ITP and Pregnancy Induced Thrombocytopenia

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• The prevalence of a platelet count <150K/microL in the third trimester of pregnancy is 6.6 to 11.6%.

• When a more stringent platelet count threshold is used (eg, platelet count <100,000/microL), the incidence is <1 percent

Causes of Thrombocytopenia

- vary with the duration of gestation, the severity of thrombocytopenia, and the patient's clinical status

Pregnancy imposes additional urgency on determining the cause of thrombocytopenia and additional management decisions related to the potential for complications that may affect the patient and the fetus
Causes of Thrombocytopenia in Pregnancy

In a retrospective series of 199 pregnant women with moderate to severe thrombocytopenia (platelet count <100,000/microL),

- Gestational thrombocytopenia (GT) – 59%
- Preeclampsia with severe features/HELLP syndrome – 22%
- Immune thrombocytopenia (ITP) – 11%
- Other causes – 8% (includes antiphospholipid syndrome, disseminated intravascular coagulation, dilutional thrombocytopenia, myeloproliferative neoplasm)

ITP — Immune thrombocytopenia

• 1 to 3 in 10,000 pregnancies.
• more frequent CBC testing
• increased incidence of autoimmune disorders in young women, and
• possibly unmasking of mild ITP due to the increased platelet turnover in pregnancy.
ITP

• Autoimmune

• Antiplatelet autoantibodies interfere with platelet production and cause destruction of circulating platelets.

• However, tests for antiplatelet antibodies are neither sensitive nor specific.

• The diagnosis of ITP is based only on the exclusion of other causes of thrombocytopenia.
• May occur during any trimester.
• Severity of thrombocytopenia is variable
• Platelet count may decline further as pregnancy progresses and improve postpartum
• Risk of bleeding is higher with platelet counts <20,000 to 30,000/microL,
Prospective study of 119 pregnancies in 92 women over the course of 11 years.

- Moderate bleeding -18%; described as epistaxis or mucous membrane bleeding
- Severe bleeding -3%; described as hematuria or gastrointestinal.
- Most deliveries were vaginal, and one-fourth of the infants had thrombocytopenia.

Gestational thrombocytopenia (GT)

Pregnancy Induced Thrombocytopenia

• Incidental
• Benign and a self-limiting condition
• Uncommon in first trimester, more frequent as pregnancy progresses.
• Highest frequency at the time of delivery - 5 to 7%
• Mild thrombocytopenia (≥80,000/microL, typically 100,000 to 150,000/microL)
• No increased bleeding or bruising
• No associated abnormalities on CBC
• No fetal or neonatal thrombocytopenia
The mechanism(s) – unclear

• Dilutional-increased plasma volume,
• Pooling or consumption of platelets in the placenta, or
• other physiologic changes
• GT and ITP cannot be distinguished in pregnant patients with mild thrombocytopenia
• GT is 100-fold greater than the frequency of ITP during pregnancy.
• GT will resolve postpartum, may take up to 8 weeks.
<table>
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<tr>
<th>Gestational age</th>
<th>Incidental finding of asymptomatic thrombocytopenia (platelet count 80,000 to 149,000/microL)</th>
<th>Platelet count &lt;80,000/microL</th>
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<tr>
<td>≤20 weeks</td>
<td>- Most often GT&lt;br&gt;- ITP cannot be excluded, but no evaluation or management would be required&lt;br&gt;- Occurrence of other disorders not different from non-pregnant patients</td>
<td>- Not GT&lt;br&gt;- May be ITP&lt;br&gt;- Occurrence of other disorders not different from non-pregnant patients</td>
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<td>&gt;20 weeks, at delivery, and postpartum</td>
<td>- Almost always GT&lt;br&gt;- ITP cannot be excluded, but no evaluation or management would be required&lt;br&gt;- Occurrence of other disorders not different from non-pregnant patients</td>
<td>- Almost never GT&lt;br&gt;- If asymptomatic, ITP likely&lt;br&gt;- If hypertension, preeclampsia&lt;br&gt;- If symptoms of systemic illness as well as MAHA:&lt;br&gt;  - HELLP syndrome, if LFTs increased&lt;br&gt;  - DIC, if coagulation abnormalities present; suspect sepsis&lt;br&gt;  - C-TMA, if AKI is severe&lt;br&gt;  - TTP, if transient focal neurologic abnormalities occur&lt;br&gt;The frequency of these disorders increases with gestation, with a peak occurrence at delivery and the first postpartum week.</td>
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Helpful information includes the following:

- Course of the pregnancy so far, including presence or absence of complications.
- Symptoms of infection such as fever and chills.
- New daily medications within the past three weeks, or occasional medications taken immediately before symptoms occurred.
- Personal or family history of excessive bleeding, bruising, pregnancy complications, or known thrombotic microangiopathy (TMA) syndrome.
- Systemic lupus erythematosus or other autoimmune disorder.
- History of liver disease.
- Timing of the drop in platelet count (which trimester, how rapidly).
- Presence of anemia more severe than expected for the stage of pregnancy.
- Abnormalities of the peripheral blood smear, such as abnormal white blood cells, Schistocytes or nucleated red blood cells.
- Rule out Pseudothrombocytopenia- due to clumping- Peripheral smear
The evaluation

- CBC - other cytopenias (e.g., leukopenia, anemia out of proportion to the stage of pregnancy) and the red blood cell indices;
- Peripheral blood smear - Pseudothrombocytopenia, Schistocytes or abnormal white blood cells
- Prothrombin time (PT) and activated partial thromboplastin time (aPTT),
- Fibrinogen level; D-dimer
- Metabolic panel with renal function and hepatic function tests;
- Urinalysis, lactate dehydrogenase (LDH) and bilirubin to assess hemolysis;
- At least one additional platelet count to identify a declining trend.
Isolated thrombocytopenia – Severe ITP, drug-induced ITP
Fever, chills – Infection, DIC
Severe hypertension – Preeclampsia with severe clinical features/HELLP, possible TMA
Hypotension – Bleeding, DIC
Neurologic findings – Possible central nervous system bleeding, preeclampsia, DIC, TTP
Bloody diarrhea – ST-HUS, possible TMA
Hemolytic anemia (drop in hemoglobin, increased LDH and bilirubin) – Preeclampsia with severe clinical features, DIC, TTP
Schistocytes on the blood smear – TTP, C-TMA, preeclampsia with severe clinical features/HELLP, possibly DIC
Leukopenia or leukocytosis – Infection, possibly DIC
Prolonged PT and aPTT, low fibrinogen – DIC, severe liver disease
Rapidly increasing creatinine – C-TMA, ST-HUS, DIC
Elevated liver function tests – Preeclampsia with severe clinical features/HELLP, acute fatty liver of pregnancy (AFLP), infection (eg, viral illness)
Hypoglycemia – AFLP
Proteinuria – Preeclampsia/HELLP
The risk of severe bleeding - platelet counts below 50,000/microL.

Platelet counts of 50,000 to 100,000/microL, increased bleeding may occur with invasive procedures, but will not occur spontaneously.

Platelet counts $<50,000$ and severe bleeding (bleeding into a closed space, bleeding requiring transfusion, bleeding that will not stop) or bleeding that is expected to become severe, platelet transfusion should be given immediately, regardless of the underlying cause of thrombocytopenia.

Platelet transfusions are not appropriate for pregnant women without active bleeding, unless surgery and/or delivery is imminent.
In the absence of bleeding,

- **Vaginal delivery** – Transfuse to a platelet count of 30,000/microL
- **Cesarean delivery** – Transfuse to a platelet count of 50,000/microL
- **Neuraxial anesthesia** – above 50,000 to 80,000/microL
- **Invasive procedure** – above 50,000/microL
Review of 119 pregnancies ITP

- 17 of 110 women (15 percent) had platelet counts <50,000/microL at delivery.

- Hemorrhagic complications were uncommon and did not correlate with the platelet count.

- The greatest blood loss was in four women with platelet counts between 54,000 and 321,000/microL.

*Individuals with platelet dysfunction may require higher platelet counts*

In this same series of 119 pregnant women with ITP over a 10-year period:

- 42 women - epidural anesthesia,
- None had a complication related to the catheter placement.

- Platelet counts were <100,000/µL in 19 women (45 percent),
- <75,000/µL in six women (14 percent), and
- <50,000/µL in one woman (2 percent).
ITP

Goal of therapy is to reduce the risk of bleeding, not to normalize the platelet count

Indications:
- the platelet count is below 20,000 to 30,000/microL or
- if an invasive procedure is needed.
- if the patient has a history of bleeding at a higher count, or
- if there are other factors that increase the risk of bleeding

Persistent platelet counts less than 30,000/microL may not require treatment during pregnancy if they were not receiving it prior to conception, except in preparation for delivery.

ITP:
Glucocorticoids or intravenous immune globulin (IVIG) approximately one week prior to a scheduled delivery.

For platelet count <20,000 to 30,000/microL at the time of delivery platelet consider platelet transfusion

Cesarean delivery for standard obstetrical considerations

This practice is consistent with guidelines published by the American Society of Hematology, the British Society of Haematology, and an international consensus report

Forceps and vacuum-assisted delivery are relatively contraindicated in the setting of severe maternal thrombocytopenia.

If we have to – Forceps is used over Vacuum.

Platelet transfusions are for clinically important bleeding or for prevention of bleeding with an invasive procedure or delivery.

Increase in platelet count with transfusion will/may only be temporary.
High-dose dexamethasone (typical dose, 40 mg per day for four days)

Prednisone (typical dose, 1 mg/kg per day for two weeks followed by a gradual taper) - especially in early pregnancy - less fetal exposure.

If preterm birth, then dexamethasone or betamethasone given antenatally

IVIG - +/- glucocorticoid, if there is a need to raise the platelet count more rapidly.
Typical times for these therapies to take effect are as follows:

- **IVIG** – 1 to 3 days for initial response, 2 to 7 days to peak response.
- **Dexamethasone** – 2 to 14 days for initial response, 4 to 28 days to peak response.
- **Prednisone** – 4 to 14 days for initial response, 7 to 28 days to peak response.

Outcomes in pregnant women within retrospective studies:
- Treatment is needed in 30 - 40 % of pregnancies, and
- serious complications are rare
- Avoid splenectomy, rituximab, and thrombopoietin receptor agonists during pregnancy due to concerns about maternal and fetal adverse effect
**Splenectomy** –
For patients unresponsive to glucocorticoids, IVIG, and rituximab

Greater risk as the uterus becomes larger during later pregnancy

**Thrombopoietin receptor agonists** (eg, romiplostim, eltrombopag) Their safety during pregnancy is unknown.
Rituxan: Safety unknown
Neonatal testing:

Maternal ITP
Neonatal thrombocytopenia in a previous pregnancy.
Overall risk of thrombocytopenia in infants of ITP mothers 10-15%
No evidence that ITP therapy for the mother raises the fetal platelet count
Gestational thrombocytopenia (GT)-

Commonest cause of thrombocytopenia in pregnancy a benign, physiologic condition that requires no evaluation or treatment
Followed by-immune thrombocytopenia (ITP)

GT and ITP can occur at any stage of the pregnancy
Both are diagnoses of exclusion.

Platelet transfusions for severe thrombocytopenia with bleeding, require a procedure, or are nearing delivery.

ITP if require treatment - Glucocorticoids or IVIG
References


UpToDate: Thrombocytopenia in Pregnancy.
Thank you!