

# Thromboembolic Disease

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## Objectives:

1. The implication of thrombo-embolic disease(TED) on pregnant women
2. Why pregnancy is associated with increased tendency for clotting
3. Risk factors for TED
4. Clinical Symptoms & signs of DVT and diagnostic difficulties
5. Types of DVT
6. Diagnostic tests
7. Treatment of acute phase DVT & subsequent management
8. Clinical presentation of pulmonary embolism, symptoms & signs and confirmatory lab tests
9. Management of PE

## Introduction

- Venous TED (thromboembolic disease) 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 **Due to increased endothelial trauma.**
- 75% of DVT occur antepartum (equally distributed among all three trimesters)
- 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.** Hemorrhage is the major obstetric cause of maternal mortality. (2/100,000 pregnancies Fatality rate 15% ) **Especially in the 1st hour.**

### Why is Pregnancy Associated with an Increased Tendency for Clotting ?

- Venous stasis **Pressure of the uterus on the pelvic veins +the hormonal changes that occur lead to venous stasis.**
- Increased production of clotting factors V, VIII, Von Willebrand, fibrinogen
- Decreased anticoagulants protein S and antithrombin
- Decreased fibrinolytic activity via increased plasminogen activator inhibitor
- Endothelial damage during pregnancy and delivery

**These changes happen to minimize postpartum hemorrhage but could lead to clotting.**

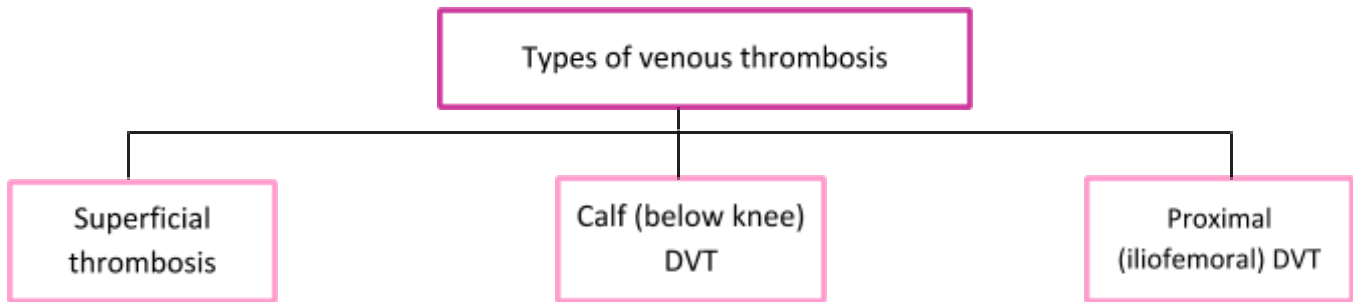
### Risk factors for TED:

- **Age over 35 yrs**
- **Multi parity (  $\geq 4$  )**
- **Obesity ( over 80 kg )**
- PET (pre-eclamptic toxemia) **They have abruption, DIC.**
- Immobility
- Infections **Any septic infection is a source of septicemia, DIC and thrombin release to vessels.**
- Pelvic or leg trauma **e.g. RTA**
- **Smoking**
- Atrial fibrillation
- Personal or family H/O TED
- Thrombophilia (antithrombin deficiency, factor V Leiden, protein C, protein S deficiency.)
- Antiphospholipid antibodies and lupus anticoagulant **They have vascular changes and high BP so they're more prone to thrombus formation.**



- Operative delivery (Emergency C/S > elective ) In c-section there is immobility and endothelial damage. That's why we give them prophylactic heparin during their stay in the hospital and maybe even at home if they're high risk.
- Previous history of IUFD, early PET, severe IUGR, abruption In these patients always think about antiphospholipid syndrome, especially if they have history of recurrent abortions/ IUFD.

## Venous Thrombosis



### Diagnosis

- Clinical diagnosis is difficult and inaccurate in over 60% of cases of TED.
- Why? Bc Leg symptoms (oedema and pain) and dyspnea are common in pregnancy/ mimic symptoms of DVT/PE 40% are normal. But if you're suspecting then it's better to test.
- Tachycardia may be a normal physiologic response.

|              | Superficial thrombophlebitis   | Calf deep venous thrombosis   | Proximal/ Iliofemoral DVT  |
|--------------|--|---|--|
| General info | <ul style="list-style-type: none"> <li>• The condition is misnamed. It is not infective. The redness surrounding the affected vein is a reaction to clot</li> <li>• It is the commonest form of venous thrombosis in pregnancy &amp; puerperium. It occurs in about 1% of patients and nearly always arise in existing <b>varicose veins</b></li> <li>• Superficial thrombophlebitis does not predispose to thromboembolism but</li> </ul> | <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> | <ul style="list-style-type: none"> <li>• It occurs more commonly than CVT and over 80% is left-sided Due to anatomical changes, (left common iliac vein is compressed by the right common iliac artery.)</li> <li>• DVT does predispose to thromboembolic disease.</li> <li>• Lower limb edema usually is both sides without pain. If you see pain and swelling in one side only then</li> </ul> |



|                       |  |  |   |
|-----------------------|--|--|---|
|                       | may mimic more severe disease.   |  | suspect proximal/ iliofemoral DVT.  |
| Clinical presentation | (tenderness, erythema, palpable cord-like veins)   | The most common clinical features are pain, local tenderness, swelling, change in skin colour and temperature  | <ul style="list-style-type: none"> <li>Symptoms are more dramatic with pain and swelling involving the entire limb, calf pain on foot dorsiflexion (Homan sign)</li> <li>If the arterial supply is unimpaired, the leg appears swollen, blue &amp; warm. On the other hand if arterial spasm occurs secondary to irritation from the nearby clotted vein, the leg becomes swollen, painful, white &amp; cold</li> </ul> |
| Investigation         | <ul style="list-style-type: none"> <li>The diagnosis is clinically obvious</li> <li>In some pt's DVT need to be excluded as it may co-exist with it . Even more extension to involve deep veins rarely occurs (Diagnosis is one of exclusion after ruling out DVT.)</li> </ul> | <ul style="list-style-type: none"> <li>Contrast venography</li> <li>Duplex ultrasonography /commonly used with a sensitivity and specificity of 97%. If its equivocal → go for MRI,CT</li> <li>Compression ultrasonography</li> <li>MRI (sensitivity and specificity 100% in nonpregnant Pt ).</li> <li>Pelvic vein ultrasound, CT scan and MRI are all tests that can be used to look for pelvic clot.</li> <li>D dimer test is <b>not useful</b> in pregnancy because it normally increases with gestational age.</li> </ul> |   |
| Treatment             | <ul style="list-style-type: none"> <li>Treatment is usually symptomatic with compression bandage, leg elevation and to encourage mobility. We may give <b>local</b> Anti-Inflammatory drugs.</li> </ul>  | Discussed later  |   |

## Pulmonary embolism (PE)

- A high index of **suspicion** is always needed for the diagnosis of PE especially in patients with DVT or risk factors for VTE (c-section, fracture, obesity...)
- 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%

### The common symptoms & signs of PTE

These S &S are non-specific and in most cases there is no prior clinical evidence of DVT

- Tachypnoea
- Dyspnoea **most common**
- Haemoptysis
- Pleuritic chest pain
- Tachycardia
- Cyanosis
- Pyrexia
- Syncope or varying degree of shock

These S &S are non-specific and in most cases there is no prior clinical evidence of DVT

### Investigations for suspected PTE

| Routine  | Diagnosis  |
|--|--|
| <ul style="list-style-type: none"> <li>• Chest X- ray <b>often normal</b></li> <li>• ECG <b>may show tachycardia, Right axis deviation inverted T</b> (but usually is normal)</li> <li>• Blood gases <b>showing low pO<sub>2</sub></b> (but often in the normal range) <b>Check O<sub>2</sub>, CO<sub>2</sub>, PH</b></li> </ul> | <ul style="list-style-type: none"> <li>• <b>Compression duplex Doppler</b> to exclude DVT. <b>commonly we use it.</b></li> <li>• Ventilation-perfusion isotope lung scan (V/Q)</li> <li>• Helical or spiral CT scan is regarded superior to V/Q scan</li> <li>• <b>Spiral CT</b></li> <li>• Arteriography. <b>If needed</b></li> <li>• CT angiography. <b>If needed</b></li> </ul> |

Diagnosis depends on the pulmonary **imaging** modalities used. Spiral CT scan of the chest is the **best initial** test for suspected PE. Pulmonary angiography is the **most definitive** diagnostic method; most common indication is a negative spiral CT scan in a high-risk and symptomatic patient.

## 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%.**
- **Teratogenicity**
  - No increase in pregnancy loss, growth or mental retardation

Suspect PE? no problem go to X-ray because we're dealing with a life threatening condition that outweighs the very low risk (0.1%) of malignancy (oncogenicity) in fetus

## Treatment of Acute Phase TED

- **Standard heparin IV or the more preferred LMWH S.C should be started once the diagnosis is clinically suspected until excluded by objective testing. Don't wait for investigations to prevent progression to PE.**
- 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. **IV heparin, Once therapeutic levels are achieved, subcutaneous heparin is used once.**
- For PE it should be continued for 4-6 months post-nataly
- **Heparin is the anticoagulant of choice in pregnancy.** It does not cross the placenta and in overdose action can be reversed by protamine sulphate. Oral anticoagulant is contraindicated. **(If she is on warfarin switch to heparin)**  
**Patient on heparin came in for emergency c\c → give her protamine sulphate**
- Osteoporosis & thrombocytopenia are complications of prolonged heparin treatment. Therefore **platelet count should be monitored regularly**
- Legs should be elevated & graduated elastic compression stocking should be worn to reduce oedema
- In DVT, calf circumference should be measured daily to help monitoring the response to treatment
- Massive PE requires ICU & multi-disciplinary team approach **hematologist and vascular surgeon**
- 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
- **Perform thrombophilia workup.**

### Oral anticoagulants (Warfarin)

- Cross the placenta and are potentially teratogenic at any stage of pregnancy **contraindicated in 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

- Thrombo-embolism 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 (like warfarin) should not be given at any stage during pregnancy **due to teratogenicity** but they are safe & may be more convenient after delivery **+ safe for lactation**
- High clinical suspicion with early full anticoagulation and objective diagnosis are the **best** ways to minimize maternal Mortality & Morbidity and avoiding risks of the unnecessary treatment

## Summary

### Thrombo-Embolic Disease (TED)

#### Risk factors of TED:

**Age** (>35), multiparity ( $\geq 4$ ), obesity, **immobility**, infection, pelvic or leg trauma, **smoking**, atrial fibrillation, **personal or family history of TED**, thrombophilia, **operative delivery**, antiphospholipid antibodies.

|                  | Venous Thrombosis  |  |  |
|------------------|--|--|--|
| Types            | Superficial thrombophlebitis                               | Calf deep venous thrombosis (CVT)  | Proximal deep venous thrombosis  |
| Notes            | Commonest form of venous thrombosis in pregnancy.          |  | More common than CVT and over 80% is left-sided.   |
| Signs & Symptoms | Tenderness, erythema, palpable cord-like veins.            | Pain, local tenderness, swelling, change in skin colour and temperature.   | Pain and swelling of entire limb.<br>Leg is blue & warm → artery unimpaired.<br>Leg is white and cold → secondary arterial spasm |
| Diagnostic tests | Clinically obvious.  | <b>Duplex ultrasound</b> , compression ultrasound, contrast venography, MRI.<br>Note: pelvic clot → pelvic vein US + CT + MRI<br>D-DIMER <b>NOT USEFUL IN PREGNANCY!</b> |  |
| Treatment        | Symptomatic: compression bandage, leg elevation, mobility. | Low molecular weight heparin (Note: most resolve spontaneously (75-80%) except if it spreads to proximal deep veins)   | Low molecular weight heparin → anticoagulant of choice in pregnancy (note: continue prophylactic dose 6 - 12 weeks postnatally)  |

| Types   | Pulmonary embolism   |
|---------|--|
| Notes   | Untreated PE → maternal mortality rate 13% within 1 hour!<br>Early treatment and diagnosis of PE → 92-95% survival rate! |
| Signs & | Tachypnea, dyspnea, hemoptysis, pleuritic chest pain, tachycardia, cyanosis,   |





|                  |   |
|------------------|---|
| Symptoms         | pyrexia.  |
| Diagnostic tests | CXR, ECG, blood gases, <b>compression duplex US, V/Q scan, spiral CT</b> , arteriography, CT angiography.                               |
| Treatment        | Low molecular weight heparin (LWMH) (note: continue prophylactic dose 4-6 months postnatally) / Major PE → ICU + multidisciplinary team |

## MCQs

1- Which of the following patients has the highest risk for DVT?

- A- Primigravida
- B- 33 year old
- C- Vaginal delivery
- D- smoker

2- A 32 year old pregnant female presented to your clinic complaining of tenderness and erythema over her leg. You suspect thrombophlebitis, how will you manage the patient?

- A- Low molecular weight heparin subcutaneously
- B- Warfarin orally
- C- Leg elevation and compression bandage
- D- Admit and monitor patient

3- On a prenatal visit, a patient complains of pain and swelling in her leg. What investigation will you order for this patient?

- A- D-dimer
- B- Duplex US
- C- V/Q scan
- D- Leg xray

4- A patient was diagnosed with DVT during pregnancy and treated with LWMH. After delivery she asked if she could switch the medicine and take something orally instead of by injection. How will you proceed?

- A- Explain to her that oral medication can harm her baby.
- B- Switch the patient to oral warfarin.
- C- Switch the patient to oral heparin.
- D- The patient does not need further medication after delivery.

5- A 38 year old female presented to your clinic for a prenatal visit. She complains of dyspnea, palpitations, and tachycardia. She has no chest pain, no swelling or pain in her legs. On examination she is overweight and appears cyanotic. How will you proceed?

- A- Reassure her that these are normal changes in pregnancy.
- B- Start her on LWMH and continue for 4 month after delivery.
- C- Order ECG + spiral CT and if normal reassure patient.
- D- Refer her to internal medicine.

Answers: 1- D. 2- C. 3- B. 4- B. 5- C.