ABSTRACT
Von Willebrand's disease (VWD) is the most common inherited bleeding disorder with estimated prevalence of 1% in general population which has high incidence of postpartum haemorrhage type 3 VWD which is the most severe form of disease with autosomal recessive inheritance has prevalence of 1 in 250,000 to 1 in 1,000,000. We hereby present an interesting case of pregnancy with type 3 von willebrand disease and its outcome. Secondary postpartum bleeding unresponsive to medical approaches was successfully managed with selective uterine artery embolization as the last chance of preservation of uterus. Women with VWD require a multidisciplinary approach with careful monitoring during and after pregnancy for several weeks. The risk is higher in those with type 2 and 3 disease and persists for several weeks after delivery as hypercoagulability of pregnancy returns to normal state after delivery.

Keywords: Von Willebrand Disease, Pregnancy, Uterine Artery Embolisation.

INTRODUCTION
Von willebrand's disease (VWD) is the most common inherited bleeding disorder that is caused by deficiency or dysfunction of Von Willebrand factor (VWF), a plasma protein that mediates the initial adhesion of platelets at sites of vascular injury and also binds and stabilizes blood clotting factor VIII in the circulation. It affects around 1% of general population. Type 1 disease usually autosomal dominant is due to a partial, quantitative deficiency of a structurally normal VWF, and accounts for 70–80% of all VWD patients. Type 2 (20% of VWD patients) includes qualitative defects in VWF that affect its multimeric structure or function with four variants (2A, 2B, 2M, 2N) on the basis of the phenotype. Type 3 VWD (5–10% of VWD patients) – severe form with autosomal recessive inheritance and has prevalence of 1 in 2,500,000 to 1 in 1,000,000 with a complete deficiency or very low level of VWF and a secondary severe deficiency of FVIII. There is a higher frequency of symptomatic VWD in women because of the hemostatic challenges of menses, pregnancy and delivery. Initial tests to determine VWD is by factor VIII, VWF Antigen, VWF: Ristocetin Cofactor activity in blood and to determine type of the disease the tests are Ristocetin induced platelet agglutination; plasma VWF multimer analysis.

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CASE REPORT
History: A 19 year old primigravida with 37 weeks of gestation, was referred to us by a gynaecologist. The initial diagnosis was made at the age of 17 years, when she presented with anemia, menorrhagia to the haematologist. Her menstrual cycles were irregular with cycle length of 13-15 days with passage of clots. Based on the following investigations, the haematologist had diagnosed the disease as Von Willebrand Disease Type 3. She had a hemoglobin = 5.6gm%, Platelet count=3.98lakh /cmm , Bleeding Time > 20 min, and APTT = 60sec. Factor VIII level <10 IU/dL. PT was normal. Prolonged APTT which gets corrected with factor IX deficient plasma and does not get corrected with factor VIII deficient plasma. Ristocetin induced platelet aggregation was absent. In her childhood, she had episodes of epistaxis, gum bleeding and prolonged bleeding following any injury. Her family history revealed that her 21 year elder sister had the same disease. Whereas both the parents and brother were not affected suggestive of autosomal recessive inheritance. Patient presented to the haematologist at 5 month of amenorrhoea with episodes of bleeding gums which subsided with oral tranexemic acid tablets. She was kept under strict antenatal surveillance, aemoglobin and other routine blood investigations were within normal limits. BT>15min, CT> 20 min, APTT=52sec. Serial sonography scan showed healthy growth of the fetus. Frequent antenatal check ups, complete hemogram and clotting profile were done periodically throughout the course of pregnancy. NSAIDS and intramuscular injections were completely avoided. In view of limited facilities for
procuring cryoprecipitate/ FVIII/VWF concentrates in emergency situation, and to avoid any untoward bleeding catastrophe, the gynaecologist referred the patient to tertiary care centre. She was admitted at 37 weeks of gestation. Examination: General condition was good, vitals were within normal limits. Per abdomen; uterus was term, with breech presentation. Per vaginal examination; Cervix 1finger dilation, noneffaced. Non-Still Test showed reactive pattern. Investigations: BT > 20 min, CT>10 min, APTT = 66.5sec (control = 26-40sec), Hb = 13.7gm%, Platelet Count = 1.71lakh/ cmm. Management: Decision of elective caesarean section was taken because of obstetric indication. According to haematologist's advise, 10 bags of cryoprecipitate were transfused 4 hours before surgery. Inj. Tranexemic acid was given 2 hours before surgery. Elective caesarean section under general anaesthesia was performed. A 2.6 kg live healthy female child was delivered with APGAR of 7/7/8. Coagulation profile and all other investigations of the baby were normal. Immediate post-operative period, the patient was transfused with 5 bags of cryoprecipitate. 5 bags of cryoprecipitate were transfused twice daily for 5 days. DDAVP nasal spray was given in the immediate postoperative period. Injectable Tranexemic acid were given twice daily for 5 days. Post-operative period was uneventful. Baby and mother were discharged on 9th post operative day. But patient presented to us with secondary postpartum hemorrhage on 10th day of discharge with episodes of heavy bleeding and passage of clots. She was anemic , with Hb= 4.2gm% , Wbc- 6,280/cmm and Platelet count =2,48,000/cmm. BT>20 min, CT>12 min. Factor VIII level was 20IU/dl (N=50 to150IU/dl). Ultrasonography Pelvis suggested of 5*3cm sized heterogenous lesion in the lower uterine segment without vascularity suggestive of clot. According to haematologist’s advice, 2 units of packed cell volumes and 8 units of fresh frozen plasma, 10 units of cryoprecipitate were given. Injectable tranexemic acid, ethamsylate was started. DDVAP nasal spray was given for 3 days. 10 units of cryoprecipitate twice daily was given for 7 days. Tab. Misoprostol 600µg kept per rectally. Vaginal packing was done. Gentle evacuation of the uterine cavity was done. But there was no improvement in the general condition of the patient, bleeding episodes continued. Hematologist was consulted for Recombinant factor VIII/VWF concentrates. According to the haematologists advice, she was transfused 1000 IU of concentrates twice daily for first two days and 500 IU twice daily for next three days, following which the patient had no active bleeding episodes. But within 2 days of stopping the treatment with factor VIII/VWF concentrates she developed massive bleeding again with severe anemia (Hb= 4.1gm%). Decision of selective uterine artery embolisation was taken as the haemorrhage was not controlled by medical methods. Bilateral uterine artery embolisation was done with cook coiling by interventional radiologist (fig 1 and 2). Postoperative period was uneventful. Bleeding was controlled post embolisation procedure. (fig-3). Hemoglobin =10gm % and coagulation profile were normal. She was observed for 5 days and discharged with oral hematinics. 

**Figure 1:** Pre-coiling fluoroscopy of uterine artery

**Figure 2:** Cook coil inserted in uterine artery

**Figure 3:- Post coiling fluoroscopy**

**DISCUSSION**

Women with VWD require monitoring during and after pregnancy. Because of the rapid fall in FVIII and VWF levels after delivery, women with VWD are at substantial risk for postpartum hemorrhage (30%). The risk is higher in those with type 2 and 3 disease and persists for several weeks after delivery. Meticulous surgical hemostasis, effective uterine contraction and the avoidance of antiplatelet drugs will reduce the risk of postpartum hemorrhage. However, there are no data defining a threshold level of FVIII or VWF as a reliable predictor of bleeding. There is limited evidence regarding DDAVP and factor VIII level use in pregnancy and lactation. As DDAVP can cross placental barrier, it is usually not prescribed in antenatal period. Patients who have type 3 VWD almost never experience a clinically relevant rise in VWF:RCo or FVIII activities, and DDAVP is not considered clinically useful in these patients. Women who receive...
DDAVP should limit their fluid intake to reduce the risk of hyponatremia. DDAVP and Factor VIII/VWF concentrates may be used only if clearly needed during pregnancy and lactation. Plasma concentrates containing factor VIII and VWF treated with virucidal methods are safe and treatment of choice. The ultimate goal of surgical prophylaxis is to achieve a therapeutic level of 100 IU/dL VWF:RCo and, at least for the first 3 days of treatment, a nadir of 50 IU/dL VWF:RCo, as well as similar targets for FVIII. The required dosage can be calculated by the formula Required units = body weight(kg) × desired factor VIII rise(%) × 0.5. But in developing countries due to restricted and low resource settings cryoprecipitate and fresh frozen plasma still remains the treatment of choice.

Uterine artery embolization has several advantages, including easy identification of the bleeding site, preservation of the uterus and fertility and decreased rebleeding from collaterals with more distal occlusion of the bleeding vessels. Complications of pelvic embolization for postpartum haemorrhage occur at a rate of 8.7%. The commonest complication is low-grade fever and rarer ones include pelvic infection, groin haematoma, iliac artery perforation, transient buttock ischaemia, transient foot ischaemia and bladder gangrene. Thus with a multidisciplinary approach involving obstetrician, anaesthesiologist, haematologist, interventional radiologist, neonatologist a healthy maternal and fetal outcome was achieved.

REFERENCES