Thrombophilia in Pregnancy

What We Know

› Thrombophilia, defined as the tendency to develop venous thrombosis (i.e., blood clots) because of a coagulation abnormality, is commonly used to refer to a group of hypercoagulability disorders that predispose affected persons to venous thrombosis (VT), usually manifested as deep vein thrombosis (DVT) or pulmonary embolism (PE)\(^{(11,12,13)}\)
  • Thrombophilia is caused by a shift in balance between procoagulant and anticoagulant factors toward a hypercoagulable state and thrombosis
  • Thrombophilia can be acquired or inherited; thrombophilic conditions that increase clotting tendency include:
    – Factor V Leiden is characterized by impaired response to activated protein C (APC) and is the most common cause of inherited hypercoagulability in White individuals
    – Hyperhomocysteinemia (i.e., elevated homocysteine levels) can be inherited or caused by a nutritional deficiency of folic acid, vitamin B12, or vitamin B6
    – Antithrombin III deficiency (i.e., antithrombin levels that are too low to inhibit thrombin and other normal coagulation factors) is a common hereditary condition
    – Prothrombin G20210A mutation (PTm), which increases plasma prothrombin levels, is an inherited gene mutation
    – Protein C and/or S deficiencies (i.e., reduced levels of endogenous anticoagulant protein C and/or S) can be either inherited or acquired
    – APC resistance, characterized by an impaired anticoagulant effect of APC, can be either inherited or acquired
    – Antiphospholipid syndrome, is an autoimmune disorder in which the immune system produces antibodies in response to phospholipids in endothelial cell and platelet membranes (i.e., antiphospholipid antibodies [aPLs]), resulting in a hypercoagulable state that is associated with significant difficulties during pregnancy, including maternal thrombosis and recurrent pregnancy loss.\(^{(1)}\) (For more information, see Quick Lesson About … Antiphospholipid Syndrome and Pregnancy)
  – Researchers who analyzed 1,717 females undergoing thrombophilic mutations, such as those to factor V or the prothrombin G20210A mutation, found that these mutations do not affect IVF outcomes\(^{(15)}\)

› Normal pregnancy also disrupts the usual balance among coagulation factors and is considered a hypercoagulable state\(^{(2,10,14)}\)
  • Pregnancy in a woman with a preexisting clotting disorder is associated with still greater risk for VT and vascular complications
  – Venous thromboembolism (VTE) occurs in 1:1,000 pregnancies
  – Inherited thrombophilia is present in 30–50% of women with pregnancy-associated VTE

› Thrombophilia is an important cause of maternal morbidity and mortality\(^{(10,11)}\)
  • Signs and symptoms (S/S) of DVT include pain, heaviness, swelling, discoloration, and erythema of the affected area (e.g., leg)
  • PE during pregnancy can cause dyspnea, chest pain, hemoptysis, and tachycardia
  • Thrombophilia is commonly associated with recurrent, unexplained fetal loss\(^{(7,8,10,11,13,14)}\)
Thrombophilia is implicated as the main cause in > 40% of cases.

Fetal loss can occur because of hypercoagulability impairing placental blood flow affecting placental function and fetal growth.

Thrombophilia can also be associated with other obstetric complications, including:
- preeclampsia, characterized by increasing hypertension, proteinuria, and edema
- fetal growth retardation (i.e., below-average fetal development and lower weight compared with statistical averages)
- placental abruption (i.e., sudden placental detachment from the uterus)

Thrombophilia can be a risk factor for perinatal stroke.

No consensus exists regarding screening for thrombophilia in pregnancy, and the condition is likely underdiagnosed.

Routine screening of women without risk factors for thrombophilia is not recommended.

The American College of Obstetricians and Gynecologists recommends screening women with a history of 1 fetal loss or ≥ 3 recurrent embryonic or fetal losses, personal history of unexplained VTE, new VTE in pregnancy, or history of VTE in women not previously screened.

The American College of Chest Physicians (ACCP) recommends screening women with recurrent early pregnancy loss (≥ 3 miscarriages at < 10 weeks) for aPLs.

Thrombophilia screening should be considered for women with severe PE or HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count) occurring before 34 weeks’ gestation.

ACCP guidelines for management of thrombophilia in pregnancy include the following:
- Pregnant women with acute VTE should receive adjusted-dose low molecular weight heparin (LMWH) for the duration of pregnancy and ≥ 6 weeks’ postpartum (minimum 3 months total treatment duration).
  - LMWH does not cross the placenta and is considered safe for use in pregnancy.

ACCP recommends screening women with confirmed thrombophilia can be managed expectantly with close monitoring only, or treated with LMWH.

- Existing clinical guidelines recommend that women who test positive for aPLs should receive prophylactic LMWH plus aspirin.

Authors of a systematic review suggest that for women with unexplained recurrent miscarriage, with or without inherited thrombophilia, the evidence does not support use of prophylactic anticoagulant drug therapy to increase live birth rates.

However, a small study of 50 pregnant women with inherited thrombophilia found that treatment with LMWH reduced the incidence of intrauterine fetal death.

Pregnant women with mechanical heart valves are at extremely high risk for valve thrombosis and cerebral or peripheral embolization and require individualized and closely monitored anticoagulation.

All women with a history of DVT should wear graduated elastic compression stockings during pregnancy and for 6–12 weeks’ postpartum.

Although combined use of LMWH and aspirin is recommended for treatment of patients with recurrent miscarriage and thrombophilia in pregnancy, this treatment strategy is largely based upon expert opinion and has not been well-studied.

Researchers performing a meta-analysis of data from 19 clinical trials involving 2,391 patients concluded that their findings did not support the use of LMWH plus aspirin as treatment for this condition.

A meta-analysis of studies covering 222 women with hereditary thrombophilia found no evidence which showed any benefit of LMWH with aspirin compared to aspirin alone.

What We Can Do

Learn about the latest research on thrombophilia and its treatment so you can accurately assess your patients’ personal characteristics and health education needs; share this information with your colleagues.

Consider timing recommendations for placement and removal of epidural or spinal catheters to minimize the risk for patients on any anticoagulant drugs or delay administration of such drugs to decrease the risk of spinal column bleeding, hematoma, and subsequent paralysis after spinal injections.

Include questions about thrombophilia risk factors in routine nursing assessment of your pregnant patients; suggest that they talk with their obstetric clinician about any family history, personal risk, symptoms, screening, and treatment, if appropriate.
Educate patients with thrombophilia about signs and symptoms of DVT and discuss the need for anticoagulant therapy, when indicated.

Educate patients in the importance of early and frequent mobility in the postnatal period to aid in prevention of DVT.

Provide emotional support for coping with a potentially serious condition and support in decision making regarding treatment.

Encourage peer networking in pregnant women with thrombophilia.

References


