Pathophysiology of Obstetrics VTE

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MFM, HoSHAS
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HoSHAS
Key Message

Pregnancy is an independent risk factor for VTE
Key Message

Pregnancy is an independent risk factor for VTE

When pregnant, think VTE!!
## Outline

<table>
<thead>
<tr>
<th>What</th>
<th>VTE in Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Why</td>
<td>Why VTE in Pregnancy?</td>
</tr>
<tr>
<td>Who</td>
<td>Women at risk (risk factors)</td>
</tr>
<tr>
<td>Where</td>
<td>Site</td>
</tr>
<tr>
<td>When</td>
<td>Which phase of pregnancy</td>
</tr>
<tr>
<td>How</td>
<td>Thromboprophylaxis</td>
</tr>
</tbody>
</table>

**Kipling Method**

I keep six honest serving-men,
They taught me all I knew;
Their names are **What** and **Why** and **When**
And **How** and **Where** and **Who**.
Venous thromboembolism

• Venous thromboembolism (VTE) is a major health problem
• It is the 3rd most common cardiovascular disease after myocardial infarction and stroke
• 3 million VTE-related deaths per year worldwide
• 10% of hospital deaths are due to pulmonary embolism

Naess IA, JTH 2007
VTE CPG 2013
Cohen AT, Thromb Haemost 2007
VTE in Pregnancy

VTE incidence 1-2/1000 pregnancies
Pregnancy : 10x risk
Any stage of pregnancy
Highest during puerperium:
  → 5x risk vs pregnancy
  → 50x risk vs non-pregnant
Elective CS  2x risk vs Vaginal delivery
Emergency CS  2x risk vs Elective CS
Emergency CS  ≈4x risk vs Vaginal delivery

**75-80% pregnancy-associated VTE is DVT and 20-25% PE (≠ HoSHAS data)

RCOG Green-top Guideline No.37a, Nov 2009
### HoSHAS Obstetric VTE
(July 2013-April 2017)

<table>
<thead>
<tr>
<th></th>
<th>Antepartum</th>
<th>Postpartum</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DVT</strong></td>
<td>5</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td><strong>PE</strong></td>
<td>3</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td><strong>DVT + PE</strong></td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>8</td>
<td>17</td>
<td>25</td>
</tr>
</tbody>
</table>

**Overall incidence of Obst VTE:** 0.85/1000 deliveries

*Prior to Sept 2015: 1.0/1000 deliveries*

*After Sept 2015: 0.61/1000 deliveries*
Obstetric VTE: Facts

- Pregnant women are 4-5x more likely to suffer from VTE
- 75-80% pregnancy-associated VTE is DVT and 20-25% PE
Obstetric VTE : Facts

• PE occurs in 15-24% of untreated DVTs with a mortality rate of 15-30%
• PE occurs in 4.5% of treated DVTs with a mortality rate of 1%
Virchow’s Triad

**Hypercoagulability**
- Major surgery / trauma
- Malignancy
- Pregnancy (post-partum)
- Inherited thrombophilia
- Infection and sepsis
- Inflammatory Bowel Disease
- Autoimmune condition
- Estrogen therapy
- Inflammation
- Dehydration

**Vascular Damage**
- Thrombophlebitis
- Cellulitis
- Atherosclerosis
- Indwelling catheter / heart valve
- Venepuncture
- Physical trauma, strain or injury
- Microtrauma to vessel wall

**Circulatory Stasis**
- Immobility
- Venous obstruction (obesity, tumour, pregnancy)
- Varicose veins
- Atrial fibrillation or left ventricular dysfunction
- Congenital abnormalities affecting venous anatomy (e.g., May-Thurner and Paget-Schroetter syndrome)
- Low heart rate (bradycardia) and low blood pressure
Virchow’s Triad during Pregnancy

Hypercoagulability in pregnancy
- Increase clotting factors (VIII, IX, X) & fibrinogen
- Reduced levels of anti-coagulators (protein S, antithrombin)

Vascular compression at delivery
Assisted / operative Delivery

Compression of left iliac vein (by gravid uterus, right iliac art & left infundibulopelvic vessels);
Immobilisation; Hormonally mediated venous dilatation
Pathophysiology of thrombosis

• Thrombosis occurs when there is disruption of Virchow’s triad.

• Modifications of haemostasis by pregnancy renders blood hypercoagulable.

• Hyperemesis and pre-eclampsia further contribute to thrombogenesis.

• Excessive fluid loss in hyperemesis concentrates blood and the resultant bed rest further promotes stasis of blood flow.
(1) Hypercoagulability

• Hypercoagulability in pregnancy, in preparation for parturition.

a) **Increased** concentration of clotting factors VIII, IX and X. Fibrinogen level increase by 50% while fibrinolytic activity is decreased.

b) Levels in **anticoagulators** such as antithrombin and protein S **fall**.

c) Levels in PAI-1 & PAI-2 (placenta) increase 5-fold → Hypofibrinolytics
(1) Hypercoagulability (cont’)

• These changes are observed from 1st trimester to 6 weeks after delivery.

• Peak in coagulation in immediate postpartum which tails off after 3 weeks postpartum.

Pregnancy: blood is in procoagulant state
(2) Venous stasis

- a) Venous dilatation (hormonal effect)
- b) Compression of the gravid uterus on the IVC
- c) Compression of the Lt iliac vein by left infundibulopelvic vessels & Rt Iliac Artery
(3) Endothelial injury

a) Vascular compression at delivery

b) Assisted / operative delivery
Pregnancy.....

....an **independent risk factor**

for VTE
Direct Causes of maternal deaths in Malaysia: 2008-2014

<table>
<thead>
<tr>
<th>CAUSES OF MATERNAL DEATHS (MALAYSIA)</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>MMR</td>
<td>N</td>
<td>MMR</td>
<td>n</td>
<td>MMR</td>
<td>n</td>
</tr>
<tr>
<td>Pulmonary Embolism</td>
<td>13</td>
<td>2.6</td>
<td>15</td>
<td>3.1</td>
<td>10</td>
<td>2.0</td>
</tr>
<tr>
<td>Amniotic fluid embolism</td>
<td>10</td>
<td>2.0</td>
<td>15</td>
<td>3.1</td>
<td>6</td>
<td>1.2</td>
</tr>
<tr>
<td>PPH</td>
<td>20</td>
<td>10.5</td>
<td>13</td>
<td>2.6</td>
<td>19</td>
<td>3.7</td>
</tr>
<tr>
<td>Hypertensive Disorders in Pregnancy</td>
<td>18</td>
<td>13.7</td>
<td>25</td>
<td>5.1</td>
<td>25</td>
<td>4.9</td>
</tr>
<tr>
<td>Obstetric Trauma</td>
<td>4</td>
<td>5.4</td>
<td>10</td>
<td>2.0</td>
<td>12</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Family Health Division, MOH Malaysia
Direct Causes of maternal deaths in Malaysia 2008-2014

<table>
<thead>
<tr>
<th>CAUSES OF</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
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<td>4.9</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td>Obstetric Trauma</td>
<td>4</td>
<td>10</td>
<td>12</td>
<td>2.3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

An average of 13-14 deaths from pulmonary embolism per year!
Maternal Deaths Cause-Specific MMR 2001 – 2013p

Year


Pulmonary Embolism 2.1 2.7 3.3 1.9 3.0 1.9 1.5 2.4 3.3 2.0 1.8 2.6

PPH 3.3 3.3 4.7

HDP

Med Cond

Pulm Emb

Source: Family Health Development Division & Health Informatics Centre
Malaysia: VTE MMR

Pulm Embolism 2.5/100K LB in 2009-2011p
12.3% of Direct Mat Deaths in 2009-2011p

Sabah:
1.6/100K LB in 2012 (1 PE)
4.61/100K LB 2013 (both cerebral vein thrombosis)
1.6/100K LB in 2014 (1PE)

Pahang:
8.3/100K LB in 2012 (2 PE)
4.1/100K LB in 2013 (1 PE)
7.9/100K LB in 2014 (2 PE)
3.92/100K LB in 2015 (1 PE)
3.92/100K LB in 2016 (1 CVT)

Temerloh: 7.4/100K LB in 2004-2016 (7 PE)

Pahang State Health Department
Sabah State Health Department
Pahang VTE Maternal Deaths
Analysis of pattern of Pahang MMR
? Temerloh women are more thrombogenic
• Lacking in thromboprophylaxis – not systematic, not using the recommended agent, inadequate
• Failure to diagnose, delay in treatment

➔ Essentially .......

NOT thinking VTE!
Obstetric VTE in Malaysia

• No local publication on Obstetric VTE incidence
• Poor understanding by HCP
• Lack thromboprophylaxis program
• Fragmented care in current system
• Issue of LMWH (sourced from porcine)
• Costly thromboprophylaxis program
VTE in Malaysian women?

• Not that uncommon (It is as common as in the West!)
• Under-diagnosed, unsuspected
• Lack of awareness, does not believe (in denial?!) 
• Similar risk factors

The eyes do not see what the mind does not know!!

Blind Mind = Blind Eye
Some of the Risk Factors for Obstetric VTE:

- Obesity
- Medical Co-Morbidities
- LSCS
- IVF / ART pregnancy

Frequent factors we encounter nowadays

VTE risk in pregnancy & puerperium exist not only during admission but also as out patient.

Walking VTE Risks!
Risk Factor for VTE

- Pre-existing risk factors
  - Eg: Previous VTE
  - High risk thrombophilia
  - Medical co-morbidities
  - Obesity
  - Smoker, etc

- Obstetric risk factors
  - Eg: LSCS – EMLSCS, ELLSCS
  - Pre-eclampsia
  - ART/IVF
  - Mid-cavity or rotational operative delivery
  - Eg: OHSS (T1 only)

- Transient risk factors
  - Any surgical procedure in pregnancy or puerperium except immediate repair of perimeum
  - Hyperemesis
  - Current systemic infection
  - Immobility
  - Dehydration

Risk factors are scored accordingly from 1-4.

RCOG 2015
RCOG 2009 vs 2015 guidelines

Risk factors:

• Readmission (new 2015)
• Surgical procedure in puerperium (except immediate repair of the perineum) \(\rightarrow\) intermediate risk (low risk in 2009)
• T1DM with nephropathy (new 2015)
• Preterm delivery in this pregnancy (new 2015)
• Stillbirth in this pregnancy (new 2015)
• Transient risk factors (dehydration, hyperemesis, current systemic infection, long-distance travel)
Scoring:

• New system
• May start from 28 weeks (score 3)
• Postpartum thromboprophylaxis now extends from 7 to 10 days
Training Manual – Prevention & Treatment of Thromboembolism in Pregnancy & Puerperium, 2\textsuperscript{nd} Ed (2017)
## Pre-existing risk factors

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous VTE</td>
<td>4</td>
</tr>
<tr>
<td>High-risk thrombophilia (anti-thrombin, protein C, protein S deficiency)</td>
<td>3</td>
</tr>
<tr>
<td>Medical comorbidities e.g. cancer, heart failure, active SLE, nephritic syndrome, Type 1 DM with nephropathy, current IV drug user, TB, thalassemia major or intermedia, post splenectomy</td>
<td>3</td>
</tr>
<tr>
<td>Obesity BMI ≥ 40kg/m²</td>
<td>2</td>
</tr>
<tr>
<td>Obesity BMI 30-39kg/m²</td>
<td>1</td>
</tr>
<tr>
<td>Family history of VTE</td>
<td>1</td>
</tr>
<tr>
<td>Low-risk thrombophilia (Factor V Leiden, High Factor VIII)</td>
<td>1</td>
</tr>
<tr>
<td>Current smoker (≥ 10/day)</td>
<td>1</td>
</tr>
</tbody>
</table>

## Obstetric risk factors

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>All caesarean sections (both Emergency &amp; Elective)</td>
<td>2</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>1</td>
</tr>
<tr>
<td>IVF (1(^{st}) trimester only)</td>
<td>1</td>
</tr>
<tr>
<td>Mid-cavity or rotational operative delivery</td>
<td>1</td>
</tr>
<tr>
<td>Prolonged labour &gt;24hr</td>
<td>1</td>
</tr>
<tr>
<td>PPH of&gt;1L or requiring blood transfusion</td>
<td>1</td>
</tr>
<tr>
<td>Stillbirth (current)</td>
<td>1</td>
</tr>
</tbody>
</table>
## Transient risk factors

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical procedures (excluding episiotomy, 1\textsuperscript{st} &amp; 2\textsuperscript{nd} degree perineal repair, ERPOC)*</td>
<td>4</td>
</tr>
<tr>
<td>Hyperemesis gravidarum/OHSS*</td>
<td>4</td>
</tr>
<tr>
<td>Systemic infection / infection requiring IV antibiotics</td>
<td>1</td>
</tr>
<tr>
<td>Immobility, dehydration</td>
<td>1</td>
</tr>
<tr>
<td>Admission beyond 3 days</td>
<td>1</td>
</tr>
<tr>
<td>Non-stop long distance travel (&gt;4 hrs)</td>
<td>1</td>
</tr>
</tbody>
</table>

* thromboprophylaxis cover is advised until the patient has sufficiently recovered from surgery or her signs and symptoms of hyperemesis gravidarum or OHSS
## Score summary

<table>
<thead>
<tr>
<th>Period</th>
<th>Score</th>
<th>Duration of thromboprophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal</td>
<td>≥4</td>
<td>Consider giving from 1&lt;sup&gt;st&lt;/sup&gt; trimester up to 6 weeks postnatal (up to 6 weeks postnatal if there is a single risk with a score of 4. If a combination score of ≥4, then give up to 3 weeks postnatal then to be reviewed by an O&amp;G specialist to decide if a further 3 weeks of prophylaxis is warranted)</td>
</tr>
<tr>
<td>Antenatal</td>
<td>3</td>
<td>Consider prophylaxis from 28 weeks till 3 weeks postnatal</td>
</tr>
<tr>
<td>Postnatal</td>
<td>2</td>
<td>Consider prophylaxis for 10 days</td>
</tr>
<tr>
<td>Postnatal</td>
<td>&gt;2</td>
<td>Consider prophylaxis for 10 days or longer, specialist to decide</td>
</tr>
</tbody>
</table>

All antenatal and postnatal patients, even those considered low risk should be counselled on VTE prevention and recognition of VTE signs & symptoms
New MOH Obst VTE Checklist


• The difference:
  1) Weightage / Risk score
  2) Risk factors – some were taken off
  3) Duration of postnatal thromboprophylaxis

Risk Factors - removed

• Age
• Parity
• Varicose vein
• Multiple pregnancy
• Preterm delivery
Risk Factors - modified

• Smoker - ≥10/day

• All LSCS – same score of 2*

*start thromboprophylaxis the evening before scheduled ELLSCS (at least 12hr from LSCS)
Cadangan Penambahbaikan Dalam Pengendalian Kes Berisiko dan VTE/PE:

- Beri pilihan kepada pesakit semasa kaunseling: antara UFH & LMWH
- Memurnikan SOPs
- Senarai semak faktor risiko disimpan di dalam *smart phone*
- Bertanya tentang faktor risiko dan simptom DVT / Pulm Embolism semasa membuat postnatal ward rounds
- Bekerjasama dengan kakitangan kesihatan primer dan komuniti.
- Perancang keluarga perlu diberi perhatian – tawarkan penggunaan kaedah yang sesuai, contoh: implan.
- Latihan – fokus kepada penjagaan kesihatan di peringkat primer

➔ VTE boleh dicegah!
Ringkasan

• Kehamilan merupakan risiko untuk mendapat VTE. LSCS; puerperium – risiko lebih tinggi
• Semua unit obstetrik mesti mempunyai SOP untuk thromboprophylaxis
• Semua wanita (antenatal & postnatal) mesti dinilai untuk risiko VTE (semasa booking, admission, selepas kelahiran)
• Penilaian perlu direkodkan.
• Latihan berterusan perlu dijalankan untuk meningkatkan kesedaran dan pengetahuan
• Berhati-hati dalam mengendalikan pesakit yang mengambil anticoagulant semasa antenatal.
Mesej Penting: (5Ws1H)

APA (what) Kehamilan ialah risiko untuk mendapat VTE

KENAPA Kehamilan memenuhi ketiga-tiga ciri dalam (why) Virchow’s Triad

BILA (when) Boleh berlaku pada mana-mana fasa kehamilan dan pueperium

DI MANA (where) Pulmonary Embolism, DVT

SIAPA (who) Warga emas, obes, kadar LSCS yang tinggi, ↑ART pregnancy (senarai semak)

BAGAIMANA (how) Kenalpasti risiko, latihan, SOP, tingkatkan kesedaran.

... JANGAN LUPA PERANCANG KELUARGA!
The task of science is to stake out the limits of the knowable, and to center consciousness within them.

- Rudolf Virchow