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Assessment of Risk Factors and Risk Stratification for Venous Thromboembolism (VTE) in Pregnancy: A Study Conducted in A Tertiary Level Hospital

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ABSTRACT

Background: *Pregnancy itself is one of the most provoking factors for the development of venous thromboembolism (VTE) with an incidence of 5-12 per 10,000 pregnancies and 3-7 per 10,000 deliveries postpartum. As a continuum of care, GTG 37a (RCOG) guideline has also proposed careful review of post-partum risk factors. The objective of this study is to apply the documented assessment scoring system according to the RCOG Guideline 37a mainly based on clinical risk factors to detect and stratify antenatal patients according to risk of VTE and to institute appropriate preventive intervention.* ***Method:*** *This is a prospective cross-sectional study involving 50 antenatal/pregnant women randomly selected over a period of 6 months undergoing antenatal care in Bangladesh Medical College. For the assessment of risk of VTE in these patients, RCOG guideline 37a risk assessment tool was used. A score ranging from 0 to 4 or more was objectively found among these patients. Based upon the score, each patient was categorized as high risk, intermediate risk, and lower risk. Then thromboprophylaxis with LMW (Low Molecular Weight) Heparin (Enoxaparin) and/ or mobilization was advised for variable durations depending upon the timing of presentation and scores. The patients were reassessed after admission and post-delivery using the same tool for change in transient factors and advised according to the score.* ***Results:*** *Among the fifty antenatal patients, RCOG guideline 37a risk assessment tool revealed 1 patient scored 0, 18 patients scored 1, 16 scored 2, 9 scored 3, 6 scored 4. Those who scored 0 and 1 (19 patients) required no thromboprophylaxis. The sixteen patients with a score of two were advised for post-natal thromboprophylaxis with Enoxaparin for 10 days. They were reassessed/ re-scored in the postnatal period for VTE risk and 5 of these patients down scored to one. There by they were judged as not to require post-natal thromboprophylaxis and were advised early mobilization and avoidance of dehydration. The remaining 11 patients with a score of two on postnatal review were put on LMW Heparin (Enoxaparin) at a dose of 20 mg daily subcutaneous (s.c.) (<50 kg), 40 mg daily (50-90 kg), 60 mg daily in 2 divided dose (91-130 kg) for 10 days.* ***Conclusion:*** *LMW heparin in pregnancy and post-partum in prophylactic and therapeutic doses according to body weight was found to be safe and cost-effective.*

Keywords: *Venous thromboembolism, Assessment in pregnancy, LMW Heparin.*

Introduction:

Venous thromboembolism (VTE) which includes Deep vein thrombosis and pulmonary embolism is the third most common cardiovascular disorder after ischemic heart attack and stroke.[1,2] The death of a mother either in pregnancy or post-delivery is a devastating obstetric complication. In 2017 globally, approximately 810 women died every day from preventable causes related to pregnancy and childbirth. In 2015, there were an estimated 303,000 maternal deaths throughout the world, which summated to a maternal mortality ratio (MMR) of 216 per 100,000 live births. Ninety-four percent of all maternal deaths occurred in low and lower middle-income countries, whereas high-resource settings with an MMR of 12 per 100,000 live births are still striving to achieve further reduction of MMR.[3] Among the preventable causes of maternal mortality, VTE/PE stands out. However, it is difficult to prove cause and effect since VTE, and especially death due to VTE is relatively uncommon. Thus, properly designed trials are difficult to conduct, and recommendations are largely based on expert opinion and theoretical benefits, rather than high-quality empirical evidence.[4,5] Implementation of low-cost clinical risk scoring systems for risk stratification is highly justified in our country's context. Bangladesh is passing through the phase II in the Obstetric transition model, approaching the Phase III with a high MMR. Obesity, advanced maternal age, caesarean delivery, and co-morbid conditions such as diabetes mellitus and hypertension are increasingly prevalent among the pregnant population going through the Phase III of obstetric transition and are now considered as risk factors for VTE. The maternal mortality rate of Bangladesh for 2017 was 173, a 6.99% decline from 2016; for 2016 was 186, a 7% decline from 2015; for 2015 was 200, a 6.54% decline from 2014 and for 2014 was 214, a 5.73% decline from 2013. Haemorrhage, hypertensive disorders in pregnancy and sepsis are the main contributing factors of maternal death. Pulmonary embolism as a consequence of DVT is contributing to death reported in intensive care units/ critical care obstetric units. Often overlooked as "the oedema in pregnancy" DVT is discovered later in patients with clinically suspected PE with disastrous outcomes. (Figure: 1,2,3) Thromboembolic disease is linked with both adverse maternal & foetal/neonatal outcome. (Lippincott) Pregnant women are 4-5 times more likely to experience a VTE than age matched non-pregnant women. The absolute incidence of VTE in pregnancy varies between 0.025 & 0.1%. Majority of VTEs occur antenatally (around 65%) occurring prior to 15 weeks gestation; hence the need for early risk identification (even pre-pregnancy) & thromboprophylaxis.[6] Approximately 80% of VTEs in pregnancy are DVT & 20% are PE. Caesarean delivery imparts a 3-5 times greater risk than a vaginal delivery.[7] Therefore, in the context of our country, risk stratification of VTE in pregnancy can contribute to reducing disastrous maternal and perinatal outcome. An apparent 50% reduction in maternal deaths due to VTE from 2006 to 2008 compared to 2003 to 2005 in the UK works as evidence .[4,5,7] Recent data from the UK show that fatal PE can occur in the antepartum period and after vaginal delivery and caesarean section.[7] Therefore preventive strategies must focus on both antepartum and postpartum periods and after both vaginal and caesarean delivery. Institution of LMW Heparin according to the risk score can reduce the risk of serious VTE. LMW heparin provides advantages over heparin in that it has better bioavailability and longer half-life, simplified dosing, predictable anticoagulant response, lower risk of Heparin-induced -thrombocytopenia (HIT), and lower risk of osteoporosis. However, if monitoring is necessary

particularly in case of ≥Class II obesity, renal insufficiency and presence of mechanical heart valve anti-factor Xa levels must be measured because LMWH preparations have little effect on activated Partial Thromboplastin Time (aPTT).

Materials and Methods:

This is a prospective cross-sectional study involving 50 antenatal women randomly selected over a period of 6 months treated in Bangladesh Medical College. For the assessment of risk of VTE in these patients RCOG guideline 37a risk assessment tool was used.[1] (Appendix 1) A score ranging from 0 to 4 or more was objectively found among these patients. Based upon the score, each patient was categorized as high risk, intermediate risk, and lower risk. Then thromboprophylaxis was advised for variable durations depending upon the timing of presentation and scores. The patients were reassessed after admission and post-delivery using the same tool for change in transient factors and advised according to the score. Addressing this risk stratification tool resulted in improved patient care and counselling, the pregnancy outcome of each case was followed up.

Results:

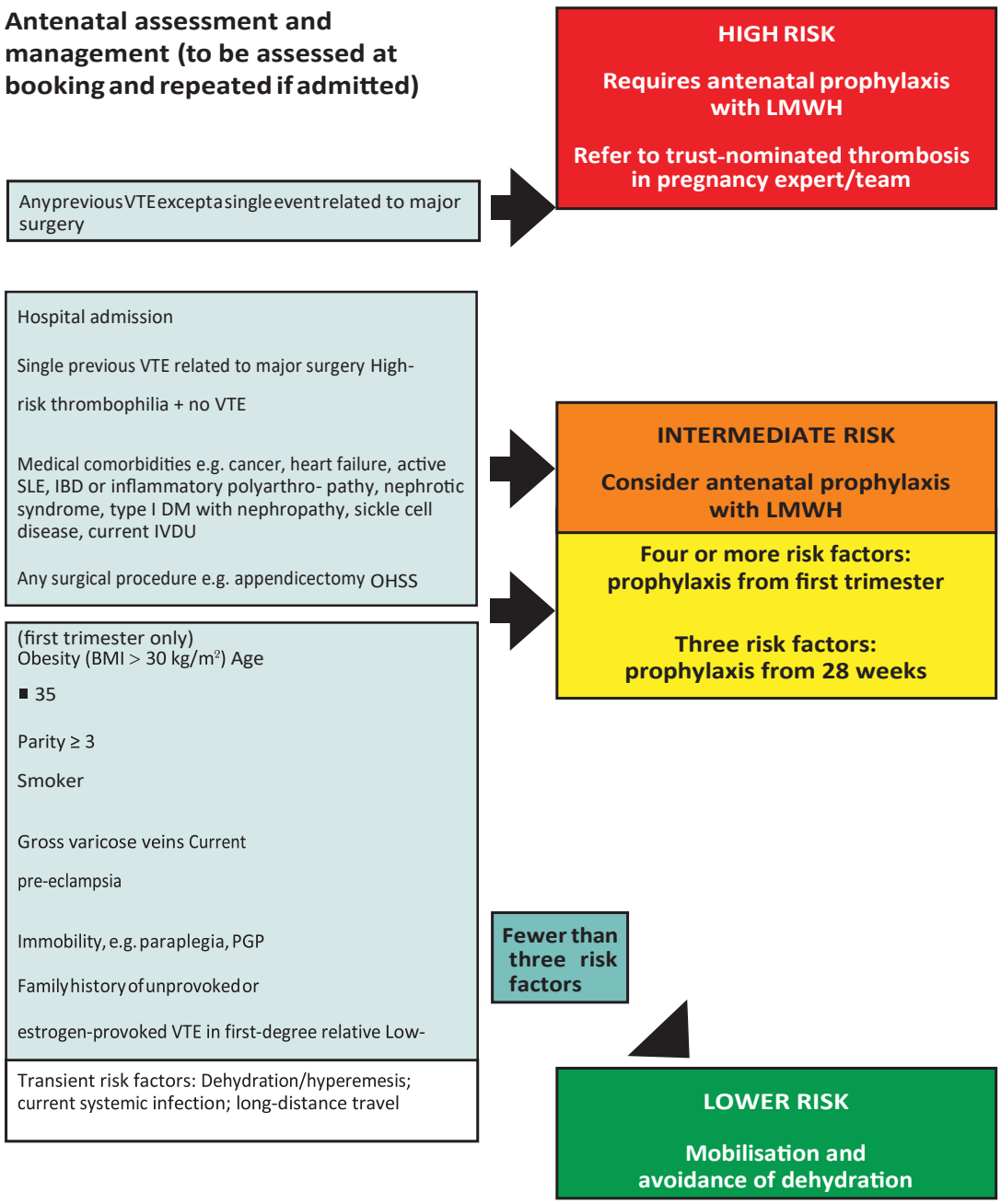
Among the fifty antenatal patients, one patient scored zero. Eighteen patients scored one. Sixteen patients scored two. Nine patients scored three. Six patients scored four. Those who scored 0 and 1 (19 patients) required no thromboprophylaxis. The sixteen patients with a score of two were advised for post-natal thromboprophylaxis with Low molecular weight Heparin (LMWH) for 10 days. They were re-scored after delivery for VTE risk. Five of these patients down scored to one and thereby assessed as not to require post-natal thromboprophylaxis. They were counselled about early mobilization and avoidance of dehydration. The remaining 11 patients with a post-natal score of two were put on Inj. Enoxaparin at a dose of 20 mg daily s.c. (<50 kg), 40 mg daily (50-90 kg), 60 mg daily (91-130 kg) for 10 days.

Details of patients with scoring profile: Antenatal thromboprophylaxis was started for nine antenatal patients who scored 3 and presented at 28 weeks and beyond. Only one patient presented at 31 weeks with a BMI 31.7 and para 4. The remaining eight patients were pregnant for 36+ weeks and beyond. All nine patients were put on 40 mg Enoxaparin daily for the rest of pregnancy based on their body weight. All these patients had a post-natal reassessment and found to have a score of ≥ 2. They were advised 10 days postnatal therapy with LMWH.

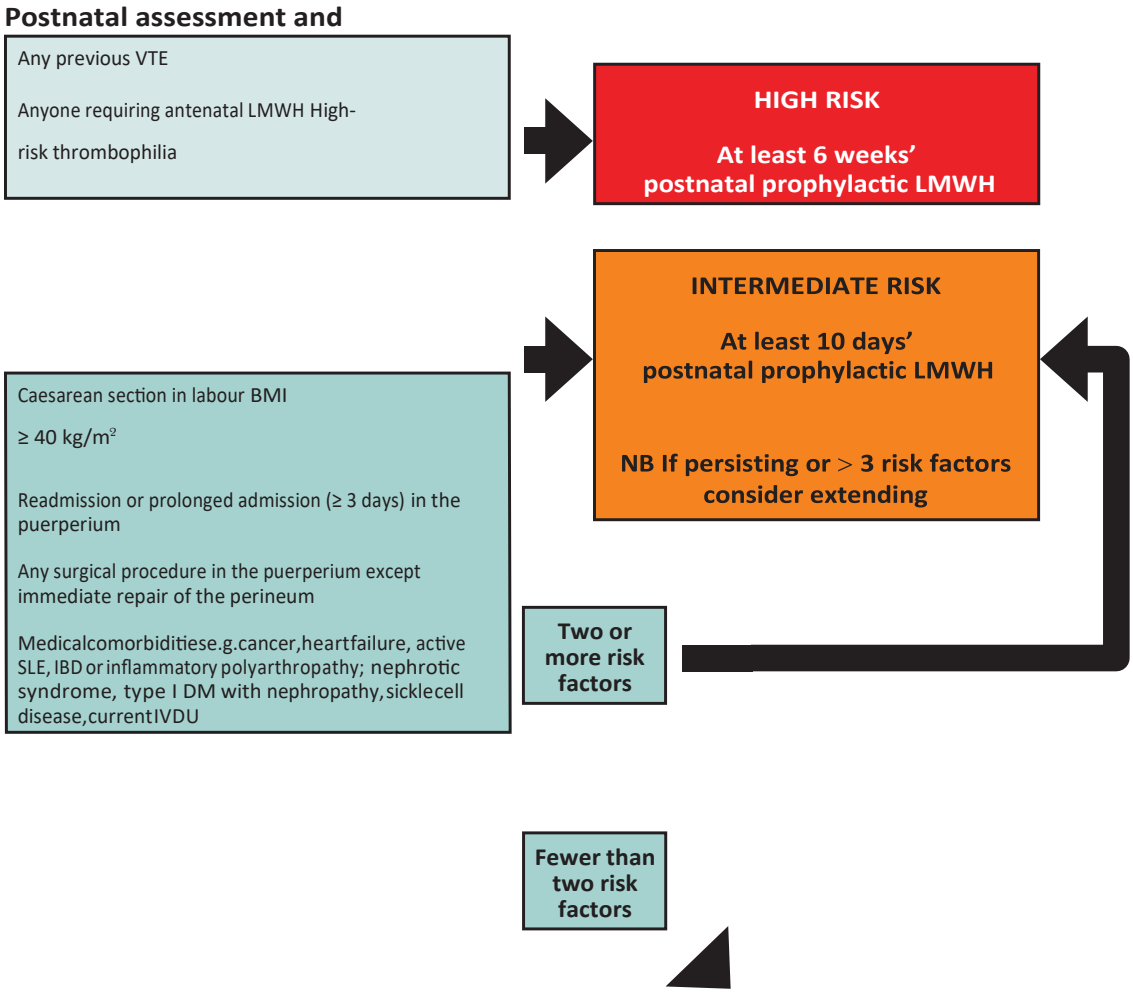
Among the six antenatal patients who scored 4, two patients presented at 32+ weeks; of them, one suffered from active Systemic Lupus Erythematosus (SLE) and the second patient was pregnant with twins and diagnosed as pre-eclampsia with severe features and had conceived upon Artificial reproductive technique (ART). The remaining 4 patients presented at 36+weeks of pregnancy and beyond. All these 6 patients were put on antenatal thromboprophylaxis at a dose 40 mg daily (bearing BMI ranging from 26.72 to 30.3) and 60 mg daily in 2 divided doses (bearing BMI of 42.96). These patients on antenatal LMWH were advised to continue the prophylaxis up to 38 completed weeks; in case of spontaneous onset of labour or caesarean section for emerging obstetric indication, the dosing was modified by simple omission of that day's LMWH as the half-life of LMWH is only3 to 6 hours after subcutaneous injection. No patients experienced post–partum haemorrhage either after vaginal delivery or caesarean section. These patients were reassessed post-natal and 2 patients scored ≥2. They were advised 10 days LMW Heparin prophylaxis along with Anti-Embolism Socks.

No patients were screened for hereditary thrombophilia or had any previous history of arterial or venous thrombosis except for one patient who was a known case of SLE.

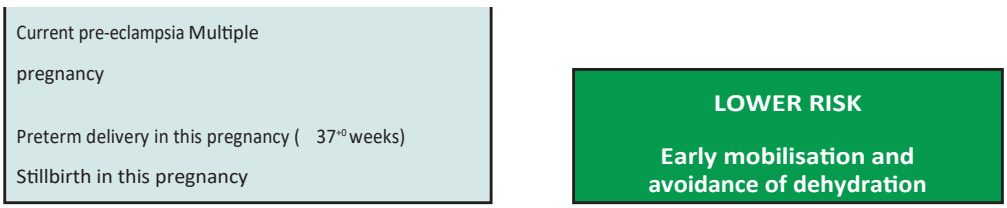
Obstetric thromboprophylaxis risk assessment and management[1]



APL = antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, $_{2}$-glycoprotein 1 antibodies); ART = assisted reproductive technology; BMI based on booking weight; DM = diabetes mellitus; FHx = family history; gross varicose veins = symptomatic, above knee or associated with phlebitis/oedema/skin changes; high-risk thrombophilia = antithrombin deficiency, protein C or S deficiency, compound or homozygous for low-risk acquired; VTE = venous thromboembolism.



thrombophilias; IBD = inflammatory bowel disease; immobility = ≥ 3 days; IVDU = intravenous drug user; IVF = in vitro fertilisation; LMWH = low-molecular-weight heparin; long-distance travel = 4 hours; low-risk thrombophilia = heterozygous for factor V Leiden or prothrombin G20210A mutations; OHSS = ovarian hyperstimulation syndrome; PGP = pelvic girdle pain with reduced mobility; PPH = postpartum haemorrhage; thrombophilia = inherited or



Antenatal and postnatal prophylactic dose of LMWH

Weight 50 kg = 20 mg enoxaparin/2500 units dalteparin/3500 units tinzaparin daily
Weight 50–90 kg = 40 mg enoxaparin/5000 units dalteparin/4500 units tinzaparin daily
Weight 91–130 kg = 60 mg enoxaparin/7500 units dalteparin/7000 units tinzaparin daily
Weight 131–170 kg = 80 mg enoxaparin/10000 units dalteparin/9000 units tinzaparin daily
Weight 170 kg = 0.6 mg/kg/day enoxaparin/ 75 u/kg/day dalteparin/ 75 u/kg/day tinzaparin

Appendix III: Risk assessment for venous thromboembolism (VTE)

- If total score ≥ 4 antenatally, consider thromboprophylaxis from the first trimester.
- If total score 3 antenatally, consider thromboprophylaxis from 28 weeks.
- If total score ≥ 2 postnatally, consider thromboprophylaxis for at least 10 days.
- If admitted to hospital antenatally consider thromboprophylaxis.
- If prolonged admission (≥ 3 days) or readmission to hospital within the puerperium consider thromboprophylaxis.

For patients with an identified bleeding risk, the balance of risks of bleeding and thrombosis should be discussed in consultation with a haematologist with expertise in thrombosis and bleeding in pregnancy.

Risk factors for VTE

Pre-existing risk factors	Tick	Score
Previous VTE (except a single event related to major surgery)		4
Previous VTE provoked by major surgery		3
Known high-risk thrombophilia		3
Medical comorbidities e.g. cancer, heart failure; active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug user		3
Family history of unprovoked or estrogen-related VTE in first-degree relative		1
Known low-risk thrombophilia (no VTE)		1[a]
Age (> 35 years)		1
Obesity		1 or 2[b]
Parity ≥ 3		1
Smoker		1
Gross varicose veins		1
Obstetric risk factors		
Pre-eclampsia in current pregnancy		1
ART/IVF (antenatal only)		1
Multiple pregnancy		1
Caesarean section in labour		2
Elective caesarean section		1
Mid-cavity or rotational operative delivery		1
Prolonged labour (> 24 hours)		1
PPH (> 1 litre or transfusion)		1
Preterm birth < 37^{+0} weeks in current pregnancy		1
Stillbirth in current pregnancy		1
Transient risk factors		
Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation		3
Hyperemesis		3
OHSS (first trimester only)		4
Current systemic infection		1
Immobility, dehydration		1
TOTAL		

1. **Abbreviations:** ART assisted reproductive technology; IVF in vitro fertilisation; OHSS ovarian hyperstimulation syndrome; VTE venous thromboembolism.

[a] If the known low-risk thrombophilia is in a woman with a family history of VTE in a first-degree relative postpartum thromboprophylaxis should be continued for 6 weeks.

2. [b] BMI ≥ 30 = 1; BMI ≥ 40 = 2

No patients developed any significant problem during anti-coagulation except for subcutaneous haemorrhage at the site of injection. Cost and compliance were a problem along with the need for a specialist nurse who was able to administer the dose appropriately daily. Each patient required counselling in order to continue the LMWH injections and was well motivated to continue therapy. The theoretical risk of excessive haemorrhage in the event of a sudden obstetric indication for termination of pregnancy or in the event of spontaneous onset of labour was discussed with, but no patient on antenatal thromboprophylaxis developed any complications related to post-partum haemorrhage or VTE. The patients were compliant with the 10 days postnatal LMW Heparin and came back for their post-natal visits after 2 weeks.

Table I: Distribution of antenatal patient's profile according to risk factors

Parameters	**n=50(%)**
Age >35	5(10%)
Parity≥ 3	12(24%)
BMI >30kg/m^2	7(14%)
BMI>40 kg/m^2	1(2%)
Smoker	0
Gross varicose vein	1(2%)
Current pre-eclampsia	2(4%)
Immobility (paraplegia, pelvic girdle pain with reduced mobility)	0
Multiple pregnancy	1(2%)
Known Thrombophilia (Low-risk or high risk without VTE)	0
IVF/ART	1(2%)
Family history of unprovoked or oestrogen provoked VTE in first-degree relative	0
Transient risk factor: Dehydration/hyperemesis, Current systemic infection, long distance travel (more than 4 hours)	18(36%)
Any previous VTE except a single event related to major surgery	0
Single previous VTE related to major surgery	0
Medical comorbidities e.g., cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy, nephrotic syndrome, type 1/2 DM with nephropathy, sickle cell disease	3(6%)
Any surgical procedure in pregnancy (e.g., appendicectomy)	0
OHSS (Ovarian hyperstimulation syndrome)	0
Hospital admission	47(94%)

Pregnancy outcome: The pregnancy outcome in terms of gestational age at the time of delivery, mode of delivery, need for blood transfusion, birth weight and need for neonatal support was collected by contacting the patient after delivery over telephone or during post-natal visit. The COVID-19 status of each patient was also recalled.

Table II: Pregnancy outcome of 50 antenatal patients(n=50)

Gestational age ≥ 37 weeks	44(88%)
Operative delivery	35(70%)
Need for blood transfusion throughout pregnancy	10(20%)
Birth weight ≥ 2.5 Kg	43(86%)
Live birth	48(96%)
Need for neonatal support	12(24%)
COVID Positive status	6 (12%)

Discussion:

The purpose of the study is to implement the proposed recommendation by GTG (Green Top Guideline) 37a that all pregnant women should undergo a documented assessment of clinical risk factors for VTE in early pregnancy which should be repeated if the woman requires admission or develops other inter-current problems and should be repeated again intra-partum or immediately postpartum; individualized prophylaxis for VTE should be implemented according to a standard recommendation.[1,2]

VTE results from the complex interactions of genetic and environmental factors that influence the coagulant, inflammatory procoagulant, anticoagulant, and fibrinolytic system, leading to hypercoagulability or hypofibrinolysis, or both. Among them, pregnancy is an independent factor for the development of VTE in one's lifetime.[7,8] Each pregnant woman has some definable non-modifiable and transient risk factors which are summated to make an objective score using the GTG RCOG 37a guideline, individual details of which are discussed below:

Advanced maternal age and VTE: Studies have shown that the relative risk of VTE in pregnant women over 35 years old has increased approximately 2-fold. A large cohort study in the United States found that maternal women aged 35-44 were twice as likely to develop VTE as non-pregnant women aged 25-34.[8,9] In this study, 10% of women were aged over 35 years and 24% had high Parity (p≥3).

Obesity and VTE: Although the association between obesity and VTE appears to be moderate, obesity can interact with other environmental or genetic factors and pose a significantly greater risk of VTE among individuals who are obese and who are exposed simultaneously to several other risk factors for VTE. A prospective cohort study of 87,226 women in the Nurses' Health Study (NHS) showed that the relative risk of unprovoked PE that was not associated with prior surgery, trauma, or cancer raised by about 8% per 1 kg/m^2 increase in BMI and approached a nearly six-fold greater risk among individuals with a BMI ≥35 kg/m^2 ($p < 0.001$).[10] There was a positive monotonic association between BMI and VTE risk. Individuals with a BMI ≥35 kg/m^2 had a HR for VTE of 3.09 (95% CI: 2.26-4.23) compared to those with normal BMI (<25 kg/m^2). Among the well-established CVD risk factors, only current smoking and obesity were independently associated with VTE risk corroborating that the pathogenesis of venous disease differs from that of atherosclerotic disease. Obesity appeared to be associated with a higher risk of pulmonary embolism (adjusted OR: 14.9 (95% CI: 3.0, 74.8) than of deep venous thrombosis (adjusted OR: 4.4, 95% CI: 1.6, 11.9).[11] In this study, 16% of women had a BMI above 30.

Smoking and VTE: Current smoking were associated with increased risk of VTE during pregnancy and the puerperium (adjusted OR 2.7 (95% CI: 1.5, 4.9), however concomitant obesity works as a confounding factor in risk estimation.[12] Thirty-two observational studies about risk of smoking and VTE in women involving 3,966,184 participants and 35,151 VTE events have been identified. Compared with never smokers, the overall combined relative risks (RRs) for developing VTE were 1.17 (95% CI 1.09-1.25) for ever smokers, 1.23 (95% CI 1.14-1.33) for current smokers, and 1.10 (95% CI 1.03-1.17) for former smokers, respectively. The risk increased by 10.2% (95% CI 8.6%-11.8%) for every additional ten cigarettes per day smoked or by 6.1% (95% CI 3.8%-8.5%) for every additional ten pack-years.[13,14] However, none of the pregnant women were smokers in this study.

Gross varicose vein/ chronic venous insufficiency and VTE: Varicose veins are generally recognized as a weak risk factor of venous thromboembolic diseases. The presence of lower extremity varicose veins adds one point to the total Modified Caprini/Padao score used for post-operative VTE risk assessment.[15] Caprini score includes pregnancy and history of unexplained/ recurrent spontaneous abortion as a scoring parameter, that may result in VTE prophylaxis upgrade.[16] In this study, only one patient had gross varicose veins and was advised ambulation and intermittent pneumatic stockings as her overall score was 2.

Thrombophilia (heritable/ acquired) and VTE: Women with previous VTE associated with Anti-thrombin III (AT-III) deficiency and those with antiphospholipid syndrome (APS) are considered as high- risk thrombophilia and presence of this risk factor is sufficient to offer thromboprophylaxis with higher dose LMWH (either 50%, 75% or full treatment dose) throughout pregnancy and for 6 weeks postpartum or until returned to oral anticoagulant therapy after delivery. Management of AT -III deficient patients or those with recurrent VTE should be undertaken in collaboration with a haematologist with expertise in thrombosis in pregnancy and consideration given to antenatal anti-Xa monitoring /or anti-thrombin replacement at initiation of labour or prior to caesarean section in cases associated with morbid obesity.[1,17] Other heritable thrombophilic defects are lower risk and can be managed with standard doses of thromboprophylaxis. Pregnant women with APS and prior VTE or arterial thromboses should also be managed in collaboration with a haematologist and/or rheumatologist with expertise in this area. Women on long-term warfarin or other oral anticoagulants should be counselled about the risks of the foetus and advised to switch to LMWH preferably prior to the sixth week of gestation.[1] Fortunately, no patients in our study group gave a suggestive history of thrombophilia, though no one performed the tests although being offered.

Medical co-morbidity complicating pregnancy (e.g., type 1/type 2 DM with nephropathy, active SLE, IBD or inflammatory poly-arthropathy, nephrotic syndrome, sickle cell disease, cancer, heart failure) and VTE: Venous thromboembolism shares many risk factors with atherosclerotic cardiovascular disease, including obesity, hypertension, dyslipidaemia, smoking, and diabetes.[13,17] Diabetes was an independent predictor of recurrent deep vein thrombosis. The increased risk of venous thromboembolism associated with diabetes ranges from 40% in a large prospective cohort from the US to 50% in a meta-analysis of more than 63,000 patients.[5] The risk of VTE appears to be elevated in both type 1 and type 2 diabetic patients.[18] Hypercoagulability due to increased thrombin generation and higher concentration of procoagulant cell-derived circulating microparticles in patients

with type 2 diabetes plays an important pathogenic role in the increased frequency of venous thromboembolism.[9] Moreover, proteinuria regardless of the aetiology confers a pro-thrombotic state and it has been found that the presence of proteinuria in the first 20 weeks of pregnancy is associated with a significantly higher risk of VTE.[19,20,21] In this study, 2 patients had Type 2 Diabetes with renal impairment as evidenced by proteinuria before 20 weeks of gestation.

Studies conducted among SLE patient reveal that 42% of the Lupus Anticoagulant (LAC)-positive and 40% of the Anti-Cardiolipin Antibody (ACA)-positive individuals had a history of thrombosis; in contrast, the prevalence of thrombosis in LAC negative or ACA-negative SLE patients was only10-18%; conferring a subgroup of pregnant SLE patients at an additive risk of VTE.[22] Glucocorticoids administered in high doses in SLE have been also associated with thrombosis, probably mediated by endothelial damage and accelerated atherosclerosis.[23,24] One patient in our study was a known case of SLE but in the quiescent stage.

Transient factors provoking intracellular dehydration (e.g., long haul travel, sepsis, immobilization, Ovarian hyperstimulation) and VTE: The most serious complication associated with Ovarian hyperstimulation syndrome (OHSS) is thrombotic phenomena on both arterial and venous side.[25] Therefore, thromboprophylaxis should be initiated in patients with thrombophilia and who develop moderate-to-severe OHSS. However, none of our patients had OHSS though one patient had conceived upon IVT-ET with twins. One patient had sustained a Fracture of the Tibia at 14 weeks of gestation and required 6 weeks immobilization with thromboprophylaxis.

ART (Artificial reproductive technique) and VTE risk: According to a national register-based cohort study over a period of 10 years, the venous thrombosis incidence was found significantly increased in pregnancies after in vitro fertilization: especially in the first trimester and in the first 6 weeks post-partum.[25] Several mechanisms support this clinical association such as pharmacological ovarian stimulation and its induced acquired thrombophilia, possible presence of inherited thrombophilia that represents a risk to develop VTE per se and the occurring of pregnancy with its spontaneous hypercoagulable state.[25,26] It has been concluded that if thrombophilia is considered as a possible cause of repeated ART failure in order to prevent VTE, a thorough anamnesis focused on additional transient or permanent thrombotic risk factors (e.g., type of hormonal drugs, timing of exposition to hormonal treatment and dosages of hormonal treatment, smoking habits, obesity,

suggested or prolonged bed rest after ART), should be performed in order to understand if antithrombotic treatment may be helpful. In repeated ART failure, LMWH seems to have more efficacies if compared to aspirin alone toward relevant outcome as to prevent VTE and\or to increase pregnancy rate.[27,28,29] In our study, one patient had conceived upon controlled ovarian stimulation but developed no complications.

The strength of this study is that the scoring system is clinically reproducible and can be applied in everyday obstetric practice. Upon this scoring, patient counselling is also more formative particularly regarding the dosing and duration of LMW heparin therapy. The limitations are also there which actually serve as the points of improvement of our current obstetric care (e.g., as inclusion of thrombophilia screening in selected high-risk cases with clinical history suggestive of recurrent thrombosis).

Conclusion:

Individualized scoring of the risk of VTE or early detection of deep venous thrombosis with subsequent prophylaxis and treatment can reduce the risk of maternal death or morbidity related to VTE. During implementation of risk stratification for VTE of antenatal patients in this study, a change of antenatal care emphasizing precise preventive measures such as mobilization and anticoagulation according to the individual objective scoring system was observed. The risk of VTE should be discussed with women at risk and the reason for individual advice was explained to bring about a good perinatal outcome. Previous VTE or high-risk thrombophilia or a score of 4 or more are considered a condition for LMW Heparin throughout pregnancy with post-natal reassessment. Prophylactic LMWH from 28 weeks is for pregnant patients with a score of three. As per the GTG 37a, women with VTE associated with either antithrombin deficiency or APS or with recurrent VTE (who will often be on long-term oral anticoagulation) should be offered thromboprophylaxis with higher dose LMWH (either 50%, 75% or full treatment) antenatally and for 6 weeks postpartum or until returned to oral anticoagulant therapy after delivery. Unprovoked/idiopathic VT or related to estrogen (estrogen-containing contraception/ pregnancy) should be offered thromboprophylaxis with LMWH throughout the antenatal period. In VTE provoked by major surgery, thromboprophylaxis with LMWH can be withheld antenatally until 28 weeks provided no additional risk factors are present (in which case they should be offered LMWH). Prophylactic LMWH for 10 days postpartum is recommended for those with a post-natal reassessment score of 2. This clinical factor-based scoring has scope for widespread implementation in the context of our country.

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Reference:

1. Royal College of Obstetricians and Gynaecologists, Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium. Green-top Guideline No. 37a. April 2015. Available from: https://www.rcog.org.uk/media/qejfhcaj/gtg-37a.pdf [Accessed 19 December 2022]
2. Simpson EL, Lawrenson RA, Nightingale AL, Farmer RD. Venous thromboembolism in pregnancy and the puerperium: incidence and additional risk factors from a London perinatal database. BJOG. 2001;108(1):56-60.
3. Macrotrends. Bangladesh Maternal Mortality Rate 2000-2022. Available from: https://www.macrotrends.net/countries/BGD/bangladesh/maternal-mortality-rate [Accessed 19 December 2022]
4. Yu T, Vollenweider D, Varadhan R, Li T, Boyd C, Puhan MA. Support of personalized medicine through risk-stratified treatment recommendations - an environmental scan of clinical practice guidelines. BMC Med. 2013 Jan 9;11:7. doi: 10.1186/1741-7015-11-7.

5. Zhang W, Shen J, Sun JL. Risk scores, prevention, and treatment of maternal venous thromboembolism. World J Clin Cases. 2020 Jun 6;8(11):2210-2218. doi: 10.12998/wjcc.v8.i11.2210. PMID: 32548151; PMCID: PMC7281061.

6. Amarnath Bhide, Sabaratnum Arulkumaran, Kaizad R Damania. Arias Practical Guide to High-risk Pregnancy & Delivery: a South –Asian Perspective, 5th edition, (p. 163) 2019.

7. Betty Chou, Jessica Bienstock, Andrew J. Satin. The Johns Hopkins Manual of Gynaecology and Obstetrics. Sixth Edition, 2021.

8. Chaves Sda C, Cecatti JG, Carroli G, Lumbiganon P, Hogue CJ, Mori R, Zhang J, Jayaratne K, Togoobaatar G, Pileggi-Castro C, Bohren M, Vogel JP, Tunçalp Ö, Oladapo OT, Gülmezoglu AM, Temmerman M, Souza JP. Obstetric transition in the World Health Organization Multicountry Survey on Maternal and Newborn Health: exploring pathways for maternal mortality reduction. Rev PanamSalud Publica. 2015 May;37(4-5):203-10. PMID: 26208186.

9. World Health Organization. Maternal Mortality. Available from: https://www.who.int/news-room/fact-sheets/detail/maternal-mortality [Accessed 19 December 2022]

10. Geerts WH, Bergqvist D, Pineo GF. Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). Chest. 2008;133(6 suppl):381S–453S.

11. Jobin S, Kalliainen L, Adebayo L, Agarwal Z et al. Venous thromboembolism prophylaxis. Bloomington (MN). Institute for Clinical Systems Improvement (ICSI). 2012 Nov; p. 51.

12. Yang G, De Staercke C, Hooper WC. The effects of obesity on venous thromboembolism: A review. Open J Prev Med. 2012 Nov;2(4):499-509. doi: 10.4236/ojpm.2012.24069. PMID: 26236563; PMCID: PMC4520798.

13. Kabrhel C, Varraso R, Goldhaber SZ, Rimm EB, Camargo CA. Prospective study of BMI and the risk of pulmonary embolism in women. Obesity. 2009; 17:2040–2046.

14. Larsen TB, Sørensen HT, Gislum M, Johnsen SP. Maternal smoking, obesity, and risk of venous thromboembolism during pregnancy and the puerperium: a population-based nested case-control study. Thromb Res. 2007; 120(4):505-9. doi: 10.1016/j.thromres. 2006.12.003. Epub 2007 Jan 25. PMID: 17257657.

15. Wattanakit K, Lutsey PL, Bell EJ. Association between cardiovascular disease risk factors and occurrence of venous thromboembolism. A time-dependent analysis. Thrombosis and Haemostasis. 2012 Sep;108(3):508-515.

16. Cheng YJ, Liu ZH, Yao FJ, Zeng WT, Zheng DD, Dong YG, Wu SH. Current and former smoking and risk for venous thromboembolism: a systematic review and meta-analysis. PLoS Med. 2013;10(9):e1001515. doi: 10.1371/journal.pmed.1001515. Epub 2013 Sep 17. PMID: 24068896; PMCID: PMC3775725.

17. Li R, Chen Z, Gui L, Wu Z, Miao Y, Gao Q, Diao Y, Li Y. Varicose Veins and Risk of Venous Thromboembolic Diseases: A Two-Sample-Based Mendelian Randomization Study. Front Cardiovasc Med. 2022 Apr 14;9:849027. doi: 10.3389/fcvm.2022.849027. PMID: 35498031; PMCID: PMC9047357.

18. Fuentes HE, Paz LH, Al-Ogaili A, Andrade XA, Oramas DM, Salazar-Adum JP, Diaz-Quintero L, Acob C, Tafur A, Caprini J. Validation of a Patient-Completed Caprini Risk Score for Venous Thromboembolism Risk Assessment. TH Open. 2017 Oct 20;1(2):e106-e112. doi: 10.1055/s-0037-1607339. PMID: 31249916; PMCID: PMC6524847.

19. Piazza G, Goldhaber SZ, Kroll A, Goldberg RJ, Emery C, Spencer FA. Venous thromboembolism in patients with diabetes mellitus. Am J Med. 2012 Jul;125(7):709-16. doi: 10.1016/j.amjmed. 2011.12.004. Epub 2012 May 3. PMID: 22560173; PMCID: PMC3424058.

20. Tsai AW, Cushman M, Rosamond WD. Cardiovascular risk factors and venous thromboembolism incidence: the longitudinal investigation of thromboembolism etiology. Arch Intern Med. 2002; 162:1182-1189.

21. Ageno W, Becattini C, Brighton T. Cardiovascular risk factors and venous thromboembolism: a meta-analysis. Circulation. 2008; 117:93-102.

22. Tripodi A, Branchi A, ChantarangkulV.. Hypercoagulability in patients with type 2 diabetes mellitus detected by a thrombin generation assay. J ThrombThrombolysis. 2011; 31:165-172.

23. Akbari A, Kunkel E, Bota SE, Harel Z, Le Gal G, Cox C, Hundemer GL, Canney M, Clark E, Massicotte-Azarniouch D, Eddeen AB, Knoll G, Sood MM. Proteinuria and venous thromboembolism in pregnancy: a population-based cohort study. Clin Kidney J. 2021 Jan 11;14(9):2101-2107. doi: 10.1093/ckj/sfaa278. PMID: 34671466; PMCID: PMC8521786.

24. Al-Homood IA. Thrombosis in systemic lupus erythematosus: a review article. ISRN Rheumatol. 2012; 2012:428269. doi:10.5402/2012/428269.

25. Roman MJ, Shanker BA, Davis A. Prevalence and correlates of accelerated atherosclerosis in systemic lupus erythematosus. New England Journal of Medicine. 2003;349(25):2399-2406.

26. Ruiz-Irastorza G, Hunt BJ, Khamashta MA. A systematic review of secondary thromboprophylaxis in patients with antiphospholipid antibodies. Arthritis Care and Research. 2007;57(8):1487-1495.

27. Mor YS, Schenker JG. Ovarian hyperstimulation syndrome and thrombotic events. Am J Reprod Immunol. 2014 Dec;72(6):541-8. doi: 10.1111/aji. 12310. Epub 2014 Aug 22. PMID: 25146913.

28. Strina I, Alviggi C, Rosa PD, Avino L, Amoroso R, Marrone V, Mascia M, Cioffi G, Placido GD. Venous Thromboembolism (VTE) and Assisted Reproductive Technologies (ART): A Complex Relationship. J Blood Lymph. 2018;8(1):199. doi:10.4172/2165-7831.1000199

29. Hansen AT, Kesmodel US, Juul S, Hvas AM. Increased venous thrombosis incidence in pregnancies after in vitro fertilization. Hum Reprod. 2014 Mar; 29(3): 611-7. doi: 10.1093/humrep/ det458. Epub 2014 Jan 6. PMID: 24399508.