OBSTETRICS AND GYNAECOLOGY
CLINICAL PRACTICE GUIDELINE

Thrombocytopenia in obstetrics

[NEW 2023]

Scope (Staff):	WNHS Obstetrics and Gynaecology Directorate staff
Scope (Area):	Obstetrics and Gynaecology Directorate clinical areas at KEMH and OPH

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Contents

Background

Thrombocytopenia develops in 5-10% of women during pregnancy or postpartum. Three diagnostic categories explain the majority of cases of thrombocytopenia seen in pregnancy.

Gestational thrombocytopenia (GT) is the commonest cause of thrombocytopenia in pregnancy, accounting for 70-80% of cases. Onset is typically in the mid-second to third trimesters and the platelet count tends to fall progressively with advancing gestation. It is generally mild with most platelet counts remaining >100 x 10^9/L; It is unlikely if the platelet count is <50 x 10^9/L. The exact cause of GT is unclear, with contributing mechanisms thought to include increased clearance and haemodilution. It resolves postpartum and there is no impact on the neonate.

Immune thrombocytopenia (ITP) is the second commonest cause of thrombocytopenia in pregnancy. It is an autoimmune disorder characterised by isolated thrombocytopenia (<100 x 109/L) in the absence of other causes. Unlike GT, thrombocytopenia may be seen outside pregnancy. Platelet counts <50 x 10^9/L may be seen in approximately 10% of newborns of mothers with ITP.

Hypertensive disorders such as pre-eclampsia account for 20-40% of cases of thrombocytopenia at term. While thrombocytopenia may be the initial manifestation of these disorders, other symptoms/signs often follow.

Differential diagnosis of thrombocytopenia in pregnancy

It can be difficult to differentiate between gestational thrombocytopenia and ITP. Both are a diagnosis of exclusion. The **differential diagnosis includes:**

	Pregnancy specific	**Not pregnancy-specific**
Isolated thrombocytopenia	• Gestational thrombocytopenia	• ITP • Secondary ITP • Medication therapy/drugs • Type 2B von Willebrand disease • Congenital thrombocytopenia
Thrombocytopenia associated with systemic disorders	• Pre-eclampsia • HELLP* syndrome • Acute fatty liver of pregnancy	• TTP/HUS† • Systemic lupus erythematosus (SLE) • APLS‡ • Viral infections (HIV, HBV etc) • Bone marrow disorders • Nutritional deficiency • Splenic sequestration

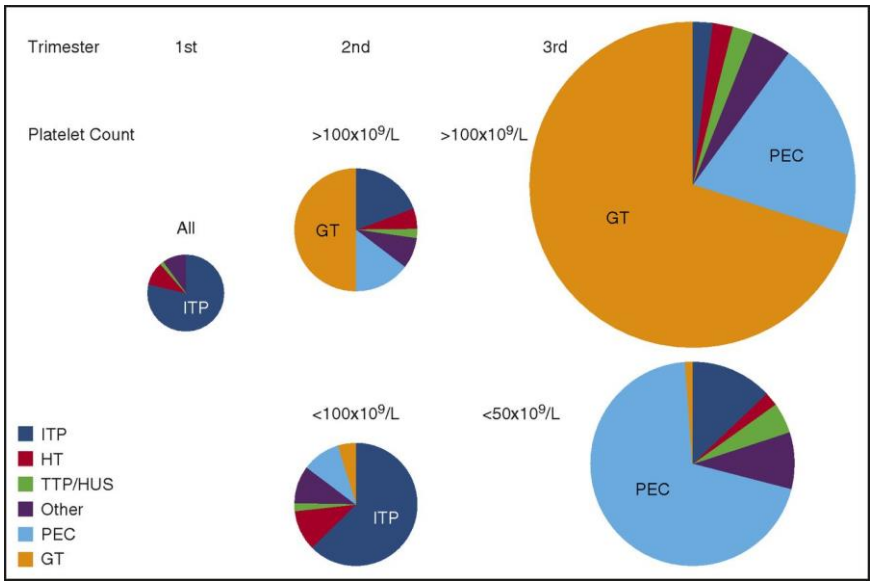
*Haemolysis, Elevated Liver enzymes, Low Platelets

†Thrombotic Thrombocytopenic Purpura/Haemolytic Uraemic Syndrome

‡Antiphospholipid Syndrome

HBV- hepatitis B virus; HIV- human immunodeficiency virus

Figure 1: Prevalence of thrombocytopenia causes in trimester of presentation and platelet count



Acknowledgement: Reproduced with permission 2023. Cines D, Levine L. Thrombocytopenia in pregnancy, Hematology Am Soc Hematol Educ Program, 2017, Figure 1.

Investigation

Thrombocytopenia requires further investigated if:

- it develops in the first trimester
- the platelet count is <80 x 10^9/L, or is likely to be <80 x 10^9/L by time of birth
- thrombocytopenia has been demonstrated pre-dating pregnancy

All women with a platelet count <80 x 10^9/L should be referred to a haematologist for review and management.

- Initial investigations:
  - Full blood count (FBC) and blood film
  - Coagulation studies
  - Urea, electrolytes and creatinine (UEC), Liver function tests (LFT)
  - Thyroid function tests (TFT)
  - Vitamin B12 / folate levels, iron studies
  - Epstein-Barr virus (EBV) / Cytomegalovirus (CMV) serology
  - Viral serologies if not already done (HIV, HBV, Hepatitis C virus (HCV))
  - Autoimmune scree (lupus anticoagulant, antiphospholipid antibodies, dsDNA, ANA)
- Second line investigations to be **arranged by a haematologist**
  - Haemolytic screen (direct antiglobulin test, reticulocyte count, haptoglobin, LDH, bilirubin)
  - ADAMTS13 assay (tested at Fiona Stanley Hospital; in fragmentation syndromes)
  - Von Willebrands screen to exclude Type 2B VWD
  - *Helicobacter pylori* serology (in confirmed ITP)

Diagnosis

1. Gestational thrombocytopenia

There is no specific laboratory test to confirm the diagnosis. Gestational thrombocytopenia is a diagnosis of exclusion, based on the following:

- Normal platelet count outside of pregnancy and in the first trimester
- Onset of thrombocytopenia in second or third trimester
- Platelet count is generally >80 x 10^9/L.

2. Immune thrombocytopenia

There is no specific laboratory test to confirm the diagnosis. ITP is a diagnosis of exclusion though the diagnosis is supported by one or more of the following:

- Severe thrombocytopenia (platelets <50 x 10^9/L) with normal blood film.
- Steroid responsiveness
- Positive autoimmune serology

3. Hypertensive disorders in pregnancy

- Full clinical review, including blood pressure and urinalysis, is vital to identify other features associated with these disorders.
- The table below summarises other clinical manifestations of hypertensive and other serious causes of thrombocytopenia in pregnancy.
- The blood film may show a few red cell fragments, but overt/frank haemolysis is more suggestive of HELLP syndrome or TTP. Similarly, renal dysfunction may occur in severe pre-eclampsia, but severe acute renal impairment is more suggestive of TTP or atypical HUS.
- The platelet count and other laboratory parameters usually improve within 48-72 hours after birth. If they do not improve or deteriorate, consider alternate diagnoses.

Typical features in pregnancy- associated microangiopathies

	MAHA	Thrombo-cytopenia	Coagulopathy	HBP	Abdominal symptoms	Renal impairment	Neurological symptoms
PET	+	+	±	+++	±	±	++
HELLP	+	+	±	+	+++	+	±
TTP	++	+++	-	±	+	++	+++
HUS	+	++	±	++	+	+++	±
AFLP	±	+		+	++	+	±
SLE	+	+	±	+	±	++	+
APS	+	++	±	++	-	++	++

Abbreviations: AFLP- acute fatty liver of pregnancy; **APS**- antiphospholipid syndrome; **HBP**- high blood pressure; **HELLP**- haemolysis, elevated liver enzymes and low platelets; **HUS**- haemolytic uraemic syndrome; **MAHA**- microangiopathic haemolytic anaemia; **PET**- pre-eclamptic toxaemia; **SLE**- systemic lupus erythematosus; **TTP**- thrombotic thrombocytopenia

Notes: ± possibly occurs; +++ definitive feature

Acknowledgment: Pavord S, Hunt B (Eds). The obstetric hematology manual. 2nd ed. United Kingdom: Cambridge University Press. 2018.

General management strategies

Antepartum management

- Monthly platelet counts, increasing to fortnightly at 32 weeks, then weekly at 36 weeks are recommended.
- If the platelet count falls to <80 x 10^9/L (or is likely to do so imminently) and it is not possible to differentiate gestational thrombocytopenia from ITP, discuss with haematology who may suggest a trial of prednisolone/prednisone 25mg daily for 4 days a few weeks prior to delivery. A rise in platelet count suggests ITP.

Hypertensive disorders in pregnancy

- Management is based on gestational age. In some patients who are <34 weeks gestation, expectant inpatient management may be carefully considered.
- The definitive management is delivery of the placenta.
- Worsening thrombocytopenia, HELLP, severe hypertension or deterioration in the maternal or fetal condition are indications for delivery.

Peripartum management:

- Thrombocytopenic patients should have a haematology management plan prior to birth.
- If the platelet count is <80 x 10^9/L near to term, urgent haematology review is recommended.
- A platelet count of ≥50 x 10^9/L is considered safe for vaginal and Caesarean birth.
- Women with a platelet count below 50 X 10^9/L may require a platelet transfusion for birth. These cases **must** be discussed with a haematologist. Note: platelets are not routinely kept on site at KEMH and need to be ordered in specifically for individual patients, therefore good communication with the haematologist and Transfusion Medicine Service is required to ensure platelets are available around the time of birth.
- Decisions regarding neuraxial anaesthesia must be individualised. Consider with stable platelet counts >70 x 10^9/L and a normal coagulation profile. A higher platelet threshold may be desired if thrombocytopenia is rapid in onset or if there is a history of bleeding. In women with severe pre-eclampsia / HELLP syndrome and/or rapidly declining platelet counts, the platelet count and coagulation parameters must be checked no longer than 6 hours prior to neuraxial insertion. Even with this interval, rapid changes from normal platelet counts to low platelet counts can occur, so each case should be approached with a degree of caution.
- For women receiving ≥5mg prednisolone/prednisone daily over three weeks, adrenal insufficiency is possible. Consider peri-partum hydrocortisone.

Prevention and management of postpartum haemorrhage (PPH)

- Prevention and treatment of iron deficiency is important to optimise the haemoglobin prior to delivery.
- Active management of the third stage of labour is recommended to reduce the risk of PPH.
- If PPH occurs, consider other contributing factors. Early use of tranexamic acid is recommended, as is use of a ROTEM-guided critical bleeding protocol.

Management of the neonate

- The only reliable predictor of whether a neonate will be thrombocytopenic is a history of thrombocytopenia in previous siblings.
- Management at delivery:
  - Haematologist may suggest to avoid fetal scalp blood sampling, vacuum or high abdominal forceps delivery in some cases
  - Take an umbilical cord platelet count
- After initial platelet count:
  - If platelet count <100 x 10^9/L, daily platelet counts
  - If platelet count <50 x 10^9/L, arrange a cranial ultrasound
  - If platelet count >100 x 10^9/L, repeat at day 3-5 days
- Management of neonatal thrombocytopenia
  - Liaise with haematologist
  - Intervention is generally not required in asymptomatic infants if the platelet count is >30 x 10^9/L
  - If the platelet count is <30 x 10^9/L or the infant is bleeding, urgent haematology consult for investigation and management which may include platelet transfusion +/- IVIg

Postpartum maternal management:

- Avoid non-steroidal anti-inflammatories if platelet count <70x10^9/L.
- Assess for the risk of venous thromboembolism (VTE). If at increased risk for VTE (e.g. caesarean section, antiphospholipid antibodies), consider appropriate thromboprophylaxis. Pharmacological thromboprophylaxis is generally safe if the platelet count is >50 x 10^9/L though treatment decisions must be individualised. Discuss with haematologist.
- Check FBC on day 1 postpartum. Further follow-up depends on clinical factors but a repeat count approximately 2 and 6 weeks postpartum are generally advised.
- Consider referral to haematologist outside KEMH (if not already known) for ongoing management of persisting thrombocytopenia.

Specific management

Immune thrombocytopenia

- Treatment is generally indicated in the following situations:
    - platelet count <30 x 10^9/L
    - platelet count <50 x 10^9/L and imminent birth or upcoming invasive procedures
    - platelet count <80 x 10^9/L with significant bleeding
- In a patient with newly diagnosed ITP in pregnancy, refer to haematology who will arrange a trial of steroid therapy in the early third trimester. If an adequate response is achieved, arrange for an additional course of treatment prior to delivery.
- First line therapy is oral prednisolone/prednisone. Second line therapy is IVIg. Dexamethasone is NOT recommended as it crosses the placenta.
    - Prednisolone/prednisone:
        - It is recommended to start prednisolone/prednisone at a low dose (25mg daily) to minimise the cumulative dose and side effects.
        - If the platelet count is <30 x 10^9/L, a higher initial dose (e.g. 40-50mg daily) may be considered.
        - Side effects of prolonged corticosteroids include gestational diabetes, weight gain, hypertension, insomnia, gastritis and mood disturbances.
    - IVIg:
        - Generally used in steroid resistant/refractory cases.
        - Occasional patients need regular IVIg to maintain a safe platelet count during pregnancy.
        - IVIg administration requires approval via BloodStar. It is administered in the Infusion Unit, in liaison with the Haematologists and CNC Patient Blood Management (Haematology).
- Other treatment options, including splenectomy, may need to be considered in patients with ITP unresponsive to IVIg and corticosteroids.

Hypertensive and other thrombocytopenias

- Significant red cell fragmentation syndromes require urgent intervention. Specific therapy depends on the cause and ranges from therapeutic plasma exchange in TTP to renal support and complement inhibitors (e.g. eculizumab) in atypical HUS.
- Urgent referral to a haematologist, if not already involved, and consideration of transfer to a tertiary site with expertise in renal and intensive care medicine is recommended.

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- Obstetrics and Gynaecology:
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  - Postpartum Complications (PPH)
  - VTE

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Version history

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1	July 2023	First version

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