Original Research Paper

Volume - 11 | Issue - 06 | June - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Gynaecology

VENOUS THROMBOEMBOLISM DURING PREGNANCY- A REVIEW ARTICLE

Dr.Madhu Meena*	M.S., Assistant Professor, Department Of Gynae & Obs, Govt. Medical College Kota. *Corresponding Author
Dr Ramawatar Meena	M.D Assistant Professor Department Of Medicine, Govt. Medical College Kota.
Dr Khushbu Meena	M.D. Assistant Professor Department Of Gynae & Obstetric, Govt. Medical College Kota.

ABSTRACT Deep vein thrombosis and pulmonary embolism are two clinical entities of single diseases causes venous thromboembolism. VTE is an important causes of maternal morbidity and mortality. Diagnosis and treatment of VTE in pregnant women are much more difficult than in non pregnant women. To date numerous studies have evaluated the risk factor and treatment of VTE during pregnancy. In this review we aim to summarise recent literature published within the past few years.

KEYWORDS :

INTRODUCTION

Pregnancy and the puerperium are well-established risk factors for venous thromboembolism, a disease that includes pulmonary embolism and deep venous thrombosis. Approximately 30% of apparently isolated episodes of PE are associated with silent DVT and in patients presenting with symptoms of DVT, the incidence of silent PE ranges from 40–50%. VTE is both more common and more complex to diagnose in those patients who are pregnant than in those who are not. Among pregnant women pulmonary embolism is the most serious complication of DVT and remains one of the leading cause of maternal death in the developed world.(1) Thrombo-embolic disease can lead to a number of long-term health problems, including post-phlebitic syndrome with chronic leg swelling and pain, and pulmonary hypertension following PE.

EPIDEMIOLOGY

Women are at an increased risk of both venous and arterial thromboembolism during pregnancy. Compared to women who are not pregnant, the risk of arterial Thrombo embolism (strokes and heart attacks) is increased 3-to 4-fold (2)and the risk of venous thrombo embolism increased 4- to 5-fold. (3) Postpartum, the risk is even high 20-fold (3). The overall prevalence of thrombo embolic event during pregnancy is approximately 2 per 1000 deliveries (2). Approxymately 20% of these events are arterial, and the other 80% are venous (2). VTE accounts for 1.1 deaths per 100000 deliveries, or 10% of all maternal deaths.(2).

Approximately 80% of venous thromboembolic events during pregnancy are deep vein thrombosis (DVT) and 20% are pulmonary emboli. Approximately one third of pregnancy related DVT and half of pregnancy-related pulmonary emboli occur after delivery. When DVT occurs during pregnancy, it is more likely to be proximal massive, and in the left lower extremity. Distal thromboses are as likely to occur on the right as on the left, but proximal thromboses occurring under the influence of estrogen are more likely to be on the left. This left-sided predominance is thought to be attributable to a relative stenosis of the left common iliac vein where it lies between the lu+mbar vertebral body and the right common iliac artery, but the true mechanism is unknown. DVT is 3-16 times more common after caesarean section than after spontaneous vaginal delivery.

PATHOPHYSIOLOGY

Pregnancy is a prothrombotic state; it has all components of Virhow's triad: venous stasis, endothelial damage and hypercoagulability. Venous stasis results from a hormonally induced decrease in venous tone and obstruction of venous flow by the enlarging uterus. A reduction of venous flow velocity of approximately 50% occurs in the legs by weeks 25–29 of gestation. This lasts until approximately six weeks postpartum, at which time normal venous velocities return. Among pregnant and postpartum women, the left lower extremity is the most common site of DVT (82%). Anatomic reasons (compression of the left common iliac vein by the right common iliac artery which is accentuated by the enlarging uterus) have been postulated.

Endothelial damage in pelvic veins can occur at the time of delivery or from venous hypertension. Pelvic vein thrombosis, which is uncommon outside of pregnancy, accounts for 6–11% of DVT during pregnancy and the puerperium.

The most important reason for the increased risk of VTE during pregnancy is hypercoagulability. Normal pregnancy is accompanied by increased concentrations of factors VII, VIII, X, and von Willebrand factor and by pronounced increases in fibrinogen. Factors II, V, and IX are relatively unchanged. Free protein S, the active, unbound form, is decreased during pregnancy secondary to increased levels of its binding protein, the complement component C4b. Plasminogen activator inhibitor type 1(PAI-1) levels increase 5-fold. Levels of PAI-2, produced by the placenta, increase dramatically during the third trimester. Markers of thrombin generation such as prothrombin F1+2 and thrombin-antithrombin (TAT) complexes are increased. These changes, which may not completely return to baseline until more than 8 weeks postpartum begin with conception. As a result of these pro thrombotic changes, the incidence of pregnancy-associated VTE is 0.1%(,3) and in women with a previous VTE the risk of recurrence is 2–3%.

The hypercoagulability of pregnancy has likely evolved to protect women from hemorrhage at the time of miscarriage or childbirth. Indeed, in the developing world, the leading cause of maternal death is still hemorrhage, but in Western Europe and the United States, where hemorrhage is successfully treated or prevented, the leading cause of maternal death is thromboembolic disease.

Risk Factors for Thrombosis in Pregnancy

A previous unprovoked or oestrogen related (associated with oral contraceptive or pregnancy) venous thrombo embolism is one of the strongest risk factors(4) for antepartum and postpartum venous thromboembolism. A recent systematic review and meta-analysis of 1003 patients showed that around 1 in 20 women (4.27% (95% confidence interval 1.20% to 7.30%), P=0.001) will experience a recurrent venous thromboembolism in a subsequent pregnancy (5).Besides a history of thrombosis, the most important risk factor for VTE in pregnancy is thrombophilia. which is inherited and acquired. Inherited thrombophilias are present in at least 15% of the general population But approximately 50% of gestational venous thromboses are associated with inherited thrombophilias. Multiple studies have looked at the relationship between inherited thrombophilias and VTE. However, limitations in their methods have made it difficult to make accurate assessments of their risk. The highest risk has been found with homozygosity for factor V Leiden and homozygosity of the prothrombin G20210A variant (7). The more common inherited thrombophilias such as heterozygous factor V Leiden and heterozygous prothrombin G20210A variant were associated with lower risk (7). Deficiencies of endogenous anticoagulant such as antithrombin, protein C and protein S were associated with moderate risk (7). Given the background incidence of VTE during pregnancy of approximately 1/1,000 deliveries, it is clear that the absolute risk of VTE in women without a prior event remains modest for those women with the most common inherited thrombophilias. Acquired

thrombophilias have been less well studied, but persistent APLAs (lupus anticoagulants or anticardiolipin antibodies) are likely associated with an increased risk of pregnancy related VTE (7). The American College of Obstetricians and Gynecologists (ACOG) recommends testing for antiphospholipid antibodies and inherited thrombophilias if there is a prior history of VTE (8).

Other factor that increase the risk of VTE are family history, maternal age over 35years, obesity, null parity, multiple gestation, operative delivery, prolonged labour, gross varicose veins immobility after delivery, prolonged bed rest, air travel, dehydration, pre-eclampsia, major obstetric haemorrhage, intra venous drug abuse, hyperemesis gravidarum, Nephrotic syndrome, sickle cell disease, myeloproliferative disease, ovarian hyperstimulation, heart disease, lupus, anemia, diabetes, hypertension, and smoking.

Clinical assessment of pregnant women with suspected VTE

Clinical suspicion is essential for the diagnosis of VTE, because many of the classic signs and symptoms of VTE, including lower limb edema, tachycardia, dyspnea, tachypnea, are normally found in pregnancy. However, women with clinical findings suggestive of VTE should be further investigated to rule out VTE. Timely diagnosis of DVT is crucial because up to 24% of patients with untreated DVT will develop PE. The main clinical symptoms of DVT in pregnant women include discomfort (with a prevalence of 79% and 95% during pregnancy and postpartum, respectively), edema in the lower extremities (with a prevalence of 88% and 79% during pregnancy and postpartum, respectively)(9,10). Symptoms are more likely to be left sided. Other symptoms of DVT include difficulty in walking, in 21% of pregnant and 32% of post partum women . Erythema was reported in 26% of both groups. The incidence of isolated DVT in the iliac veins is higher during pregnancy .Abdominal pain, pain in the back, and swelling of the whole leg which is more common in isolated iliac DVTs, compared to other veins (11). It should be noted that in most cases, these symptoms are not examined due to overlap with discomfort and swelling in the leg; therefore, they do not give rise to the suspicion of isolated iliac DVT.

Sometimes the symptoms are so mild that they are not treated on time, rather they attract the attention of physicians with pain and edema all over the leg due to the spread of thrombosis in distal veins, such as the femoral vein (11). Therefore, DVT should be taken into account when dealing with pregnant women who suffer from such symptoms as edema and pain. Moreover, necessary diagnostic tests are needed to minimize the risk of embolic complications and post-thrombotic syndrome by timely identification and treatment. **Pulmonary Embolism** occurs when a blood clot that develops in a blood vessel in the body break loose, travel through the bloodstream, and block an artery in the lungs (12**).** Clinical feature of PE include breathlessness, dry cough,, chest discomfort, perspiration , cyanosis , haemoptysis, and sign of shock if embolism is massive.About 40-50% of PE episodes are asymptomatic without any symptoms during pregnancy. Nonetheless, due to the serious complications of PE, such as hemorrhage, renal failure, and maternal death, early diagnosis and treatment of PE is of utmost importance (13). Post-thrombosis syndrome refers to a set of symptoms, such as chronic leg pain, edema, and leg ulcers, which occur after thrombosis. According to a case report, the prevalence of the post-thrombotic syndrome is 42% in pregnant women with a history of DVT (14,15).

Increased thigh circumference is one of the most commonly used diagnostic tests and reliable symptoms to confirm DVT. The results of a meta-analysis showed that patients with a difference in thigh circumference leg diameters were twice as likely to develop DVT. Homan's sign (discomfort behind the knee upon forced dorsiflexion of the foot) is not reliable for the diagnosis of DVT.

Diagnosis of DVT in pregnancy

It is essential that objective diagnosis is sought in pregnant women with suspected VTE. If there is a delay in obtaining objective testing, anticoagulant therapy should be commenced until testing is available unless there are strong contraindications to its use **Compression duplex ultrasound** of the entire proximal venous system is considered the optimal first-line diagnostic test for DVT in pregnancy.(16) If the initial ultrasound shows an abnormality in the popliteal or femoral veins, the diagnosis of proximal DVT is confirmed and therapeutic anticoagulation should be used. An apparently normal ultrasound examination in a patient with significant symptoms and signs or risk factors for VTE does not exclude a calf DVT, so serial ultrasound examinations should be repeated on days 3 and 7**.** (16). If repeat testing is negative, anticoagulant treatment can be discontinued. For pregnant women with negative result from single or serial compression ultra sonography in whom iliac vein thrombosis is suspected pulsed Doppler, magnetic resonance venography, or conventional contrast venography should be considered.(16) The usefulness of **D-dimer** blood measurement is well established in diagnosis of venous thromboembolism in the non-pregnant population.(18) However, a physioalogical gradual increase,in D-dimer level is normal as gestation advances. D-dimer levels will be outside of the normal range at term and postpartum in most normal pregnancies. D-dimer levels also increase with complications such as preeclampsia and abruption, which are themselves associated with an increase in risk for VTE.(16,17) Further, false-negative D-dimer results have been reported in cases of VTE in pregnancy. In view of these issues and because D-dimer assays have not been evaluated in prospective management studies, it is practice to proceed directly to compression ultrasound venography in women with suspected DVT and to repeat this as required rather than use D-dimer measurements.

Wells' score

The most common clinical prediction rule Wells' score used for estimating the pre-test probability of DVT is not validated in pregnant women. It does not take into account pregnancy as a risk factor for DVT, nor the left sided predilection of pregnancy related DVT. Current evidence and guidelines do not support the use of pretest probability in the diagnosis of DVT in pregnancy.

Diagnosis of pulmonary thromboembolism

In the woman with a suspected PTE who is hemodynamically stable, **a chest X-ray** is valuable to identify other pulmonary diseases such as pneumonia or pneumothorax. Pregnant women in general have low rates of pre existing pulmonary disease and, more than 50% of cases, the chest X-ray will be normal. Non specific features of PTE on chest X-ray include atelectasis, effusion, focal opacities, regional oligemia, and pulmonary edema. The radiation dose to the fetus from a chest X-ray performed at any stage of pregnancy is negligible and this test should not be withheld from a pregnant woman with a potentially fatal condition. If the chest X-ray is abnormal with a high clinical suspicion of PTE, then ventilation perfusion scanning, the preferred objective test for suspected PTE in pregnancy, is unreliable and computed tomography pulmonary angiography (CTPA) should be Performed. It is important to consider the issue of radiation exposure in the context of diagnosis of PTE. Concerns over radiation exposure for the fetus are often cited as reasons for avoiding radiation-based investigations in pregnancy. However, the tests used most commonly are not associated with high levels of fetal exposure. In addition, the context of a potentially fatal disorder for the mother and the fetus if the event is antenatal should be considered.

CTPA is associated with less radiation exposure to the fetus than ventilation/perfusion (V/Q) lung scans in all trimesters of pregnancy. It has been estimated that the risk of fatal cancer up to the age of 15 years is 1 in 1 000000 after in utero exposure to CTPA and 1 in 280000 after a perfusion scan. Perhaps of more concern is that although CTPA is associated with a lower dose of radiation for the fetus than a V/Q scan, it exposes the mother to a relatively high radiation dose: as much as 20 mGy to the thorax and in particular breast tissue. It has been calculated that this is associated with a significant increase in the lifetime risk of breast cancer, because breast tissue is especially sensitive to radiation exposure during pregnancy. Pulmonary angiography carries the highest radiation exposure (at least 0.5 mSv to the fetus and 5-30 mSv to the mother). To summarize, the main techniques for objective diagnosis of PTE are V/Q lung scans or CTPA. The choice may be restricted by local availability and guidelines**.** Where available, V/Q scans are generally preferred because of the lower radiation dose to the mother and the low incidence of comorbid pulmonary problems that often reduce the value of such scans in the non-pregnant patient.. In the non pregnant woman, CTPA is usually the first-line investigation for non massive PTE due to better sensitivity and specificity than the V/Q lung scan. It can also identify other pathology such as aortic dissection, but, as noted, the radiation dose is an important concern when only approximately 5% of such investigations will have a positive result.

When the chest X-ray is normal, then to Doppler ultrasound venography because a diagnosis of DVT may confirm PTE indirectly and anticoagulant therapy is the same for both conditions. Therefore further pulmonary investigation may not be necessary, thus avoiding the radiation doses, particularly those associated with CTPA, for the mother and fetus.

Management of VTE during pregnancy

Anticoagulation is the mainstay of treatment. In the initial assessment of the pregnant patient before commencing therapeutic

anticoagulation for VTE, complete blood count, coagulation screen, urea, electrolytes, and liver function tests should be performed to exclude renal or hepatic dysfunction, which are risk factors for anticoagulant therapy. Thrombophilia screen should not be performed because many factors are disturbed by both pregnancy and the presence of thrombus and because the results will not alter the acute management of VTE.

Anticoagulants in pregnancy

Unique aspects of anticoagulation in pregnancy include both maternal and fetal issues. The main therapeutic option are LMWH, UFH, and oral anticoagulant. Altohgh for many years the standard anticoagulant used in pregnancy and postpartum was UFH, but current guide lines recommend LMWH as the first choice medication for VTE treatment and prophylaxis in pregnancy. Advantages of LMWH are better bioavailability, predictable pharmacokinetics, no need of monitorning and lower rates of adverse effects, including heparin-induced thrombocytopenia, symptomatic osteoporosis, bleeding, and allergic reactions. In pregnancy a systemic review concluded that LMWH is safe and effective and there is no evidence to favour one LMWH over another. In non pregnant women, randomized trials have shown LMWHs to have equivalent or better effectiveness compared with UFH. Excretion in breast milk is minimal. There are now substantial data from randomized controlled trials in non pregnant patients confirming that LMWH is more effective than vitamin K antagonists in preventing recurrent VTE and post thrombotic syndrome without increasing the risk of serious bleeding events(19,20).

However in pregnancy treatment with LMWH is more difficult. Maternal weight gain and increased renal clearance of LMWH during pregnancy has led to the suggestion that the dose of LMWH should be adjusted over the course of pregnancy however this remains controversial. Routine laboratory monitoring of dose of LMWH is not warranted. The activated partial thromboplastin time which is useful in monitoring UFH is not changed significantly in patients on LMWH and therefore can not be used to assess response to therapy. Anti-Xa levels need only be obtained in patients who are at extremes of weight (< 55 kg or >90 kg) or have abnormal renal function. If LMWH therapy requires monitoring the aim is to achieve a peak anti factorXa level of 0.6-1.0 unit/ml if a twice daily regimen is used and slightly higher if a once daily regimen is chosen. Routine platelet count monitoring for evidence of HIT is not required in pregnant patients who have received only LMWH. However, if the patient is receiving LMWH after first receiving UFH or if she has received UFH in the past, making HIT more likely, the platelet count should be monitored every other day from days 4-14 or until LMWH is stopped, whichever occurs first.

Therapeutic Dosing of Heparin in Pregnancy are

LMWH (enoxaparin) 1 mg/kg subcutaneously every 12 hours UFH 5000IU iv loading dose followed by continuous iv infusion for a total of at least 30000IU over 24 hours. OR 10000IU subcutaneously every 8 hours OR 20000IU sub cutaneously every 12 hours, APTT should be monitored and the dose should be adjusted to maintain APTT 1.5-2 times higher than the control.

Warfarin should be avoided during pregnancy. It crosses the placenta and increases the risk of miscarriage, stillbirth, embryopathy (nasal hypoplasia or stippled epiphyses), central nervous system abnormalities, and maternal and fetal hemorrhage. However it can be used postpartum if required because there is no significant excretion in breast milk.

Fondaparinux is a new selective factor Xa inhibiter used for thrombo prophylaxis. As there is limited high quality evidence for the use in pregnancy and lactation, its use is recommended only when LMWH cannot be used, such as in cases of heparin allergies(21). The safety and efficacy of direct thrombin inhibitors (such as dabigatran) and factor Xa inhibitors (such as rivaroxaban) for treating venous thromboembolism in pregnancy have yet to be determined, and their use is not recommended during pregnancy or breast feeding(21).

With life-threatening PE, Intravenous UFH, thrombolytic therapy, percutaneous catheter thrombus fragmentation, or surgical embolectomy may be used, depending on local resources. Intravenous UFH remains the preferred treatment in massive PTE because of its rapid effect and our extensive experience of its use in this situation. This is a situation in which there is a strong case for considering systemic thrombolytic therapy because anticoagulant therapy will not reduce the obstruction of the pulmonary circulation. An infusion of UFH can be given after thrombolytic therapy. There is growing evidence(22) on the use of thrombolytic agents in pregnancy. Streptokinase, and probably other thrombolytic agents as well, do not cross the placenta. No maternal deaths associated with thrombolytic therapy have been reported, and the maternal bleeding complication rate is approximately 6%, which is consistent with that in nonpregnant patients receiving thrombolytic therapy. Most bleeding events occur around the catheter and puncture sites and, in pregnant women, in the genital tract. If the patient is not suitable for thrombolysis or is moribund, cardiothoracic surgeons should be consulted urgently for consideration of emergency thoracotomy.

Graduated elastic compression stockings

These are thought to be effective and are recommended as adjuvant therapy for reducing DVT related pain and oedema(21,23). However, a recent meta-analysis of six randomised controlled trials involving 1462 non-pregnant patients revealed that the use of compression stockings was not associated with prevention of post-thrombotic syndrome as compared with controls (odds ratio 0.56 (95% confidence interval 0.27 to 1.16); 36% (269/739) *v* 45% (322723), P=0.12(24).

Inferior vena cava filters

Clinical guidelines and a recent systematic review of 124 pregnancies advise that inferior vena cava filters in pregnancy should be used only temporarily and for the following indications.**1.** Acute venous thromboembolism when anticoagulation is contraindicated**. 2**. The development of acute DVT close to the time of delivery (to prevent risk of pulmonary embolism) **3**.The recurrence of venous thromboembolism despite adequate anticoagulation(21,23). Inferior vena cava filters are usually placed via an intravenous route by an interventional radiologist and serve as a mechanical obstacle to clot dissemination. A single centre, retrospective study of 70 patients showed similar rates of complications for placement of the filter above the renal veins (where there is potential for developing renal vein thrombosis) as for placement below the veins, suggesting that such a procedure can be safely performed in experienced hands(25).

Management during labour and delivery:

The risks of anticoagulant-related maternal hemorrhage and epidural hematoma in women using anticoagulants at the time of delivery can be minimized with careful planning. The plan for delivery should take account of obstetric, hematological and anesthetic issues. In order to avoid an unwanted anticoagulant effect during delivery (especially with neuraxial anesthesia), women receiving therapeutic subcutaneous UFH or LMWH should generally have a planned delivery. Twice daily therapeutic doses of subcutaneous UFH or LMWH should be discontinued 24 hours before induction of labor or cesarean section, while patients taking once daily therapeutic doses of LMWH should take only 50% of their dose on the morning of the day prior to delivery. Pregnant women receiving LMWH or UFH should be instructed to withhold their injection if they believe they have entered labor spontaneously (either contraction or rupture of the membranes). If spontaneous labor occurs in fully anticoagulated women, neuraxial anesthesia should not be used. In case of an emergency cesarean section this will be done with general anaesthesia. Where the level of anticoagulation is uncertain and where laboratory support allows for rapid assessment of heparin activity, testing can be considered to guide anesthetic and surgical management. If bleeding occurs that is refractory to management of an obstetric cause protamine sulphate may provide partial neutralization.

Women with a very high risk for recurrent VTE (e.g. proximal DVT or PE within 2-4 weeks) can be switched to therapeutic intravenous UFH, which is then discontinued 4-6 hours prior to the expected time of delivery or epidural insertion. In exceptional cases for instance in such women who also have a contraindication to anticoagulation transiently(need for a cesarian section) the use of a temporary inferior vena caval filter may be considered.

Management during Postpartum and duration of anticoagulant treatment

Anticoagulation should be restarted after delivery as soon as possible, depending on the amount of estimated vaginal blood loss and the type of delivery. Generally, restarting therapeutic dose anticoagulation 6 to 24 hours after delivery is feasible, but this period should be longer if hemostasis is not adequate. If the anticipated interval is >24 hours because of bleeding, a prophylactic dose, 24 hours after delivery should be considered.

In most women in whom the intention is to stop anticoagulation 6 weeks after delivery, continuation with therapeutic-dose LMWH until 6 weeks postpartum (or until discontinuation if VTE occurred in late pregnancy) is the most practical option. In women who will continue

anticoagulation indefinitely and who plan to breastfeed their babies, we first restart LMWH and initiate the first loading dose of VKAs at least 1 day later. LMWH can be discontinued after at least 3 days of VKAs and as soon as the international normalized ratio is >2.0 . It is important to reassure women that they can breastfeed during use of either LMWH or VKAs, particularly nonlipophilic types such as acenocoumarol and warfarin .

We treat women with therapeutic-dose LMWH until 6 weeks postpartum and for a minimum duration of 3 months(21) If the pregnancy related VTE was the first episode, we advise discontinuation of anticoagulation after 3 months total duration or after 6 weeks postpartum. In the recent European Society of Cardiology 2019 PE guideline, pregnancy is considered a minor transient risk factor leading to an intermediate risk (3% to 8% per year) of recurrence after discontinuation of anticoagulants, with a recommendation to consider extending anticoagulation in women with pregnancy-related VTE(27).

Prevention of thrombosis in pregnancy

Ideally, evaluation of the woman who may require anticoagulation during pregnancy should occur before conception,or at least early in pregnancy. Women who have not had a complete thrombophilia work-up may be tested. Although the results of thrombophilia testing will not alter the general recommendation for anticoagulation in pregnancy. Women with conditions that place them at a high risk of maternal mortality because of thrombosis may best be counseled against pregnancy. These conditions include mechanical heart valves, chronic thromboembolic pulmonary hypertension, a history of recurrent thrombosis while fully anticoagulated, and a history of myocardial infarction. Women who are already on full anticoagulation will likely need to continue. They should be counseled about the harmful effects of warfarin on the fetus and offered the opportunity to be converted to low-molecular-weight heparin before conception. In the antiphospholipid syndrome, several studies have demonstrated that anticoagulation improves the outcome of pregnancy **The American college of chest physician (ACCP) and ACOG** recommend prophylaxis with LMWH for all pregnant patients with a previous history of venous thrombosis, and documented thrombophilia ,as well as those with a history of multiple >2 episode of DVT(28,29). For patients with history of a single idiopathic DVT but no thrombophilia or those with a transient risk factor that has resolved the recommendation from two agencies is for close clinical surveillance during pregnancy and prophylaxis postpartum(28,29) For pregnant patients with a heritable or acquired thrombophilia but no prior history of venous thrombosis the recommendation of the ACCP is not to routinely use prophylaxis during pregnancy but to perform an individual risk assessment however post partum anticoagulation is recommended.(28) The ACOG recommends prophylaxis for all women with documented thrombophilia during pregnancy and postpartum(28) but the ACCP recommends anti parum and postpartum prophylaxis with anti thromboin deficiency(28).

Prophylactic Dosing of Heparin in pregnancy

LMWH	(50 to 90 kg)	40 mg SC daily
	<50 kg	20 mg SC daily
	>90 kg	40 mg SC every 12 hours
UFH	First trimester	5000 IU SC twice daily
	Second trimester	7500 IU SC twice dail
	Third trimester	10000 IU SC twice daily

Low-dose aspirin (75 to 81 mg) is sometimes used for women with an increased risk of thrombosis that does not meet the threshold for prophylactic heparin (e.g., a woman with a mild thrombophilia and no history of VTE(29). Due to the lack of studies of aspirin for this indication, such treatment is of unknown benefit; however, low-dose aspirin is safe to use during pregnancy(31).

Acknowledgements

No financial support for this work.

Conflicts of interest

None

Abbreviation=

Venous thromboembolism(VTE), Deep venous thrombosis (DVT), Pulmonary embolism(PE), Low molecular weight heparin(LMWH), Unfractioned heparin(UFH), Computed tomography pulmonary angiography(CTPA)

REFERENCES

1. KnightMTD, Kenyon S, Shakespeare J, Gray R, Kurinczuk JJ, eds, on behalf of MBRRACE-UK. *Saving lives, improving mothers' care—surveillance of maternal deaths in the UK 2011-13 and lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-13*. National Perinatal. lEpidemiology Unit, University of Oxford, 2015.
2. James AH, Jamison MG, Biswas MS, Brancazio LR, Swamy GK, Myers ER. Acute myocardial infarction in pregnancy: a United States population-based study. *Circulation*. 2006;113:1564 –1571.
3. Heit JA, Kobbervig CE, James AH, Petterson TM, Bailey KR, Melton LJ, III. Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. *Ann InternMed*. 2005;143:697–706. James Venous Thromboembolism in Pregnancy *329* Downloaded from http://ahajournals.org by on January 5, 2021
4 Greer IA. Pregnancy complicated by venous thrombosis. *N Engl J Med* 2015;357:540-7. doi:10.1056/NEJMcp1407434 pmid:26244307
5 Kourlaba G, Relakis J, Kontodimas S, Holm MV, Maniadakis N. A systematic review and meta-analysis of the epidemiology and burden of venous thromboembolism among pregnant women. *Int J Gynaecol Obstet* 2016;357:4-10. doi:10.1016/j.ijgo.2015.06.054 pmid:26489486.
6 Bates SM, Middeldorp S, Rodger M, James AH, Greer I. Guidance for the treatment and prevention of obstetric-associated venous thromboembolism. *J Thromb Thrombolysis* 2016;357:92-128. doi:10.1007/s11239-015-1309-0 pmid:26780741. 120895 pmid:23318405.
7. Bates SM, Greer IA, Middeldorp S. Venous Thromboembolism, thrombophilia, antithrombotic therapy and pregnancy: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence- based clinical practice guidelines. Chest 2012;141:e691s-736s.
8. Bates SM, Middeldorp S, Rodger M. Guidance for the treatment and prevention of obstetric associated venous thromboembolism. J Thromb Thrombolysis 2016;41:92-128.
9. Verma V, Mohil R, Kumar S, Gupta A. Comparing ultrasound guided foam sclerotherapy with surgical treatment in patients of varicose veins. Int Surg J 2016;3(4):2239-45. Link
10. Hull CM, Rajendran D, Barnes AF. Deep vein thrombosis and pulmonary embolism in a mountain guide: awareness, diagnostic challenges, and management considerations at altitude. Wilderness Environ Med 2016;27(1):100-6. PMID: 26723546
11. Diagn Ther 2017;7(Suppl 3): 45. Devis P, Knuttinen MG. Deep venous thrombosis in pregnancy: incidence, pathogenesis and endovascular management. Cardiovasc S309-19. PMID: 29399535
12. Goldhaber SZ, Bounameaux H. Pulmonary embolism and deep vein thrombosis. Lancet 2012;379(9828):1835-46. PMID: 22494827
13. Khan F, Vaillancourt C, Bourjeily G. Diagnosis and management of deep vein thrombosis in pregnancy. BMJ 2017;357:j2344. PMID: 28566284
14. Greer I, Thomson AJ. Green-top Guideline No. 37b-thromboembolic disease in pregnancy and the puerperium: acute management. London: Royal College of Obstetricians and Gynaecologists; 2015. Link
15. Wik H, Jacobsen A, Sandvik L, Sandset PM. Prevalence and predictors for post.thrombotic syndrome 3 to 16 years after pregnancy.related venous thrombosis: a population.based, cross.sectional, case.control study. J Thromb Haemost 2012;10(5):840-7. PMID: 22452811
16. Bates SM, Jaeschke R, Stevens SM et al Diagnosis of DVT.*Chest.* 2012;141(2 Suppl):e351S-e418S.
17. Bates SM, Greer IA, Middeldorp S, Veenstra DL, PrabulosAM, Vandvik PO. VTE, thrombophilia, antithrombotic therapy,and pregnancy. *Chest*. 2012;141(2 Suppl):e691S-e736S.
18. Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-dimer in the diagnosis ofsuspected deep-vein thrombosis.
19. Bates SM, Greer IA, Middeldorp S, Veenstra DL, Prabulos AM, Vandvik PO. VTE, thrombophilia, antithrombotic therapy, and pregnancy. *Chest*. 2012;141(2 Suppl):e691S-e736S.
20. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy forVTE disease: antithrombotic therapy and prevention of thrombosis. American College of Chest Physicians evidencebased clinical practice guidelines. 9th Ed. *Chest.* 2012;141(2 Suppl):e419S-e494S.
21 Green-top Guideline No. 37b — thromboembolic disease in pregnancy and the puerperium: acute management. London:*Royal College of Obstetricians and Gynaecologists, April2015(www. rcog. org. uk/ globalassets/ documents/ guidelines/ gtg- 37b. pdf)*.
22. Holden EL, Ranu H, Sheth A, Shannon MS, Madden BP. Thrombolysis for massive pulmonary embolism in pregnancy– a report of three cases and follow up over a two year period. *Thromb Res.* 2011;127(1):58-59.
23. Greer IA. Pregnancy complicated by venous thrombosis. *N Engl J Med* 2015;357:540 7 doi:10.1056/NEJMcp1407434 pmid:26244307.
24. Subbiah R, Aggarwal V, Zhao H, Kolluri R, Chatterjee S, Bashir R. Effect of compression stockings on post thrombotic syndrome in patients with deep vein thrombosis: a meta-analysis of randomised controlled trials. *Lancet Haematol* 2016;357:e293-300.. doi: 10.1016/S2352-3026(16)30017-5 pmid:272640
25. Kalva SP, Chlapoutaki C, Wicky S, Greenfield AJ, Waltman AC, Athanasoulis CA. Suprarenal inferior vena cava filters: a 20-year single-center experience. *J Vasc Interv Radiol* 2008;357:1041-7. doi:10.1016/j.jvir.2008.03.026 pmid:18589318.
26. Harris SA, Velineni R, Davies AH. Inferior vena cava filters in pregnancy: a systematic review. *J Vasc Interv Radiol* 2016;357:354-60.e8.. doi:10.1016/j.jvir.2015.11.024 pmid: 26746328.
27. Konstantinides SV, Meyer G, Becattini C, et al; The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): the task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Respir J. 2019;54(3): 1901647.
28. Bates SM, Greer IA, Middeldorp S. Venous Thromboembolism, thrombophilia, antithrombotic therapy and pregnancy: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence- based clinical practice guidelines. Chest 2012;141:e691s-736s
29. Bates SM, Middeldorp S, Rodger M. Guidance for the treatment and prevention of obstetric associated venous thromboembolism. J Thromb Thrombolysis 2016;41:92-128.
30. Nelson-Piercy C. Thromboprophylaxis during pregnancy, labour and after vaginal delivery. Royal College of Obstetricians and Gynaecologists, 2004. Guideline no. 37. http://www.rcog.org.uk/resources/Public/pdf/ Thromboprophylaxis_no037.pdf. Accessed February 23, 2008.
31. Bates SM, Greer IA, Hirsh J, Ginsberg JS. Use of antithrombotic agents during pregnancy: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest.* 2004;126(3 suppl):627S-644S.