Pregnancy and VTE
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Introduction
Georgia Thrombosis Forum (GTF, www.gtfonline.net) is an affiliate of North American Thrombosis Forum (NATF, www.natfonline.org). GTF is dedicated to the advocacy of thrombosis in the community and conducting research in the area of various aspects of management of thrombosis. GTF is also focused on training the next generation of leaders, and encourages youth volunteers as a medium for action in the community. This research project is focused on the relationship between pregnancy and venous thromboembolism (VTE). It will involve the incidence of VTE, risks and contributing factors, pathophysiology of VTE, signs and symptoms of VTE, diagnosing techniques and prevention.

My aunt was inactive during her most recent pregnancy. I started wondering if my aunt’s inactivity during her pregnancy would increase her chances of having VTE. In order to gain some background information on the correlation between pregnancy and VTE, I read the Rose case; a 32 year old patient who suffered from cerebral hematoma after the delivery of her second child and she had to undergo surgery for removal of the hematoma. These events sparked my interest to conduct research in this field.

Incidence of VTE in Pregnant Patients
The annual incidence of VTE in the pregnant population is high (1 out of 1000, or 0.1%, CDC). Between 1991 and 1999, pulmonary embolism (PE) was the leading cause of maternal mortality (CDC). Pregnancy increases the risk of VTE 4- to 5-fold over that in the non-pregnant state, as seen below.

VTE may occur at any time during gestation. Of the 4,200 pregnancy related deaths reported in the United States between 1991 and 1999, 20% were attributed to PE, surpassing deaths due to pregnancy-related hypertensive disorders, postpartum hemorrhage, and infection, as seen in the figure below.
Pregnancy-related mortality has been increasing over the past several years, significant percent of this number is from VTE during pregnancy (CDC), as shown in the figure below. The incidence of VTE has almost doubled from 1987 (ratio of 7.2 deaths per 100,000 live births) to 2013 (now a ratio of 17.3 deaths per 100,000 live births):

Risk and Contributing Factors of VTE

❖ Normal physiologic alterations during pregnancy
- Personal or family history of VTE
- Presence of a thrombophilic disorder
- Cesarean delivery (risk of VTE is twice that of vaginal delivery)
- Obesity
- Maternal cardiac disease
- Premature delivery
- Thrombophilia

Pathophysiology of VTE in pregnancy

- Pregnancy is a state of hypercoagulability due to alterations of coagulation proteins.
  - Factors I, II, VII, VIII, IX, and X increase
  - Increased resistance to the anti-thrombotic factors
  - Thrombophilias can exacerbate these changes in coagulation proteins, further increasing the patient's risk for VTE.
- It follows Virchow’s triad:

Virchow's triad is composed of three parts: hypercoagulability - defined by factor V, IX, and X - vessel damage - composed of vascular compression at delivery - and stasis - expounded as compression of the iliac vein. We can see the other factors defining each of the three parts in the graphic below:
Signs and Symptoms of VTE

They are mostly non-specific. Common ones are mild tachycardia (fast heart rate), dyspnea (shortness of breath), chest pain, cough, and edema. There might be pain and swelling of the lower extremity due to DVT. Syncope, hypotension, loss of pulse, or death are possible in patients with PE.

Laboratory Diagnosis of VTE
Imaging studies.
➢ Compression UltraSonography (CUS) of the lower extremity veins for DVT.
➢ Chest radiography for PE.
➢ Ventilation/perfusion (V/Q) scanning for PE.(infrequently used now)
➢ Spiral Computed Tomography Pulmonary Angiography (CT-PA).
➢ D-dimer for DVT (limited usage).

Imaging Studies
➢ Compression UltraSonography (CUS) of the lower extremity veins: 95% sensitive and specific for proximal lower extremity DVT.
➢ CUS is less accurate for the diagnosis of pelvic DVT.
➢ In pregnancy, CUS should be performed with the patient in the left lateral decubitus position and with Doppler analysis of flow variation during respiration to maximize the study’s ability to diagnose pelvic DVT.
➢ Magnetic Resonance Imaging (MRI) with a 97% sensitivity and 95% specificity for pelvic DVT in nonpregnant patients.
➢ CT scanning
➢ Spiral computed tomography pulmonary angiography (CT-PA)
➢ Chest radiography (x-ray)

Prevention and Management
➢ Therapeutic anticoagulation in the absence of contraindications.
➢ Common anticoagulant agents:
  ➢ Indirect thrombin inhibitors: unfractionated heparin and Low-Molecular-Weight Heparin (LMWH), synthetic heparin, pentasaccharides and orally administered Factor Xa inhibitors (Rivaroxaban, Apixaban, Edoxaban).
  ➢ Direct thrombin inhibitors (Argatroban, Lepirudin, Bivalirudin, Dabigatran).
  ➢ Vitamin K antagonist: warfarin.

Complications of VTE medication during pregnancy
➢ Fetal complications:
  ➢ Warfarin crosses the placenta and may cause fetal bleeding and teratogenicity.
➢ Maternal complications:
  ➢ Major bleeding in patients.
  ➢ Heparin-Induced Thrombocytopenia (HIT).
  ➢ Osteoporosis.
➢ The incidence is highest in the first 3 weeks post-partum. It then gradually reduces.
Summary and Conclusions

Thrombosis may attack at any time during pregnancy. Each pregnancy carries a certain amount of risk of thrombosis. If a pregnant woman maintains a healthy lifestyle (food intake and in exercise), before, during, and after the pregnancy, these risks could easily be avoided altogether. VTE during pregnancy is absolutely preventable.

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