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Thromboembolism and Thrombosis during Pregnancy and After Delivery between 2009 and 2012 in Al-Zahra Educational Center

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ABSTRACT

Venous thromboembolism (VTE) is considered as one of the leading causes of maternal mortality during pregnancy and postpartum period. In this retrospective study the medical records of 81 women diagnosed with Pulmonary thromboembolism (PTE) and Deep venous thrombosis (DVT) between 2009 and 2012 in Tabriz Al-Zahra hospital was participated. These cases were evaluated regarding frequency, maternal and fetus risk factors associated with VTE. During 3 years 33 patients were diagnosed as PTE; 7 women were diagnosed as DVT and PTE; and 41 women were diagnosed as DVT. Most frequent underlying disease was hypertension (13.5%) and most frequent symptoms of PTE and DVT were dyspnea (100%) and swelling of lower limb (100%) respectively. 93% of PTE and 79% of DVT incidences occurred during and after the third trimester of pregnancy. Additionally, 38% of PTE occurred during or after childbirth (33% following cesarean and 5% following vaginal delivery). Therefore, it seems that vaginal delivery is safer than cesarean surgery. In addition, the importance of third trimester of pregnancy and postpartum period is obvious.

Introduction

Venous thromboembolism events (VTE) include pulmonary thromboembolism (PTE) and deep venous thrombosis (DVT), occurring in one in every 1000 pregnancies. However, VTE is considered as one of the serious complications of pregnancy.[1,2]

Pregnancy due to hypercoagulability, venous stasis, and vascular damage is considered as typical example of Virchow triad.[3] Therefore, the prevalence of this complication increase about four to five times in pregnant women and about 20 times in postpartum period.[4,5]

In the absence of prevention and timely diagnosis,[6] the VTE may lead to irreversible consequences for mother and her fetus. So, pulmonary embolism is a leading cause of maternal death worldwide.[7-9] Unfortunately, despite the strong association between pregnancy and VTE there is inadequate evidence about preventive or curative methods for VTE.[1] So, the aims of this study were to investigate frequency, risk factors, complications, medical treatments, and their complications of VTE in pregnant women.

Materials and methods

This retrospective study was conducted on medical records of pregnant women diagnosed with VTE in Al-Zahra educational center between 2009 and 2012. The census sampling method was used to access all medical records. The total suspected cases of VTE was 98 cases, and after the accurate evaluation of each medical record the number decreased to 81 cases. A checklist was designed including these parts: demographic characteristics, risk factors, symptoms of VTE, pregnancy status, thrombosis location, type of treatment,

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duration and dosage of drugs, maternal complication, and labor and fetus outcomes.

Based on review of textbooks and scientific articles.

Risk factors examined were included: age, parity, history of abortion, history of multiple births, past medical history (pregnancy-induced hypertension, chronic hypertension, heart disease, diabetes, cholecystectomy), past history of VTE during pregnancy or non-pregnancy periods, antiphospholipid syndrome, obstetric history, and mode of delivery.

Thrombophilia tests were included identifying protein C and S, mutation of factor V Leiden, homocysteine, and mutations of prothrombin and antithrombin-3 genes. The first six weeks after delivery was considered as a determined period for diagnosis of VTE. Diagnosis of pelvic venous thrombosis was performed by changes in the flow of femoral veins by Color Doppler Sonography and confirmation of PTE with CT scan or MRI. Fetus outcome was analyzed based on major fetus anomalies, apgar score of infant and neonatal complications during hospitalization. The validity of prepared checklist was determined by using content validity conducted by 10 academic staff of Tabriz University of Medical Sciences, Relialolity of checklist.

Data analysis was performed using descriptive statistic including frequency, percent, mean and standard deviation using SPSS statistical software ver. 13. This research project was approved by Students Research Committee at Tabriz University of Medical Sciences.

Results

Participants were diagnosed with the following complications: 33 women (41%) with PTE; 7 women (9%) with DVT and PTE; 41 women 50% with DVT. The average age were 28.76 (7.69) years. 65 women 85% did not report history of abortion. 11 women had a history of twin pregnancy and one% had a history of triple pregnancy. 65 women (62%) did not have a history of previous illness and most frequent disease in them was hypertension 13.5% that include chronic hypertension 6.1% and pregnancy-induced hypertension 7.4%. Other risk factors and obstetric history of women is reported in table 1 and table 2.

The occurrence of PTE in one women (2.5%) were in the first trimester of pregnancy; in 2 women (5%) were in the second trimester of pregnancy; in 22 women (55%) were in third trimester of pregnancy; and in 15 women (38%) were during or after delivery (33% after cesarean and 5% after vaginal delivery). Also, three cases of DVT (6.2%) occurred in first trimester of pregnancy; and in 7 (14.5%), 32 (66.6), and 6 (12.5) cases occurred in second and third trimester of pregnancy and after delivery respectively.

In 12 cases (14.8%) the DVT occurred in the right leg, in 27 cases (33.3%) in the left leg and in 3 cases (3.7%) in both legs. All VTE patients reported dyspnea, but only 17 cases (43.5%) observed change in their lung sounds. Among 48 DVT patients, limb swelling was evident in all of them and painful and red extremities were observed in 5 cases (10.4%) and two cases (4.1%) respectively.

All patients were received drug therapy and there was no need for orokinase or inferior vena cava filter. Heparin therapy: Starts with IV infusion of 1000 units per hour and was modified based on heparin protocol.

Heparin as a prophylaxis: 5000 unit each hour. Enoxaparin therapy: 1 mg per kg of body weight daily. Enoxaparin as a prophylaxis: 40 mg daily.

In all cases of PTE Heparin was discontinued from 4 hours prior to delivery.

In 15 cases Enoxaparin did not change to Heparin. In two cases Varfarin was used and changed to Enoxaparin during pregnancy. In both of these cases, the fetal death had occurred in eighth week of pregnancy. In the remaining 13 cases during the onset of labor

the treatment regimen include 40 mg Enoxaparin (two times a day) caused a large hematoma after normal vaginal delivery in three cases (20%). In 12 cases the patients had been used Enoxaparin as prophylaxis before delivery. In these cases the Enoxaparin was changed to Heparin and no complication occurred. In other patients (54 cases) Heparin was used for prophylaxis and treatment and only in one case 1.8% excessive bleeding occurred following vaginal delivery. 67.4% intrauterine fetal death (IUFD) was occurred and 92.6% the remaining infants had apgar scores of 8 or above. There weren't any cases of neonatal abnormalities and bleeding.

Table 1. Risk factors and underlying disease in participants

Risk factors	N (%)	Risk factors	N (%)
Without any underlying disease	62 (76.5)	Diabetes	1 (1.2)
Pregnancy-induced hypertension	6 (7.4)	Cholecystectomy	1 (1.2)
Chronic hypertension	5 (6.1)	History of VTE during pregnancy	1 (1.2)
Artificial heart valves	1 (1.2)	History of VTE in non-pregnancy periods	2 (2.4)
Ventricular septal deficit	1 (1.2)	Antiphospholipid syndrome	1 (1.2)

Table 2. Frequency of obstetric history of women

Obstetric history	N (%)
Without obstetric complication	67 (82.7)
Preterm birth	7 (8.6)
Intrauterine fetal death	2 (2.4)
Preeclampsia	4 (4.9)
Decolement	1 (1.2)

Discussion

PTE is the most common cause of maternal death during pregnancy and in the postpartum period.[10] In this study, all PTE and DVT patients complained of dyspnea and swelling of the lower limb respectively.

So, it is important to pay more attention to these symptoms in pregnant women. The study of James et al., on a sample of 34 pregnant women and 19 postpartum women with DVT showed that in 80% of pregnant women and 79% of postpartum women edema was evident and in 70% of pregnant women and 95% of postpartum women severe discomfort was obvious. In addition, erythema was noted in 26% of patients in both groups.[1]

High dose of anticoagulant therapy is administered for women diagnosed with VTE during pregnancy and in the postpartum period in order to reduce the risk of PTE and death.[7] It should be noted that, pregnant women and the their fetus may be at risk for side effects of therapeutic or prophylactic dosage of anticoagulation therapy.[8,11] Heparin does not pass through the placenta and breast milk and is not associated with maternal and fetal complications.[12] However, administration of Heparin may be associated with some complications such as osteoporosis, allergies, and thrombocyto- penia.[13,14]

In this study, the incidence of major heparin- related bleeding was 1.8%. In contrast, a study on pregnant women by Gillis and colleagues showed that prophylaxis with low molecular weight Heparin (LMWH) results in no any hemorrhage and Enoxaparin is well tolerated during pregnancy.[15] Another study that compared the LMWH with UHF (Unfractionated Heparin) during pregnancy

showed that LMWH is preferred to VHF due to lower incidence of thrombocytopenia.[14]

The total numbers of infant deaths in this study were 6 cases (7.4%) and all of them were intrauterine fetal death (two cases because of using warfarin before pregnancy and four deaths because of unknown etiology). We didn't find any similar studies in this area. But in one study that conducted on a sample of 100 pregnant women the rates of early puberty, miscarriage, stillbirth, neonatal mortality, and congenital anomalies in women who receiving Heparin prophylaxis during pregnancy similar to the normal population and heparin-induced bleeding occurred in two cases.[12]

In this study, 93% of all PTE and 79% of all DVT accidents occurred the third trimester of pregnancy onwards. In a similar study, 48% of DVT events occurred during third trimester of pregnancy, and 32% and 22% of these accidents were occurred during second and first trimester respectively.[16] This shows the importance of considering this time in prevention of VTE in pregnant women.

In present study DVT event occurred in 48 patients, 12 cases in right leg and 27 cases in left leg. Previous studies also show that the majority of DVT occurs in the left leg[1,16] This may be due to the pressure of right iliac artery and the ovarian artery on left iliac vein. Both of these arteries pass only on the left side of the vein.[7] As reported, 38% of cases diagnosed with PTE had occurred during or after delivery (33% following cesarean and 5% following vaginal delivery).

Also, one study reported similar results (60% in cesarean and 40% in normal vaginal deliveries).[1]

In previous studies the main risk factors of VTE are presented as follows: over age pregnancy, history of VTE, smoking, hypertension, obesity, dehydration,[7] surgery, trauma, hospitalization in hospital or home, neoplasms with or without chemotherapy, central venous catheters, cardiac pacemakers, superficial vein thrombosis and neurologic disease associated with paralysis of the extremities.[17] In the present study 7.4%, 12%, 1.02%, and 1.2% of women have a history of pregnancy-induced hypertension, artificial heart valves, VSD, and cholecystectomy respectively. Similarly, Salenon et al., conducted a study on a sample of one million deliveries in Sweden and calculated the risk of PE, in comparison with uncomplicated deliveries, as a 4.8%, 3.8%, 2.7% and 2.3% for women with severe preeclampsia, cesarean delivery, history of diabetes, and multiple pregnancies respectively.[18]

Although thrombophilia test was not evaluated in this study, but the diagnosis of thrombophilia was confirmed in 1.2% of patients. In the similar study in 8 cases 24% of women diagnosed with DVT the thrombophilia diagnosis were confirmed.[1]

Conclusion

Results of this study showed a high rate of VTE in caesarean deliveries. So, there is an urgent need for essential revise in providing educational programs for pregnant women emphasizing on the benefits of vaginal delivery. Also, there is a need for better follow up of women diagnosed with VTE.

Also, due to the higher incidence of VTE in the third trimester of pregnancy the importance of this period in prevention and early detection of VTE is obvious.

In addition, dyspnea and swelling of extremities were reported by all women. So, health care providers should consider these symptoms in taking medical history from all suspected patients. Also, education of pregnant women on preventive procedures of VTE such as varicose socks, proper exercise, and using medications seems reasonable. As well, because of lack of specific antidote, using Enoxaparin for the treatment of VTE in pregnancy can be problematic. The main limitation of present study is low sample size. Therefore, there is a need for further studies with larger sample size to better evaluation of risk factors of VTE during pregnancy.

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Ethical issues

None to be declared.

Conflict of interest

The authors declare no conflict of interest in this study.

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