

Extra-Hepatic Portal Venous Obstruction in Pregnant Women of South-Asian Descent: A Case Series

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ABSTRACT

Liver diseases complicate approximately 3% of pregnancies worldwide, and require specialized care to ensure optimal pregnancy outcomes. Extra-hepatic portal venous obstruction (EHPVO), even though asymptomatic in a majority of the cases, has a higher risk of variceal bleeding in pregnancy and adverse pregnancy outcomes. In this series, we describe five cases of EHPVO presenting during pregnancy at our tertiary care hospital, their antenatal management, and delivery outcomes. In our case series on EHPVO in pregnancy, a majority of the women were diagnosed during childhood and adequately asymptomatic before pregnancy. Two women underwent Endoscopic band ligation for esophageal varices and one woman underwent splenectomy before pregnancy for disease control. One woman was Anti-nuclear antibody (ANA) positive and another was Anti-phospholipid antibody (APLA) positive, while the other three did not have pre-existing thrombotic tendencies. One patient required Endoscopic band ligation during pregnancy. Pregnancy complicated by hypertension was noted in two of the five women (40%). Four of the five women (80%) had thrombocytopenia requiring blood products during delivery. Two women underwent preterm vaginal delivery, and one woman underwent preterm Caesarean section because of placental abruption. Three women had a post-partum hemorrhage, which was effectively managed with uterotonics and blood products. All five women and their neonates were discharged in good health. Multi-disciplinary approach with standardized antenatal care can give positive pregnancy outcomes in women with EHPVO.

Keywords: EHPVO; Esophageal varices; Portal Hypertension

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Introduction

Liver diseases complicate approximately 3% of pregnancies worldwide and require specialized care to ensure optimal pregnancy outcomes (1,2). Extra-hepatic portal venous obstruction (EHPVO) is one such entity, with a predisposition in Asian women of the reproductive age group (3). EHPVO is a condition characterized by the occlusion of the extra-hepatic portion of the portal vein and may also involve the superior mesenteric or splenic veins. While portal hypertension is

asymptomatic in a majority of cases, pregnant women are at higher risk of variceal bleeding and adverse pregnancy outcomes. Though 70-80% of the cases of EHPVO in adults are idiopathic, it may be attributed to other causes such as polycythemia, Anti-phospholipid antibody syndrome (APLA), Protein C and Protein S deficiencies, malignancies, portal vein abnormalities, and traumatic injury (4-6). The hyperdynamic state of pregnancy can exacerbate the disease (3).

In this case series, we describe five cases of EHPVO presenting during pregnancy to our tertiary care hospital, their antenatal management as well as delivery outcomes. Informed consent was obtained from all five patients before including them in the study. These high-risk pregnancies require a multi-disciplinary team approach to optimize both maternal and fetal outcomes.

Case 1

A 27-year-old third gravida with previous two Caesarean deliveries, presented at 24 weeks of pregnancy with a two-day history of hematemesis. She had no prior history of bleeding episodes. Her vital signs on admission were stable and mild pallor was noted on examination. Hepato-splenomegaly was noted on abdominal examination. The obstetric assessment revealed a live fetus with growth corresponding to gestational

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age. Her blood picture revealed mild anemia (Hb=81 g/L) and a platelet count of $67 \times 10^9/L$. Liver function and coagulation parameters were within normal limits. APLA and Anti-nuclear antibody (ANA) were negative.

Abdominal ultrasonography showed hepatosplenomegaly, hetero-enhancement of liver parenchyma, and portal vein dilation (Figure 1A). Endoscopy was performed by the Medical Gastroenterology team, which revealed grade 4 esophageal varices (Figure 1B). The varices were ligated by banding in the same sitting. Following the procedure, the patient was monitored for a week and was symptomatically better. No further episodes of bleeding were observed during pregnancy.

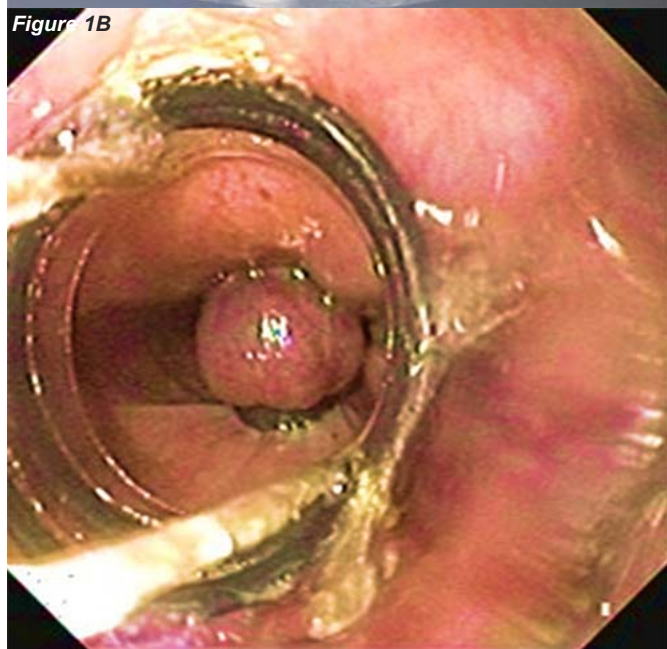


Figure 1(A): Hepatomegaly on abdominal ultrasound **(B):** Endoscopic band ligation of esophageal varices

Anaemia was corrected with intravenous iron sucrose, and close monitoring of platelets and liver function tests was carried out until full-term gestation. Fetal growth was monitored monthly on an outpatient basis which was indicative of stage

1 fetal growth restriction at term (Barcelona Stage 1 FGR). Elective Caesarean delivery was planned at 37 weeks due to two previous Caesarean sections with FGR. Platelet count at delivery was $54 \times 10^9/L$, requiring two single donor platelet (SDP) transfusions and one red blood transfusion intraoperatively due to increased bleeding. She delivered a healthy baby of 2.300 grams and had an uneventful post-operative period. Both mother and baby were discharged in good health on post-operative day 5.

Case 2

A 26-year-old primigravida presented at 32 weeks of pregnancy with mild anemia (Hb=101 g/L). She was a known case of chronic liver disease, diagnosed with EHPVO at 12 years of age after she presented with hematemesis, tarry stools, and severe anemia. Ultrasound suggested portal vein thrombosis with cavernoma. Endoscopic esophageal variceal ligation was performed for grade 3 varices. She underwent open splenectomy for hypersplenism after five years and had no further symptoms.

During pregnancy, she was referred to our tertiary care hospital due to EHPVO. She had a history of elevated blood sugars in the second trimester and was managed with oral Metformin 500 mg twice daily for Gestational Diabetes Mellitus. Coagulation profile, platelet count, and liver function tests were within normal limits. Ultrasonography suggested coarsened hepatic echotexture and nodularity. An endoscopy was performed and reported no fresh varices (Figure 2). Obstetric examination findings were normal, showing a live fetus with adequate growth.



Figure 2: Oesophago-Gastro-Duodenoscopy revealing no fresh varices

She underwent spontaneous preterm vaginal delivery at 35 weeks, delivering a healthy 2.500-gram baby. There were no intrapartum difficulties or excessive blood loss. The postnatal period was uneventful, and the patient was discharged in

healthy condition on day 3. Her blood sugars reverted to normal on oral glucose testing six weeks later.

Case 3:

A 33-year-old second gravida with previous intra-uterine fetal death presented at 18 weeks of pregnancy for routine care at our tertiary care center. She was diagnosed with EHPVO and chronic liver disease in childhood when she presented with epistaxis, hematemesis, and tarry stools. Her esophageal varices were treated with oral Propranolol 40 mg once daily, which was continued through both pregnancies. Her first pregnancy was associated with preeclampsia and Barcelona stage 3 FGR, which resulted in intra-uterine fetal demise at 32 weeks of pregnancy due to poor antenatal follow-up.

In the current pregnancy, she had multiple episodes of epistaxis due to persistent thrombocytopenia (in the range of $48\text{-}54 \times 10^9/\text{L}$). She was managed by a multidisciplinary team with hematology, Ear-Nose-Throat (ENT), and medical gastroenterology. Her bleeding episodes were symptomatically treated. Liver function tests and coagulation parameters were normal. Abdominal ultrasonography showed a dilated portal vein, splenic artery pseudo-aneurysm, splenomegaly, and features of chronic parenchymal liver disease (Figure 3). Her blood pressure recordings were elevated at admission but maintained between 140/100mmHg and 130/90mmHg on monitoring.



Figure 3(A),(B): Abdominal ultrasound with Doppler findings suggestive of parenchymal liver disease

She went into spontaneous labor at 36 weeks of pregnancy and delivered a girl baby of 2600 grams. The platelet count at the time of delivery was $58 \times 10^9/\text{L}$. Blood loss during delivery was approximately 900 milliliters, managed with uterotonics, one packed red blood transfusion, and eight platelet transfusions. The baby was monitored in the Neonatal ICU for five days for respiratory distress. Blood pressures were normal post-delivery, and both mother and baby were discharged on day 6 in good condition.

Case 4

A 20-year-old primigravida was referred to our hospital at 34 weeks of gestation because of thrombocytopenia and severe features of preeclampsia. She was a known case of portal hypertension with EHPVO, diagnosed when she developed fever and jaundice two years earlier. An endoscopy was done and revealed grade 4 esophageal varices, for which she underwent endoscopic variceal ligation before pregnancy. On routine workup, ANA was positive, and Anti-smooth muscle antibody (ASMA), Anti-mitochondrial antibody (AMA), and Liver-Kidney-Microsomal antibody (LKM) were negative. She was managed with oral Propranolol 40 mg once daily thereafter. She was advised Ecospirin 150 mg during pregnancy and given a positive Pregnancy-induced hypertension (PIH) screen.

At admission to our hospital, her blood pressure was 160/100mmHg, but otherwise stable. She was managed with antihypertensives and four single platelet transfusions due to a low platelet count of $38 \times 10^9/\text{L}$. Her liver function tests were within normal limits. Abdominal ultrasound was suggestive of hepatomegaly and portal hypertension; hepato-fugal flow in the portal vein, dilated splenic vein with hilar lienorenal peripancreatic collaterals (Figure 4).

The patient developed sudden onset abdominal pain with per-vaginal bleeding at 36 weeks and was taken up for emergency Caesarean section because of fetal bradycardia. Intraoperatively, revealed abruption was noted. Bleeding was managed with two packed cells and two SDP transfusions. A 2450-gram baby was delivered, but because of poor APGAR, required resuscitation and prolonged neonatal ICU care.





Figure 4(A), (B): Hepatomegaly on abdominal ultrasound

The post-operative platelet count was $63 \times 10^9/L$. Persistent tenderness and distension of the abdomen mandated an abdominal ultrasonography which revealed ascites and rectus muscle hematoma. Following conservative management over seven days, she was discharged in healthy condition with blood pressure under control. The neonate was diagnosed with stage 1 Hypoxic ischemic encephalopathy (HIE) but was doing well at discharge after a month.

Case 5:

A 19-year-old primigravida was referred to our hospital due to thrombocytopenia and splenomegaly at 23 weeks of pregnancy. She was asymptomatic at admission, with mild pallor. On evaluation, her hemoglobin was 92 g/L and her platelet count was $37 \times 10^9/L$. Liver function tests and coagulation parameters were within normal limits. Abdominal ultrasonography was suggestive of hepatosplenomegaly, dilated splenic vein, and portal vein thrombosis, resulting in a diagnosis of EHPVO with portal hypertension (Figure 5A). An antiphospholipid antibody workup was done, which was positive for anti-cardiolipin IgG and $\beta 2$ -Glycoprotein.



Figure 5A: Hepatomegaly on abdominal ultrasound

She was started on Ecospirin, low molecular weight heparin, and hydroxychloroquine based on the advice of our Immunology team. Pulse dexamethasone was given to im-

prove platelet count. At 28 weeks of pregnancy, she developed hematemesis, for which endoscopy was done. Grade 3 esophageal varices were noted, requiring band ligation (Figure 5B).



Figure 5B: Dilated esophageal varices

She was asymptomatic until term and induced at 39 weeks of gestation to deliver a healthy male infant of 2700 grams. The platelet count at the time of delivery was $65 \times 10^9/L$, and one SDP was transfused peri-delivery. Low molecular weight heparin was continued for seven days post-delivery and the patient with her baby was discharged in healthy condition.

Discussion

Extra-hepatic portal vein obstruction involves the obstruction of the extra-hepatic portion of the portal vein, which may be associated with the splenic or intra-hepatic portal vein (7).

There is limited data available in the literature that depicts the outcomes and management of EHPVO in pregnancy. Subbaiah, in his retrospective analysis of pregnancies in 12 women with EHPVO concluded that prenatal diagnosis and treatment of the disease by a multidisciplinary approach is of utmost importance to ensure good pregnancy outcomes (7).

Aggarwal et al. described the management experience of 14 women retrospectively, which showed successful pregnancy outcomes when EHPVO is treated before pregnancy. In this study, the stillbirth rate was 7.7%, and a preterm birth rate of 15.4% (6). Jacob described outcomes in 20 women with EHPVO over seven years. 60% of the women had thrombocytopenia, and preterm labor was noted in 35% of the women (3). Mandal suggested that women with variceal bleeds during pregnancy had poorer outcomes, and therefore recommended pre-pregnancy evaluation and management of varices (8). The high risk of preeclampsia in pregnancies with EHPVO was described in several case reports (7,9,10).

In our case series on EHPVO in pregnancy, a majority of the women were diagnosed during childhood and adequately asymptomatic before pregnancy. One woman each was ANA and APLA positive, while the other three did not have pre-ex-

isting thrombotic tendencies. Four of the five women (80%) had thrombocytopenia requiring blood products during delivery. One patient required endoscopic band ligation of esophageal varices during pregnancy. Hypertension complicating pregnancy was noted in two of the five women (40%).

Two women underwent preterm vaginal delivery and one woman underwent preterm cesarean section because of abruptio placenta. Only two women required cesarean section (40%), both for obstetric indications. Three women had a postpartum hemorrhage, which was managed adequately with uterotonics and blood products. All five women and their neonates were discharged in healthy condition, indicating that a multidisciplinary approach with standardized antenatal care can give positive pregnancy outcomes in women with EHPVO. It is important to optimize the blood parameters and hemodynamic status before delivery for enhanced patient recovery.

Informed Consent: Informed consent for the use of data was obtained from all the participants of the study. The study was conducted in accordance with the Declaration of Helsinki. The case data was obtained retrospectively from hospital records and the Institutional Ethical Committee (IEC) waived off the ethical approval.

Availability of data and materials: The data supporting this study is available through the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

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