Risk Asessment and Thromboprophylaxis for Venous Thromboembolism (VTE) in the Antenatal Population in a Tertiary Health Facility in Nigeria

Mkpe Abbey[1*] and Green Kinikanwo[2]

[1]*Department of Obstetrics and Gynaecology, Rivers State University Teaching Hospital, Port Harcourt, Nigeria.*
[2]*Department of Obstetrics and Gynaecology, University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.*

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Original Research Article	

ABSTRACT

Aim: To review the venous thromboembolism (VTE) risk assessment and thromboprophylaxis in the antenatal population in a tertiary health facility in Nigeria and to perform a retrospective VTE risk assessment of the patients with a view of determining those patients that would have needed VTE prophylaxis.
Design: It was a retrospective cross-sectional study.
Place and Duration of Study: The study was carried out at the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Nigeria from the 1st of February to the 30th of April, 2020.
Materials and Methods: The following data were extracted from the hospital notes of 347 consecutive antenatal patients: history/demographic characteristics, risk factors for VTE, thromboprophylaxis, diagnosis and treatment of VTE, using the RCOG guideline 37a of 2015 as a benchmark for comparison. Data was analysed with the aid of a Statistical Package for Social Science (SPSS) software, version 18.
Results: VTE risk assessment and thromboprophylaxis was not a routine practice at the UPTH.

_____

Corresponding author: E-mail: mkpeabbey@aol.com;

Apart from antenatal admission, the most frequent VTE risk factors in pregnancy were BMI ≥30, Parity ≥ 3, Age > 5 years and current pre-eclampsia at 48.48%, 41.04%, 36.04% and 15.56% of the study population respectively. 131 (37.75%) of the 347 antenatal population fulfilled the criteria for venous thromboprophylaxis with low molecular weight heparin (LMWH) but they were not assessed and the drug was not given. 63 (18.16%) of the study population was to receive LMWH from 28 weeks of pregnancy while 68 (19.60%) of them were to be given from the first trimester. The prevalence of VTE was however very low at 0.02% (1 patient out of the 347 maternities), irrespective of the fact that 41 (11.82%) of the patients had symptoms and signs of VTE.

Conclusion: 131 (37.75%) out of the total 347 antenatal patients fulfilled the criteria to be given thromboprophylaxis but the prevalence of VTE was low at 0.02%. It was therefore recommended that a unified Nigerian national guideline should be written.

1. INTRODUCTION

Venous thromboembolism (VTE) is a leading cause of maternal morbidity and mortality in the developed world [1, 2]. Pregnant women were at a two- to 5-fold higher risk of developing VTE versus nonpregnant women; [3]. its incidence was 1.2 to 1.6 per 1,000 deliveries [4, 5]. There was however paucity of information on the prevalence of VTE and its associated risk factors in pregnancy in Nigeria [6, 7]

There was clear evidence that identification of risk factors with subsequent thromboprophylaxis of the at-risk population will reduce the occurrence of morbidity and mortality caused by the disease. For instance, in the UK, there was a significant fall in the maternal mortality rate from pulmonary embolism from 1.56 per 100000 maternities in 2003–2005 (33 deaths) to 0.70 per 100 000 maternities in 2006–2008 (16 deaths), due largely to reductions in deaths from antenatal VTE (which fell from 11 to 3) and deaths from VTE after vaginal delivery (which fell from 8 to 2) and attributed to thromboprophylaxis [8, 9]. 79% and 89% of the women who died from PE in the UK between 2003 and 2005 and between 2006 and 2008 respectively had identifiable risk factors [8]. Low-molecular-weight heparin (LMWH) reduced VTE risk in medical and surgical patients by 60% and 70% respectively [10].

Therefore, VTE can be prevented by careful assessment of pre-existing and new-onset/transient risk factors, and employing optimum thromboprophylaxis [11].

1.1 Aim

To assess the practice of VTE risk assessment and thromboprophylaxis in the antenatal population in a tertiary health facility in Nigeria. The secondary goal was to perform a retrospective VTE risk assessment of the antenatal patients with a view of determining those who would have needed VTE prophylaxis.

2. METHODOLOGY

Design: It was a retrospective cross-sectional study.

Place and Duration of Study: The study was carried out at the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Nigeria from the 1st of February to the 30th of April, 2020.

Population: 347 consecutive antenatal population.

Inclusion and exclusion criteria - Pregnant women who had objectively (ultrasound) confirmed pregnancies, visiting for the first prenatal consultation in the first 14 weeks of pregnancy. Women with a VTE event in the preceding 4 months or those using concurrent antithrombotic therapy for other medical reasons were excluded.

Procedure: Files of patients who delivered in UPTH between January 2019 and January 2020 were reviewed for the following information: history/demographic characteristics, risk factors for venous thromboembolism, thromboprophylaxis, diagnosis of VTE and treatment of venous thromboembolism. A dedicated Research Fellow was trained in data collection. Data was collected on a semi-structured pretested validated questionnaire by the Research Fellow and then fed onto SPSS 2018. The standard that was used for comparison was the Royal College of

obstetricians and gynaecology guideline, United Kingdom [12].

2.1 Statistics

Sample size: The outcome measure in the study was the number of obstetric patients that had risk factors for venous thromboembolism. Therefore the sample size for the study was calculated by applying the sample size formula for cross-sectional study with a categorical outcome.

$$n = Z_{1-\alpha/2}^2 \, P \, (1-P) \, / \, d^2$$

where

$Z_{1-\alpha/2}^2$ = Standard normal variate. At 5% type I error (p<0.05), it is 1.96. If we decide to raise the degree of precision with less error, i.e. at 1% type1 error (p<0.01), it will be 2.58. That will increase the power of the study. In many studies, p value is considered significant at p<0.05. Therefore 1.96 was used in the present calculation of the sample size for the study.

P – Expected proportion in population based on previous studies.
D = Absolute error or precision.

There was no study in Nigeria at the time that the present study was planned, that dealt with assessment of risk factors specifically in pregnancy, except the only one study that was carried out in Lagos University Teaching as a part of an international multi-country study [13]. Unfortunately the data from Nigeria was not analysed separately. The data from South Africa which was also part of the international study was used; it showed that 126/220 (57.2%) of the women that were assessed were at risk of developing VTE during pregnancy and in the puerperium.

Therefore   n = 1.96 x 0.572 (1-0.572) / 0.05^2
= 1.96 X 0.572 X 0.428 / 0.0025
= 191.94
= 192

The required number of patients for the study was therefore 192. Giving allowance for attrition rate of 10%, the final power for the study was 10/100 x 192 + 192
= 19.20 + 192
= 211.2
= 211 Patients.

Data analysis: Data was entered into SPSS 2018 for analysis. Simple proportions were used

in the descriptive analysis. Quantitative data were summarized and presented as mean and standard deviation while qualitative data were presented as numbers and percentages.

3. RESULTS

3.1 Socio-demographic and Obstetric Characteristics of the Patients

A total of 347 patient's notes were reviewed. All the demographic indices were not available for all the patients. The availability was as shown in the table 1 below. Age distribution was computed using modified WHO standard age groups [14]. The average age of the patients was 32.26 ± 5.61 years. The highest number of the patients was in the age bracket of 25-35(168) and >35-44 years (111), indicating that majority of the women had children late in life. Those at age. >35-44, 111(36.04%), although do not constitute high risk for venous thromboembolism, they scored ''1'' (Table 2) for venous thromboembolism risk and in association with other factors they can sum up to constitute a significant risk for venous thromboembolism (VTE).

The average weight of the patients was 77.20 ± 14.78 kg while the average BMI was 30.04 ± 6.42. 64(32.32%) of the women had BMI 30.0–34.9 (Class I Obesity) while 26(13, 13%) had BMI 35.0–39.9 (Class II Obesity) (Tables 1 and 2). Patients in both BMI bracket sore ''1''each for venous thromboembolism risk. Those with BMI ≥ 40.0 (Class III Obesity) scored 2 (Table 2). 142 (41.04%) out of the total 147 of the patients were Para 3; each patient scored 1 for venous thromboembolic risk. Associated risk of VTE disease with other demographic factors (education, employment, education, social history and marital status could not be assessed because only one of the patients developed VTE.

3.2 Frequency of Individual Risk Factors for Venous Thromboembolism

The risk factors for venous thromboembolism were those factors, if present could predispose the patient to developing venous thromboembolism (VTE) during pregnancy. The RCOG guideline, UK was adopted and used in the present study (Table 2) [12].

Each of the factors was given a number which is an indicator of the degree of the risk associated with it. The identified risk factors in the present

study with their frequencies were as shown in Table 3. They were classified into high, intermediate and low risk categories.

3.3 Scoring of the Risk Factors for VTE and the Need for Thromboprophylaxis

The identified risk factors in the study population were scored with a view of determining the percentage of the women that would have needed thromboprophylaxis. The scoring was based on the RCOG guideline [12] The guideline was clear on the indications and the schedules for thromboprophylaxis based on the scores by each patient. So, if the total scores ≥ 4 (high risk for VTE), low-molecular weight heparin (LMWH) was to be given from the first trimester and continued 6 weeks postnatal.

Table 1. Demographic, obstetric and general characteristics
n=347

Demographic obstetric and general characteristics		Frequency	Percentage %
Maternal age (n=308) (years)	15-24	29	9.42
	25-35	168	54.55
	>35 – 44	111	36.04
Education (n=285)	Primary	2	0.70
	Secondary	65	22.81
	Tertiary	218	76.49
Employment (n=250)	Employed	114	45.60
	Self-employed	88	35.20
	Unemployed	48	19.20
Occupation (n=309)	Business/Trader	107	34.63
	Teacher	59	19.09
	Civil servant	51	16.50
	Student	36	11.65
	House wife	20	6.47
	Nurse	17	5.50
	Professional (Accountant, Lawyer, Engineer)	7	2.27
	Applicant/Unemployed	4	1.29
	Allied Health Professional	3	0.97
	Artisan	3	0.97
	Farmer	2	0.65
Social History(n=347)	Nil	327	94.24
	Drinking	17	4.90
	Smoking	3	0.86
Marital Status(n=258)	Married	243	94.19
	Single (Never Married)	15	5.81
	Single (Divorced)	0	0
Weight at booking(n=229)	< 80 Kg	129	56.33
	≥ 80 kg	100	43.67
Parity (n=346)	Para1 & Para 2	162	46.82
	Para 3 and above	142	41.04
	Para 0	42	12.14
BMI at booking (n=198)	< 18.5 (Underweight)	3	1.52
	18.5–24.9 (Normal weight)	37	18.69
	25.0–29.9 (Overweight)	56	28.28
	30.0–34.9 (Class I Obesity)	64	32.32
	35.0–39.9 (Class II Obesity)	26	13.13
	≥ 40.0) (Class III Obesity)	12	6.06
BMI at booking (n=198)	<30	96	48.48
	30 or more	102	51.52

Table 2. Antenatal risk assessment for venous thromboembolism (VTE) (RCOG guideline) [12]

Risk factors	Score
Pre-existing Risk factors	
Previou 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) [a]	1
Age (> 35 years)	1
Obesity (BMI ≥ 30 Kg/m2 but < 40 Kg/m2)	1
Obesity (BMI ≥ 40 Kg/m2)	2
Parity ≥ 3	1
Smoker	1
Gross varicose veins	1
Obstetric Risk factors	
Multiple pregnancy	1
Pre-eclampsia in current pregnancy	1
ART/IVF	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
Current systemic infection	1
Reduced mobility, dehydration	1
OHSS (first trimester only)	4

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.

A score of 3 (moderate risk for VTE) was an indication for VTE prophylaxis (LMWH) from 28 weeks of pregnancy and to continue for 6 weeks postpartum. If total score = 0-2 (low risk), early mobilisation and avoidance of dehydration would have been advocated. An admission to the antenatal ward was an indication for consideration for LMWH while administration.

The LMWH that was normally prescribed was Enoxaparin (Clexane). TED stockings were recommended for all that were at risk of developing VTE when admitted. In the index project, out of the 347 case notes that were reviewed, 3 (0.86%) did not have any risk factor at all and therefore would not have qualified for VTE prophylaxis. 84 (24.21%) patients scored ''1'' each while 128 (37.18%) scored ''2'' each and therefore avoidance of dehydration and early mobilisation would have been advocated for them (Table 4). 53 (15.27%) of the patients scored ''3'' and therefore, they were supposed to be given VTE prophylaxis (LMWH) from 28

weeks of pregnancy and to be continued for 6 weeks postpartum.

The highest scores and therefore high risk patients for VTE were as following: ''4'' for 55 (15.85%), ''5'' for 7 (2.31%), 6 for (0.86%) and ''7'', ''8'' and ''9'' for 1 patient respectively, totalling 3(0.86%) out of the 347 patients.

3.4 Patients that Presented with Symptoms and Signs of Venous Thromboembolism

Some of the patients that were admitted on the ward had some symptoms and signs of VTE (Table 5). They were as follows: maternal tachycardia, dyspnoea, tacypnoea, chest pain, calf pain and redness of the calf. 41 (11.82%) of the patients had associated risk factors for venous thromboembolism (Table 6). None of the patients with no risk factors for VTE had its Symptoms and signs.

Table 3. Frequency of individual risk factors for VTE (n= 347)

Categories of risk	Risk factors	Frequency (N (%))	
		Yes	No
High risk factors -	Any previous VTE except a single event related to major surgery	0 (0)	0 (0)
Intermediate risk factors.	Hospital admission	331 (95.39)	16 (4.61)
	Chronic hypertension(Complicated)	8 (2.31)	339 (97.69)
	1 previous VTE related to major surg.	0 (0)	0 (0)
	High-risk thrombophilia + no VTE	0 (0)	0 (0)
	Any surgical procedure e.g. appendicitis.	0 (0)	0 (0)
	OHSS (first trimester only	0 (0)	0 (0)
Other Intermediate risk factors -Medical co-morbidities	Sickle-cell disease	11 (3.16)	336 (96.84)
	Type I diabetes(with nephropathy) (n=257)	7 (2.72)	250 (97.28)
	Heart failure	5 (1.14)	342 (98.56)
	Inflammatory polyarthritis	4 (1.15)	343 (98.85)
	Retroviral disease (with complications)	6 (1.73)	341 (98.83)
	IBD (347)	7 ()2.02	340 (97.98)
	Asthma (Acute severe)	2 (0.58)	345 (99.42)
	Epilepsy (Poorly controlled)	1 (0.29)	346 (99.71)
Low risk factors	BMI ≥30 (n=198)	96 (48.48)	102 (51.52)
	Age >35 years (n=308)	111 (36.04)	197 (63.96)
	Parity ≥ 3 (n=346)	142 (41.04)	204 (58.96)
	Gross varicose veins (n=347)	10 (2.88)	337 (97.12)
	Current pre-eclampsia (n=347)	54 (15.56)	293 (84.44)
	Family history of unprovoked or estrogen-provoked VTE in first-degree relative	0 (0)	0 (0)
	Low-risk thrombophilia	0 (0)	0 (0)
	Multiple pregnancy	14 (4)	332 (95.6)
	IVF/ART	6 (1.73)	341 (98.27)
Low risk (Transient risk factors)	Dehydration/hyperemesis	9 (2.59)	338 (97.41)
	current systemic infection	10 (2.88)	337 (97.12)
	long-distance travel	2 (0.58)	345 (99.42)

Table 4. Scoring of the risk factors for VTE and the need for thromboprophylaxis.
n = 347

Risk Scores	Frequency N (%)	Total N (%)	Need for Thromboprophylaxis	Total
0 (No risk)	3 (0.86)	3 (0.86)	Not needed	
1 (Low risk)	84 (24.21)	213 (61.39)	Mobilisation	216 (62.25%)
2(Low risk)	129 (37.18)		Avoid dehydration.	
3 (Intermediate risk)	63 (18.16)	63 (18.16))	To give LMWH from 28 weeks of pregnancy and continue for 6 weeks postpartum.	131 (37.75)
4 (High risk)	55 (15.85)		To give LMWH from the first trimester and continue 6 weeks postnatal	
5 (High risk)	7 (2.02)	68 (19.60)		
6 (High risk)	3 (0.86)			
7, 8, 9 (High risk)	1 for each = 3 (0.86)			
Total	347 (100)	347 (100)		
Admitted to hospital	331 (95.39)		To consider giving thromboprophylaxis when on admission.	

Table 5. Venous Thromboembolism and its presentations (n=347)

VTE and its presentations	Frequency N(%)	
	No	**Yes**
Pain in the calf	331 (95.39)	16 (4.61)
Redness of the leg	340 (97.98	7 (2.02)
Tachycardia	340 (97.98)	7 (2.02)
Tachypnoea	343 (98.85)	4 (1.15)
Chest pain	336 (96.54)	12 (3.46)
Pulmonary Embolism	346 (99.71)	1(0.29)
Deep venous thrombosis	347 (100)	0 (0)
Death	0 (0)	0 (0)

Out of the 84 patients that scored ''1'' for the risk of VTE, 2 of them had chest pain, 6 had pain in the calf while 3 had redness of the leg, 1 had tachycardia and chest pain while another 1 had calf pain and lower limb redness (Table 6). The rest of the associations of the risk factors with the signs and symptoms of VTE were illustrated in Table 6.

4. DISCUSSION

The study, although retrospective, was the second study in Nigeria, assessing the risk of VTE in pregnancy. The first was the study that was carried out in Lagos state University Teaching Hospital as a part of a multinational study [13]. Unfortunately, the study unlike the one that was done in South Africa as a part of the same multinational study was not published separately and the prevalence of risk factors and VTE was not clearly stated.

Out of the 347 patients, 3 (0.86%) of the patients did not have any risk factor for VTE and therefore no thromboprophylaxis was to be given. Another 84 (24.21%) and 129 (37.18%) of the total patients population, had VTE sores of ''1'' and ''2'' (low risk) respectively and the recommendation for them would have been mobilisation and to avoid dehydration as per RCOG guideline [12].

16 (4.61%) out of the 347 antenatal patients were managed as outpatients while 331 (95.39%) of them were admitted into the antenatal ward of the hospital and therefore certified the criteria for consideration for VTE prophylaxis in accordance to the RCOG guideline [12]. 63 (18.16%) of the 147 patients had a risk score of ''3'' (intermediate risk) for VTE and therefore, were supposed to be given LMWH from 28 weeks of pregnancy and continued

Table 6. Association of signs and symptoms of VTE and actual VTE with its risk factors N = 347

VTE Scores (Frequency)	Symptoms and signs and their frequencies						
	No Signs	**Tachy cardia**	**Chest pain**	**Tachyp noea**	**Calf pain**	**Leg redness**	**Pulmonary Embolism**
0 (3)	3	0	0	0	0	0	
1 (84)	71		2		6	3	
		1				1	
2 (129)	118	1	3		4		
			2			1	
3 (63)	57	1	2	2		1	
4 (55)	46	3	3		1		1
			1				
5 (7)	6	Calf pain + Leg Redness =			1		
6 (3)	3	0	0	0	0	0	
7 (1)	1	0	0	0	0	0	
8 (1)	1	0	0	0	0	0	
9 (1)	0	0	0	0	1	0	
347	306	41 (11.82%)					

for 6 weeks postpartum but that did not happen. 68 (19.60%) of them had risk scores of ''4-9'' (high risk for VTE) for VTE and therefore were supposed to be given LMWH from the first trimester and continued 6 weeks postnatal but no assessment was done and it was not given. So, apart from the risk associated with antenatal admission, 131 (37.75%) of the entire antenatal population fulfilled the criteria to be given thromboprophylaxis in the form of LMWH but they were not assessed and the LMWH was not given.

Patients might not be able to fully give account of their medical history but the result of the hospital notes review showed that none of the patients had a history of thrombophilia or venous thromboembolism in the past. Only 1(0.29%) patient had pulmonary embolism in the index pregnancy. Her VTE risk score was ''4'' for maternal age of 40 years, grade I obesity, para 4 and preeclampsia apart from been an inpatient. Paucity of information and lack of knowledge about the diseases may be responsible for the low prevalence of VTE in the present study irrespective of high prevalence of risk factors in the study population.

It may be that some patients had the disease in the past and in the index review but unfortunately the diagnosis was not established; spontaneous recovery might have occurred. Although only one patient had the disease, 41 (11.82%) of the 347 patients had symptoms and signs of VTE. 16 (4.61%) of them had pain in the calf, 12 (3.46% had chest pain, 7 (2.02%) had tachycardia and another 7 (2.02%) had tachypnoea. 306 (88.18%) of them did not have any symptom or sign of VTE. It might be that some patients who had VTE actually died and because of paucity of knowledge and information about the disease, the diagnosis was not established.

5. LIMITATION

The study was retrospective. It was powered enough to determine the prevalence of risk factors in the study population but not to ascertain the prevalence of VTE. The RCOG guideline which was used as a benchmark for comparison in the study might not be suitable for Nigerian population due to cultural, social and economic differences.

6. CONCLUSION

The study showed that irrespective of the morbidity and mortality that VTE could cause

assessment for its risk and prophylaxis was not a routine practice at the UPTH in Nigeria. The prevalence of risk factors for VTE was high among the study maternity population. 131 (37.75%) of the entire antenatal population fulfilled the criteria to be given thromboprophylaxis in the form of LMWH but they were not assessed and the LMWH was not given. 63 (18.16%) of the 347 patients was to receive LMWH from 28 weeks of pregnancy while 68 (19.60%) of them was to be given from the first trimester. The prevalence of VTE was however very low at 0.02% (1 patient out of 347 maternities), irrespective of the fact that 41 (11.82%) out of the patients had symptoms and signs of VTE. It was therefore recommended that a unified national guideline should be written, seminars on the topic should be organised for doctors and patient's education carried out.

7. RECOMMENDATIONS

It was recommended that a unified national guideline on thromboembolic risk assessment and prophylaxis be written, taking into consideration the Nigerian disease pattern, cultural diversity, level of economic development and the peculiarities of maternal care in the country. It was also highly recommended that a prospective well powered study should be carried out, using the created guideline as a benchmark for comparison.

ETHICAL APPROVAL

Ethical approval for the study was granted by the University of Port Harcourt Teaching Hospital Ethical Committee.

CONSENT

Since it was a retrospective study individual Patient's consent was not sought. The study was carried out in a Teaching Hospital where at booking Patients were informed that their data may be used for research. Patient's confidentiality was preserved.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1.   Kuriya A, Piedimonte S, Spence AR, Czuzoj-Shulman N, Kezouh A, Abenhaim

HA. Incidence and causes of maternal mortality in the USA. J Obstet Gynaecol Res. 2016;42(06):661–668

2. Knight M, Kenyon S, Brocklehurst P, Neilson J, Shakespeare J, Kurinczuk JJ, eds.; on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care: Lessons learned to inform future maternity care from the UK and Ireland. Confidential Enquiries into Maternal Deaths and Morbidity 2009–2012. Oxford, UK: University of Oxford; 2014.

3. Pomp ER, Lenselink AM, Rosendaal FR, Doggen CJ. Pregnancy, the postpartum period and prothrombotic defects: risk of venous thrombosis in the MEGA study. J Thromb Haemost. 2008;6(04):632–637.

4. Abbasi N, Balayla J, Laporta DP, Kezouh A, Abenhaim HA. Trends, risk factors and mortality among women with venous thromboembolism during labour and delivery: a population-based study of 8 million births. Arch Gynecol Obstet. 2014;289(02): 275–284.

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;132(01):4–10.

6. Kamdem F, Ngahane BHM, Hamadou B, Mongyui A, Doualla MS, Jingi AM, et al. Epidemiology, clinical presentations and in-hospital mortality of venous thromboembolism at the douala general hospital: A cross-sectional study in Cameroon, Sub-Saharan Africa. World Journal of Cardiovascular Diseases. 2008;8:123-132.

7. Korubo KI, Ekeke ON. Awareness of venous thromboembolism among doctors in a Nigerian tertiary centre. East African Medical Journal. 2015;92(12).

8. Lewis G, editor. The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer - 2003-2005. The Seventh Report on Confidential Enquiries into Maternal Deaths in the United Kingdom. London: CEMACH; 2007.

9. Centre for Maternal and Child Enquiries (CMACE). Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006–08. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. BJOG. 2011; 118 Suppl 1:1–203.

10. National Institute for Health and Clinical Excellence. Venous thromboembolism: reducing the risk. Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital. NICE clinical guideline 92. London: NICE; 2010.

11. Sultan AA, Tata LJ, West J, Fiaschi L, Fleming KM, NelsonPiercy C, et al. Risk factors for first venous thromboembolism around pregnancy: a population-based cohort study from the United Kingdom. Blood. 2013;121:3953–61.

12. RCOG greentop guideline No. 37a. Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium. April 2015.

13. Jean-Christophe Gris, Joseph Aoun, Leyla Rzaguliyeva, Rowshan Begum, Hassan Salah, Tatia Tugushi. The save study group. risk assessment and management of venous thromboembolism in women during pregnancy and puerperium (SAVE): An international, cross-sectional study. TH Open. 2018;2:2.

14. Ahmad Cynthia Boschi-Pinto, Alan D, Lopez Christopher JL, Murray Rafael Lozano Mie Inoue. Age standardization of rates: a new WHO standard. GPE discussion paper series: no.31 eip/gpe/ebd world Health Organization; 2001.