Hematologic Disorders in Pregnancy: What to expect when you’re expecting

Chantalle Menard – MD FRCPC (PGY-5)

Arjuna Ponnampalam - MD FRCPC
Presenter Disclosure

- **Faculty / Speaker’s name:** Chantalle Menard & Arjuna Ponnampalam

- **Relationships with commercial interests:**
  - Grants/Research Support: None
  - Speakers Bureau/Honoraria: None
  - Consulting Fees: None
  - Other: None
Mitigating Potential Bias

• Not applicable
Learning Objectives

1. Recognize expected physiologic changes in hematologic parameters with pregnancy
2. Identify causes of thrombocytopenia and anemia in pregnancy.
3. Know when referral is necessary based on information provided by the CBC
Hematological Changes in Pregnancy

• Plasma volume expands 40-60%
  – Red blood cell mass expands by only 20-50% → physiologic anemia develops (hematocrit 30-32%)
  – Hemoglobin levels typically >110 g/L.

• Prevalence of anemia increases in each trimester
  – 8% → 12% → 34%
Hematological Changes in Pregnancy

Figure 2. Distribution of platelet counts in healthy pregnant women at term. Reprinted from Boehm et al.10 with permission.

Cines & Levine. *Thrombocytopenia in Pregnancy*. ASH Education. 2017
Hematological Changes in Pregnancy

• White blood cell count increases (leukocytosis)
  – Predominantly neutrophilia
• Occurs due to increased drive of hematopoiesis under physiologic stress
• Monocyte count increases
  – Particularly in the first trimester
Case 1

- 32 year old female, G2P1 at 28 weeks
- Routine bloodwork:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>12 x 10⁹/L</td>
<td>4.5-11.0 x 10⁹/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>115 g/L</td>
<td>120 – 160 g/L</td>
</tr>
<tr>
<td>MCV</td>
<td>88 fL</td>
<td>80– 98 fL</td>
</tr>
<tr>
<td>Platelets</td>
<td>98 x 10⁹/L</td>
<td>140 – 440 x 10⁹/L</td>
</tr>
</tbody>
</table>
Case 2
- 32 year old female, G2P1 at 32 weeks
- Diagnosed with preeclampsia at 28 weeks
- Complains of RUQ pain

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>$12 \times 10^9$/L</td>
<td>4.5-11.0 $\times 10^9$/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>83 g/L</td>
<td>120 – 160 g/L</td>
</tr>
<tr>
<td>MCV</td>
<td>88 fL</td>
<td>80– 98 fL</td>
</tr>
<tr>
<td>Platelets</td>
<td>$45 \times 10^9$/L</td>
<td>140 – 440 $\times 10^9$/L</td>
</tr>
</tbody>
</table>
Case 3

- 32 year old female, G2P1 at 8 weeks
- Routine bloodwork:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>$10.6 \times 10^9$/L</td>
<td>4.5-11.0 $\times 10^9$/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>123 g/L</td>
<td>120 – 160 g/L</td>
</tr>
<tr>
<td>MCV</td>
<td>88 fL</td>
<td>80– 98 fL</td>
</tr>
<tr>
<td>Platelets</td>
<td>$62 \times 10^9$/L</td>
<td>140 – 440 $\times 10^9$/L</td>
</tr>
</tbody>
</table>
# Thrombocytopenia in Pregnancy

<table>
<thead>
<tr>
<th>Isolated thrombocytopenia</th>
<th>Pregnancy-specific</th>
<th>Not pregnancy specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational Thrombocytopenia (70-80%)</td>
<td>Primary ITP (1-4%)</td>
<td>Secondary ITP (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Drug-induced thrombocytopenia (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Congenital thrombocytopenia (&lt;1%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thrombocytopenia associated with systemic disorders</th>
<th>Severe preeclampsia (15-20%)</th>
<th>TTP/HUS (&lt;1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia associated with systemic disorders</td>
<td>HELLP syndrome (&lt;1%)</td>
<td>SLE (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>AFLP (&lt;1%)</td>
<td>Antiphospholipid syndrome (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Viral infections (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bone marrow disorders (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nutritional deficiencies (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Splenic sequestration (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thyroid disorders (&lt;1%)</td>
</tr>
</tbody>
</table>

Gestational Thrombocytopenia

• 5% of all pregnancies
• 75% of all cases of thrombocytopenia in pregnancy
• Mid-second to third trimester
• Platelet counts typically 70 – 149 x10⁹/L
  – Only 1-5% develop counts <100 x10⁹/L
• No adverse health consequences to the fetus or the mother
  – May affect candidacy for neuro-axial anesthesia

Cines & Levine. Thrombocytopenia in Pregnancy. ASH Education. 2017
Gestational Thrombocytopenia

• Treatment
  – No therapy is recommended
  – Resolves 1-2 months post-partum
    • Confirm with CBC
  – Monitor at antepartum visits
  – May (or may not) recur with subsequent pregnancies

Cines & Levine. *Thrombocytopenia in Pregnancy.* ASH Education. 2017
Preeclampsia

• New onset of hypertension ≥20 weeks gestation with proteinuria
• 15-20% of thrombocytopenia in pregnancy
• Severe cases may be accompanied by:
  – Thrombocytopenia ≤100 x10⁹/L
  – Impaired liver function
  – New onset renal impairment
  – Pulmonary edema
  – New onset cerebral or visual disturbance

Cines & Levine. *Thrombocytopenia in Pregnancy*. ASH Education. 2017
Preeclampsia

• Treatment:
  – Urgent referral to obstetrics
  – Expedient delivery of the fetus (if severe)

Gernsheimer et al. *How I treat thrombocytopenia in pregnancy*. Blood; 121 (1).
HELLP Syndrome

• Hemolysis, Elevated Liver Enzymes, Low Platelets
• Occurs with (80%) and without (20%) preeclampsia
• <1% of all thrombocytopenia in pregnancy

Gernsheimer et al. *How I treat thrombocytopenia in pregnancy*. Blood; 121 (1).
HELLP Syndrome

• Diagnosis:
  – 28-36 weeks of gestation
  – Hemolysis
    • Schistocytes, Elevated bilirubin & LDH, low haptoglobin
    – Liver enzyme elevation
    – Thrombocytopenia (often <50 $\times 10^9$/L)
  
• Can be difficult to differentiate from TTP!!

Gernsheimer et al. *How I treat thrombocytopenia in pregnancy*. Blood; 121 (1).
HELLP Syndrome

• Treatment:
  – Urgent referral to obstetrics
  – Transfer to tertiary care center
  – Expedient delivery of the fetus

Gernsheimer et al. *How I treat thrombocytopenia in pregnancy*. Blood; 121 (1).
Acute Fatty Liver of Pregnancy (AFLP)

- Third trimester
- Can overlap with symptoms of HELLP and severe preeclampsia
- <1% of all thrombocytopenia in pregnancy
Acute Fatty Liver of Pregnancy (AFLP)

• Clinical Features:
  – Severe thrombocytopenia (<20x10⁹/L)
  – Evidence of disseminated intravascular coagulation
    • Elevated INR
    • Bleeding
  – Liver transaminases >1000 IU/L
  – Elevated bilirubin
  – Hypoglycemia

Gernsheimer et al. *How I treat thrombocytopenia in pregnancy*. Blood; 121 (1).
Acute Fatty Liver of Pregnancy (AFLP)

- Treatment:
  - Urgent referral to obstetrics
  - Transfer to tertiary care center
  - Expedient delivery of the fetus

Gernsheimer et al. *How I treat thrombocytopenia in pregnancy*. Blood; 121 (1).
Immune Thrombocytopenia (ITP)

- 1-4% of all pregnancies
- 3% of thrombocytopenia in pregnancy
  - Most common cause of a platelet count <50 x 10⁹/L
- Suspect when otherwise healthy woman develops platelets <70 x 10⁹/L at any point in pregnancy, or thrombocytopenia in the first trimester.

Gernsheimer et al. *How I treat thrombocytopenia in pregnancy*. Blood; 121 (1).
Immune Thrombocytopenia (ITP)

• Management
  – Treatment not indicated unless bleeding, or platelets <30 x10⁹/L
  – Refer to Hematology if requiring treatment
  – If counts stable, monitor platelet counts monthly, and then weekly once 32-34 weeks

Gernsheimer et al. *How I treat thrombocytopenia in pregnancy*. Blood; 121 (1).
Immune Thrombocytopenia (ITP)

• Management (continued)
  – May need treatment prior to neuro-axial anesthesia
  – Newborn should be monitored for thrombocytopenia at delivery, and 4-7 days post delivery
Common Causes of Anemia in Pregnancy

1. Iron deficiency
2. Iron deficiency
3. Iron deficiency

• 75% of all cases of non-physiologic anemia in pregnancy
  • Ferritin <20 ng/mL = diagnostic
  • Ferritin 20-50 ng/mL = probable
  • Ferritin >50 ng/mL = unlikely*

• Supplementation of oral iron (15-30mg/day) recommended
## Less Common Causes of Anemia in Pregnancy

<table>
<thead>
<tr>
<th>Pregnancy-specific</th>
<th>Not pregnancy specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>HELLP</td>
<td>Megaloblastic anemia</td>
</tr>
<tr>
<td>AFLP</td>
<td>Thalassemia</td>
</tr>
<tr>
<td>Severe preeclampsia</td>
<td>Sickle cell disease</td>
</tr>
<tr>
<td></td>
<td>Bone marrow failure disorders</td>
</tr>
<tr>
<td></td>
<td>Bone marrow infiltrative disorders</td>
</tr>
<tr>
<td></td>
<td>TTP/HUS</td>
</tr>
</tbody>
</table>
Case 1

- 32 year old female, G2P1 at **28 weeks**
- Routine bloodwork:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>12 x 10⁹/L</td>
<td>4.5-11.0 x 10⁹/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>115 g/L</td>
<td>120 – 160 g/L</td>
</tr>
<tr>
<td>MCV</td>
<td>88 fL</td>
<td>80– 98 fL</td>
</tr>
<tr>
<td>Platelets</td>
<td>98 x 10⁹/L</td>
<td>140 – 440 x 10⁹/L</td>
</tr>
</tbody>
</table>
**Thrombocytopenia in Pregnancy** (Platelets <130 x10⁹/L)

**Consider:** Pre-eclampsia, HELLP, AFLP

**Investigations:** Creatinine, glucose, uric acid, AST, ALT, LDH, bilirubin, INR, urine protein/creatinine, haptoglobin

Are any of the following present?
- Proteinuria
- Elevated liver enzymes
- Elevated blood pressure
- Hemolysis

**URGENT** Obstetrics Referral

Are any of the following present? (hemoglobin <110g/L)?

- Yes: See Anemia Algorithm
  - Is cause of anemia unrelated to thrombocytopenia? i.e. Iron deficiency anemia

- No: 2nd or 3rd trimester
  - Yes: Platelets >7 x10⁹/L
    - Yes: Gestational thrombocytopenia likely
      - Monitor – CBC monthly
    - No: Thrombocytopenia Algorithm
  - No: Thrombocytopenia Algorithm
## Case 1

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref. Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>110/75</td>
<td>&lt;140/90</td>
</tr>
<tr>
<td>Creatinine</td>
<td>52 µmol/L</td>
<td>50 – 90 µmol/L</td>
</tr>
<tr>
<td>LDH</td>
<td>175 U/L</td>
<td>90 – 230 U/L</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>16 µmol/L</td>
<td>&lt;26 µmol/L</td>
</tr>
<tr>
<td>Haptoglobin</td>
<td>1.4 g/L</td>
<td>0.3 – 2.0 g/L</td>
</tr>
<tr>
<td>ALT</td>
<td>23 U/L</td>
<td>5 – 32 U/L</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>Protein Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>
Thrombocytopenia in Pregnancy
(Platelets <130 x10⁹/L)

Consider: Preeclampsia, HELLP, AFLP
Investigations: Creatinine, glucose, uric acid, AST, ALT, LDH, bilirubin, INR, urine protein/creatinine, haptoglobin

Are any of the following present?
Proteinuria, elevated liver enzymes, elevated blood pressure, hemolysis

NO

URGENT
Obstetrics Referral

Anemia (hemoglobin <110g/L)?

NO

2nd or 3rd trimester

See Thrombocytopenia Algorithm

NO

Yes

Platelets >7 x10⁹/L

Gestational thrombocytopenia likely
Monitor – CBC monthly

NO

See Anemia Algorithm

Is cause of anemia unrelated to thrombocytopenia?
i.e. Iron deficiency anemia

YES

YES

YES
Case 1

- 32 year old female, G2P1 at 28 weeks
- Routine bloodwork:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>$12 \times 10^9$/L</td>
<td>4.5-11.0 $\times 10^9$/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>115 g/L</td>
<td>120 – 160 g/L</td>
</tr>
<tr>
<td>MCV</td>
<td>88 fL</td>
<td>80– 98 fL</td>
</tr>
<tr>
<td>Platelets</td>
<td>$98 \times 10^9$/L</td>
<td>140 – 440 $\times 10^9$/L</td>
</tr>
</tbody>
</table>
Thrombocytopenia in Pregnancy (Platelets <130 x10^9/L)

- **Consider:** Preeclampsia, HELLP, AFLP
- **Investigations:** Creatinine, glucose, uric acid, AST, ALT, LDH, bilirubin, INR, urine protein/creatinine, haptoglobin

Are any of the following present?
- Proteinuria, elevated liver enzymes, elevated blood pressure, hemolysis

- **URGENT** Obstetrics Referral

Anemia (hemoglobin <110g/L)?

- **Yes**
  - See Anemia Algorithm
  - Is cause of anemia unrelated to thrombocytopenia? i.e. Iron deficiency anemia

- **No**
  - 2nd or 3rd trimester
    - **No**
      - See Thrombocytopenia Algorithm
    - **Yes**
      - Platelets >70 x10^9/L
        - Gestational thrombocytopenia likely
          - Monitor – CBC monthly
Case 2

- 32 year old female, G2P1 at 32 weeks
- Diagnosed with preeclampsia at 28 weeks
- Complains of RUQ pain

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>12 x 10⁹/L</td>
<td>4.5-11.0 x 10⁹/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>83 g/L</td>
<td>120 – 160 g/L</td>
</tr>
<tr>
<td>MCV</td>
<td>88 fL</td>
<td>80– 98 fL</td>
</tr>
<tr>
<td>Platelets</td>
<td>45 x 10⁹/L</td>
<td>140 – 440 x 10⁹/L</td>
</tr>
</tbody>
</table>
Thrombocytopenia in Pregnancy
(Platelets <130 x10^9/L)

Consider: Preeclampsia, HELLP, AFLP
Investigations: Creatinine, glucose, uric acid, AST, ALT, LDH, bilirubin, INR, urine protein/creatinine, haptoglobulin

Are any of the following present?
Proteinuria, elevated liver enzymes, elevated blood pressure, hemolysis

NO

URGENT Obstetrics Referral

Anemia (hemoglobin <110g/L)?

YES
See Anemia Algorithm

NO

2nd or 3rd trimester

Platelets >7 x10^9/L

Gestational thrombocytopenia likely
Monitor – CBC monthly

NO

Is cause of anemia unrelated to thrombocytopenia?
i.e. Iron deficiency anemia

See Thrombocytopenia Algorithm

YES

YES

YES

YES
Case 2

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref. Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>145/95</td>
<td>&lt;140/90</td>
</tr>
<tr>
<td>Creatinine</td>
<td>83 µmol/L</td>
<td>50 – 90 µmol/L</td>
</tr>
<tr>
<td>LDH</td>
<td>800 U/L</td>
<td>90 – 230 U/L</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>45 µmol/L</td>
<td>&lt;26 µmol/L</td>
</tr>
<tr>
<td>Haptoglobin</td>
<td>&lt;0.1 g/L</td>
<td>0.3 – 2.0 g/L</td>
</tr>
<tr>
<td>ALT</td>
<td>95 U/L</td>
<td>5 – 32 U/L</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>Protein 3+</td>
<td>Negative</td>
</tr>
</tbody>
</table>
Thrombocytopenia in Pregnancy
(Platelets <130 x 10^9/L)

Are any of the following present?
Proteinuria, elevated liver enzymes,
elevated blood pressure, hemolysis

Investigations: Creatinine, glucose, uric acid,
AST, ALT, LDH, bilirubin, INR, urine protein/
creatinine, haptoglobin

Consider: Preeclampsia, HELLP, AFLP

Are any of the following present?
Proteinuria, elevated liver enzymes,
elevated blood pressure, hemolysis

Anemia
(hemoglobin <110g/L)?

2nd or 3rd trimester

Platelets >70 x 10^9/L

Is cause of anemia unrelated to thrombocytopenia?
i.e. Iron deficiency anemia

Gestational thrombocytopenia likely
Monitor – CBC monthly

See Thrombocytopenia Algorithm

URGENT
Obstetrics Referral

See Anemia Algorithm

Yes

No

See Thrombocytopenia Algorithm
Case 3

• 32 year old female, G2P1 at 8 weeks
• Routine bloodwork:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>10.6 x 10⁹/L</td>
<td>4.5-11.0 x 10⁹/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>123 g/L</td>
<td>120 – 160 g/L</td>
</tr>
<tr>
<td>MCV</td>
<td>88 fL</td>
<td>80– 98 fL</td>
</tr>
<tr>
<td>Platelets</td>
<td>62 x 10⁹/L</td>
<td>140 – 440 x 10⁹/L</td>
</tr>
</tbody>
</table>
Thrombocytopenia in Pregnancy (Platelets <130 x10^9/L)

Consider: Preeclampsia, HELLP, AFLP

Investigations: Creatinine, glucose, uric acid, AST, ALT, LDH, bilirubin, INR, urine protein/creatinine, haptoglobin

Are any of the following present?
Proteinuria, elevated liver enzymes, elevated blood pressure, hemolysis

- YES
- NO

URGENT Obstetrics Referral

Are any of the following present?

Anemia (hemoglobin <110g/L)?

- YES
- NO

2nd or 3rd trimester

Is cause of anemia unrelated to thrombocytopenia? i.e. Iron deficiency anemia

- YES
- NO

See Anemia Algorithm

Platelets >7 x10^9/L

Gestational thrombocytopenia likely
Monitor – CBC monthly

See Thrombocytopenia Algorithm
<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref. Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>105/67</td>
<td>&lt;140/90</td>
</tr>
<tr>
<td>Creatinine</td>
<td>51 µmol/L</td>
<td>50 – 90 µmol/L</td>
</tr>
<tr>
<td>LDH</td>
<td>140 U/L</td>
<td>90 – 230 U/L</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>15 µmol/L</td>
<td>&lt;26 µmol/L</td>
</tr>
<tr>
<td>Haptoglobin</td>
<td>2.1 g/L</td>
<td>0.3 – 2.0 g/L</td>
</tr>
<tr>
<td>ALT</td>
<td>18 U/L</td>
<td>5 – 32 U/L</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>Protein negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>
## Case 3

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Ref Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>10.6 x 10^9/L</td>
<td>4.5-11.0 x 10^9/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>123 g/L</td>
<td>120 – 160 g/L</td>
</tr>
<tr>
<td>MCV</td>
<td>88 fL</td>
<td>80– 98 fL</td>
</tr>
<tr>
<td>Platelets</td>
<td>62 x 10^9/L</td>
<td>140 – 440 x 10^9/L</td>
</tr>
</tbody>
</table>
Work-Up of THROMBOCYTOPENIA

Peripheral Blood Smear Platelets 130 x 10^9/L

Artificial thrombocytopenia (Pseudothrombocytopenia)
  - Pseudothrombocytopenia (EDTA phenomenon)
    - Thrombocyte Satellitism
  - Familial Macrothrombocytopenia

Real thrombocytopenia
  - Isolated thrombocytopenia
    - Direct Antiglobulin Test Negative
      - Evans Syndrome
    - Direct Antiglobulin Test Positive
  - Non-isolated thrombocytopenia
    - Other Cells
    - Schistocytes
    - Leukopenia
      - Normal Hb
      - MAHA
        - Hypersplenism
      - Bone Marrow Infiltration
        - TTP
        - HELLP
        - DIC
        - Eclampsia
        - Fatty liver
    - Bone marrow examination
      - AML
      - ALL
      - MDS
      - Solid tumor
      - Pregnancy (Gestational)
      - Alcohol
Take home messages

• Gestational thrombocytopenia is the most common cause of thrombocytopenia in pregnancy
• Rule out hemolysis, and look for systemic concerns (BP, liver enzymes, urinalysis)
• Thrombocytopenia that occurs in the first trimester, or is severe (<70 x10⁹/L), requires investigation
• Iron deficiency anemia is common in pregnancy
Thank you

cmenard@cancercare.mb.ca
aponnampalam@cancercare.mb.ca