Deep Vein Thrombosis during Pregnancy Workup

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ABSTRACT

Background: During pregnancy deep vein thrombosis (DVT) is a considerable factor which contributed to increase maternal fatal mortality and morbidity. It may transpire when there is thrombophilia, because of compression of inferior vena cava (IVC), hormonal changes or venous stasis.

Aim: To assess patients who were pregnant or just given birth and with the condition of deep vein thrombosis in lower limbs.

Method: The study was conducted at Department of Gynaecology and Obstetrics, Lohdran during from August 2016 to May 2018, pregnant were assessed and puerperal patients when there was doubt of deep vein thrombosis. During study period there were 4000 childbirths at hospital in which cesarean were 89%, normal births were 7.5% and forceps deliveries were 3.5%. Eighty four cases were clinically diagnosed as DVT, out of total referred patients with clinical status suggesting deep vein thrombosis, confirmed through venous duplex scan. The age group of pregnant females was 21-years to 39-years.

Results: Out of 84 DVT patients, primigravida were 64 (with no thrombophilia changes there were six twin pregnancies, four resulting from in vitro fertilization), 16 were second birth mothers and at third birth were 4. DVT was occurred in pregnancy first trimester in 8 patients (9.52%), in second trimester DVT was present in 22 patients (26.19%) and in third trimester of pregnancy DVT was developed in 54 (64.29%) patients. Of the 84 DVT diagnosed patients, 36 (42.85%) occurred in infrapatellar veins. In a thirty seven year old patient, there was a case of pulmonary thromboembolism which submitted to in vitro fecundation, with twin pregnancy after C-section a diagnostic of DVT (no thrombophilia). Of the 84 patients, 32 (38.09%) had cause of their deep vein thrombosis (DVT) determined, with prevalence of heterozygous mutation of factor-V Leiden in 12 (14.28%) patients followed by phospholipid syndrome as well as other reasons.

Conclusion: Despite having low frequency during pregnancy DVT is a major reason of increase maternal fetal morbidity. In selected cases thrombophilia investigation should be conducted, such as family or personal history of thrombotic phenomena and thrombophilia. Artificial insemination, twin pregnancy and cesarean births were also observed as a leading factor of DVT.

Keywords: Deep Vein Thrombosis, Pregnancy, Thrombosis, Heparin, Anticoagulant, Maternal-fetal Morbidity.

INTRODUCTION

Pregnancy toxemia is the most common cause of maternal mortality, resulted by pulmonary embolism.¹-⁴ High ratio of C-section deliveries is the major effect of increasing thromboembolic cases in the gynaecology departments. During pregnancy and puerperium period, deep vein thrombosis and pulmonary thromboembolism are the main factors to increase the maternal fatal mortality and morbidity.

There were various reports between 0.5 and 3 deep vein thrombosis (DVT) cases for each thousand pregnancies. In pregnant females deep vein thrombosis is five times more frequent as compared to non-pregnant females in the same age group as estimated by some authors in their studies. Pregnancy is a condition of preliminary hypercoagulability for delivery, by production of endothelial plasminogen activator 1 and 2 through the placenta, decreasing fibrinolytic activity and increase the platelet accumulation. There are also increase in I, VII, VIII and X factors and reductions in S level of proteins and gradual resistance to the activity of protein-C. Concomitantly, inferior vena cava compression by the pregnant womb contribute to venous stasis, therefore, favoring thrombotic phenomena⁵. Thrombophilia define as tendency of thrombosis development, can be acquired or hereditary. The example of acquired hereditary thrombophilia is hyperhomocysteinemia. Both reasoning increase in plasma homocysteine and high possibility of thrombosis³.

In pregnancy and postpartum period deep vein thrombosis significantly increase the maternal fatal mortality and morbidity and also place two lives at risk. Our hospital maternity experience associated with these factors which inspired us to conduct this study. In this study, during pregnancy and postpartum period analyze the reasons of thrombosis with lower limb deep vein thrombosis in patients.

MATERIAL AND METHODS

The study was conducted at Department of Gynaecology and Obstetrics, Lohdran during from August 2016 to May 2018. Eighty four pregnant females between the age group of 21-years to 39-years with clinical suspicion of deep vein thrombosis were analyzed, when there was record of four thousand childbirths. On the basis of symptoms clinically the diagnosed was made. Family & personal history of thrombosis and thrombophilia was thoroughly examined. More than in 80% of patients edema, calf tenderness and pain were present. At lower proportion cyanosis, superficial venous dilatation and homans’ signs were observed. All
patients were clinically examined of deep vein thrombosis resulted by venous duplex scan. After confirmation of deep vein thrombosis, inclusion criteria were established for thrombophilia. To evaluate the comorbid conditions and treatment, D-dimer, echocardiogram, coagulogram and blood count were performed. First choice drug was low molecular weight heparin being carefully control dosage to elude level of activated partial thromboplastin 1.5 to 2 times higher than the normal value. Due to the high cost of this drug its use was limited and all patients not maintain the treatment of low molecular weight heparin due to their financial conditions. We select subcutaneous unfractionated heparin (UHF) in these cases. Through coagulogram monitor the platelet control.

Three months were the minimum anticoagulation time. In thrombosis patients group 1st, 2nd pregnancy trimester, reaches the puerperal period in thrombophilia incidences. Before 24-hours of delivery the therapy was ceased and 6-hours after anesthesia, it was resumed. After 2-months of delivery the treatment was suspended due to thrombophilia suspicion when in 12 cases the results of thrombophilia were confirmed. Three patients did not have laboratory confirmation after therapy who initially considers positive thrombophilia during pregnancy. Thrombophilia patients were referred to hematologist. Surgical treatment through aortic arch ligation was chosen in cases of great saphenous thrombosis using local anesthesia. In any case oral anticoagulation was not use, neither implantation of inferior vena cava filter or fibrinolytic drugs.

Heparin maternal fetal side effects controversial in literature. Heparin is safe for fetus as reported by others whereas, fetal complications in 30% of cases approximately as reported by some authors.\(^1\) No teratogenic complication was found our study. With unfractionated heparin (UHF) two patients with small metrorrhagia were treated, but treatment did not have to suspend.

**RESULTS**

During the period of this study, 4000 deliveries were performed out of which 3560 (89%) deliveries were cesarean, normal deliveries were 300 (7.5%) and 140 (3.5%) deliveries were forceps (Table 1). According to patients’ choice or clinical signs decision regarding procedure was made, any interference was excluded, which recommend normal delivery as 1st option. Patients were referred with DVT suspicion and 84 patient were confirmed examined by expertise. Out of the 84 DVT patients, primigravida were 64 (76%), of whom 6 have twin pregnancy without any thrombophilic change and 4 had in vitro fecundation, patients giving 2nd delivery were 16 (19%) and mothers at 3rd birth were 4 (5%) [Table 2]. 21-years to 39-years range of age of patients. In the first pregnancy trimester, DVT was occurred in 8 (9.52%) patients, in 2nd trimester occurred in 22 (26.19%), in 3rd trimester occurred in 54 (64.28%) included four post C-sections as shown in Table 3. On first post cesarean day there was one case of PTE (Pulmonary Thromboembolism) in a thirty seven year old patient, no thrombophilic change observed in twin pregnancy, whose diagnosed infrapatellar deep vein thrombosis was done after pulmonary thromboembolism (PTE). Between 9th and 36th week DVT was developed in seventy six patients. Between the 1st and 3rd post-operative day eight thrombosis 9.5% were occurred. In forceps deliveries or normal deliveries there was no DVT.

As compared to right lower limb, the left lower limb was prevalent: 38 (42.23%) and 46 (54.76%) respectively as shown in table IV, the most frequent affected was infrapatellar territory, with 36 (42.85%) cases followed by 20 (23.80%) patients in the popliteal veins, 14 (16.66%) patients were in the femoral vein, iliac veins 10 (11.90%) and in the great saphenous veins there were 4 (4.76%) cases (Tables 4-5).

**DISCUSSION**

There are multiple variation happens during pregnancy which contributed to hypercoagulability.\(^6\) Pregnancy can consider a shape of DIC (disseminated intravascular coagulation) impacted to decreased fibrinolytic activity and increase platelet aggregation. There are alterations throughout pregnancy like protein-C activity resistance,
factor-I fibrinogen elevation, VII, VIII hemophilic, X & non willebrand, reduced antithrombin and protein-S\(^3\). These thrombogenic nature changes are introductory resources for deliveries, decreasing bleeding risk for mothers.

There is increase venous pressure during first trimester of pregnancy due to hyperflow in hypogastric and communal iliac arteries, resulting from arterio venous anastomoses due to activity of progesterogen. In addition to these factors, during 2\(^{nd}\) and 3\(^{rd}\) trimesters, due to pregnant uterus there is inferior vena cava compression which results decreased venous flow.\(^5\) We observed in current research that in the 3\(^{rd}\) trimester of pregnancy deep vein thrombosis (DVT) was more frequently occurred, in 54 (64.28%) cases, possibly due to similarity of procoagulating factor and stasis, follow by 2\(^{nd}\) and 3\(^{rd}\) trimester respectively. In the instantaneous post-cesarean duration eight (9.52%) patients had deep vein thrombosis. It is because of pelvic trauma of femoral, tributary veins and iliac.

The happening of VT (venous thromboembolism) is usually higher 2 to 4 times after cesarean delivery when compare to normal deliveries as reported by Ginsberg & Shannon.\(^7,6\) During the 3\(^{rd}\) trimester of pregnancy thrombosis risk is considered high, and specially up to six weeks after delivery (puerperium). However, objective diagnostic tests used by prospective studies not show any dissimilarity between DVT frequency and trimesters of pregnancy.\(^2\) Similarly the present analysis shows that deep vein thrombosis in pregnancy as common as postpartum deep vein thrombosis\(^9\).

Deep vein thrombosis is similar incidence in males and females and most frequent in Caucasian females as compared to Asian.\(^10\) Before twenty years of age its occurrence in not common but after forty years its occurrence is double at each decade. There is high tendency of DVT impacted because of increase in cesarean sections.\(^11\) It is worth mentioning here that more than half of pulmonary thromboembolercency surgery (PTE) episodes results from deep vein thrombosis and seventy five percent of these occur in 1\(^{st}\) episode\(^13\).

Most frequently thrombosis occurred in the left lower limb in this study. As compared to right lower limb 38 (45.23%) the occurrence is higher in left lower limb 46 (54.76%). Despite that difference is not considered important. It is stated that, due to left iliac vein abnormal compression by right common iliac artery the thrombosis occur in left leg about 8% of cases in many studies.\(^2\) In our population, Infrapatellar location was most frequent which is in accordance with these studies. Deep vein thrombosis frequency was observed as high in primigravida females (76.19%) but it was low in months at 2\(^{nd}\) birth (19.04%) and at 3\(^{rd}\) birth (4.76%). It was also observed that deep vein thrombosis frequently occurred in three primigravida, who have twin pregnancy, due to inferior vena cava high compression as a result of large pregnant uterus.

Four parturient female had in vitro fertilization. This fecundation type supports thrombogenic phenomena due to high doses therapy of hormone with progesterone and estrogen. Ovarian hyperstimulation syndrome (OHSS) caused by in vitro fertilization and in little frequent locations supports the thrombosis such as Jugular and subclavian arteries as reported by Korintoya\(^12\).

As regard to thrombophilia, it was observed that a high prevalence of factor V Leiden (FVL) mutation (twelve cases) was present and in six cases antiphospholipid syndrome followed by deficiency of protein-S, C and antithrombin (two cases each).

Inherited thrombophilia may cause of placental vessel thrombosis and repeated abortions with factor V Leiden (FVL) in patients and Prothrombin alterations. About in 5% of population factor V Leiden mutation is present, which is a more frequent alteration. In population, persistence of that characteristic has been attributed to decreased bleeding risk during labour. Deficiency of protein C and S is comparatively uncommon. Recently a study shown that symptomatic females with deficiency of protein-C, protein-S or antithrombin have about 8 times more chances of deep vein thrombosis during pregnancy as compared to normal females\(^3\).

In our population, the most present cause was factor V Leiden (FVL) mutation. FVL mutation is more frequent in individuals of North Europe (3% to 8%) but in Africans and Asian it is rare.

Its prevalence in USA is 4% to 6%\(^5\). In a study conducted by Langan et al\(^14\) reported that factor V Leiden alteration persuade to preeclampsia due to marked fibrin deposition which resulted in endothelial lesion which causes vasospasm, coagulation and platelet activation.

Di Stefano et al\(^15\) described that deficiency of protein-C, S and antithrombin decrease placental perfusion.\(^16\) We observed in the present study that there were two patients in each group. When occurred prothrombin alteration is a causing factor of deep vein thrombosis.\(^17\)

A multi centered study published by McCool et al\(^18\) involved STP (superficial thrombophlebitis) in pregnant females. An average of 0.68 per thousand deliveries founded by McCool et al\(^18\) and concluded that thrombophilia can be lowest etiology of STP in pregnancy.

In our population one patient had deep vein thrombosis with polycythemia vera. One twenty cases of polycythemia vera linked with pregnancy reported by Robinson which related to fetal death and premature birth. Therefore, hematocrit needs careful attention.\(^19,20\) In a study published by Fokkin et al\(^21\) on sixteen cases of temporary vena cava filter implantation during 3\(^{rd}\) trimester of pregnancy.

**CONCLUSION**

There was low occurrence of deep vein thrombosis in pregnancy but significantly increased the maternal, fetal morbidity, bring high to the pregnancy. There was high risk of DVT in primigravid patients, cesarean sections, twin pregnancies and puerperium. In vitro fertilization has much vulnerability to deep vein thrombosis due to progesterone and estrogen high doses require to that pregnancy model. During pregnancy oral anticoagulants & fibrinolytic should not be used. During and after pregnancy recommended the prophylactic doses of heparin for females who are confirmed thrombophilic and have past history of venous thromboembolism.
REFERENCES