Challenges of thromboprophylaxis in pregnancy: A 12 months audit and a review of the literature

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Keywords: thromboprophylaxis, pregnancy, risk factors, nurse role, adherence

Abstract_The presentation is going to comprise of two parts: The first part will be about the role of the nurse in management of women and girls with inherited bleeding Disorder (IBD) in a comprehensive care centre. The role of the nurse within the multidisciplinary team is to provide educational and emotional support to the women and the facilitate and coordinate person-centred care. This will be followed by presentation of an audit that was carried out on antenatal thromboprophylaxis in a single centre. Over the recent decades, there is increasing focus on women with inherited bleeding disorders (WBD) which has brought more patients into Haemophilia Treatment Centres (HTC) around the globe. These women require input of a multidisciplinary team to improve outcomes in their gynaecological and obstetric care. Nurses play a pivotal role in patient and family education and in the coordination of the multidisciplinary team. Carriers of Haemophilia and women with IBD experience heavy menstrual bleeding, bleeding from dentistry, surgery, injury or childbirth. Symptoms are treated leading to full and active lives. The nurse is often the point of contact for women who are pregnant, to organise and schedule attendance at a multidisciplinary clinic. The nurse is able to offer regular monitoring of the outcome of interventions in an ongoing relationship with the woman.

The number of WBD in HTC has increased and the nurse should play an active role in outreach and education in the developing world where the numbers of identified WBD falls further below the expected numbers based on prevalence.

BACKGROUND

In pregnancy the risk of thromboembolism is doubled. Venous thromboembolism (VTE) can occur at any time during pregnancy but increases 20-fold during the post-partum period. In order to provide appropriate prevention NICE guidelines recommended referral into dedicated clinics. The NICE's (2012) Quality statement for service providers state that "pregnant women at high and intermediate risk of venous thromboembolism at the booking appointment have specialist advice provided about the care". If necessary, thromboprophylaxis is prescribed [1].

The audit considered the appropriateness of referrals from antenatal clinic to a thrombosis clinic and checked if management plans prescribed during pregnancy for antenatal, peri and post-partum treatment were followed. Referrals were grouped into primary and secondary risk categories and not all referrals were appropriate for the antenatal - thrombosis clinic. This service is provided in the Haemophilia Centre & Thrombosis Unit where pregnant women are assessed by the haematologist consultant and supported by named specialist nurse. The audit gave an insight as to why some women were not compliant to self-injecting with low molecule weight heparin (LMWH).

I. INTRODUCTION

Pregnancy-related venous thromboembolism (VTE) is one of the leading causes of maternal deaths in developed countries. Despite improved prophylaxis and treatment options, and current risk-assessment tools, morbidity and mortality related to VTE remains high in pregnant women [2]. VTE in pregnancy are potentially preventable, since two-thirds of these women have identifiable risks factors and may benefit from appropriate thrombo-prophylaxis. Royal College of Obstetricians & Gynaecologists (RCOG) guideline (No.37b 2015) provide practical recommendations for risk assessment of VTE at the time of antenatal booking, categorising risks into low, intermediate, and high risk [3]. In case series study, Shirazi et al showed lack of recognition of high-risk women and lack of provision of thromboprophylaxis with LMWH were important causes of maternal mortality, The study highlighted the need for accurate screening of high-risk mothers and designing a standard form [4]. Women with pre-eclampsia are at risk of thromboembolic events, three times more than healthy women, especially in the post period. There

is also a correlation between smoking and the increased risk of VTE [6].

Careful assessments of the personal and family history as well as the pre-existing and new onset /transient risk factor during pregnancy and after delivery are mandatory for an effective prevention of VTE [5]. Timely diagnosis and referral to dedicated thrombosis clinic depends on the awareness of the condition and recognition of the risk factors. These factors include family history of VTE, thrombophilia (heritable: antithrombin deficiency, protein C deficiency protein S deficiency, factor V Leiden, prothrombin gene mutation), anti-phospholipid antibodies, persistent lupus anticoagulant, obesity, increased maternal age and parity and reduced mobility [5]. Therefore, thromboembolism risk assessment should be carried out at any time during pregnancy; in early pregnancy and specially at delivery to assess if risk factors change [6].

It is established that pregnancy changes the haemostatic system into a hypercoagulable state, which increase throughout pregnancy and is highest around term [7]. Anticoagulation with LMWH is a well-known antithrombotic practice for primary and secondary thromboprophylaxis during pregnancy. There is increasing evidence in favour of the use of heparin with pregnancy and an increasing number of women undergoing invitro fertilisation (IVF) found that the administration of LMWH may increase clinical pregnancy and live birth rates.

In context of the audit, referral forms that were received from antenatal clinic highlighted the risk factors. Scoring system used is based on the Royal College of Obstetrician and Gynaecologist (RCOG) guidelines 2015. If total score is 4 or more, anticoagulation administration with prophylaxis dose starts at the beginning of the pregnancy. In score 3, it is recommended to start coagulant with prophylactic dosage at 28weeks of pregnancy.

Cohort

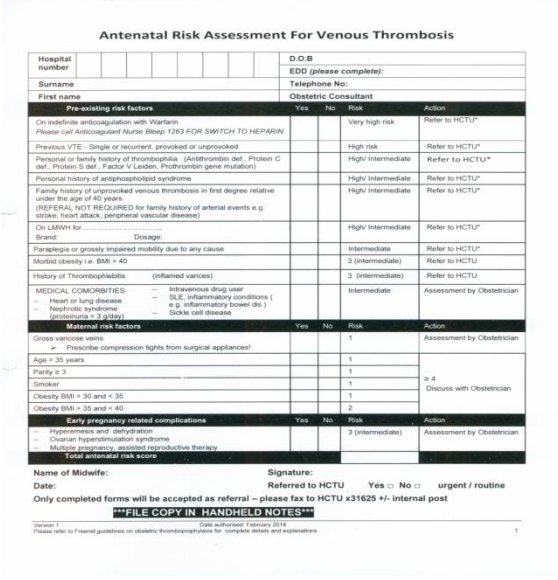
- Data collected between August 2013-July 2014
- A total of 288 new referrals, 211 of which were seen.
- 77 DNAs or cancellations
- Majority of data discussed here is reflective of one clinic.
- 120/211(56%) completed forms
- 92/211 (44%) not captured.
- Age range 20-46 years, mean age 31 years
- National average age 30-34years

II. METHODOLOGY

- Prospective data collection capturing the following
  - Antenatal VTE risk factors
  - Management advice given
  - Follow up with phone call or clinic review after delivery to check on adherence with advice.

Data was collected during the clinic and sometimes after the clinic consultation. More information was also extracted from the women's maternity notes and the referral form. The referral form classified risk factor into three categories; those with pre-existing risk factors (these women were deemed as high to intermediate risk group), women with maternal risk factors (obstetricians further assessed those with risk score 4 or more) and those with early pregnancy complications (those with score of 3 were classified as having intermediate risk). See table 1.

TABLE 1.



Antenatal Risk Assessment For Venous Thrombosis

Hospital number			D.O.B	
			EDD *(please complete)*:	
Surname			Telephone No:	
First name			Obstetric Consultant	
Pre-existing risk factors	**Yes**	**No**	**Risk**	**Action**
On indefinite anticoagulation with Warfarin *Please call Anticoagulant Nurse Bleep 1263 FOR SWITCH TO HEPARIN*			Very high risk	Refer to HCTU*
Previous VTE - Single or recurrent, provoked or unprovoked			High risk	Refer to HCTU*
Personal or family history of thrombophilia (Antithrombin def., Protein C def., Protein S def., Factor V Leiden, Prothrombin gene mutation)			High/ Intermediate	Refer to HCTU*
Personal history of antiphospholipid syndrome			High/ Intermediate	Refer to HCTU*
Family history of unprovoked venous thrombosis in first degree relative under the age of 40 years. (REFERAL NOT REQUIRED for family history of arterial events e.g. stroke, heart attack, peripheral vascular disease)			High/ Intermediate	Refer to HCTU*
On LMWH for..... Brand: Dosage:			High/ Intermediate	Refer to HCTU*
Paraplegia or grossly impaired mobility due to any cause			Intermediate	Refer to HCTU*
Morbid obesity i.e. BMI > 40			3 (intermediate)	Refer to HCTU
History of Thrombophlebitis (inflamed varices)			3 (intermediate)	Refer to HCTU
MEDICAL COMORBITIES – Heart or lung disease – Nephrotic syndrome (proteinuria > 3 g/day) – Intravenous drug user – SLE, inflammatory conditions (e.g. inflammatory bowel dis.) – Sickle cell disease			Intermediate	Assessment by Obstetrician
Maternal risk factors	**Yes**	**No**	**Risk**	**Action**
Gross varicose veins ➢ Prescribe compression tights from surgical appliances!			1	Assessment by Obstetrician
Age > 35 years			1	≥ 4 Discuss with Obstetrician
Parity ≥ 3			1	
Smoker			1	
Obesity BMI > 30 and < 35			1	
Obesity BMI > 35 and < 40			2	
Early pregnancy related complications	**Yes**	**No**	**Risk**	**Action**
– Hyperemesis and dehydration – Ovarian hyperstimulation syndrome – Multiple pregnancy, assisted reproductive therapy			3 (intermediate)	Assessment by Obstetrician
Total antenatal risk score				

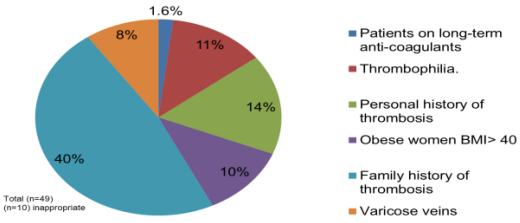
Name of Midwife: Signature:
Date: Referred to HCTU Yes ☐ No ☐ urgent / routine
Only completed forms will be accepted as referral – please fax to HCTU x31625 +/- internal post
FILE COPY IN HANDHELD NOTES
Version 1 Date authorised: February 2014
Please refer to Freenet guidelines on obstetric thromboprophylaxis for complete details and explanations 1

Out of 120 women, those with primary risk factors were 103, with the highest percentage of which were those with a family history of VTE of which 10 women were inappropriately referred as they had family history of strokes and heart attacks. A total of 17 women had secondary risk factors and were deemed appropriate.

Statistics: referrals

Table 2. Primary Risk factors (=103)

1. Patients on warfarin	1
2. Personal history of Thrombophilia	13
3. Personal History of Thrombosis	18
4. Obese women BMI>40	12
5. Family History of Thrombosis	49 N=10 Inappropriate N= 39 appropriate
6. Varicose	10 (N=2 with phlebitis)
Others	
Maternal Age >35 = 38/120 (31%)	
BMI ≥35 and <40 = 7/120 (5%)	
BMI ≥30 and <35 = 12/120 (10%)	



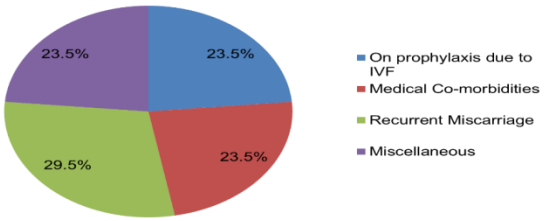
Secondary Risk factors (=17)

On prophylaxis after IVF = 4

Medical Comorbidities = 4

Recurrent miscarriages = 5

Miscellaneous: Thrombocytopenia = 4

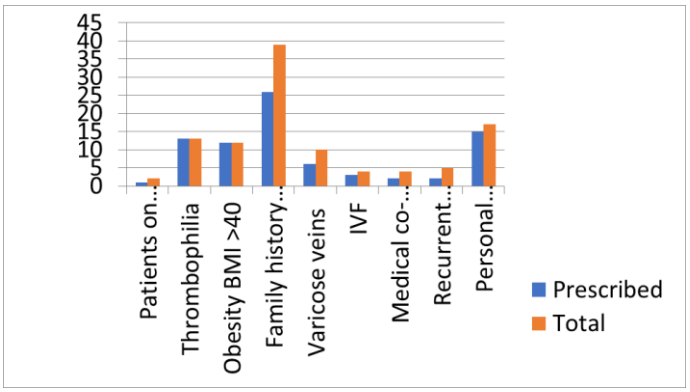


III. RESULTS

According to the RCOG recommendations, 80 women out of 120 had Thromboprophylaxis prescribed. All 13 women with a personal history of thrombosis and obese pregnant women with a BMI of >40 was prescribed and started on LMWH. Not all women with family history of thrombosis were started on prophylaxis as they did not any other additional risk factors, hence 71% were prescribed LMWH.

Table 3.

1. Patients on long-term anticoagulation	1/2
2. History of Thrombophilia (eg Factor V Leiden)	13/13 (100%)
3. Personal History of Thrombosis (PE or DVT)	15/17 (94%)
4. Obese women BMI>40	12/12 (100%)
5. Family History of Thrombosis	26/39 (71%)
6. Varicose Veins	6/10 (60%)
IVF	3/4 (75%)
Comorbidities	2/4 (75%)
Recurrent miscarriage	2/5 (60%)



The pregnant women on thromboprophylaxis were supported throughout their pregnancies by the specialist nurse whose role was to educate and teach them how to do self-injection with LMWH. Those who had PE or DVT while pregnant, they were monitored in the centre by measuring their anti-Xa levels and adjusting their therapeutic doses. Injection sites were checked, and the technic of injection taught by the nurse. Booklets and videos were given so that women could build confidence in self injection. The nurse facilitated new prescriptions and other accessories required to ensure women adhered to prescribed LMWH. Some women were needles phobic and their spouses/ partners were taught how to inject LMWH and required psychological and emotional support was provided as required.

There was follow up by telephone by the nurse to ensure the correct prescription was given post-partum as showed in Table 4. In total 46 women received prescription for 6 weeks of LMWH, 31 received a prescription for 2 weeks. Only 3 women received 4 weeks prescription of LMWH. Those women at high risk of VTE and were already on prophylaxis, they received their 6 weeks prescription as recommended by RCOG guidelines.

Table 4. Post-partum prescription on discharge

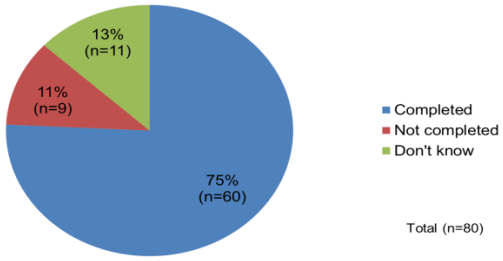
	Prescription		
	6 weeks	**4weeks**	**2weeks**

Patient on warfarin	1		
History of Thrombophilia (eg Factor V Leiden)	13		
Personal History of Thrombosis	13		2
Obese women BMI>40	1	2	9
Family History of Thrombosis	9	1	16
Varicose	3		3
IVF	3		
Comorbidities	1		1
Recurrent miscarriage	2		
Total	**46**	**3**	**31**

Interestingly, in the post-partum follow up by telephone, 75% completed the prescribed LMWH. 11% of women failed to complete their prescription and 13%. The high number of women who were compliant to their treatment post-partum were those who has primary risk factor such as history of thrombosis.

Table 5. Follow-up Post-Partum – Adherence to prescribed therapy

	completed	**Not completed**	**Don't Know**
Patients on warfarin	1		
History of Thrombophilia (eg Factor V Leiden)	10		3
Personal History of Thrombosis	11	1	3
Obese women BMI>40	9	2	1
Family History of Thrombosis	19	4	3
Varicose	4	1	1
IVF	3		
Comorbidities	1	1	
Recurrent miscarriage	2		
Total (%)	**60 75%**	**9 11%**	**11 13%**



IV. DISCUSSION

Overall, the audit shows that timely referral to dedicated specialist clinic improved the outcome for the women as risk of developing VTE. Even though referrals deemed inappropriate in some women, 80 out of 120 women were prescribed LMWH as recommended by RCOG. Women who developed PE or DVT in pregnancy were treated with therapeutic doses of subcutaneous LMWH and this was employed during the remainder of the pregnancy and for 6 weeks postnatally and until at least 3 months of treatment was given in total [9].

However, there was variation for the women who had a BMI >40, only one received the treatment for 6 weeks; reason being that she had an elective caesarean section as mode of delivery. Nine obese women only got a prescription for 2 weeks reasons being that they did not have other related risk factors. Three women received a prescription of 4 weeks, it was not clear whether another assessment was at time of discharged.

The 2015 ROCG guidelines highlight that prophylaxis should be used from the start of pregnancy in women with four risk factors, from 28 weeks in those with three risk factors, and women with two risk factors should receive 10 days of post-partum prophylaxis [10]. This indicates that nearly half of pregnant women are eligible for post-partum prophylaxis. Evaluation by Brenner et al (2019), showed that in Italy, experts used a fixed dose of LMWH for prophylaxis in pregnant women with a history of thrombosis. In Netherlands, a study by Roeters Van Lennep et al, showed that women at intermediate risk of VTE were managed without pharmacological intervention during pregnancy and were prescribed LMWH for 6 weeks postpartum. Women at high risk of VTE are given low-dose LMWH during the entire pregnancy and for 6 weeks postpartum [10]. Since VTE risk is high in the first week following a caesarean section, thromboprophylaxis is given for 10 days in the UK. In Germany, post-partum prophylaxis depends on the type of caesarean section, ie, for elective caesarean section lasts for 10-14days where as in an emergency caesarean section is extended for up to 3 months. ,

There were several reasons that contributed to some women to be non-adherence with thromboprophylaxis:

- Needle phobia was the main reason. despite the correct injection technic being demonstrated to them, the fear of needles became an obstacle and they struggled to complete their prescription
- Communication barriers: - not all women use English as their first language, the

interpreter would not be accessed easily once woman was at home. Some women relied on their partner of other family members to translate the instructions of self-injection

- Delivered out of the country – by the time of delivery a few women relocated to other countries. Women may choose to deliver nearer to their family members for better support.
- Medication not prescribed on discharge. This may explain partly why some women did not get their correct prescription. Every woman had a plan written on the antenatal notes explaining the need for a prescription at time of discharge.
- Personal objections, "I felt the treatment was over the top (OTT)." this was comment to a few ladies who deemed themselves as having minimal risk of VTE. they received the prescription on discharge but simply could not care to self-inject.
- Advised not needed by midwife - contradicting advise on discharge and again this could have been after assessment was made post-partum, there was no evidence
- No data in 11% (unable to contact women) – this was due to communication breakdown; the phones were unreachable and/ or no reply. some women changed their contact details, and they may not have been updated in the system.

Nurse role

Nurse as a first point of call, plays a vital role in education the women and provide psychological and emotional support during and after pregnancy. Nurse monitored investigations and facilitated appointments with other healthcare professionals and coordinated a person-centred care [10]. This is in accordance with the 2015 RCOG guidelines, which states that women should be taught to self-inject with LMWH and arrangements made to allow safe disposal of needles and syringes. During the outpatient visit, the nurse checks the dosing and reviews for any red flags such sudden shortness of breath, swollen/painful leg, and excessive bruising. For those women who developed heparin-induce thrombocytopenia or have heparin allergy and require continuing anticoagulant therapy alternate anticoagulant were offered by specialist haematologist [10]. Outpatient follow-up should include clinical assessment and advice with monitoring of blood platelets and peak anti-Xa levels if appropriate [11]. In the UK, monitoring of the anti-Xa activity is recommended, aiming to t ensure adequate dosing of LMWH. In Israel, anti-Xa levels, are measured for both treatment and prophylaxis these doses need to be adjusted at around 20-25 weeks of pregnancy. The interactive role by the nurse in collaborating with other health professionals in awareness, training and better screening tools should continue. Guelcher et al (2021), encourage specialist nurse to play an active part in outreach and education in the developing world , however resources are needed to support the extension of this role[15]

Safety

The nurse and dedicated haematologist spent time educating women about the subcutaneous LMWH and its safety in pregnancy and while breastfeeding. Continued encouragement and education to women to self-inject with LMWH reassured the women who doubted the safety of LMWH and their compliance improved. In Greece, a study by Papadakis et al, revealed that there is increasing evidence in favour of using heparin in women with pregnancy complications. Though is no scientific evidence, all women were followed up until end of 6 weeks post-partum to monitor safety and efficacy of anticoagulation, any thrombotic or bleeding and non was recorded. Their study demonstrated the safety and efficacy of LMWH 's use in a high-risk pregnancy setting.

Strengths

The audit gave an insight that the dedicated specialist clinic worked closely with the antenatal clinic, and this brought about the smooth pathway for referral throughout the TRUST and this pathway of referral is being used in other hospitals. Good collaborations between these specialities have built a recognisable MDT in the TRUST.

This study also included review of literature and guidelines to help better understanding of the risk factors and implementation of risk assessment and thromboprophylaxis. The literature review was performed with a member Cihan university (MAH) with the aim of motivating Health care professionals in Erbil to be actively involved in VTE risk assessment not only in relation to pregnancy but in all at risk in hospital patients and adopt a similar approach of auditing their practice.

Limitations

- Inconsistent data collection - women booked in clinic on different days were missed.
- Clinics were busy and limited time, and staff shortage

- Scoring system on referral form was confusing/unclear to other healthcare professionals

Recommendations

- Review and re-design referral form
- Maintain dedicated antenatal thromboprophylaxis assessment clinics within the HCTU with dedicated named nurse
- Continuing education link with antenatal clinic midwives and obstetric consultants
- Develop patient information relating to risk of VTE post-partum in high-risk groups, to try and improve compliance in this group.
- Further sessions with specialist named nurse to support women to engage fully with prescribed treatment.
- Further education of labour ward midwives in post-natal period to reduce prescription errors.
- Further studies are required on this subject and how best can the assessment tools can be standardised.
- Further collaboration with healthcare professionals in Erbil to support them in providing a better VTE risk assessment and management with regular audits.

In conclusion, there is evidence that timely referrals together with correct diagnosis can reduce and prevent event of VTE in pregnant women. Current guidelines on thromboprophylaxis in pregnancy and post-partum are being followed and has resulted in reduced the maternal mortality. There is strong evidence that nearly half of pregnant women are eligible for post-partum prophylaxis. Nurse plays a pivotal role in educating and supporting women throughout their while on thromboprophylaxis and in the coordinating of the MDT and in ensuring the women receive person-centred care. Low molecular weight heparin (LMWH) is still the preferred anticoagulant for both prophylaxis and treatment during pregnancy. However, guidelines and opinions differ on how to stratify risk during pregnancy.

Consent for publication

Not applicable

Ethical approval and consent to participate

Not applicable

Competing interest

Not applicable

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