2021 Chinese consensus on the diagnosis and management of primary immune thrombocytopenia in pregnancy

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Immune thrombocytopenia (ITP) is an acquired disease characterized by isolated thrombocytopenia, which is one of the most common causes of thrombocytopenia during pregnancy. Women with ITP who have severe thrombocytopenia are at an increased risk for life-threatening obstetric complications. Therefore, we established this consensus statement on the diagnosis and management of ITP during pregnancy (detailed information is available in the Supplementary File, http://links.lww.com/CM9/A978).

Recommendations for diagnosis of ITP in pregnancy

1. Patients with suspected ITP prior to pregnancy or those with a platelet count $<100 \times 10^9$/L should be assessed for ITP.
2. The recommended examinations for all patients include the following: a detailed patient and family history; a physical examination; complete blood count panels; reticulocyte and reticulated platelet counts; a peripheral blood smear; coagulation screening; human immunodeficiency virus, hepatitis B virus, and hepatitis C virus testing; liver and renal function tests; thyroid function tests; antinuclear antibody; and anti-phospholipid antibody tests.
3. Detection of *Helicobacter pylori* infection should be considered in patients with digestive symptoms and in those from areas of high prevalence. Polymerase chain reaction for cytomegalovirus and Epstein–Barr virus is also recommended, when clinically indicated.
4. Direct anti-globulin test combined with haptoglobin, lactate dehydrogenase, and bilirubin tests should be considered to assess hemolysis.
5. A bone marrow examination is not routinely recommended unless there are atypical features in the peripheral blood counts or peripheral blood smears that are inconsistent with isolated thrombocytopenia.
6. Anti-platelet antibody and testing of thrombopoietin levels are not routinely recommended.

Recommendations for preconception counseling

Preconception counseling should be performed for women diagnosed with ITP before pregnancy. Details of the diagnosis of ITP, history of bleeding, previous medical treatment, splenectomy, response to treatment, and obstetric history, including a previous neonate platelet count, should be explored during this counseling.

Recommended timing for intervention

1. Patients with a platelet count $\geq 30 \times 10^9$/L, without bleeding or any risk factor for bleeding who can be observed and followed up until delivery is imminent.
2. In patients with a platelet count $<30 \times 10^9$/L, treatment should be considered in order to achieve a safe platelet level.
3. Patients with active bleeding symptoms should be treated regardless of the degree of thrombocytopenia.
4. The platelet count should be raised to a target level when a medical procedure or surgery is planned.
5. Late in the third trimester, the platelet count should be maintained at $\geq 50 \times 10^9$/L for vaginal delivery and at $\geq 80 \times 10^9$/L for cesarean section and spinal/epidural anesthesia in patients with otherwise normal coagulation.
6. Pregnancy may complicate the management of ITP. A multidisciplinary team including a hematologist, an obstetrician, a neonatologist, and an anesthetist, if necessary, is recommended for the treatment of ITP during pregnancy.

Recommended platelet levels for patients undergoing medical procedures

- Dentistry: a platelet count $\geq 20 \times 10^9$/L
- Tooth extractions and regional dental block: a platelet count $\geq 30 \times 10^9$/L
- Minor surgery: a platelet count $\geq 50 \times 10^9$/L
- Major surgery: a platelet count $\geq 80 \times 10^9$/L
- Anticoagulant therapy: a platelet count $\geq 50 \times 10^9$/L

Recommendations for first-line treatment

1. Prednisone started at a dose of 10 to 20 mg/day is recommended for initial treatment. It can be tapered subsequently to the minimum maintenance dose (5–10 mg/day) to maintain a target platelet count. The dosage should be tapered rapidly to discontinuation in patients who do not respond to prednisone.
2. Intravenous immunoglobulin (IVIg) is recommended for patients who fail to respond to prednisone, for those with severe adverse effects, or for those with an urgent need for elevated platelet counts. A dose of 400 mg/kg per day for 3 to 5 days, or 1000 mg/kg for 1 to 2 days, is recommended; this protocol may be repeated after 1 or 2 weeks, if necessary.
3. In consideration of the safety of the fetus, prednisone is recommended for use in the second and third trimesters of pregnancy. Prednisone should be used with caution during the first trimester. IVIg can be considered when treatment is needed in the first trimester.

Recommendations for emergency treatment

1. Emergency treatment is needed for severe thrombocytopenia, which is defined as severe, life-threatening bleeding with a platelet count $<10 \times 10^9$/L, to rapidly stop bleeding and improve the platelet count, raising it to a relatively safe level.
2. High-dose methylprednisolone (1000 mg/day for 3 days) and IVIg (1000 mg/kg per day for 1–2 days), either alone or in combination, with platelet transfusions are recommended for emergency treatment. If used in combination with high-dose methylprednisolone, which can contribute to increased catabolism, a reduced dosage of IVIg at 400 mg/kg per day for 3 to 5 days could be considered in women who have an increased risk of acute kidney injury.
3. Other therapeutic measures include discontinuing medications that may have an antiplatelet or anticoagulation effect and controlling hypertension.

Recommendations for second-line treatment

1. Prednisone or high-dose methylprednisolone combined with IVIg is recommended for patients who fail to respond to initial treatment.
2. Recombinant human thrombopoietin could be considered a second-line alternative for patients who are refractory to corticosteroids and IVIg, ideally in the third trimester and only at an experienced center.
3. Thrombopoietin receptor agonists could be considered in pregnancy only in extremely severe cases when the benefits outweigh the potential harm or when other treatments have failed or are not accessible.
4. Splenectomy is rarely performed during pregnancy. When a splenectomy is deemed necessary, it is best carried out in the second trimester by laparoscopy, if possible.
5. Other cytotoxic and immunosuppressive drugs not listed in these recommendations should be avoided in pregnancy.

Recommendations for platelets transfusion

1. When delivery is approaching, platelet transfusion should be prepared in patients whose platelet counts are still below the recommended level despite standard treatment.
2. When pregnant patients with ITP undergo surgery or a procedure, or when they have active bleeding, platelet transfusion can be used to achieve a safe platelet count and rapidly stop bleeding.
3. A combination of IVIg and/or corticosteroids may improve the effectiveness of platelet transfusion.

Recommendations for delivery

1. ITP is not an indication for cesarean section. The mode of delivery should be considered based on obstetrical indications.
2. In the third trimester, as delivery nears, an adequate platelet count should be maintained to reduce the risk for maternal hemorrhage. Vaginal delivery is generally considered safe at platelet counts above 50×10^9/L. A platelet count $\geq 80 \times 10^9$/L is required for cesarean sections with epidural anesthesia.
3. Platelet infusion in combination with IVIg or corticosteroids can be used to rapidly increase platelet levels in emergency situations.

Assessment of postpartum hemorrhage (PPH)

We recommend evaluating PPH risk for ITP patients routinely to prevent life-threatening events associated with ITP by using the MONITOR model (maternal complication, World Health Organization bleeding score, antepartum platelet transfusion, placental abnormalities, platelet count, previous uterine surgery, and primiparity).

Recommendations for the management of neonates born to women with ITP

1. The fetal platelet levels cannot be predicted by measuring the maternal platelet counts. Neonates who have a sibling with previous thrombocytopenia are more likely to experience thrombocytopenia at or after birth.
2. The umbilical cord platelet count should be examined at delivery, if possible.
3. Neonatal platelet counts should be closely monitored after delivery. Repeat platelet monitoring as required based on platelet levels, trends in the count, and response to treatment (if any).
4. It should be considered that the incidence of pseudothrombocytopenia is high in neonates due to the difficulty of collecting blood.
5. Cranial ultrasound should be performed to rule out intracranial hemorrhage if the platelet count is below 50×10^9/L at birth.
6. For neonates with a platelet level $<30 \times 10^9$/L or with symptomatic bleeding, IVIg at a dose of 1 g/kg can be administered, and can be repeated if necessary. If bleeding is severe and uncontrollable, platelet transfusion can be considered.
7. For neonates with thrombocytopenia, fetal/neonatal alloimmune thrombocytopenia should be considered and differentiated.

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Conflicts of interest

None.

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