Original Article

Venous thromboembolism during pregnancy and the post-partum period: Incidence and risk factors in a large Victorian health service

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Background: There is a strong recommendation for post-partum thromboprophylaxis following emergency caesarean sections, particularly in overweight women, and following prolonged labour.

Aims: To analyse the incidence and epidemiological factors associated with antepartum and post-partum venous thromboembolism in a large Victorian health service.

Methods: A retrospective study of all 6987 women delivering at Ballarat Health Services between March 1999 and June 2006. Case notes of women with confirmed venous thromboembolism during this period were subjected to detailed analysis. The data were analysed for possible risk factors, the timing of thromboembolism in relation to the pregnancy and any correlation with thromboprophylaxis, if administered.

Results: The rate of venous thromboembolism was 1.14 per 1000 deliveries, with risk factors of age > 30 (100%), obesity (75%), previous history of thromboembolism (62.5%) and caesarean section (37.5%). Majority of cases were diagnosed in first trimester (62.5%), and in the right lower limb (75%). None of the patients had been given thromboprophylaxis.

Conclusion: While the incidence and risk factors were similar to those generally quoted, a much higher incidence was found in early pregnancy, and in the right lower limb. The importance of meticulous screening for risk factors in early pregnancy cannot be overemphasised.

Key words: deep-vein thrombosis (DVT), epidemiology, risk factors, thromboprophylaxis, thromboembolism.

Introduction

Venous thromboembolism (VTE) continues to be an important cause of maternal morbidity and mortality worldwide.1 While the leading cause of maternal death in the developing world is haemorrhage, in Australia, UK and USA, thromboembolic phenomena were found to be a major cause of maternal deaths. The incidence of pregnancy-related venous thromboembolism in the Caucasian population is reported to range between 0.7 and 1.3 per 1000 deliveries.2-4 Chan et al.5 recently reported a similar incidence of 1.88 per 1000 deliveries in pregnant Chinese women. Heightened awareness of the condition among clinicians and availability of easier diagnostic methods partly account for the increased detection of what was once considered an uncommon condition among Asians.

VTE occurs infrequently but is a leading cause of illness and death during pregnancy and the puerperium and remains a diagnostic and therapeutic challenge. The risk of VTE is five times higher in a pregnant woman than in a non-pregnant woman of similar age.6 The increased risk is related to the hypercoagulable state of pregnancy, which is probably the nature's way of protecting women from haemorrhage during delivery. Available evidence suggests that post-partum VTE is more common than antepartum VTE, and it appears more likely that the risks of both initial and recurrent deep-vein thrombosis (DVT) are higher post-partum than antepartum. In the Leiden Thrombophilia Study,7 pregnancy was associated with a fourfold increased risk of thrombosis and the puerperium was associated with a 14-fold increased risk. Other studies have also reported a significantly higher incidence of VTE in the post-partum period.8,9

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Women with previous VTE have an approximately 3.5-fold increased risk of recurrent VTE during pregnancy compared to non-pregnant periods. In a review of maternal mortality in Singapore over a 10-year period (from 1990 to 1999), the rate of maternal deaths from thromboembolism (0.21 per 10 000 live births) and stillbirths appears to be comparable to that reported in the Confidential Enquiries into Maternal Deaths in the UK. This review reported a lack of awareness of the risk of venous thromboembolism occurring in the first trimester of pregnancy. The importance of paying special attention to any woman developing chest or leg symptoms during pregnancy and puerperium, and carrying out appropriate investigations cannot be overemphasised.

Our ability to diagnose DVT clinically is generally poor and is further hampered during pregnancy since dyspnoea, tachypnoea, swelling and discomfort in the legs are common, particularly at term and must be interpreted with caution during pregnancy.

The objectives of this study were (i) to determine the incidence of thromboembolism in pregnancy and puerperium in a large hospital in regional Victoria, and (ii) to study the profile of patients predisposed to thromboembolism in regional obstetric practice.

Methods

A retrospective study of all 6987 women delivering at Ballarat Health Services between March 1999 and June 2006 was undertaken to determine the incidence of thromboembolism. Data were obtained from the Health Information System Database after acquiring ethics committee approval. Admission notes of all women who had venous thromboembolism during pregnancy or post-partum period were studied in detail. The post-partum period was defined six weeks after a miscarriage, stillbirth or delivery. Case notes were scrutinized to determine factors that may precipitate thromboembolism in pregnancy and puerperium in a large hospital in regional Victoria, and (ii) to study the profile of patients predisposed to thromboembolism in regional obstetric practice.

Inclusion criteria: A patient was deemed to have DVT or pulmonary embolism if symptoms and signs suggested this, physician confirmed the diagnosis, full anticoagulation was administered and radiological confirmation was obtained by Doppler ultrasonography or CT pulmonary angiogram. This group of women constituted the study group. Women who had only short-term anticoagulation while awaiting results of diagnostic evaluation were not included.

For comparison where appropriate, the control group consisted of all other women who delivered during the study period, with no thromboembolic episode during pregnancy or puerperium.

Data from the study group of eight women with thromboembolism related to pregnancy have been presented in a descriptive format, given the small number. Where information was available, comparisons have been made with the remaining 6978 women for average age, parity, smoking, duration of labour and type of delivery.

Results

Eight patients (Table 1) were found to have an episode of thromboembolism during pregnancy giving an overall incidence of 1.14 per 1000 deliveries. All the patients in the study group were older 30 years of age (average age was 35), while the average age in the control group was 29.8 years. Six (75%) patients were morbidly obese and one (12.5%) mildly obese.

Five patients (62.5%) had previous episode of thromboembolism. Unfortunately, details of the previous episode were unavailable from the admission history in two of these cases. Of the three available details, it appeared that two were attributed to limb trauma/operation and a third was attributed to oral contraceptive pill and smoking, with no cause actually determined. From the records, it appeared that thrombophilia panel was tested and was found negative in all these, and the plan was for post-partum thromboprophylaxis for six weeks. None of these women were anticoagulated during the index pregnancy, prior to this episode of VTE. Two patients (25%) were smokers in the group that developed DVT, which also compares well with the 23.4%
Table 1  Profile of patients who suffered deep-vein thrombosis during pregnancy and puerperium

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Para</th>
<th>Weeks pregnant at time of diagnosis</th>
<th>Family history</th>
<th>Previous DVT/Stroke</th>
<th>Thrombophilia screen</th>
<th>BMI/weight</th>
<th>Smoker</th>
<th>Site</th>
<th>Method of diagnosis</th>
<th>Assisted delivery</th>
<th>Duration of labour</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33</td>
<td>Multi</td>
<td>8</td>
<td>Negative</td>
<td>DVT</td>
<td>Positive</td>
<td>&gt; 35</td>
<td>No</td>
<td>R</td>
<td>Doppler/U/S</td>
<td>No</td>
<td>1:32</td>
</tr>
<tr>
<td>2</td>
<td>39</td>
<td>Multi</td>
<td>9</td>
<td>Positive</td>
<td>None</td>
<td>Negative</td>
<td>&gt; 35</td>
<td>No</td>
<td>R</td>
<td>Doppler/U/S</td>
<td>No</td>
<td>1:48</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>Multi</td>
<td>Post-partum</td>
<td>Positive</td>
<td>DVT</td>
<td>Negative</td>
<td>32</td>
<td>Yes</td>
<td>R</td>
<td>Doppler/U/S + CT scan</td>
<td>LSCS</td>
<td>1:27</td>
</tr>
<tr>
<td>4</td>
<td>33</td>
<td>Multi</td>
<td>34</td>
<td>Negative</td>
<td>DVT</td>
<td>Negative</td>
<td>31</td>
<td>No</td>
<td>R</td>
<td>Doppler/U/S</td>
<td>No</td>
<td>1:72</td>
</tr>
<tr>
<td>5</td>
<td>31</td>
<td>Primi</td>
<td>30</td>
<td>Positive</td>
<td>None</td>
<td>Negative</td>
<td>25</td>
<td>Yes</td>
<td>R</td>
<td>Doppler/U/S</td>
<td>No</td>
<td>8:07</td>
</tr>
<tr>
<td>6</td>
<td>35</td>
<td>Multi</td>
<td>9</td>
<td>Negative</td>
<td>SVT</td>
<td>Negative</td>
<td>&gt; 35</td>
<td>No</td>
<td>L</td>
<td>Doppler/U/S + CT scan</td>
<td>LSCS</td>
<td>1:58</td>
</tr>
<tr>
<td>7</td>
<td>31</td>
<td>Multi</td>
<td>8</td>
<td>Positive</td>
<td>DVT and PE</td>
<td>Positive</td>
<td>&gt; 35</td>
<td>No</td>
<td>R</td>
<td>Doppler/U/S</td>
<td>Elective LSCS</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>33</td>
<td>Multi</td>
<td>12</td>
<td>Negative</td>
<td>None</td>
<td>Not done</td>
<td>&gt; 35</td>
<td>No</td>
<td>R</td>
<td>Doppler/U/S + CT scan</td>
<td>Delivered outside BHS</td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index; BHS, Ballarat Health Services; DVT, deep-vein thrombosis; LSCS, lower segment caesarean section; PE, pulmonary embolism; SVT, superficial venous thrombosis.
smokers in the control group. Two patients (25%) had positive thrombophilia screen, one prothrombin gene mutation and one heterozygous factor V Leiden mutation. Both were identified after the episode of VTE in the current pregnancy. One (12.5%) patient had pre-eclampsia. Seven patients (87.5%) were multigravida which compares well with the average gravida status of 2.63 for the control group. Five (62.5%) were diagnosed with thromboembolism during first trimester, two (25%) during third trimester and only one (12.5%) during post-partum period. None had prolonged labour, with the average duration of labour being 2.57 h as compared to 6.46 h for the control group. Three patients (37.5%) had caesarean section and the rest had uncomplicated normal vaginal delivery. Six patients (75%) had DVT detected in the right lower limb and two (25%) in the left lower limb. All patients were diagnosed using Doppler ultrasound. Only one patient (12.5%) developed pulmonary embolism which was diagnosed using CT scan. Full anticoagulation with low molecular weight heparin was instituted in all eight patients subsequent to diagnosis.

Discussion

This interesting study is the first reported from regional Australia, to analyse the epidemiology, incidence and the risk factors in a largely Caucasian population.

We undertook this study in view of recent evidence revealing venous thromboembolism as the leading cause of death in many parts of the world, including Australia. In addition to the immediate morbidity associated with venous thromboembolism, there is significant long-term morbidity associated with post-thrombotic syndrome. It is also increasingly recognised that women with thrombophilias, which are risk factors for thrombosis, are at greater risk of poor pregnancy outcomes including recurrent miscarriage, pre-eclampsia, intrauterine growth restriction, placental abruption and stillbirth.

The incidence of VTE with pregnancy was 1.14 per 1000 deliveries, which is similar to that reported from studies worldwide. The lowest reported incidence was 0.7 per 1000 from Missouri, USA and interestingly, the highest incidence that has been reported so far is 1.88 per 1000 deliveries from Hong Kong. Ballarat seemed to follow the international trends. We acknowledge that the prevalence could be underestimated, given that women could have gone to another hospital for delivery. Without any database linkages, an accurate determination was not possible. However, this is a large referral hospital in the region, and most women with any complication are transferred here for further management. One woman who was diagnosed at 12 weeks and was booked for delivery at the hospital had a quick delivery at home prior to arrival to hospital. She was included in the statistics as she was diagnosed here, booked for delivery here and nursed at Ballarat Hospital post-partum.

The other epidemiological factors including age, obesity and parity also did not differ from those found in population subgroups worldwide. The risk factors identified in the Hong Kong study also followed generally reported international trends with operative delivery, older maternal age, greater body mass index and pre-eclampsia being commonly associated with thromboembolism.

Two patients were found to have positive thrombophilia screen, though this was tested after the episode. One had heterozygous prothrombin gene mutation, and the other had heterozygous factor V Leiden mutation with activated protein C resistance. Five women had an episode of VTE earlier, with negative thrombophilia screen. It is interesting that the guidelines for management of these conditions, in the absence of any complications, focus mainly on post-partum thromboprophylaxis.

The focus of VTE prophylaxis has been heparin or LMWH administration in high risk patients – emergency caesarean section, prolonged labour and obese patients. This practice has not been implemented across the board because of a lack of consensus. It is, however, interesting to note that only a small proportion (12.5%) of VTE actually occurred post-partum. The Leiden Thrombophilia Study reported a fourfold increased risk in pregnancy and 14-fold increased risk in puerperium. De Stefano et al. studied women with past history of VTE. They reported 7.5% antepartum and 15.5% post-partum recurrence when the first VTE was unprovoked. A large study from the USA found 50% of VTE occurred post-partum. Contrary to popular belief and conventional teaching we found that the highest incidence of VTE in the antepartum period: 62.5% in first trimester, 25% in third trimester and none in the second. On detailed analysis, 87.5% of these actually had risk factors including family history (50%), positive thrombophilia screen (25%) and previous VTE (62.5%). In retrospect, it is difficult to predict how many of these could have been identified as high risk with meticulous screening process. This study has highlighted the importance of a careful antenatal screening process and a low threshold for testing for thrombophilia screen.
This study did not identify prolonged bed rest as a risk factor in VTE development. Whether prolonged bed rest is actually a factor is debatable, though stasis forms one component of Virchow's triad. Many studies found it to be an important contributory factor in precipitating VTE but Carr et al. have categorically ruled out prolonged bed rest as a risk factor. Changing trends in management of pregnancy complications have shown lower incidence of admission for bed rest, with due emphasis on ambulation to prevent thromboembolic episodes!

While an attempt was made to study labour and delivery variables, the relevance of this information is debatable as seven of eight events occurred antepartum. Most women were on low molecular weight heparin and had elective induction after omitting LMWH for the day, thus any comparison of labour duration or mode of delivery seems incongruous. An argument could be made that thromboprophylaxis instituted post-caesarean may have reduced the risk for some women in the control group, but such a conclusion is impossible without a formal randomised controlled trial. Moreover, given multiple variables, finding matched controls would be difficult if not impossible. In our hospital, the usage of post-partum heparin has been irregular at best, a need for thromboprophylaxis tempered with concern about post-caesarean bleeding, and varying with personal opinions.

This study had preponderance of VTE in right leg (75%), which differs from the results of most other studies. Meta-analysis by Ray and Chan found a 77.2% incidence in left leg. This was explained by a spur phenomenon exclusively in the left common iliac vein. Physiological dextrorotation of the pregnant uterus could explain a higher incidence of right leg thrombosis in third trimester but we could find no explanation for this significantly higher incidence through all trimesters of pregnancy.

Diagnosis and treatment of VTE in pregnancy and puerperium has been the subject of most studies reporting VTE in pregnancy. In this study, no delay in diagnosis or institution of heparin for VTE was noted. Given that VTE in pregnancy is stressed as a high-risk condition, most doctors in obstetrics and emergency departments have a high index of suspicion and a low threshold to request investigation and/or institute treatment.

The outcome of this study has been a shift in focus towards prevention of VTE in pregnancy. Given that majority of VTE occurred in first and third trimester of pregnancy as opposed to standard teaching of VTE occurring post-partum, more emphasis needs to be placed on careful screening in early pregnancy. Family history of stroke or positive thrombophilia screen and personal history of stroke, VTE and positive thrombophilia screen all need to be elicited meticulously. In this small study, this factor is particularly important with 62.5% of patients having previous episode of VTE.

This is much higher than some other studies. Pubinger et al. reported 3.5-fold increased risk of recurrent VTE during pregnancy, and Tengborn et al. found a recurrence rate of 12%. It has also been recommended that women with previous history of early IUGR, severe pre-eclampsia, early severe abruption and mid-trimester loss should have thrombophilia screen. Institution of LMWH from early pregnancy may prevent a potentially disastrous situation of VTE during pregnancy or post-partum period.

References


