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Thromboembolic Disease in Pregnancy

Objectives:

By the end of the lecture you should know:

- The implication of thromboembolic disease (TED) on pregnant women
- Why pregnancy is associated with an increased tendency for clotting
- Risk factors for TED
- Clinical Signs and symptoms of DVT and diagnostic difficulties
- Types of DVT
- Diagnostic tests
- Treatment of acute phase DVT & subsequent management
- Clinical presentation of pulmonary embolism, signs and symptoms and confirmatory lab tests
- Management of PE

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Thromboembolic Disease

Introduction:

- Venous TED is one of the major causes of direct maternal deaths. Those who survive suffer significant morbidity
- 2-4 fold increase compared to non-pregnant state
- Cesarean delivery > vaginal delivery

TED is more common in cesarean delivery (especially emergency) than vaginal delivery because it can cause endothelial injury which lead to clot formation.

- 75% of DVT occur antepartum (equally distributed among all three trimesters)
 - (Hacker & Moore): The greatest risk of a venous thromboembolism is during the first few weeks **postpartum**
 - 43-60% of PE occur after delivery during the first 2 weeks and in 80% of cases it is left-sided
 - **PE is the major non-obstetric cause of maternal mortality**
 - 2/100 000 pregnancies Fatality rate 15%
- All fatalities occurred in the first 1 hour after delivery. If she survive the first hour, her survival rate after that will be up to 95%.
- PE is very serious, I saw 3 or 4 cases who died immediately and we could not manage them. One of them was a sudanese lady, para 10, she started to be frothy immediately after a normal delivery, we could not manage her and she died within half an hour. Another lady had a cesarean delivery in the last 24 H, she was just talking fine then she collapsed and died within minutes. Also one day a lady collapsed after 24 H of hysterectomy, they thought that she has bleeding when I examined her there was nothing and she died because of PE.

Why is pregnancy associated with increased tendency for clotting ?

- **Venous stasis** results from compression of the pelvic veins by the gravid uterus which lead to decrease venous return from the lower extremities. As well as endocrine-mediated venodilation, often aggravated by decreased mobility.
- **Increased production of clotting factors** IV, V, VIII, IX, X, Von Willebrand, fibrinogen
- **Decreased anticoagulants** protein S and antithrombin, **this is important for thrombus formation.**
- **Decreased fibrinolytic activity** via increased plasminogen activator inhibitor
- **Endothelial damage** during preg and delivery, **especially traumatic vaginal delivery and cesarean delivery.**
- **Immobility**, especially if she was multipara or old lady (after 40s).

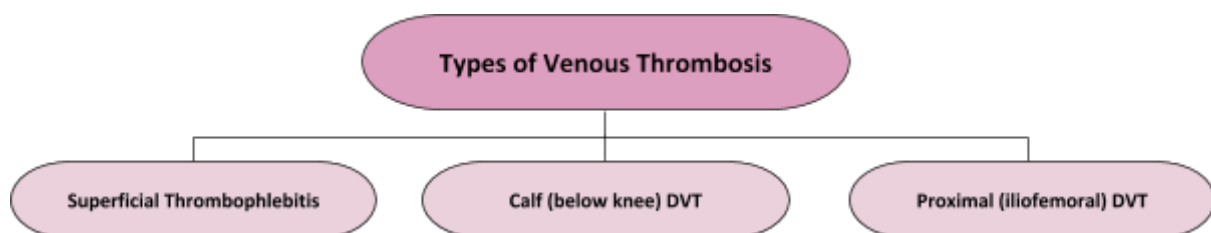
Risk factors for TED:

- Age over 35 yrs
- Multi parity (≥ 4)
- Obesity (over 80 kg)
- PET
- Immobility
- Infections
- Pelvic or leg trauma
- Smoking
- Atrial fibrillation
- Personal or family H/O TED
- Thrombophilia (antithrombin deficiency, factor V Leiden, protein C, protein S DEFF.)
- Antiphospholipid antibodies and lupus anticoagulant • Operative delivery (em. C/S > elective)
- Previous history of IUFD (intrauterine fetal death), early PET, severe IUGR, abruption or abruptio placenta.

If the patient is complaining of DVT symptoms and she has any of these factors you have to do for her doppler ultrasound to rule out DVT, although we are not worry about DVT because it is benign and we can treat it, we are worry about PE because 50% of pelvic DVT turn into PE.

but if the patient is thin and there is no predisposing factors or family history then you can neglect it.

Venous Thrombosis



- Clinical Diagnosis is difficult and inaccurate in over 60% of cases of TED
- Leg symptoms (edema and pain) and dyspnea are common in pregnancy and mimic symptoms of DVT/PE so someone may attribute it to pregnancy and may miss that it's DVT. This is a common issue that is seen even in general hospitals
- Tachycardia may be a normal physiological response

90% of pregnant ladies come to the clinic complaining of one of these symptoms so you have to choose who is the one at high risk to investigate and give her prophylactic before she develop complication.

- 50% of cases may be asymptomatic

	Superficial Thrombophlebitis	Calf Deep Venous Thrombosis (CVT)	Proximal / Iliofemoral DVT the most dangerous
	<p>The condition is misnamed (It is not inflammation). the redness surrounding the affected vein is a reaction to clot</p> <p>It is the commonest form of venous thrombosis in pregnancy & puerperium. It occurs in about 1% of patients and nearly always arise in existing varicose veins</p>	<p>Most of CVT resolve spontaneously (75-80%) and run a benign course except when the thrombus spreads up to involve the proximal deep veins (20-25%) in which case there is 50% risk of pulmonary embolism</p>	<p>It occurs more commonly than CVT and over 80% is left-sided. It is very severe that they enter the ER in a wheelchair.</p>
Clinical Presentation	<p>Tenderness, erythema, palpable cord-like veins, swelling and pain</p>	<p>Pain, local tenderness, swelling, change in skin colour and temperature (suspect it more if symptoms are unilateral)</p>	<p>-Symptoms are more dramatic with severe pain and swelling involving the entire limb. Normally the increased amount of estrogen and progesterone in pregnancy lead to softening of the joints, which cause severe backache and leg pain, the patient will tell you "I can't control my joint" , in these cases you have to differentiate and exclude proximal/ iliofemoral DVT .</p> <p>-If the arterial supply is unimpaired, the leg appears swollen, blue & warm. On the other hand if arterial spasm occurs secondary to irritation from the nearby clotted vein, the leg becomes swollen, painful, white & cold</p>
Investigation	<p>The diagnosis is clinically obvious</p>	<ul style="list-style-type: none"> - Contrast venography - Duplex ultrasonography /commonly used with a sensitivity and specificity of 97% , routinely we start with it. - Compression ultrasonography - If still suspicious do MRI: sensitivity and specificity 100% in nonpregnant Pt, MRI is not that accurate in pregnancy and not easy to do it for every pregnant. - Pelvic vein ultrasound, CT scan and MRI are all tests that can be used to look for pelvic clot. - D dimer test not useful in pregnancy because it normally increases with gestational age 	

Treatment	<p>Symptomatic treatment with compression bandage, leg elevation and to encourage mobility. Anti-inflammatory agents may be considered. In some pt's DVT need to be excluded as it may coexist with it . Even more extension to involve deep veins rarely occurs</p>	Discussed Below
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Pulmonary Embolism:

- A high index of suspicion is always needed for the diagnosis of PE especially in patients with DVT or risk factors for VTE
- The maternal mortality rate from untreated PE is 13% with the majority within 1 hr of the event
- With early diagnosis & treatment, the survival rate is between 92-95%
- **Signs and Symptoms:** Tachycardia, Tachypnoea, Dyspnoea, Haemoptysis, Pleuritic chest pain, Cyanosis, Pyrexia and Syncope or varying degree of shock. **Death may occur when the patient still under anesthesia.**
These S &S are non-specific and in most cases there is no prior clinical evidence of DVT
- **Investigation:** Chest X- ray (**mostly normal**), ECG (**only some changes**), Blood gases (**may show only low arterial blood oxygen**), Compression duplex Doppler to exclude DVT, Ventilation perfusion isotope lung scan (V/Q), Spiral CT (Helical or spiral CT scan is regarded superior to V/Q scan), Arteriography, CT angiography. **since CT is contraindicated in pregnancy you can do MRI**
- **Risk of radiologic procedures to the fetus:**
Radiation exposure of up to 0.05 Gy (5 rad) in utero:
 - Oncogenicity:
 - Relative risks of 1.2-2.4
 - Absolute risk of malignancy (baseline) in fetus is estimated to be 0.1%. **it's low percentage which may not affect the fetus, so if you have high suspicion for PE then you go for CT.**
 - Teratogenicity:
 - No increase in pregnancy loss, growth or mental retardation

Treatment of acute phase TED (PE & DVT):

- Standard heparin IV or the more preferred LMWH S.C should be started once the diagnosis is clinically suspected until excluded by objective testing
- Treatment aims at achieving APTT 2-2.5 the control for 5-7 days then continue with prophylactic dose generally for 6-12 weeks post-nataly
- **For PE** it should be continued for 4-6 months postnatally
- Heparin is the anticoagulant of choice in pregnancy. It does not cross the placenta and in overdose action can be reversed by protamine sulphate
- Osteoporosis & thrombocytopenia are complications of prolonged heparin treatment. Therefore, platelet count should be monitored regularly. This occurs more with unfractionated heparin.
- LMWH should be stopped 24 hours before delivery in the case of a planned induction or cesarean delivery. Alternatively, the patient can be switched to unfractionated heparin that can be stopped 6 hours before delivery.
- If there are no signs of postpartum hemorrhage, LMWH or unfractionated heparin can be restarted 12 to 24 hours post delivery and the patient can then be transitioned to warfarin
- **General Considerations:**
 - Legs should be elevated & graduated elastic compression stocking should be worn to reduce oedema
 - In DVT, calf circumference should measured daily to help monitoring the response to treatment
 - Massive PE requires ICU & multi disciplinary team approach
 - Recurrent PE may require inferior vena cava filter
 - Thrombolytic therapy in PE should only be given with haematologist agreement
 - Thoracotomy with embolectomy may be life saving
 - Heparin thrombo -prophylaxis has to be considered in the subsequent pregnancies or if additional risk factors appear

Oral Anticoagulants:

- Cross the placenta and are **potentially teratogenic at any stage of pregnancy**
- Complications of warfarin includes, nasal hypoplasia, depressed nasal bridge, irregular bone growth & intracranial fetal haemorrhage
- However , they **can be given after delivery** and are safe for lactation

Conclusion:

- Thromboembolism is a major cause of maternal mortality & morbidity worldwide
- Clinical diagnosis is unreliable but once strongly suspected, treatment should be started until objectively excluded
- Duplex Doppler, x-ray venogram & V/Q scan are the main diagnostic tools
- During pregnancy, LMWH is the preferred anticoagulant as it is more effective and safer than standard heparin
- Oral anticoagulants should not be given at any stage during pregnancy but they are safe & may be more convenient after delivery



- High clinical suspicion with early full anticoagulation and objective diagnosis are the best ways to minimize maternal M&M and avoiding risks of the unnecessary treatment

★ **Q1: Pregnant lady with deep vein thrombosis on heparin came with Vaginal bleeding what is the appropriate initial management for her?**

- A. Administration of protamine sulfate.
- B. Administration of tranexamic acid.
- C. Administration of vitamin k.
- D. Give fresh frozen plasma.

The Answer is: A

★ **Q2: A lady came asking for combined oral contraceptive pills. Which one of the following history is an absolute contraindication for combined oral contraceptive pills?**

- A. Ectopic pregnancy.
- B. Family history of breast cancer.
- C. Ovarian cancer.
- D. Thromboembolic disease.

The Answer is: D