Analysis of Risk Factors and Complications in Postpartum Lower Extremity Deep Vein Thrombosis Patients at a Single Center

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Abstract

Objective: The objective of this study is to elucidate circumstances surrounding postpartum patients with lower extremity deep vein thrombosis (DVT) including demographics, risk factors, comorbidities, clinical presentation, and outcomes presenting to our tertiary care center. Introduction: Postpartum is a period of increased risk of venous thromboembolism (VTE). Several risk factors such as previous history of VTE, increased maternal age, varicose veins, mode of delivery, and family history of VTE have been suggested, but data supporting these are inconsistent. In this study, we have described circumstances surrounding postpartum lower extremity DVT including demographics, risk factors, comorbidities, and clinical presentation. Materials and Methods: In this retrospective study, all women with lower extremity duplex confirmed DVT during postpartum period, presented at Jain Institute of Vascular Sciences (JIVAS), Bengaluru, from January 2010 to December 2016 were enrolled. Baseline characteristics recorded were age of the patient, index lower extremity involved, segment of the vein involved and comorbidities. Risk factor evaluated were mode of delivery, history of varicose veins, previous history of thrombophilia, VTE, abortions/ miscarriages, and tobacco use. Complications and treatments received in the hospital were documented. Results: Postpartum DVT was seen in 42 out of 1276 DVT patients (497 female patients) treated at JIVAS. The average age was 25.57 ± 5.73 years and left side (29 [69.04%]) being more commonly involved. Risk factors associated in patients were anemia 16 (38.09%), postlower segment cesarean section (LSCS) delivery 16 (38.09%) while tobacco use was seen in 2 (4.76%) patients, and varicose vein in 1 (2.38%). There were no patients with history of VTE, abortions, or thrombophilia. None of the patients had symptomatic pulmonary embolism (PE). All patients were treated with low-molecular-weight heparin and bridged to Vitamin K antagonists. Conclusion: The most common risk factors were anemia and post-LSCS delivery. There was no incidence of symptomatic PE or mortality.

Keywords: Deep vein thrombosis, lower extremity postpartum deep vein thrombosis, postpartum deep vein thrombosis

Introduction

Women are 5 times more likely to develop venous thromboembolism (VTE) during pregnancy than when not pregnant.[1] The incidence of VTE is reported to be about 13/10,000 pregnancies half of which occurs in the postpartum period. The hypercoagulable state of pregnancy has likely evolved to protect women from hemorrhage during miscarriage and childbirth. Indeed, the leading cause of maternal death in the developing world is hemorrhage,[2] but in the United States, the leading cause of maternal death is embolic disease.[3] Besides death, VTE can cause significant acute and chronic morbidity (postthrombotic syndrome).[4] Postpartum is a period of increased risk of VTE.[5] The prothrombotic changes of pregnancy do not revert completely back to normal until up to 6 weeks after delivery, especially after an emergency cesarean section.[6] Clinical data suggest the persistence of an increased risk for up to 6 weeks postpartum with an odds ratio (OR) of 84 (95% confidence interval [CI], 31.7–222.6).[5] Most cases occurred during the first 4 weeks postpartum (95%): With 18%, 42%, 20%, and 15% in the 1st, 2nd, 3rd, and 4th weeks, respectively. The risk remained increased up to 3 months postpartum (OR, 8.9; 95% CI 1.7–48.1). After the 3rd month, the OR was 0.3 (95% CI, 0.1–1.4).[6] Factors such as previous and family history of VTE increased maternal age, obesity, presence of varicose veins, smoking and mode of delivery have been suggested to increase postnatal

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VTE, although data supporting these are inconsistent.\(^5\)\(^,\)\(^7\) Recent data indicate that 50% of postpartum women had two or more risk factors and that interactions between these risk factors are important; obesity, in particular, warrants consideration.\(^6\)\(^ The increased incidence of pregnancy-related VTE among women aged 35 years and older may be partly explained by an increased prevalence of risk factors, such as cesarean delivery, hypertension, heart disease, and obesity.\(^7\)\(^ Although a history of VTE may identify women at increased risk for recurrence during pregnancy or puerperium,\(^9\) most pregnancy-associated episodes of VTE occur in the absence of such a history.\(^9\)\(^ Data regarding thrombophilia and risk of recurrent VTE specifically during postpartum are inconsistent. De Stefano et al. found that inherited thrombophilia, mainly factor V Leiden and prothrombin gene G20210A factor II (FII) polymorphisms, was not associated with a statistically significant increased risk.\(^10\)\(^ The association between cesarean delivery and VTE was previously confounded by many VTE risk factors. In an Australian registry, cesarean section carried an increased risk regardless of whether it was performed in the presence (adjusted OR [aOR] 3.7) or absence (aOR 3.11) of labor after adjustment.\(^11\)\(^ Apart from initial leg symptoms such as pain, discomfort and swelling of leg, lower extremity deep vein thrombosis (DVT) can lead to pulmonary embolism (PE) and death. Routine Heparin prophylaxis for DVT prevention is not indicated in pregnancy/postpartum as this is not cost-effective and has side effects such as heparin-induced thrombocytopenia, bleeding, and osteoporotic fractures.\(^12\)\(^ Hence, the prevalence and severity of this condition warrants careful management.

**Materials and Methods**

Data for this outcome analysis were collected retrospectively from hospital records. All women with lower extremity duplex confirmed DVT during the first 6 weeks after delivery who presented from January 2010 to December 2016 at Jain Institute of Vascular Sciences, Bengaluru, were analyzed in the study. Prior ethics committee approval was not required as this is an observational, single-center, retrospective study, and patient’s identities were not revealed in the study.

**Definitions**

Puerperium or postpartum was defined as the first 6 weeks after childbirth.

Anemia as per the WHO guidelines was defined as hemoglobin <12 mg%.

A heredity history of thrombosis was defined as one or more thromboses in first-degree relatives (father, mother, or siblings) occurring before the age of 60.

Baseline characteristics recorded were age of the patient, index lower extremity involved, segment of the vein involved and comorbidities such as diabetes, hypertension, and heart disease. Risk factor evaluated were mode of delivery, immobilization, or surgery within the last 3 months, history of varicose veins, history of thrombophilia, VTE, tobacco use, hypertension, anemia, and malignancy.

Patient’s signs and symptoms, the time duration from symptom onset to the diagnosis of DVT, and the treatment received.

**Results**

Of the 1276 patients admitted in our unit for lower extremity DVT from January 2010 to December 2016, 497 were female patients, out of which 42 (8.45%) were postpartum DVT cases as shown in Figure 1. The mean age of the patients was 25.57 ± 5.73 years while the age range was 19–37 years. The left lower limb (29 [69.04%]) was more commonly involved than the right lower limb (13 [30.95%]).

The segmental distribution of DVT is shown in Table 1. The most common segment of vein involvement was a combination of proximal and distal DVT seen in 26 (61.90%) patients, and in 1 patient (2.38%), inferior vena cava (IVC) was involved.

The distribution of risk factors is shown in Table 2. Twenty-six (61.9%) patients were delivered vaginally and the rest 16 (38.09%) by lower segment cesarean section (LSCS). Four (9.52%) patients were hypertensive. Anemia was found in 16 (38.09%) patients. Tobacco use was seen in 2 (4.76%) patients. Only one (2.38%) patient had prior history of varicose vein. Neither of the patients was previously

| Table 1: Site of deep vein thrombosis (n=42) |
|-------------------------------------------|
| **Limb involvement** | **Number of patients (%)** |
| Left lower limb | 29 (69.04) |
| Proximal with calf involvement | 19 (45.23) |
| Proximal without calf involvement | 7 (16.66) |
| Calf only | 3 (7.14) |
| Right lower limb | 13 (30.95) |
| Proximal with calf involvement | 7 (16.66) |
| Proximal without calf involvement | 5 (11.90) |
| Calf only | 1 (2.38) |

| Table 2: Distribution of risk factors (n=42) |
|-------------------------------------------|
| **Distribution of risk factors** | **Postpartum DVT patients (%)** |
| Normal delivery | 26 (61.90) |
| Anemia | 16 (38.09) |
| Post-LSCS | 16 (38.09) |
| Hypertension | 4 (9.52) |
| History of tobacco use | 2 (4.76) |
| Varicose vein | 1 (2.38) |
| Diagnosed thrombophilia | 00 |
| Previous history of VTE | 00 |
| History of malignancy | 00 |
| Superficial vein thrombophlebitis | 00 |
| Diabetes | 00 |
| Heart disease | 00 |

DVT: Deep vein thrombosis, LSCS: Lower segment cesarean section
VTE: Venous thromboembolism
diagnosed as a case of thrombophilia nor had a family history of thrombophilia or a history of VTE. No patient had a history of malignancy, superficial thrombophlebitis, diabetes, or heart disease.

The most common presenting symptom was leg edema 36 (85.71%) followed by discomfort during walking, and other symptoms included pain and erythema. The median duration of time from delivery to symptoms was 5 days (range 0–35 days) postpartum. All patients were started on low-molecular-weight heparin (LMWH) and bridged to Vitamin K antagonist (VKA) till therapeutic international normalized ratio was achieved along with Class II compression stockings. None of the patients needed IVC filter placement and thrombophilia testing was not performed.

**DISCUSSION**

The risk of VTE increased with age and increases significantly after age 35. In one study, VTE was 1.64/1000 deliveries for women under the age 35, but 2.27/1000 deliveries for women age 35 and older (38% higher).[7] The mean age our patient was 25 ± 5.73 years and 23.80% (10 patients) of these were older than 30 years. The previous studies showed anemia had an OR of 2.6, cesarian deliver 2.1, smoking 1.7, heart disease 7.1, thrombophilia 51.8, a history of thrombosis 24.8, and the antiphospholipid syndrome 15.8 in postpartum period to develop DVT.[3,9,13] The distribution of associated risk factors in our study have been listed in Table 2 of which anemia was found in 16 (38.09%), cesarean section 16 (38.09%), vaginal delivery 26 (61.90%), hypertension in 4 (9.52%), and tobacco use in 2 (4.76%). Hypertension (probably in association with preeclampsia), immobility, and recent surgery (probably cesarean delivery) appear to be important risk factors for postpartum patients.[3] Most studies showed inconsistent association of smoking with DVT. However, Jacobsen et al. reported an association of smoking with ante- and post-partum VTE (5–9 and 10–30 cigarettes/day prior or during pregnancy).[14] Even though thrombophilia is present in 20%–50% of women who experience VTE during pregnancy or postpartum,[7] at our center no previous history of thrombosis was reported. The conditions identified at the time of enrollment were included in the analysis and because testing for thrombophilia was not done as a part of study due to its false positive results when patient in on anticoagulation, thrombophilia is likely to be underreported.

Postpartum patients were hospitalized for an average of 4.3 days (range 2–7 days) at our center. The left side was more commonly involved than the right which is consistent with previous reports, and anatomic reasons are most likely the cause for same.[15] In a meta-analysis of leg of presentation during pregnancy and the puerperium, 82% of objectively diagnosed DVT occurred in the left lower extremity.[15] The most common segment of vein involved was a combination of proximal and distal DVT. None of the patients had symptoms and signs related to PE; hence, they were not evaluated further for the same.

All patients were treated with LMWH as it has longer plasma half-life, a more predictable dose response; a lower risk of heparin-induced thrombocytopenia and probably a lower risk of osteoporosis[13] and then started on oral VKA’s as bridging therapy. The treatment is offered for a minimum of 3–6 months as per the American college of chest physician (ACCP) guidelines. There is little-published data on whether LMWH’s are secreted in breast milk; in a case series of 15 women receiving LMWH after cesarean section, small amounts of heparin were detected in the breast milk of 11 patients.[16] Since neither unfractionated heparin nor LMWH is orally active, no clinical effect would be expected in the infant.[17] Coumadin is 99% bound to serum proteins which results in minimal transfer to breast milk and is not measurable in breast milk of these patients.[18,19] Currently, there is no data available on use of novel oral anticoagulants (NOAC’s) in postpartum patients. They have been treated with Class II compression stockings as per ACCP guidelines, but recent edition recommendations and Royal College of Obstetricians and Gynecologists guidelines are against their routine use.[20,21] None of the patients had in-hospital PE or any other complication. IVC filter was not indicated in any patient.

Determining which patients should receive thromboprophylaxis remains a challenge. Despite recommendations for thromboprophylaxis for women undergoing cesarean delivery,[22] a 2-fold increased risk may not be sufficient to justify thromboprophylaxis unless other risk factors are present. All published guidelines, including American, British, Australian, and French are in favor of thromboprophylaxis, usually for 6 weeks postpartum in case of previous VTE, regardless of the mode of delivery.[6]

**CONCLUSION**

Postpartum is a very high-risk period for developing VTE. There are both clinical and genetic risk factors for predicting VTE during this period; hence, it is important to systematically assess individual VTE risk, taking into account all risk factors, both antenatal and postnatal. VTE risk assessment should be performed and repeated in every pregnant woman. By improving the identification of postpartum risk factors,
health-care providers may be able to reduce the rate of maternal deaths resulting from PE.

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**Conflicts of interest**
There are no conflicts of interest.

**References**
1. National Institutes of Health. Prevention of venous thrombosis and pulmonary embolism. NIH consensus development. JAMA 1986;256:744-9.
2. World Health Organization. Maternal Mortality in 2000: Estimates Developed by WHO, UNICEF and UNFPA. Geneva: World Health Organization; 2004. p. 1-39.
3. James AH, Tapson VF, Goldhaber SZ. Thrombosis during pregnancy and the postpartum period. Am J Obstet Gynecol 2005;193:216-9.
4. Lindqvist PG, Torsson J, Almqvist A, Björgell O. Postpartum thromboembolism: Severe events might be preventable using a new risk score model. Vasc Health Risk Manag 2008;4:1081-7.
5. 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;6:632-7.
6. BrON-aNdRÉaNI, christine. Phlebolymphology 2013;20:167-73.
7. Andrea H. James, Margaret G. Jamison, Leo R. Brancazio, Evan R. Myer. Venous thromboembolism during pregnancy and the postpartum period: Incidence, risk factors, and mortality. American Journal of Obstetrics and Gynecology 2006;194:1311-5.
8. Ginsberg JS, Hirsh J. Use of antithrombotic agents during pregnancy. Chest 1998;114:524S-30S.
9. McColl MD, Walker ID, Greer IA. Risk factors for venous thromboembolism in pregnancy. Curr Opin Pulm Med 1999;5:227-32.
10. De Stefano V, Martinelli I, Rossi E, Battaglioli T, Za T, Mannucci P, et al. The risk of recurrent venous thromboembolism in pregnancy and puerperium without antithrombotic prophylaxis. Br J Haematol 2006;135:386-91.
11. Morris JM, Algert CS, Roberts CL. Incidence and risk factors for pulmonary embolism in the postpartum period. J Thromb Haemost 2010;8:998-1003.
12. Danilenko-Dixon DR, Heit JA, Silverstein MD, Yawn BP, Petterson TM, Lohse CM, et al. Risk factors for deep vein thrombosis and pulmonary embolism during pregnancy or post partum: A population-based, case-control study. Am J Obstet Gynecol 2001;184:104-10.
13. James KV, Lohr JM, Deshmukh RM, Cranley JJ. Venous thrombotic complications of pregnancy. Cardiovasc Surg 1996;4:777-82.
14. Ray JG, Chan WS. Deep vein thrombosis during pregnancy and the puerperium: A meta-analysis of the period of risk and the leg of presentation. Obstet Gynecol Surv 1999;54:265-71.
15. Richter C, Sitzmann J, Lang P, Weitzel H, Huch A, Huch R, et al. Excretion of low molecular weight heparin in human milk. Br J Clin Pharmacol 2001;52:708-10.
16. Bates SM. Pregnancy-associated venous thromboembolism: Prevention and treatment. Semin Hematol 2011;48:271-84.
17. Clark SL, Porter TF, West FG. Coumarin derivatives and breast-feeding. Obstet Gynecol 2000;95:938-40.
18. Orme ML, Lewis P, de Swiet M, Serlin MJ, Sibson R, Baty JD, et al. May mothers given warfarin breast-feed their infants? Br Med J 1977;1:1564-5.
19. Kearon C, Akl EA, Orlenas J, Blaivas A, Jimenez D, Bounameaux H, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest 2016;149:515-52.
20. Kahn SR, Shapiro S, Wells PS, Rodger MA, Kovacs MJ, Anderson DR, et al. Compression stockings to prevent post-thrombotic syndrome: A randomised placebo-controlled trial. Lancet 2014;383:880-8.
21. Royal College of Obstetricians and Gynaecologists. Thromboprophylaxis During Pregnancy, Labour and After Vaginal Delivery. Royal College of Obstetricians and Gynaecologists Clinical Guidelines. Vol. 37. London: Royal College of Obstetricians and Gynaecologists; 2004. p. 1-13.
22. Jacobsen AF, Skjeldestad FE, Sandset PM. Ante- and postnatal risk factors of venous thrombosis: A hospital-based case-control study. J Thromb Haemost 2008;6:905-12.