholm County during the corresponding years (2000–2014 for cohort 1 and 2002–2015 for cohort 2 (excluding nulliparous women)) according to data collected from the Swedish Medical Birth Registry [4]. When comparing outcomes between the first and subsequent pregnancies, each patient served as her own control. The results were also compared to the published literature for complications such as postpartum haemorrhage (PPH).

For each patient we collected baseline data for both pregnancies (age at the beginning of pregnancy, presence and type of thrombophilia, body mass index (BMI), previous thrombosis, family history for thrombosis etc.), data on obstetric history (number of previous pregnancies and deliveries, number of miscarriages, preeclampsia/eclampsia, mode of delivery, PPH etc.), data on the newborn child for each pregnancy (birth weight, APGAR score at 5 min, gestation week at partus and small for gestational age (SGA)) and data on the pelvic thrombosis (exact location, gestation week on diagnosis, recurrences, if any).

2. Statistical analysis

Descriptive statistics were used for all continuous variables. We calculated proportions and 95% CI for all categorical data. For the subgroup analyses, Kruskal-Wallis was used to compare scale values and Fisher's exact test was used for nominal values. A *p*-value of < 0.05 was considered significant for both tests.

All statistical analyses were performed by the IBM SPSS Statistics Version 23.0 software except for the 95% CI for proportions which was

Abbreviations: BMI, body mass index; FV Leiden, factor V Leiden; LMWH, low molecular weight heparin; PPH, postpartum haemorrhage; SGA, small for gestational age

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Table 1
Demographic data and obstetric outcomes of the patients included in the study.

	Number	Age (median)	Nulliparous	Thrombophilia	FV Leiden	Vaginal/ assisted vaginal delivery	Caesarean/ emergency caesarean	Epidural or spinal anaesthesia	Recurrent thrombosis	PPH/ severe PPH ^a	Children born SGA	Apgar score \geq 7 (5 min)
Cohort 1	39	31 (20–45)	32	21	16	19/11	4/5	21	0	13/1	1 ^b	40
Cohort 2	23	34 (22–40)	0	11	9	18/2	2/1	9	2	5/0	0 ^c	25

^a PPH is defined as blood loss > 500 ml (vaginal delivery) and > 1000 ml (caesarean section) and severe PPH as blood loss > 1000 ml [7].

^b Out of 40 children (one duplex pregnancy).

^c Out of 25 children (two duplex pregnancies).

calculated using the VassarStats online calculator.

3. Results

The demographic and obstetric data for both cohorts are described in Table 1. Nulliparity was almost twice as high in cohort 1 compared to controls (82.1% vs. 46.6%) [4]. The prevalence of blood group A, AB, B and O was 74.4%, 5.1%, 7.7% and 12.8% respectively (cohort 1). The prevalence of blood group A was higher in the patient cohort than the corresponding prevalence in the Swedish population (74.4% vs. 44%), whereas the prevalence of blood group O was lower (12.8% vs. 38%) [5].

The majority of pelvic thromboses were diagnosed during the second ($n = 17$, 43.6%) and the third trimester ($n = 17$, 43.6%).

The presence of factor V Leiden (FV Leiden) had no significant effect on the results from both cohorts.

In cohort 2, twenty patients received normal dose thromboprophylaxis and three received high dose thromboprophylaxis.

Two patients suffered recurrent thrombosis during the second pregnancy (cohort 2). One patient with FV Leiden was diagnosed with an upper arm thrombosis during gestation week 12. She had been hospitalized for hyperemesis twice during the first trimester, but had not started with thromboprophylaxis at the time of the thrombosis. The other patient had a recurrent, left-side pelvic vein thrombosis at gestation week 26. She had no thrombophilia and had started with normal dose thromboprophylaxis a few weeks prior to being diagnosed with the thrombosis. The reason behind the delayed start of the thromboprophylaxis is unknown.

4. Discussion

Nulliparity and the prevalence of blood group A were higher in cohort 1 compared to the women giving birth in the Stockholm County during the same time span, whereas maternal age and BMI were similar (values for control group not shown) [4]. In contrast to previous studies [6] showing that two thirds of antenatal thromboses occur during the third trimester, the majority of the events in our study occurred somewhat earlier. This could be partially attributed to the higher incidence of thrombophilia in our study compared to [6] (53.8% vs. 22%), which in turn could be explained by the fact that all the patients were screened for thrombophilia as well as the high incidence of FV Leiden in the Swedish population [3].

Compared to other studies [7, 8], our results (cohort 1) showed an increased risk (36%) for non-severe PPH despite lowering the dose according to the guidelines [3]. However, different study designs, cohort sizes and PPH definitions make it difficult to draw any conclusions. No other obstetric, maternal or foetal complications were recorded. Overall, the anticoagulant treatment, as given in cohort 1, can be

considered safe, as it did not lead to severe bleeding and obstetric complications, and effective, since no recurrent thromboses were reported.

The overall risk for non-severe PPH in cohort 2 (treated with thromboprophylaxis) was 22.5%, which is higher than the risk reported by others [9] and in controls [10]. This could be a result of not discontinuing the LMWH dosage prior to delivery as stated by the guidelines [3], or a tendency to estimate blood loss more accurately in those women. Two women in cohort 2 suffered recurrent thrombosis (8.7%). In one case the patient was not receiving thromboprophylaxis at the time of the diagnosis and in the other case the patient had started thromboprophylaxis late during pregnancy, just a few weeks prior to recurrence of thrombosis (gestation week 26). This means that the thrombus could have already been formed at the time of initiation of treatment. Our results suggest that earlier initiation of treatment is necessary to prevent even the few thromboembolic events that can occur. No other obstetric complications were reported, which means that thromboprophylaxis can be deemed as safe.

This study is, to our knowledge, the first that evaluates the outcomes and complications in women diagnosed specifically with pelvic vein thrombosis (and no other types of thrombosis) as well as following up those women in a subsequent pregnancy in order to further evaluate the safety and efficacy of the treatment. All patients were treated at the same centre and by the same protocol, which allows for systematic evaluation of its effectiveness. The main limitations of the study are the small cohort and the lack of matched controls. A multicentre study with a larger cohort would lead to increased statistical power and stronger conclusions; however, it would entail treatment with different therapeutic protocols and that would limit comparisons among groups.

Declaration of interests

None.

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