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ORIGINAL RESEARCH OBSTETRIC ANESTHESIA

Risk assessment of maternal venous thromboembolism in antenatal and postnatal period; a cross-sectional, descriptive study

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Abstract

Background: Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), is quite common disease and is associated with substantial morbidity and mortality. According to report on mortality by Iraqi Ministry of Health, maternal pulmonary embolism was the second most common cause among the direct causes of maternal deaths. We assessed the risk of thromboembolism during pregnancy and puerperium.

Methodology: This cross-sectional, descriptive study was conducted in selected primary healthcare centers in Al-Najaf during the period from April 01, 2018 to December 01, 2018. We selected 236 women (pregnant and postpartum) by convenient sampling method. All pregnant and postpartum women reporting to the hospital constituted the target population of the study.

Results: Risk assessment in antenatal group was low in 119 (74.4%) women, intermediate in 40 (25.0%) and high in one (0.6%) woman, while in postnatal group it was low in 50 (65.8%), intermediate in 25 (32.9%) and high in one woman (1.3%). According to these findings, the frequency of low risk was higher in antenatal group compared to postnatal group, while the frequency of intermediate and high risks was higher in postnatal than antenatal group; however, the differences were not significant statistically, ($P > 0.05$).

Conclusion: Women have more high and intermediate risk of thromboembolism in the postnatal period than antenatal period. The significant risk factors are multiple parity, middle age, gross obesity, medical comorbidities, preeclampsia, current systemic infection, elective cesarean section and hyperemesis gravidarum with dehydration.

Key words: Anticoagulants / therapeutic use; Antenatal period; Cesarean Section / statistics & numerical data; Female; Hospitalization; Humans; Maternal Age; Maternal Mortality; Patient Safety; Postpartum Period; Pregnancy; Pregnancy Complications, Cardiovascular / mortality; Risk Factors; Venous Thromboembolism / complications; Venous Thromboembolism / mortality

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1. Introduction

Venous thromboembolism (VTE) is a state in which blood clots in the deep veins of the leg, known as deep vein thrombosis (DVT) and can travel in the venous circulation and lodge in the lungs, leading to pulmonary embolism (PE). Together, DVT and PE are known as VTE - a dangerous and potentially deadly medical condition.[1] Thrombus formation and its dispersal depend upon three conditions, known as 'Virchow's triad'; it includes pre-existent abnormalities of blood vessel

walls, blood flow, and/or the blood clotting components. Pregnancy induces a pro-thrombotic state with an increase in coagulation factors, a decrease in natural anticoagulants, e.g., the coagulation inhibitor protein S, and failure of fibrinolysis, which is mediated by an increase in plasminogen activator inhibitor.[2]

VTE is known as one of the leading causes of maternal morbidity and mortality all over the world. The reported incidence of VTE from the developed countries is 1-2 cases per 1000 pregnancies. The risk of DVT is five times higher in pregnant women compared to non-pregnant ones. The risk of VTE is greater in postpartum than during the antenatal period.[3] The risk is comparatively increased during the first and second trimesters, and rises sharply during the third trimester and puerperium.[4] Currently, embolism is the leading cause of maternal deaths in the United States and much of the developed countries.[5]

According to Report on Mortality in Iraq (2013, 2014, 2015) by MoH/ Iraq, maternal PE was the 2nd most common cause among the direct causes of maternal deaths. It has been shown to be responsible for 19%, 17%, and 14% of all maternal deaths in 2013, 2014, and 2015, respectively. It is the most grave vascular complication that arises during in the postpartum period.[6] Also PE was the 2nd most common cause among the direct causes of maternal deaths in the years 2010, 2011, and 2012, while postpartum hemorrhage was the most common cause of maternal death.[7] The direct risk of death due to PE was associated with cesarean section, since deaths happened during the first hours following the cesarean section.[6] There are some factors that determine the extent of the risk of VTE in association with the pregnancy or the puerperium. These are identified after an extensive study search and

presented in two major guidelines published from Canada (2014) and the United Kingdom (2015).[3] Risk assessment is a dynamic process that should be done on the first pregnancy visit and repeated, whenever there was any development or admission during the pregnancy, during labor, immediately after delivery and puerperium.[3]

In Iraq, the assessment should be repeated during every visit in primary healthcare centers for all pregnant and postpartum women according to guidelines of MoH/Iraq. Low molecular weight heparins (LMWHs) are the preferred agent.[8]

2. Methodology

This cross-sectional, descriptive study was conducted at four primary healthcare centers from 1st April 2018 to 1st December 2018. All pregnant and postpartum women constituted the sample population of the study. Convenient collection of cases was done in two days of each week of the study period. A sample of 236 women (pregnant and postpartum) was studied. The primary healthcare centers were chosen by a convenient technique. History was obtained by personal interviewing and was recorded on a structured and modified questionnaire.

Sample size was calculated by using the fallowing formula:

Estimated sample size (n) = $z^2*(p)*(1-p)/d^2$

Z is equal to 1.96 (confidence interval corresponded to 95%)

P percentage of estimated prevalence that obtained from a previous study which is equal to (0.775)

d (border of error which was chose to be 0.05)

Sample size=$(1.96)^2 0.19(1-0.19)/(0.5)^2$ = 236 according to 19%.

Statistical analysis

Data were entered, managed and analyzed using the Statistical Package for Social Sciences Version 20.

the **Table 1: Demographic characteristics of the studied groups. Data given as n (%)**

Parameter		Prenatal (N=160	Postnatal (N=76)	Total N = 236	P. value
Age (year)	≥ 35	19 (11.9)	11 (14.5)	30 (12.7)	0.575
	<35	141 (88.1)	65 (85.5)	206 (87.3)	
Residence	Rural	67 (41.9)	38 (50.0)	105 (44.5)	0.241
	Urban	93 (58.1)	38 (50.0)	131 (55.5)	
Education	Illiterate	3 (1.9)	3 (3.9)	6 (2.5)	0.302
	Primary school	62 (38.8)	33 (43.4)	95 (40.3)	
	Secondary school	64 (40.0)	32 (42.1)	96 (40.7)	
	Graduate/Post graduate	31 (19.4)	8 (10.5)	39 (16.5)	
Occupation	Housewife	147 (91.9)	71 (93.4)	218 (92.4)	0.676
	Employee	13 (8.1)	5 (6.6)	18 (7.6)	

Table 2: Risk factors in prenatal group

Risk Factor	N (%)
Single VTE	1 (0.6)
Immobility	3 (1.9)
Medical comorbidities	19 (11.9)
Gross varicose vein	11 (6.9)
Current systemic infection	31 (19.4)
Preeclampsia	2 (1.3)
Surgical procedure	2 (1.3)
Dehydration hyperemesis	23 (14.4)
Multiple pregnancy or assisted reproductive therapy	1 (0.6)
Total	93 (58.3)

Table 3: Frequency distribution of the risk factors among 76 women in postnatal group

Risk Factor	N (%)
Immobility	1 (1.3)
Medical comorbidities	3 (3.9)
Gross varicose vein	3 (3.9)
Current systemic infection	7 (9.2)
Preeclampsia	1 (1.3)
Elective CS	13 (17.1)
Postpartum hemorrhage	2 (2.6)
women req. ante LM	1 (1.3)
Cesarean section in labor	3 (3.9)
Prolonged hospital admission	1 (1.3)

Descriptive statistics of the variables expressed as frequencies and percentage and compared with chi-squared test or Fisher's exact test, when chi-squared was inapplicable (more than 20 of the cells in the table had expected values < 5). $P \leq 0.05$ was considered significant.

3. Results

There were 160 antenatal women and 76 postnatal women enrolled in this study; 19 (11.9%) of women in the antenatal group and 11 (14.5%) women in postnatal group were aged ≥ 35 y, the remaining women in both groups being less than 35 y. Other demographic variables are shown in Table 1.

Comparison of both groups revealed no statistically significant differences in the frequency distribution of all variables including age, residence, education and occupation, in all comparisons (P = 0.328). Only 2/160 (1.3%) women in antenatal group were smokers out while none of those in postnatal group were smokers, (P > 0.05).

Regarding obesity, 49 (30.6%) women in antenatal group and 16 (21.1%) in postnatal group were obese with a BMI ≥ 30 kg/m^2 (P = 0.124).

Out of the 160 women in antenatal group, 53 (33.1%) had 3 or more parities compared to 47/76 (61.8%) in postnatal group, other women had less than 3 parities; the difference being statistically significant (P < 0.001).

Risk factors in antenatal group are summarized in Table 2, and main risk factors in postnatal group are summarized in Table 3.

Regarding the risk assessment, in antenatal group it was low in 119 (74.4%) women, intermediate in 40 (25.0%) and high in only one (0.6%) woman, while in postnatal group it was low in 50 (65.8%) women, intermediate in 25 (32.9%) and high in only one (1.3%) woman. According to these finding, the frequency of low risk was higher in antenatal group compared to postnatal group, while the frequency of intermediate and high risks was higher in postnatal than antenatal group, however, the differences did not reach the statistical significance, (P > 0.05) (Table 4).

In total, there were 169 (71.6%) women with low risk, 65 (27.5%) with intermediate and only 2 (0.9%) women with high risk, (Figure 1). By using ordinal multiple regression analysis, 8 factors appeared to be significant for higher risk of VTE. These factors are age ≥ 35 y (OR = 6.016), obesity (BMI ≥ 30 kg/m^2) (OR = 2.342), , Parity > 3 (OR = 3.897), presence of medical comorbidities (OR = 5.056), current systemic infection (OR = 3.444), preeclampsia (OR = 10.967), hyperemesis gravidarum (OR = 5.220) and cesarean section (OR = 7.071).

Table 4: Comparison of risk assessment between both studied groups

Risk assessment	Prenatal (N = 160)	Postnatal (N = 76)	P value
Low	119 (74.4)	50 (65.8)	P > 0.05
Intermediate	40 (25.0)	25 (32.9)	
High	1 (0.6)	1 (1.3)	

4. Discussion

The incidence of Venous Thromboembolism (VTE) in pregnancy is much higher in pregnant compared to non-pregnant women; this risk is approximately 5 times higher than the risk in non- pregnant

Table 5: The significant risk factors for high risk assessment among the studied group using ordinal regression analysis

Risk Factor	Odds ratio OR	95% CI of OR		P- value
		Lower Bound	Upper Bound	
Age > 35	6.016	3.139	8.894	< 0.001
Obesity	2.342	1.597	4.088	0.009
Parity > 3	3.897	1.960	5.834	< 0.001
Medical comorbidities	5.056	2.927	7.186	< 0.001
Current systemic infection	3.444	1.458	5.430	< 0.001
Preeclampsia	10.967	4.603	35.537	0.008
Dehydration hyperemesis gravid.	5.220	2.671	7.768	< 0.001
Elective cesarean section	7.071	2.467	11.674	< 0.001

women. there are different risk factors play an important role in the development of VTE in both pre and postnatal period. Previous studies indicated that an increase in relative risk persists until week 12 after childbirth.[3,4] We assessed the risk of thromboembolism during pregnancy and puerperium in a total of 160 antenatal and 76 postnatal women.

In general, for the 236 participant women, a higher proportion (71.6%) had the low risk, 27.5% had an intermediate risk, while only 2 women (0.9%) had high risk.

These findings agreed in part with the results of previous studies that assessed the risk of VTE in pregnancy and postnatal period. An earlier study was conducted by James et al. from USA during 2000-2001,[9] which concluded that the incidence of pregnancy-related VTE was much higher than the what was generally quoted.

The present study found that smoking was not associated with incidence of VTE in antenatal or postnatal period; no significant difference between both groups was found.

By using ordinal multiple regression analysis, the present study found that the age ≥ 35 y, BMI ≥ 30 kg/m^2, parity > 3, presence of medical comorbidities, current systemic infection, preeclampsia, hyperemesis gravidarum and cesarean section all were significant risk factors with different odds ratios.

André Luiz et al. reported that obese women were more likely to have VTE.[10] Another study from Denmark conducted in 2009 by Virkus et al. concentrated on obesity.[11] Yesim Dargaud from UK[4] agreed with all these researches and confirmed the importance of obesity as a risk factor for VTE like our study in Najaf. It is probably due to high prevalence of obesity all over the world.

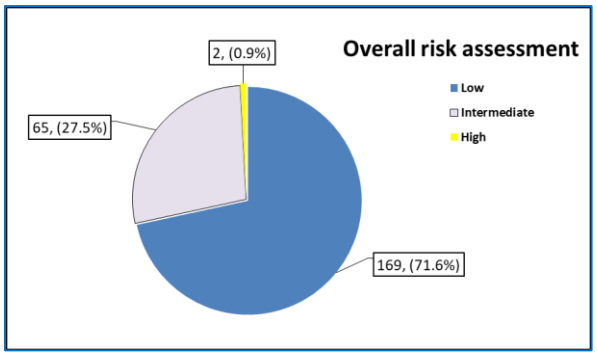

Figure 1: Risk assessment of total study participants (N = 236)

Regarding high parity which is the more frequent risk factor in the present study due to many factors; first the large family size is common in Najaf, as the Iraqis prefer to have many children, and secondly it might be due to ineffective system of family planning in our society. High parity as a risk factor was also reported in the various other studies.[4,11,12]

About thrombophilia (symptomatic and asymptomatic) no case was found in this study due to low prevalence of this disease in Iraq.[13] A study by Arab H. et al.[3] had similar results about Saudi Arabia, in contrast to a study in UK by Dargaud, which showed the prevalence to be 66.8%.[4]

Postnatal risk factors include cesarean section, particularly if this was associated with a prolonged hospital stay or emergency delivery. It was significant in this study, which might be due to increased rate of cesarean sections in the last few years in Iraq; in 2018 the rate of cesarean sections in Najaf was 43%,[14] similar that of in Saudi Arabia and in France.[3,5]

Medical comorbidities, e.g., diabetes mellitus, hypertension, heart or lung disease, cancer, sickle cell anemia etc. have been shown to be significant risk

factors in various studies.[3,9,13,14] The present study is also in agreement, due to high prevalence of medical comorbidities all over the world.

5. Conclusion

Women have high and intermediate risk more in postnatal period than the antenatal period, while the low risk is more in the antenatal period than the postnatal one. The significant risk factors in the current study were multiple parity, middle age, severe obesity, medical comorbidities, pre-eclampsia, current systemic infection, elective cesarean section and hyper emesis gravidarum with dehydration.

Conflict of interesting

No conflict of interest declared by the authors.

Data availability

Numerical data generated in this study is available with the authors.

Authors' contributions

HH: Concept and design of study or acquisition of data or analysis and interpretation of data; Drafting the paper or revising it critically for important intellectual content; and Final approval of the version to be published.

SJM: Drafting the paper or revising it critically for important intellectual content; and Final approval of the version to be published.

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