REVIEW ARTICLE

Thrombocytopenia in Pregnancy: An Approach to Diagnosis and Management

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Abstract

Thrombocytopenia, defined as a platelet count of <150,000/microliter occurs in 7–12% of pregnant women at delivery. While the most common cause of thrombocytopenia in pregnancy is benign and causes only a mild fall in platelet count, some etiologies are life-threatening. This review is a summary of some of the common causes of thrombocytopenia and outlines a systematic approach to diagnosis and management.

Keywords: High-risk pregnancy, Hypertension in pregnancy, Pre-eclampsia, Pregnancy, Thrombocytopenia.

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Introduction

Thrombocytopenia is defined as low platelet count. Although the usual cut-off is 150,000 per microliter, the American College of Obstetricians and Gynecologists suggest using a lower cut-off of 120,000 per microliter to define thrombocytopenia in pregnancy.[1,2] Late second or third trimester fall in platelet count is well known and occurs in up to 12% of normal pregnancies.[1,2] This article reviews some (but not all) causes of thrombocytopenia in pregnancy, with an aim to provide obstetricians with an evidence based approach to diagnosis and management.

General Approach to Diagnosis

An assessment of full blood count and review of the peripheral blood smear form preliminary investigations. A detailed family and personal medical history provide clues to etiology. Further diagnostic evaluation includes (but is not limited to) liver function tests, infectious screening for viral infections (hepatitis B, hepatitis C, human immune deficiency, cytomegalovirus), *Helicobacter pylori* screening and tests for markers of haemolysis.[1] Further testing is guided by history and clinical presentation. This may include tests for antiphospholipid antibody syndrome and hereditary thrmbocytopenias.[1]

Causes of Thrombocytopenia

Table 1 lists the causes of thrombocytopenia in pregnancy. This review discusses some (but not all) causes of thrombocytopenia.

Gestational Thrombocytopenia (GT)

The commonest cause of low platelets in pregnancy is GT, affecting up to 12% of all pregnancies occurring after the mid-second trimester.[1,2] Gestational thrombocytopenia is a diagnosis of exclusion.[1,3] Onset of thrombocytopenia prior to mid-second trimester, platelet count <80,000/microliter, and significant fall in platelet count is associated with a diagnosis other than GT.[1,4] Platelet counts should be monitored monthly up to 36 weeks and weekly thereafter.[5] If the platelet count (>100,000/microliter) is stable and the woman is asymptomatic, no further intervention is required.[1] Liaison with anesthetist is recommended if counts fall below 100,000/microliter. Platelet counts usually return to normal within 1–2 months of delivery.[5]

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Pre-eclampsia (PE)

Pre-eclampsia is defined as hypertension in the presence of end-organ dysfunction.[6] Thrombocytopenia (<100,000/microliter) is one of the criteria for severe PE.[6] Hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome affecting from 8 to 24% of patients with severe PE is characterized by hemolysis, a high elevation of liver enzymes with low platelets.[6–8] Patients with severe PE may develop disseminated intravascular coagulation (DIC).[6,7] Definitive management for HELLP syndrome is delivery. However, supportive care in the form of antihypertensives, magnesium sulfate for seizure prevention, and admission to high dependency care is recommended.[7,8] Management of severe PE should follow local, national or institutional guidelines.

Recurrence risk of HELLP syndrome (7%) should form part of postnatal counseling.[9]

Immune Thrombocytopenia

Immune thrombocytopenia (also known as idiopathic thrombocytopenic purpura or ITP) is an acquired autoimmune disorder. Patients with ITP demonstrate accelerated platelet destruction due to splenic sequestration of platelets coated with autoantibodies along with impaired platelet production. Accounting for 1–4% of pregnancy thrombocytopenia, ITP is the most common cause of a platelet count <50,000/microliter

Table 1: Causes of thrombocytopenia in pregnancy

Common causes	*Rare causes*
Gestational thrombocytopenia (GT)	Systemic lupus erythematosus (SLE)
Severe preeclampsia (PE)	Thrombotic thrombocytopenia (TTP)
Immune thrombocytopenia (ITP)	Hemolytic uremic syndrome (HUS)
HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome	Hematological diseases (e.g., lymphoma, leukemia, etc.)
Disseminated intravascular coagulation (DIC)	Folic acid deficiency
Drugs (heparin – HIT/ heparin induced thrombocytopenia)	Type 2B von Willebrand's disease
	Congenital thrombocytopenia
	Viral infection (HIV, Hepatitis B, Hepatitis C, etc.)

in early pregnancy (first or second trimester).[1,2] In the absence of definitive diagnostic tests, ITP is diagnosed by excluding other causes of thrombocytopenia. Corticosteroids and intravenous immunoglobulin (IVIG) (both of which are safe in pregnancy) are first-line treatment options.[2,10] The choice of treatment is determined by intolerance (to steroids) or rapidity of response (IVIG gives rapid response).[2] While there is no consensus on optimal second-line treatment, immunosuppressants, such as azathioprine and cyclosporine, have been used safely in pregnancy.[11] Rituximab can be considered in refractory cases with caution since it can cause prolonged lymphopenia in newborns.[11] Splenectomy remains an option for refractory ITP in the second trimester.[11] Routine use of thrombopoietin receptor agonists is not recommended.[11]

International consensus report (ICR) guidelines for ITP recommend a safe platelet count in pregnancy of 20 and 30,000/microliter in a nonbleeding patient.[10] Platelet count <50,000/microliter near delivery or the presence of significant bleeding are indications for platelet transfusions.[10] Idiopathic thrombocytopenic purpura per se is not an indication or contraindication for cesarean section or vaginal birth.[10,11] Induction of labor may be recommended in women following stabilization of platelet counts at term to facilitate the option of epidural analgesia.[10] For a planned vaginal birth, a platelet count >20,000/microliter and for planned caesarean delivery, a count of >50,000/microliter is recommended to prevent excessive blood loss.[10,11] Liaison with anesthetists is essential for planning safe neuraxial or general anesthesia based on platelet count (a count of >70,000/microliter is recommended for neuraxial anesthesia).[10,11] About 15% of neonates are born with thrombocytopenia.[12] However, severe neonatal thrombocytopenia and intracranial hemorrhage are rare complications.[12] Due to this risk, it is recommended that instrumental birth should be attempted with caution.[12]

Acute Fatty Liver of Pregnancy (AFLP)

Acute fatty liver of pregnancy is a rare life-threatening condition affecting between 3.8 and 6.5 per 100,000 pregnancies.[1] It should be suspected in all women who present with unexplained rapid onset of liver failure in the third trimester along with hypoglycemia and coagulopathy.[1,13,14] The pathogenesis is likely estrogen-related defective fatty acid metabolism and mitochondrial dysfunction.[15] Clinical features include abdominal pain, anorexia, nausea, and vomiting with or without overt jaundice.[13–15] Left untreated, AFLP progresses to liver failure, encephalopathy, and maternal death. The aim of management is the prevention of hepatic encephalopathy and maternal mortality. This can be achieved by a high degree of suspicion, early diagnosis, and prompt delivery irrespective of gestational age.[1,16] Supportive care includes red cell transfusions, dialysis, plasmapheresis, and management of coagulopathy.[1,15,16] Intensive care unit (ICU) admission with multidisciplinary team management involving obstetric physician, hepatologist, haematologist, intensive care specialist and obstetricians is recommended.[1,15,16]

Thrombotic Thrombocytopenic Purpura (TTP)

Thrombotic thrombocytopenic purpura is a thrombotic microangiopathy (TMA) associated with severe deficiency of ADAMTS13 enzyme activity. This enzyme is a metalloprotease responsible for the cleavage of von Willebrand factor (vWF) thus preventing it from triggering clot formation. Deficiency results in the formation of microthrombi in small vessels.[16,17] The ADAMTS13 deficiency can be congenital or acquired.[17] Symptoms of TTP include the appearance of petechiae or purpura, fever, fatigue, neurologic symptoms, and renal dysfunction.[17] Diagnosis of TTP is confirmed by low ADAMTS13 activity of <10% and/or by the presence of IgG antibodies to ADAMTS13.[17] It is crucial to commence plasma exchange and corticosteroids on the basis of the high degree of suspicion of TTP pending confirmation of diagnosis.[16] The aim of treatment should be the restoration of platelet count.[16] Rituximab may be considered in refractory cases (with caution, as above).[1,17] Thrombotic thrombocytopenic purpura in the second trimester can affect fetal growth due to placental microthrombi leading to ischemia.[17] However, TTP alone is not an indication for immediate delivery.[16]

The risk of recurrence is approximately 50% for women with both congenital or acquired TTP.[17]

Atypical Hemolytic Uremic Syndrome (aHUS)

Atypical hemolytic uremic syndrome is a rare disorder occurring in one out of every 25,000 pregnancies.[1,16] Normal physiology of pregnancy includes complement activation.[16] When this activation is uncontrolled, it leads to platelet activation and the formation of platelet thrombi, especially within the microvasculature of the kidneys.[16,18] Diagnosis of aHUS is suspected when a pregnant or postpartum woman presents with progressive renal failure and thrombocytopenia (counts >50,000/microliter).[18] It is a diagnosis of exclusion after ruling out TTP and PE/HELLP syndrome.[1] ADAMTS13 levels are helpful to exclude TTP. Management includes plasmapheresis, fresh frozen plasma infusion, and dialysis.[16,18] In cases with a high degree of suspicion, eculizumab (a monoclonal antibody targeted against complement 5) should be administered as soon as possible.[16,18] Platelet counts improve within 2–3 days but improvement in renal function can take weeks or months.[19] Although eculizumab can cross the placenta it has been used safely during pregnancy and breastfeeding.[19]

Conclusion

Thrombocytopenia is a relatively common hematological abnormality in pregnancy. Although the majority of patients will have a relatively benign courses, some causes are sinister and life-threatening. Multidisciplinary team care should be the cornerstone

in the management of complex hematological conditions. In certain conditions (eg., AFLP), immediate delivery is indicated. This could preclude the timely involvement of other specialists. Hence, obstetricians must have a good working understanding of the diagnosis and management of serious conditions associated with thrombocytopenia. Many of these conditions carry a risk of recurrence hence postnatal counseling is of vital importance to informing future pregnancy planning.

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