Thrombocytopenia in Pregnancy and the Peripartum period

University Hospitals of Leicester NHS Trust

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Contents

1. Introduction and Who Guideline applies to:

The aim of this guideline is to provide a framework for the investigation and management of thrombocytopenia in pregnancy. The guideline applies to midwives, obstetricians and haematologists who may encounter women with thrombocytopenia in pregnancy, as well as Haematology and Obstetric trainees in the Haematology Obstetric Clinic. It should also provide guidance for referral to the Haematology Obstetric Clinic.

Background:

The platelet count falls during normal pregnancy, with levels in the third trimester being approximately 10% lower than pre pregnancy levels (Myers 2012). The exact mechanism is unknown but thought to be due to haemodilution and accelerated clearance.

Thrombocytopenia is defined as a platelet count below 140 × 10^9 /L (as per UHL laboratory reference range) and is the second commonest haematological abnormality seen in pregnancy after anaemia.

For different conditions causing thrombocytopenia, see **Appendix 1**.

2. Guideline Standards and Procedures

2.1 Thrombocytopenia classification:

Severity of Maternal thrombocytopenia can be classified by platelet count as follows:

- Mild: >80 × 10^9 /L
- Moderate: 50 -80 × 10^9 /L
- Severe: <50 ×10^9 /L

In general, mild thrombocytopenia in pregnancy is benign and can be monitored with monthly FBC by the Midwife or the GP. Referral to the Haematology Obstetric clinic should be prompted if there is unexplained bruising or extensive bleeding, or if platelet counts fall below 80× 10^9 /L.

Table 1: Safe levels for intervention:

Intervention	Platelet count
Antepartum, no invasive procedures planned	>20 × 10^9 /L
Vaginal delivery	>40 × 10^9 /L
Operative or instrumental delivery	>50 × 10^9 /L
Epidural anaesthesia	>80 × 10^9 /L

2.2 When to refer to the Haematology- Obstetric Clinic:

Patients with thrombocytopenia in pregnancy should be referred to the Haematology-Obstetric clinic under the following circumstances:

- Platelet count < 80× 10^9 /L
- Unexplained bruising or bleeding
- Thrombocytopenia associated with a bleeding disorder
- A known cause of thrombocytopenia (non-obstetric) such as ITP or congenital thrombocytopenia
- Platelet count <100 x 10^9/l in the previous pregnancy

Table 2: Antenatal management of thrombocytopenia in pregnancy:

Platelet count during pregnancy	Recommended action
>140 x 10^9/l	Normal. **No action required** unless unexplained bruising or bleeding
80 – 140 x 10^9/l	Check blood pressure and urinalysis depending on gestation Send blood test for U&E, LFT **Repeat FBC every 4 weeks** Repeat FBC prior to any intervention with an associated bleeding risk Advise the women to seek medical attention in the event of bleeding symptoms Check FBC on admission if spontaneously labouring
<80 x 10^9/l	Check blood pressure and urinalysis depending on gestation Send blood test for U&E, LFT, blood film **Refer to Haematology-Obstetric Clinic for further investigation** Anaesthetic Clinic appointment
<50 x 10^9/l	Check blood pressure and urinalysis depending on gestation Send blood test for U&E, LFT, blood film **Contact the obstetric haematology team to arrange an urgent review** Anaesthetic Clinic appointment

2.3 Intrapartum management of women with thrombocytopenia

Where women with known thrombocytopenia are admitted in labour, follow specific intrapartum care plan. See appendix 2

Take bloods for FBC on admission- please note that additional bloods may be required depending on circumstances, including G&S/ Crossmatch, coagulation, and any tests specified in the intrapartum care plan.

Where women are diagnosed as having thrombocytopenia for the first time during labour, in the absence of pre-eclampsia, follow management plan for ITP (see table 3).

Inform senior Obstetrician, Anaesthetist and on call Haematologist of admission.

Table 3: Management in specific conditions

	Presentation	Management

Gestational thrombocytopenia	• Diagnosis of exclusion
	• Mild thrombocytopenia; > 80 × 10^9/L
	• Not associated with maternal bleeding
	• No past history of thrombocytopenia outside pregnancy
	• Occurs in mid-second to third trimester
	• Not associated with fetal thrombocytopenia
	• Spontaneous resolution (within 6 weeks) after delivery
	• May recur in subsequent pregnancies
		Antepartum:
		• Monthly platelet checks by midwife or GP if platelets are above 80 × 10^9/L
		• Refer to consultant care if
		  ○ platelets fall below 80× 10^9/L or
		  ○ have history unexplained bruising or extensive bleeding
		• Exclude any other pathological causes
		• Monitor platelet count every 4-6 weeks
		• If <80 × 10^9/L, anaesthetic referral to determine delivery plan in regards to regional anaesthetics
		• Consider short trial of prednisolone (20mg/d) may be helpful diagnostically and therapeutically when platelet count is 50-80 × 10^9/L.
		Intrapartum/Delivery:
		• Fetus should not be affected in gestational thrombocytopaenia
		• Caesarean section only indicated for obstetric reasons; is not indicated for thrombocytopenia alone
		• Mode of delivery should be decided on obstetric reasons as fetus not affected
		• If diagnostic uncertainty then delivery plan as for ITP should be followed (see later)

		• Regional anaesthesia, i.e. Epidural, is safe when platelet count is >80× 10^9/L • If maternal platelet count is low (<50× 10^9/L) at time of delivery, platelets should be available on standby • Can perform FBS if indicated **Postpartum:** • If maternal count was 80× 10^9/L or lower at time of delivery: - Cord sample should be taken at delivery and neonatal platelet counts on day 1 and 4 if the cord sample shows a platelet count below the normal range. - Avoid Intramuscular injection of Vitamin K until platelet count confirmed (*Consider giving orally if platelet count is <50× 10^9 /L).* • If platelet count of neonate is <50 × 10^9/L, transcranial ultrasound recommended • Verify that maternal count returns to normal after delivery within 6 weeks
Hypertensive disorders in pregnancy	See: **Pre Eclampsia and Eclampsia - Severe UHL Obstetric Guideline** - **UHL C3/2001**	
Immune Thrombocytopenia (ITP)	- Commonest cause of low platelets in 1st and 2nd trimesters. - May present with mucosal bleeding, purpura, bruising.	**Antenatal management:** - Patient should be seen in the joint Haematology – Obstetric clinic - Monitor platelet count at least monthly

- Many cases are asymptomatic.
- Around 2/3 of ITP patients in pregnancy have pre-existing disease. ITP more likely if platelets <70 $\times 10^9$ or if personal or family history of autoimmune disorders.
- No specific diagnostic test available.
- IgG Antibodies targeted against platelet surface glycoproteins can cross the placenta and cause fetal thrombocytopenia. The incidence of neonatal thrombocytopenia associated with ITP is variable however it is estimated approximately 10% have platelets < 50 x 10^9/l and 5% have platelets < 20 x 10^9/l. Even when thrombocytopenia is present the risk of intracranial haemorrhage and mortality are reassuringly low being; <1% and <1.5% respectively.

- Anaesthetics referral indicated
- Treatment indicated early in pregnancy if the platelet count drops below 20-30$\times 10^9$ /L or if the patient is symptomatic of thrombocytopenia after discussion with haematologist. The following treatments can be used:
    1. Prednisolone 10-20mg OD with ranitidine for gastric protection. Can be up titrated but usual max is 60mg/day to maintain safe platelet count ideally > 80$\times 10^9$ by the time of delivery. Ensure to counsel regarding possible side effects of steroids including exacerbation of hypertension, gestational diabetes, mood changes and osteoporosis. Should taper dose to minimum level to maintain safe platelet count.
    2. IV Immunoglobulin (Ig) 1g/kg for 2 days can be used in severe thrombocytopenia (plts< 10$\times 10^9$) or if active bleeding or if refractory to oral prednisolone. Remember IV Ig is a pooled blood product so patient should be counselled appropriately. Common side effects include headache and less common side effect of aseptic meningitis should be noted. See links below for information how to request IV Ig.
    3. Platelet transfusion may be necessary if active/life threatening bleeding in combination with above treatments.
    4. Azathioprine, Rituximab and Splenectomy can have a role in refractory cases after consultation with a Haematologist.
- If platelet count is less than 80 $\times 10^9$ /L at 34-35 weeks gestation then consider a trial of prednisolone 20mg OD. A rise in platelet count should be observed within 7-10 days. If no response then can titrate up dose to maximum of 60mg OD.
- If no response to oral steroids or a rapid rise in platelet count is needed

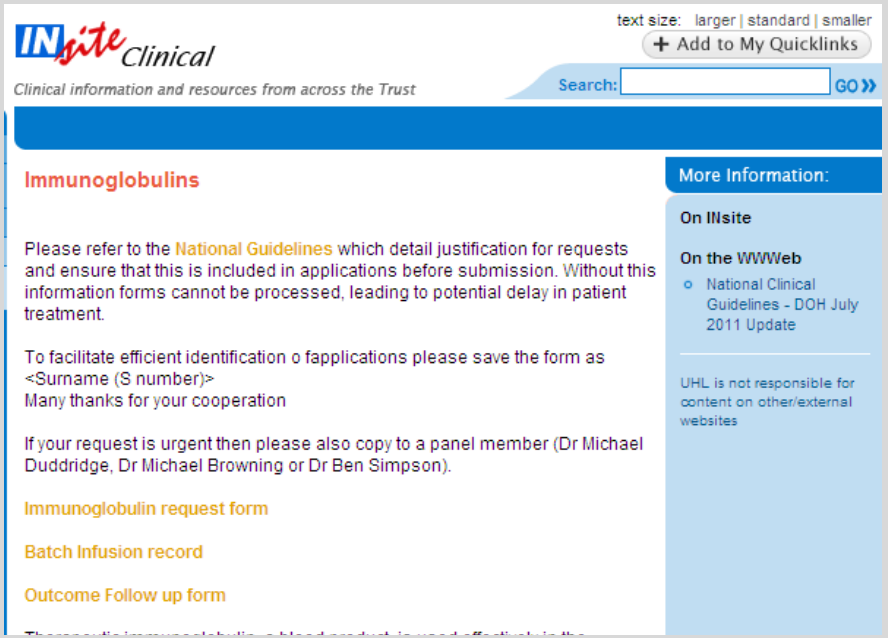
then 1g/kg IV Ig for 2 days can be used. Usually the platelet count increases within 1-2 days, with a relatively short duration of around 2-3 weeks. To request IV Ig type 'Immunoglobulins' into the search bar on insite, download the immunoglobulin request form (see link below) and send the form to Immunoglobulins.mailbox@uhl-tr.nhs.uk. Then send the Immunoglobulin Order Form (see below) to Pharmacy to issue the IV Ig. The usual product used at UHL is Privigen.

Labour/Delivery:

- Platelets should be available at labour if platelet count is < 50×10^{9}. Case should be discussed with Obstetrician, Anaesthetist and Haematologist.
- General consensus that epidural or regional anaesthesia contraindicated if platelets< 80×10^{9}.
- Avoid ventouse delivery, foetal scalp electrode, mid cavity rotational forceps and foetal blood sampling due to potential bleeding risks for the baby.
- Only proceed to caesarean section if obstetric indication.
- 10 fold increased risk of PPH, active management of third stage
- If platelets above $50x10^{9}$ and normotensive, give syntometrine IM
- If platelets below $50x10^{9}$ give 5 IU oxytocin IV
- Follow with infusion of 40 IU oxytocin

Post Natal management:

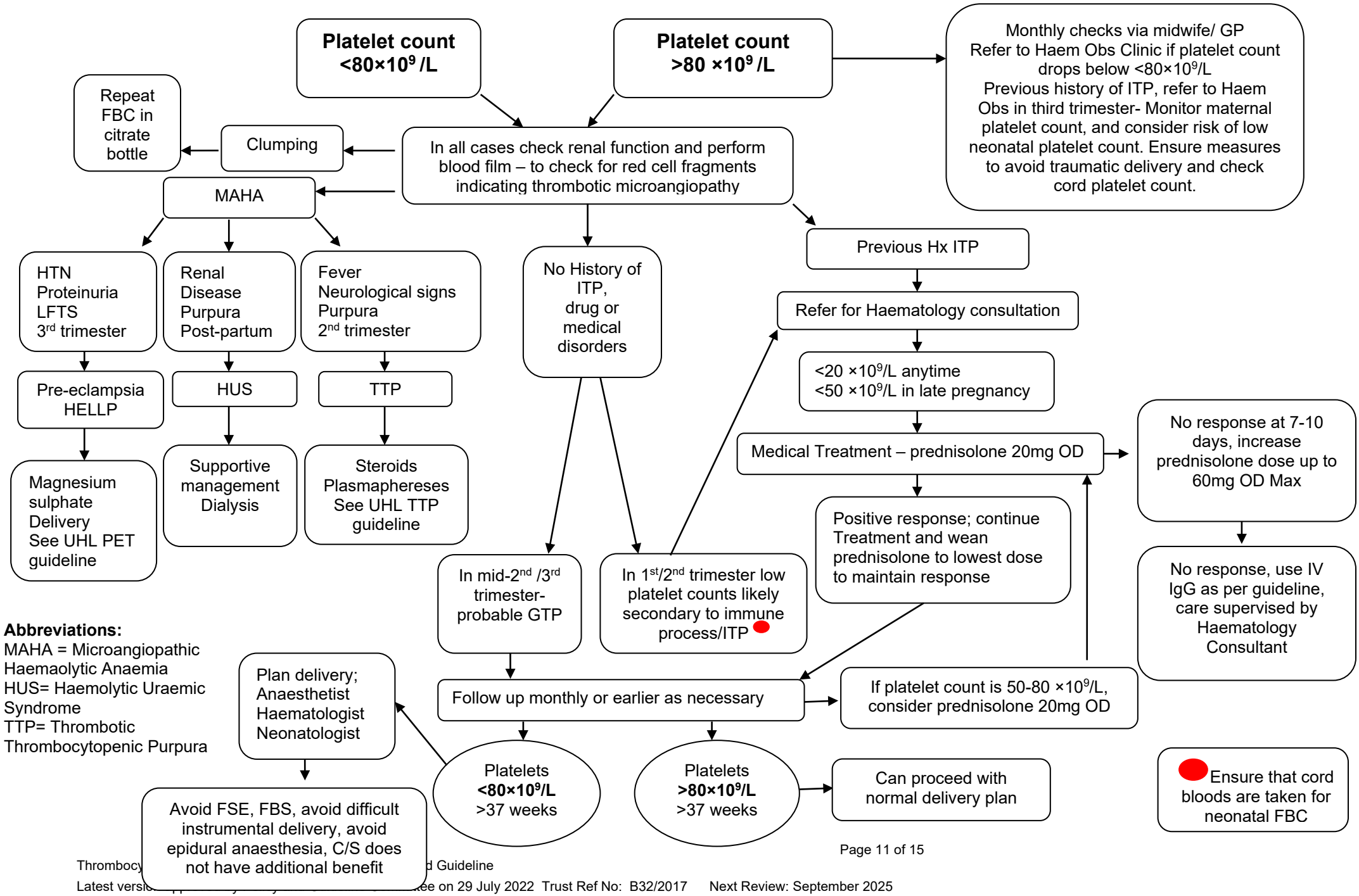
- Cord sample should be obtained for a neonatal full blood count at delivery
- If neonatal thrombocytopenia on cord blood then daily FBCs should be carried out until at least Day 5.
- If neonatal platelet count <50×10^9 a Cranial USS should be performed even if neonate is asymptomatic.
- IV IgG treatment indicated in neonate with platelet count below 30×10^9 /L.



		There is a requirement for each administration to be recorded on the national database including the batch numbers. A Batch Infusion record electronic form is available for this purpose and can be completed and emailed to immunoglobulins.mailbox@uhl-tr.nhs.uk. This enables the IVIG administrator to upload the data automatically saving time and increasing accuracy. Immunoglobulin request form The Immunoglobulin Order Form is also available electronically. Immunoglobulin Order Form	
Thrombotic Thrombocytopaenic Purpura	- Microangiopathic Haemolytic Anaemia (MAHA) - Thrombocytopenia (usual platelet count 10-30 $\times 10^9$ /L.) - Fever (temp > 37.5) - Fluctuating neurological symptoms (e.g. headache, confusion, coma) - Renal impairment (may have proteinuria and micro haematuria) - The following tests should be performed: ADAMTS 13 assay (liaise with Special Haematology lab as send away test), serum LDH, haptoglobin, clotting screen including fibrinogen, urea and electrolytes, blood film, reticulocyte count, HIV serology	- If MAHA not explained by non TTP pregnancy related condition then TTP should be suspected and urgent treatment started. - Urgent Plasma Exchange indicated after discussion with Haematologist. - Anaesthetic Involvement. - Platelet transfusion is contraindicated - Close liaison with obstetrician with special interest in fetal-maternal medicine is needed during pregnancy. - Prophylactic low molecular weight heparin should be started once platelet count is over 50×10^9 /L due to pro thrombotic nature of condition.
	- Microangiopathic Haemolytic Anaemia.	- If diagnostic uncertainty between TTP and HUS a trial of plasma

Haemolytic Uraemic Syndrome (HUS)	- Predominantly renal involvement. - Timing usually several weeks post-partum. - Associated with E.Coli infection but atypical form with no evidence of infection usually seen in pregnancy.	exchange should be given after consultation with a Haematologist. - Supportive management including renal dialysis if needed. - Caesarean section for obstetric reasons only. - Eculizumab is a new therapeutic agent that can be used in aHUS after discussion with a Haematologist/ Renal physician.

2.3 Process for Management of thrombocytopenia in pregnancy



Abbreviations:
MAHA = Microangiopathic Haemaolytic Anaemia
HUS= Haemolytic Uraemic Syndrome
TTP= Thrombotic Thrombocytopenic Purpura

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
The reasons for referral of patients with thrombocytopenia in pregnancy to the Haematology Obstetrics Clinic as specified by the guideline.	By audit	Marie Copple	6 months	Report to Maternity Governance

5. Supporting References

High Risk Pregnancy, Management Options. Fifth Edition, Chapter 37 by Bethan Myers and Richard Gooding.

6. Key Words

Coagulation, Haematology, Platelets, Pregnancy.

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details			
Guideline Lead (Name and Title) H Maybury, Consultant Obstetrician			**Executive Lead** Chief Medical officer
Details of Changes made during review:			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
June 2019	1		New guideline
May 2022	2	H Maybury	Format update Added Intrapartum care plan form to appendix

Appendix 1: Conditions resulting in Maternal Thrombocytopenia

Pregnancy-specific conditions

Diagnosis	Proportion	Pathophysiology	Typical time of onset
Gestational Thrombocytopenia	75%	Physiological dilution, accelerated destruction	Mid second- third trimester
Hypertensive disorders including: ○ pre-eclampsia ○ HELLP syndrome	15-20% Thrombocytopenia occurs in 50% cases of pre-eclampsia	Peripheral consumption with microthrombi. Accelerated destruction of platelets passing through damaged trophoblast surface of placenta	Mid second- third trimester
Acute fatty liver of pregnancy		Reduced production of platelets by the liver	Third trimester or post-partum

Pregnancy associated conditions:

Diagnosis	Proportion	Pathophysiology	Typical time of onset
Thrombotic Thrombocytopenic Purpura (TTP)	<1%	Peripheral consumption and microthombi formation; deficiency of ADAMTS 13(VWF cleaving protein)	Commonest in second trimester
Haemolytic Uraemic Syndrome (HUS)	<1%	Peripheral consumption and microthrombi formation;	Majority occur postpartum
Disseminated Intravascular Coagulation (DIC)	<1%	Activation and peripheral consumption of clotting factors and platelets	Anytime antepartum and postpartum

Incidental to pregnancy

Diagnosis	Proportion	Pathophysiology	Typical time of onset
Immune Thrombocytopenic Purpura (ITP)	3%	Immune destruction and suppressed production	Commonest in first and second trimester
Haematological Malignancy	Very rare	Bone marrow infiltration	Any time
Severe B12 or folic deficiency	Very rare	Failure of platelet production	Any time
Viral infections ○ EBV ○ HIV ○ Hepatitis B and C	<1%	Secondary immune destruction	Any time
Pseudothrombocytopenia	0.1%	Laboratory artefact	Any time

Appendix 2: intrapartum care plan

ITP in Pregnancy Management

University Hospitals of Leicester NHS Trust

Management for Patients with ITP in Pregnancy, Delivery and Postpartum

Patient details:
Surname:
Forename:

Hosp. No:
NHS No:
DOB:

Consultant Obstetricians:

Consultant Haematologists:

Booking Weight: **Expected Date Delivery:** **Parity:**

Previous neonatal thrombocytopenia: Y/N **platelet count**

Antenatal Monitoring and Management

Date									
Gestation (weeks)									
Platelet count ($x10^9$/l)									
Treatment									

Preparation for delivery

Planned mode of delivery: VD/ CS

Neuroaxial anaesthesia
Anaesthetic SpRs: if platelets ≥80 $x10^9$/l proceed as normal; 60-80 get advice from senior clinician; <60, avoid epidural.
Anaesthetic consultants: Avoid neuraxial anaesthesia if platelets <50 $x10^9$/l unless risk of GA v high, written consent advised

Check platelet count on arrival in labour and consider below treatment

Intrapartum Management of Maternal Thrombocytopenia

- ☐ No additional treatment
- ☐ Hydrocortisone 100mg 6hrly from established labour (if had oral steroids for >2/52)
- ☐ Immunoglobulins 1g/kg on admission if platelets <50 $x10^9$/l
- ☐ Tranexamic acid 1g iv in established labour if platelets <50 $x10^9$/l

- ☐ Methylprednisolone in addition to ivIg if platelets <20 x 10^9/l
- ☐ Platelet transfusion if bleeding despite the above
- ☐ Other …….

Intrapartum management for baby

Consider risk of fetal ITP and potential need to avoid
Ventouse, mid-cavity forceps, fetal scalp electrodes, fetal blood sampling

- ☐ High risk (previous sibling affected) – avoid
- ☐ Potentially high risk (severe maternal ITP, previous splenectomy) - avoid
- ☐ Low risk (previous sibling unaffected & maternal ITP unchanged) – OK to use
- ☐ unknown (no previous cord counts) - avoid

Postpartum Management: baby

Cord blood platelet count	☐
If <50x10^9/l, give vit K orally, Request cranial ultrasound scan, refer to neonatology and inform paediatric haematology.Repeat platelet count 1-2 days later	☐
If <20x10^9/l, refer to neonatology urgently. If repeat count <20 discuss with paediatric haematologist and consider giving ivIg	☐
If bleeding discuss urgently with paediatric haematologist and consider platelet transfusion in combination with IVIg and TXA	☐

Postpartum Management of mother with thrombocytopenia

Active management of 3rd stage; Prompt perineal repair	☐
Avoid NSAIDs	☐
Thromboembolic deterrent stockings	☐
Tranexamic Acid 1g tds	☐

Thromboprophylaxis contraindicated? Yes / No
Risk/benefit of thromboprophylaxis to be assessed after delivery; consider if platelet count>30, especially if operative delivery)

Completed By: **Signature** **Date:**