

*Research Article***Obstetric Venous thromboembolism: A One-year Prospective Study in a Tertiary Hospital in Egypt.****Mahmoud Hosny, Ahmed Reda, Ayman Nady, Hany Hassan and Mostafa Kamal.**

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Abstract

Background and objective: Obstetric venous thromboembolism (VTE) poses a life-threatening burden and it is one of the major causes of maternal morbidity and mortality with an increased incidence throughout the last decades. The objectives of this study were to assess the incidence of VTE, types of prophylaxis received and factors determining prophylaxis in women at VTE risk during pregnancy and puerperium at a tertiary hospital for one year. **Methods:** This is a prospective study that was carried out at Minia maternity university hospital, Egypt during the period from June 2018 to June 2019. The study included women attended the hospital at risk of VTE as per the RCOG guidelines. Full history, patient characteristics and VTE risk factors were assessed. **Results:** During the study period, a total of 901 women attended the hospital and perceived at risk of VTE (298 cases during pregnancy and 603 cases during puerperium), about half of them were mild in intensity. They comprise 8.22% of the total deliveries during the study period (n=10956). About two-thirds of them (71.5%) had a caesarean delivery. Varicose veins were found in 209 cases (23.2%), previous VTE in 189 cases (21.0%), previous superficial vein thrombosis was recorded in 240 cases (26.6%) and previous arterial ischemic events in 83 cases (9.2%). The vast majority of patients (99.6%) received the pharmacological type of prophylaxis (55.6% of them received unfractionated heparin and the rest of them 43.9% received Aspirin). Only 6 cases developed VTE from the total included cases with an incidence of 0.55/1000 maternities (0.055%). Obesity (BMI >30 kg/m²) and cesarean delivery were significant factors that determine VTE prophylaxis with an odds ratio of 1.68 (95% CI, 1.20-2.35, p<0.01) and 2.05 (95% CI, 1.49-2.80, p<0.01), respectively. **Conclusion:** The incidence of women perceived at VTE risk during the study period was 8.22% "which is lower than other studies", about half of them were mild in intensity. The risk of VTE was higher during the postpartum period than that during pregnancy. The incidence of VTE was 0.55/1000 overall maternities (0.055%). The pharmacological type of prophylaxis was the predominant used type. Obesity and cesarean delivery were significant factors determining VTE prophylaxis. Further large-scale prospective studies with longer duration are warranted to confirm our findings.

Key words: Obstetric, Venous thromboembolism, Incidence, Prophylaxis**Introduction**

Venous thromboembolism is a disease that influences venous circulation and distinctly presented by deep vein thrombosis (DVT) and pulmonary embolism (PE) ^[1]. Obstetric venous thromboembolism poses significant public health defiance and it is one of the foremost causes of maternal mortality and severe maternal morbidity, it has been reported that 51.4% of the women during pregnancy and postpartum were at risk of VTE ^[2] and about 9.2% of maternal deaths in the United States were caused by VTE with an observed increased incidence from 15.6

to 29.8 per 100,000 deliveries in short period (from 2006:2012) ^[3].

Other studies reported that the prevalence of VTE during pregnancy was 0.5-2.0/1000 pregnancies ^[4,5,6]. The risk of VTE increases by 6-fold during pregnancy however, it increases by 60-fold during puerperium ^[7,8]. Several factors are responsible for the increased risk of VTE during pregnancy "due to its related physiologic and anatomic changes" such as hypercoagulability, inferior vena cava and pelvic veins compression posed by uterus enlargement and

progesterone-related venous stasis in addition to decreased mobility^[9].

The prevention of VTE could be obtained by careful assessment of its associated risk factors and the administration of optimum prophylaxis. Multiple risk factors for obstetric VTE were confirmed but varied in their intensity. Of these, previous pregnancy-related VTE, high maternal age at delivery (>35 years), conception induced by assisted reproductive techniques (ART), caesarean delivery, smoking, preeclampsia, obesity, immobility, thrombophilia, lupus, vascular disorders, prolonged labor in addition to postpartum hemorrhage and infection^[2, 10, 11, 12, 13, 14].

The pharmacological type is the major type of VTE prophylaxis and unfractionated heparin (UFH) is the main anticoagulant used^[9]. Factors determining VTE prophylaxis were not intensively studied, but a recent large international study reported that obesity, caesarean delivery, ethnicity and immobility were of the significant factors^[2]. The objectives of this study were to assess the incidence of VTE, types of prophylaxis received and factors that could determine prophylaxis in women during pregnancy and puerperium through the period of one year.

Patients and methods

This prospective study was carried out at the department of obstetrics and gynecology, Minia maternity university hospital, Egypt during the period of one year (June 2018 to June 2019). The study included women attended to the hospital at risk of venous thromboembolism as per the latest criteria published by the Royal College of Obstetricians and Gynaecologists (RCOG) guidelines^[14]. Inclusion criteria were; age >18 years, women with confirmed pregnancy consulting for first prenatal consultation and intercurrent medical condition and those who have the ability to participate.

Exclusion criteria were; women who have experienced VTE (DVT and/or PE) in the last 4 months, women already receiving antithrombotic therapy for a specified medical reason

such as previous VTE, atrial fibrillation or mechanical prosthetic heart valves. Informed consent was taken from all participants before enrolment in the study.

Full history was taken including demographics, baseline characteristics, obstetric and medical history, history for previous abnormal pregnancies, history for pre-existing thrombotic diseases and family history of VTE. In addition, vital signs and the current treatment or medication were assessed. Also, patient characteristics were recorded such as smoking, cross varicose veins, venous insufficiency and type of current pregnancy. Also, the intensity of VTE risk according the RCOG recommendation (low-moderate-high) and laboratory risk factors were assessed. In addition, the outcome was recorded.

Statistical analysis

Data were entered and analyzed using SPSS program (Statistical Package for Social Sciences, version 20, IBM, NY, USA). Numerical data were presented as mean \pm standard deviation (SD) and range, while categorical data were presented by number and percentage. Chi-square test was used for the assessment of the factors that determine VTE prophylaxis.

Results

A total of 901 women who attended our hospital and were at risk of VTE as per the RCOG guidelines participated in the study (298 cases during pregnancy and 603 cases during puerperium, fig. 1). They comprise 8.22% of the total deliveries during the study period (n=10956), (fig. 2). The mean age of the enrolled women was 31.7 ± 9.1 years (19-47) and the mean BMI was 30.7 ± 5.5 kg/m² (22-42). Regarding parity, about half of them (486 cases, 53.9%) had 1:2 and 363 cases (40.3%) had 3 or more. About two-thirds of them (71.5%) had a caesarean delivery Table (1).

As regards VTE risk factors, varicose veins were found in 209 cases (23.2%), previous VTE in 189 cases "21.0%" (pulmonary embolism in 48 cases and lower limb proximal DVT in 91

cases), previous superficial vein thrombosis (SVT) was recorded in 240 cases (26.6%) and previous arterial ischemic events (AIE) in 83 cases (9.2%). Preexisting medical disorders were presented in 190 cases "21.1%" (136 cases of them had diabetes mellitus). Ten cases (1.1%) had thrombophilia, 17 cases (1.9%) had laboratory risk factors however, 13 (1.4%), 8 (0.9%) and 9 cases (1.0%) had positive family history of VTE, cancer and thrombophilia, respectively (Table, 2). Regarding type of prophylaxis and treatment received, the vast majority of patients (897 cases 99.6%) received pharmacological treatment (55.6% of them received unfractionated heparin and the rest of

them 43.9% received Aspirin) however, only 4 cases received mechanical treatment Table (3).

According to the intensity of VTE risk, 423 cases (46.9%) had mild risk, 352 cases (39.1%) had moderate risk and 126 cases (14.0%) had severe risk (fig. 3). Of the total included cases, 47 cases (5.2%) had dead babies (fig. 4). A total of 6 cases developed VTE from the total included cases with an incidence of 0.55/1000 maternities (0.055%). Obesity (BMI >30 kg/m²) and cesarean delivery were significant factors that determine VTE prophylaxis with an odds ratio of 1.68 (95% CI, 1.20-2.35, p<0.01) and 2.05 (95% CI, 1.49-2.80, p<0.01), respectively Table (4).

Table (1): Participant demographics.

Variable		Descriptive (n=901)
Age (year)		31.7 ± 9.1 (19-47)
Body mass index (kg/m ²)		30.7 ± 5.5 (22-42)
Smoking	-ve	830 (92.1%)
	+ve	42 (4.7%)
	Stopped	29 (3.2%)
Parity	PG	52 (5.8%)
	P 1:2	486 (53.9%)
	P ≥ 3	363 (40.3%)
Mode of delivery	Vaginal	257 (28.5%)
	Caesarean	644 (71.5%)

Table (2): Participant characteristics.

Variable		Descriptive (n=901)
Varicose veins	No	692 (76.8%)
	Yes	209 (23.2%)
Previous VTE	No	712 (79.2%)
	Pulmonary embolism	48 (5.3%)
	Lower limb proximal DVT	91 (10.0%)
	Other rare	50 (5.5%)
Previous superficial vein thrombosis (SVT)	No	661 (73.4%)
	Lower limb SVT	137 (15.2%)
	Upper limb SVT	54 (6.0%)
	Others	49 (5.4%)
Previous arterial ischemic events (AIE)	No	818 (90.8%)
	Stroke	28 (3.1%)
	MI	29 (3.2%)
	Others	26 (2.9%)
Presence of preexisting medical disorders	No	711 (78.9%)
	Chronic heart disease	11 (1.2%)
	NIDDM	49 (5.5%)
	Nephrotic	12 (1.3%)
	Chronic lung disease	11 (1.2%)
	IDDM	87 (9.7%)
	Chronic neurological disease	10 (1.1%)
	IBS	10 (1.1%)
Presence of thrombophilia	No	891 (98.9%)
	Yes	10 (1.1%)
Laboratory risk factors	No	884 (98.1%)
	Yes	17 (1.9%)
Family history	No	871 (96.7%)
	Cancer	13 (1.4%)
	VTE	8 (0.9%)
	Thrombophilia	9 (1.0%)

Table (3): Type of prophylaxis and pharmacological treatment received.

Variable			Descriptive (n=901)
Type of prophylaxis	Pharmacological (n=897)	Aspirin	395 (43.9%)
		Un-frac. heparin	501 (55.6%)
	Mechanical	4 (0.4%)	
	Both types	1 (0.1%)	

Table (4): Factors determining VTE prophylaxis.

Variable	Odds ratio (95% CI)	p. value
Obesity (BMI >30 kg/m ²)	1.68 (2.07-4.82)	<0.01**
Cesarean delivery	2.05 (1.20-2.35)	<0.01**

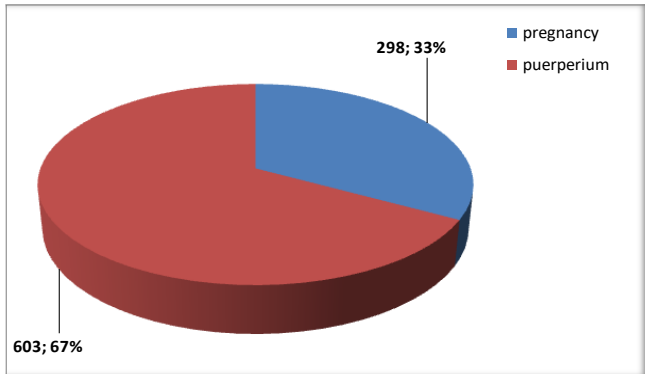


Figure (1): Women at-risk of VTE.

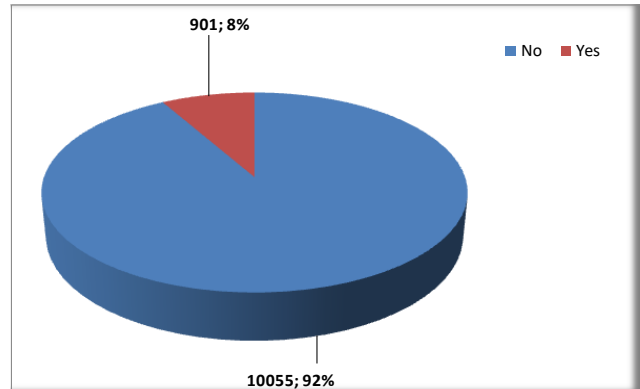


Figure (2): Incidence of women at VTE Risk.

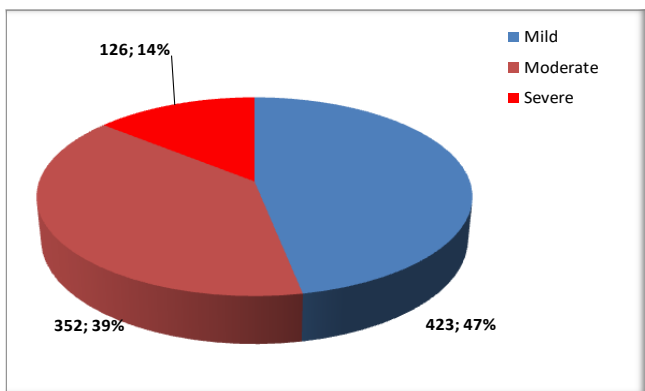


Figure (3): Intensity of VTE risk.

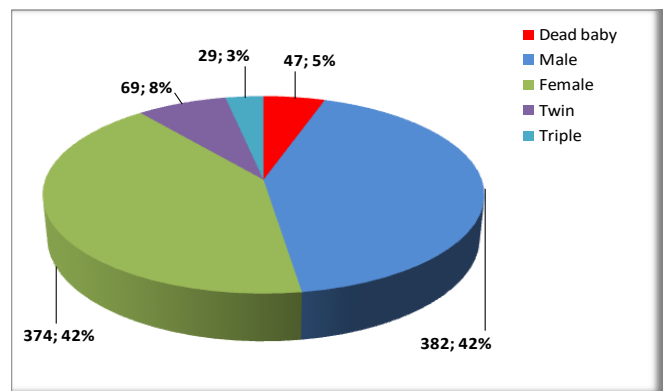


Figure (4): Outcome of the study group.

Discussion

Venous thromboembolism poses a life-threatening obstetrical burden and it is one of the major causes of maternal morbidity and mortality with an increased incidence throughout the last decades. To the best of our knowledge, very few studies assessed obstetric VTE in Egypt. Of these, a recent large multinational study included Egypt and 17 countries else^[2]. The results of the present study demonstrated that 8.22% of the

women attended the hospital during the study period were perceived at risk of VTE, about half of them (47.0%) were mild in intensity. This rate was lower than that reported in the mentioned large multinational study by Gris et al.,^[2]

who found that the rate of women at VTE risk in middle east countries was 21.0% "mostly mild in intensity" however, the global rate was 51.4% (which was obviously higher than our rate).

Also, in a previous multinational study that was carried out in the Arabian Gulf countries, they found that 32% of the pregnant women were at risk VTE^[15] however, a rate of 40% was reported in another study in Ireland ^[16].

This lower perceived risk could be attributed to less frequently risk factors (ie. smoking, gross varicose veins, previous abnormal pregnancies, previous SVT, venous insufficiency in addition to the family history of VTE, cancer, and thrombophilia) in the present study population. This was partly consistent with the results reported about Egypt "Assiut governorate" by Gris et al.,^[2] The results of our study showed that VTE risk was higher during the postpartum period than during pregnancy, this result ties well with previous studies^[2,8,17].

Currently, we found that the incidence of VTE was 0.55/1000 maternities (0.055%) and this is in line with previous reports showing that the VTE incidence was between 0.4:1 per 1000 maternities^[6,18,19]. Also, other studies reported that the incidence of VTE during pregnancy was 0.5:2.0/1000 maternities^[4,5,6]. However, in a recent meta-analysis included 27 articles, Meng et al.,^[20] studied the incidence of VTE during pregnancy and the puerperium and they found that the pooled incidence of VTE was 1.4% (1.0-1.8%).

In the present study, all included at-risk women received prophylaxis and the vast majority of them (99.6%) received the pharmacological type of prophylaxis. Similarly, Gris et al.,^[2] reported that more than 90% of at-risk women received prophylaxis and the pharmacological treatment was predominantly used in the middle east and Africa while globally, a combination of both mechanical and pharmacological treatments was used and comprised about half of the prophylaxis. Also, recent clinical practice guidelines recommended pharmacological prophylaxis in women at risk of VTE ^[14, 21].

Regarding the used type of pharmacological prophylaxis in our study, 55.6% of included cases received unfractionated heparin and the rest of them 43.9% received Aspirin. Recently,

Rybstein and DeSancho,^[9] reported that unfractionated heparin (UFH) is the main anticoagulant used for the treatment of women at VTE risk with high safety and low cost. The benefits of UFH compared to low-molecular weight heparin (LMWH) are that it has a shorter half-life and there is more complete reversal of its activity by protamine sulfate^[22]. Gris et al.,^[2] reported that aspirin was preferred "over LMWH" in some regions such as South Asia, they added that the vast majority of aspirin prescriptions are not performed for its primary indication "prevention of placenta-mediated complications" but to cover the risk of venous thrombosis.

The present results revealed that obesity (BMI >30 kg/m²) and cesarean delivery were significant factors determining VTE prophylaxis with an odds ratio of 1.68 (95% CI, 1.20-2.35, p<0.01) and 2.05 (95% CI, 1.49-2.80, p<0.01), respectively. These results agreed with those of Gris et al.,^[2] who found that obesity and caesarean delivery are from the factors determining VTE prophylaxis in Africa (OR 0.52 "0.27, 0.99" and 6.46 "1.97- 21.23", respectively). Also, earlier studies reported that high VTE incidence was strongly associated with obesity and caesarean delivery ^[12, 13, 14].

The present study has some limitations, of these, we did not assess the knowledge and the attitude of physicians toward the application of the international guidelines and toward VTE prophylaxis. The present results were restricted only for cases attended our hospital and we could not survey cases who were diagnosed and treated outside and this may falsely lower the overall obtained rate of VTE. An additional limitation is that the data were collected from one hospital, although the studied hospital is the main tertiary referral hospital in our region.

Conclusion

In conclusion, the incidence of women perceived at VTE risk during the study period was 8.22% "which is lower than other studies", about half of them were mild in intensity. The risk of VTE was higher during the postpartum period than that during pregnancy. The incidence of VTE

Obstetric Venous thromboembolism: A One-year Prospective Study in a Tertiary Hospital in Egypt.

was 0.55/1000 overall maternities (0.055%). The pharmacological type of prophylaxis was the predominant used type. Obesity and cesarean delivery were significant factors determining VTE prophylaxis. Finally, further large-scale prospective studies with longer duration and different settings are warranted for focusing on this issue.

Ethical considerations: The study protocol and all procedures were approved by the ethical committee of the Department of Obstetrics & Gynecology at Minia College of medicine. All Participants had signed a written informed consent after they have been made aware of the purpose of the study.

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Conflict of interest: None.

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