Review Article

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Thrombocytopenia in Pregnancy: Review

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Abstract

Thrombocytopenia in pregnancy is a common hematological disorder second only to anemia. Cause of thrombocytopenia may be due to an increase in destruction or consumption of platelets, dilutional effects or lack of production of platelets. Gestational thrombocytopenia mostly found in 3rd trimester of pregnancy is most common cause of thrombocytopenia in pregnancy. Neonatal mortality rate is low with ITP mother hence normal vaginal delivery advocated. Thrombocytopenia in hypertensive disorders requires multipronged approach with component therapy and antiepileptic antihypertensive. Choosing best in all treatment modality available is challenge for obstetrician.

Keywords: Thrombocytopenia; Pregnancy; Autoimmune; Preeclampsia; DIC; Platelet.

Introduction

Platelets are non-nucleated cellular fragments of megakaryocytes, they play a major part in hemostasis.Platelet count less than 150,000μl^{-1} is called as thrombocytopenia [1]. Thrombocytopenia in pregnancy is a common hematological disorder second only to anemia. Pregnancy is associated with a physiologic fall in the platelet count with a leftward shift in the platelet count distribution. Incidence of thrombocytopenia in pregnancy is about 8–10% [2].

Petechiae, ecchymosis, epistaxis, gingival bleeding etc. are presenting features. Bruising, hematuria, gastrointestinal bleeding and rarely intracranial hemorrhage mayalso appear.

Many physiological or pathological mechanisms causes thrombocytopenia in pregnant women. When the platelet count is <50,000 μl^{-1} there may be clinical signs or symptoms.If platelet function is also defective then clinical symptoms may occur even though count is is > 50,000 μl^{-1}.

Pregnancy is pro-coagulant state induced by:

1. Increased levels of Fibrinogen, Factor VIII,
2. Von Willebrand factor,
3. Suppressed fibrinolysis,
4. Reduced protein S activity.
5. Pregnant women with thrombocytopenia have fewer bleeding complications compared to non-pregnant women [3]. In very few cases where thrombocytopenia is part of a complex clinical disorder, there can be maternal and fetal mortality but most of the cases are mild.

A good diagnosis is essential to for making proper therapeutic management.

Types

Thrombocytopenia is divided according to severity into [4]

Mild	≥100,000 to <150,000 μl^{-1}
Moderate	≥50,000 to <100,000 μl^{-1}
Severe	<50,000 μl^{-1}

Etiology and Prevalance

In 8–10% of pregnancies platelet count below the normal range [5].

Causes of Thrombocytopenia in pregnancy: [6]

Benign process of gestational Thrombocytopenia	75 %
Hypertensive disorders	15-20 %
Immune process	3-4 %
Rare constitutional thrombocytopenia, infections and hematological malignancies	1-2 %

Mechanism

Cause of thrombocytopenia may be due to an increase in destruction or consumption of platelets, dilutional effects or lack of production of platelets [7].

In general, counts that are stable and above 100000/mm3 do not require further investigation but should be monitored.

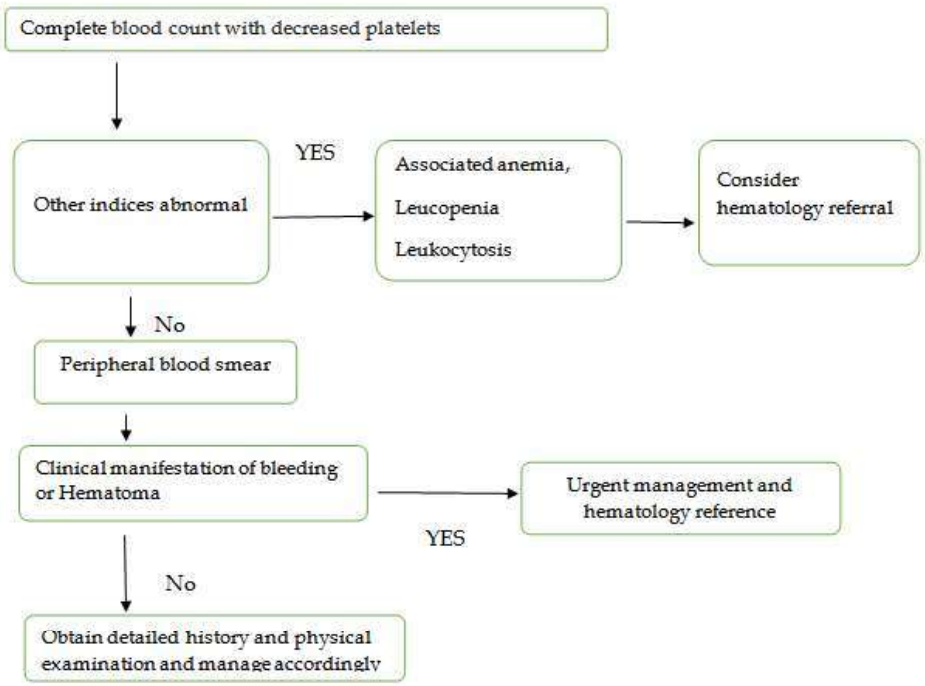
Diagnostic assessment of thrombocytopenia in pregnancy – Approach

Detailed history and systemic physical examination is important in establishing the diagnosis and evaluation the severity of thrombocytopenia.

Some significant history or some finding would quickly narrow down the diagnosis include age of the patient past medical history of any blood or autoimmune disorders, positive family history of thrombocytopenia and recent medications, vaccinations, travel history infections or other comorbidity.

Decreased Production	Increased Destruction	Others
Bone marrow failure: Eg. aplastic anaemia, paroxysmal nocturnal haemoglobinuria	Alloimmune destruction	Hypertention
Myelodysplasia	Autoimmune destruction	Liver diseases
Neoplastic bone marrow infiltration	DIC	Pulmonary emboli
Bone marrow suppression – drugs, EBV, Cytomegalovirus, HIV, Mumps, Rubella etc	TTP/HUS	Pulmonary hypertention
Genetic causes	Preeclampis, HELLP	
	Mechanical causes - mechanical valve, Cyanotic heart diseases	

Chart 1: Algorithm to Thrombocytopenia in Pregnancy



Onset duration and progress of blood loss should be evaluated. Physical examination should note location and severity of the bleeding and other abnormity like hepatomegaly splenomegaly lymphadenopathy that may show towards bone marrow infiltration or infections dysmorphism skeletal malformations that is bone marrow failure syndrome.

Other features like Pallor main point toward more than one cell line involvement [8].

Investigation

Algorithm to Thrombocytopenia in Pregnancy (Chart 1).

General Antenatal management

First initially confirm thrombocytopenia by peripheral smear examination.

Mild non symptomatic cases to be monitored. Low platelet counts in the first and second trimesters, are most likely due to an immune process, but sometimes due to a platelet production defect. In such cases obstetrician,hematologist and neonatologist and anesthesia department should be informed. Aims of the management should be adequate platelet rather than normal range. A conservative approach minimizes the risks to mother and fetus from exposure to therapeutic agents. Treat the patient if necessary if patient is symptomatic or platelet count is less than 20000/mm3 or procedure is required. A platelet count of 50000/mm3 is usually adequate for procedures. The complete blood count can be checked monthly until the 3rd trimester and then 2-weekly, increasing to weekly as term approaches. Aspirin, non-steroidal anti-inflammatory drugs, and intramuscular injections, should be avoided depending on the platelet level and function [9].

Perinatal management

Considerations for mother

Hemorrhage during delivery or post-partum remain concern. Problematic hemorrhage following vaginal delivery is not common, even with severe thrombocytopenia as main mechanism is figure of eight ligature of uterine muscle as hemostaticmechanism.

In uncomplicated obstetric cases vaginal mode of delivery is preferred rather than caesarian delivery. For a woman whose platelet count is < 80000 μl^{-1} but has not required therapy during pregnancy, oral prednisone (or prednisolone) can be started 10 days prior to anticipated delivery at a dose of 10-20 mg daily and titrated as necessary. Platelet transfusions should be managed according to time of delivery in active stage of labor as it has very short half-life as and when required [10].

Considerations for Anesthesia

Epidural analgesia should not preferred, as even a small increase in venous hemorrhage has the potential for spinal cord compression.Spinal anesthesia is preferred over epidural as needle size is negligible General anesthesia is good choice in depleted platelet [11].

Considerations for baby

Maternal thrombocytopenia of undetermined cause has been the risk of neonatal thrombocytopenia and intracranial hemorrhage (ICH). ITP and Gestational Thrombocytopenia are two entity that must be bothering to pediatrician. Immunoglobulin G (IgG) Antibodies produced in ITP in nature can cross the placenta which may cause thrombocytopenia in the fetus. But Gestational Thrombocytopenia is benign in nature. Neonatal thrombocytopenia is more likely if there is a sibling with thrombocytopenia [13].

In past caesarian section was recommended but recent evidences suggest that neonatal mortality rate is low with ITP mother. Vaginal delivery is however safe to mother. Obstetric trauma should be avoided like foceps and vacuum.A cord sample should be sent to check neonatal platelet count, and intramuscular injection of vitamin K not given until the platelet count is known [14].

Treatment of the neonate with clinical hemorrhage or platelet counts <20000–30000 μl^{-1}, treatment with intravenous immunoglobin (IVIG) 1 g/kg produces a good response, usually in 24 h [15].

Table 1: A general guideline for interventional levels in non-hemorrhagic cases of ITP in pregnancy [12].

	Platelet
Vaginal delivery	>30,000 μl^{-1}
Operative or instrumental delivery	>50000μl^{-1}
Epidural anesthesia	>80000μl^{-1}

Specific Causes

(A) Gestational thrombocytopenia (Incidental thrombocytopenia of pregnancy):

GT is mostly found in 3 rd trimester of pregnancy. Counts are typically <70000 μl^{-1} and usually <100000 μl^{-1}. These patient recover after delivery but can be present in next pregnancy. Count should be performed 6 weeks postnatally and the result documented.

B) Immune thrombocytopenia

Primary immune thrombocytopenia (ITP) occurs in 1/1000–1/10 000 pregnancies, accounting for around 3% of women thrombocytopenic at delivery. The presence of other autoimmune phenomena or a low platelet count pre-pregnancy may help diagnostically. ITP is diagnoses of exclusion [17]. There are also different opinions from studies on maternal and perinatal outcomes.Some suggest exacerbation or relapse of ITP during pregnancy some do not suggest same. Most other studies have reported a favourable outcome for neonates and mothers

Specific treatments for ITP

Primary treatment options for maternal ITP are corticosteroids and intravenous IVIG. Modality of treatment and duration depends on severity and urgency of platelet increament. ITP patients with moderate/severe thrombocytopenia (<20,000–30,000μl^{-1}). The usual first line treatment is prednisolone 10–20 mg daily for a week, adjusting to the minimum dose that achieves a safe platelet count.Response time is about 3–7 days

In the short term, low dose steroids are considered safe and effective for the mother. Prednisolone is metabolized by the placenta but high doses may cause effects on the fetus including premature rupture of membranes, adrenal suppression, and a small increase in cleft lip after use in the first trimester.

ITP patients with very severe thrombocytopenia ($\leq 10 \times 10^9/l$) or significant bleeding-

Intravenous immunoglobulin are used in similar dosage to the non-pregnant population but sometimes do not tolerate transfusions Intravenous immunoglobulin with prednisolone therapy also given. Preferably single donor platelet transfusion is given [18].

Therapeutic Options for Management of ITP during Pregnancy

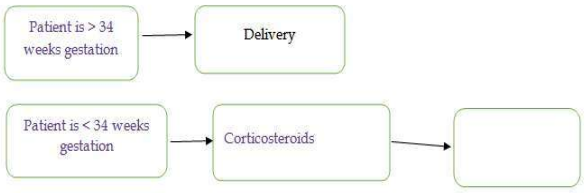
Corticosteroid and IV immunoglobin are the first line treatment for maternal ITPdringpregnancy. Limited experience is there for IV anti D, splenectomy and Azazioprin.Vinca alkaloids, rituximab, danazol, TPO receptor antagonist, immunosuopressivedrugs should not be used because of their teratogenic potential.

C) Hypertensive and microangiopathic disorders of pregnancy: thrombocytopenia + microangiopathy

Acute Onset of Thrombocytopenia in the Setting of

1) Severe Preeclampsia - Preeclampsia, which affects 5-8% of pregnant women,

2) HELLP Syndrome (hemolysis, elevated liver



enzymes, low platelets)- HELLP syndrome, which affects 0.6% of pregnant women.

3) AFLP (acute fatty liver of pregnancy) - AFLP is a rare but serious condition of the third trimester (1 in 20,000pregnancies).

Management of Severe Preeclampsia, the HELLP Syndrome, or AFLP withThrombocytopenia

The patient should be delivered as soon as she isstabilized, if the maternal and fetal status are not reassuring.

Obstetric management

Magnesium sulfate is used to prevent convulsions.

Antihypertensive are used to control blood pressure.

Hematologic management with supportive care with blood products

Therapeutic plasma exchange—if thrombocytopenia, hemolysis or renal

Failurecontinues to worsen 48-72 hours postpartum (19)

D) Miscellaneous causes of thrombocytopenia not specific to pregnancy

Microangiopathies

1)Thrombotic Thrombocytopenia Purpura (TTP)

It includepentad consist of microangiopathic haemolytic anaemia, thrombocytopenia,

neurological symptoms (varying from headache to coma), renal dysfunction and fever.

Etiology

Thrombotic thrombocytopenic purpura has been shown to be due to a severe deficiency of von Willebrand's factor-cleaving protein (ADAMTS 13).

Treatment

Plasma exchange is started by using this procedure antibodies are removed and daily 1–1.5 liter fresh frozen plasma containing the absent enzyme is infused till the platelet count is normal and the lactate dehydrogenase level is reduced.

2) DIC: Causes to be corrected with all blood component as required.

3) APLA: Mild form of thrombocytopenia is common in APLA. Treatment is low dose aspirin and low molecular weight heparin.

4) HUS (Hemolytic uremic syndrome)

This is a similar syndrome, with microangiopathic haemolytic anaemia and thrombocytopenia but with predominant renal involvement.

Type 2B von Willebrand disease (type 2B VWD)

5) Malignant hematological disorders, viral infection- HIV, Nutritional deficiencies should be treated accordingly with supportive symptomatic management.

6) Unfractionated heparin should be monitored for platelet.

Conclusions

Thrombocytopenia is the second most common hematologic condition during pregnancy and is usually a benign condition. Patients with severe preeclampsia and chronic medical condition require further investigation and treatment. But cause of thrombocytopenia during pregnancy can usually be determined with a thorough history, physical examination, and according laboratory reports. Choosing best in all treatment option available is challenge for obstetrician.

References

1. Saxena R, PatiHP, Mahapatra M. de Gruchy's clinical haematology in medical practice. Wiley pub. 6thed. 2013.p.350.
2. SaxenaR,PatiHP,Mahapatra M. de Gruchy's clinical haematology in medical practice.Wiley pub. 6thed. 2013.p.359.
3. Magann EF, Martin JN. Twelve steps to optical management of HELLP syndrome. Mississippi & Tennessee classification systems for HELLP syndrome. ClinObstet Gynecol. 1999;42(3):532–50.
4. Nisha S, Amita D, Um S, Tripathi AK, Pushplata S. Prevalence and Characterization of Thrombocytopenia in Pregnancy in Indian Women. Indian Journal of Hematology & Blood Transfusion. 2012;28(2):77-81.
5. Verdy E, Bessous V, Dreyfus M, Kaplan C, Tchernia G, Uzan S. Longitudinalanalysis of platelet count and volume in normal pregnancy. ThrombHaemost 1997;77:806–7.
6. Burrows RF, Kelton JG. Thrombocytopenia at delivery: a prospective survey of 6715 deliveries. Am J ObstetGynecol 1990;162:732–33.
7. Frances Yeap JPOG MAR/APRIL 2018 55 CME Thrombocytopenia –A clinical Review 2018.p.56.
8. Bethan Myers Diagnosis and management of maternal thrombocytopenia in pregnancyhttps://doi.org/10.1111/j.1365-2141.2012.09135.x
9. Webert, K.E., Mittal, R., Sigouin, C., Heddle, N.M. & Kelton, J.G. A retrospective 11 year analysis of obstetric patients with idiopathic thrombocytopenic purpura. Blood, 2003;102:4306–11.
10. Provan, D., Stasi, R., Newland, A., Blanchette, V.S., Bolton-Maggs, P., Bussel, J.B., Chong, B., Cines,D., Gernsheimer, T., Godeau, B., Grainger, J., Greer, I., Hunt, B., Imbach, P., Lyons, G.,McMillan, R., Rodeghiero, F., Sanz, M., Tarantino, M., Watson, S., Young, J. &Kuter, D. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood, 2010;115: 168–86.
11. Avan Dadina, Management of Autoimmunne Thromcytopenic Purpura in Pregnancy, Pregnancy at risk Usha Krishna Duru shah Vinita Salvi Nozer Sheriar K.R. Damania 5th edition page 776.
12. Christiaens, G.C., Niewenhuis, H.K. & Bussel, J.B. Comparison of platelet counts in first and second newborns of mothers with immune thrombocytopenic purpura. Obstetrics and Gynecology, 1997;90:546–52.
13. Cuker A & cines D. Immune thrombocytopenia. Haematology Am. Soc Haematol. Educ. Program 2010;377:84
14. Ballin, A., Andrew, M., Ling, E., Perlman, M. & Blanchette, V. High-dose intravenous gammaglobulin therapy for neonatal autoimmune thrombocytopenia. Journal of Pediatrics, 1988;112: 789–92.
15. Gill K.K. & Kelton J.G. Management of idiopathic thrombocytopenic purpura in pregnancy. Seminars in Haematology, 2000;37:275–89.