Original Article

Maternal and neonatal outcomes in extra hepatic portal vein obstruction: Our experience

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Abstract

Background: Women with Extra hepatic portal vein obstruction (EHPVO) are mostly young and belong to Asian countries. In the Indian subcontinent, 20–30% variceal bleeds are caused by EHPVO. Hence pregnancy is a concern in such patients. The objective of this study is to observe the maternal and neonatal outcomes in women with EHPVO. **Materials and Method:** Extra hepatic portal vein obstruction was studied retrospectively in 28 pregnancies in 20 women from Jan 2011 to July 2018 at a tertiary hospital in South India and the pregnancy outcomes were observed during this period. Institutional Review Board approval obtained. **Results:** The mean age of the women was 24.3 years and the mean age of diagnosis was 18.5 years. Splenomegaly, thrombocytopenia and anaemia were seen in 22 (78.5%), 17 (60.7%) and 8 (28.5%) of pregnancies, respectively. Rate of abortions and preterm deliveries were 2 (7.1%,n=28) and 10 (35.7%,n=28). There was one stillbirth (3.6%) in the study group. EHPVO was diagnosed in 25 (89.3%) women prenatally in our series. During pregnancy only one woman had variceal bleed, which was managed conservatively. Blood and blood product transfusion was required in 7(25%) of women and there was no maternal mortality. **Conclusion:** Pregnancies in EHPVO have good maternal and neonatal outcomes, provided they are taken care of by a multidisciplinary approach in a tertiary care centre.

Keywords: EHPVO, EST, EVL, maternal outcome, portal hypertension, pregnancy

Introduction

Extra hepatic portal vein obstruction (EHPVO) is characterised by the occlusion or obliteration of extrahepatic part of portal vein. This condition may or may not be associated with involvement of other veins, such as splenic-and/or superior mesenteric vein or intra hepatic portion of portal vein branches.[1] Patients with EHPVO are mostly young and belong to Asian countries. Among the women, leading cause of portal hypertension (40%) is contributed by thrombosis of portal vein. One third (30%) of-variceal bleed cases are caused by EHPVO in Indian adult population, but this does not lead to mortality.[1,2] However, pregnancy in such patients is of great concern. Portal venous obstruction is often asymptomatic and well tolerated.

The etiological causes of EHPVO include injury, infection, thrombotic event, umbilical vein catheterization, dehydration, myeloproliferative disorder, coagulation defects, congenital anomalies of portal vein, cirrhosis, cancers, etc.[3] However, 70% cases of EHPVO remain idiopathic.[4,5] Hypercoaguable states such as protein C and S, antithrombin III deficiency, Factor V Leiden gene mutation are linked with venous thrombosis in adults.

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Multidisciplinary approach to pre-conceptional counselling, detailed evaluation and antenatal care is important for optimisation and good obstetric outcome.

Materials and Methods

This is a retrospective observational study of all women with extra hepatic portal vein obstruction who were pregnant and took treatment in Christian Medical College, Vellore from 01/01/2011 to 01/07/2018. This study was approved by research committee and ethics committee of CMC Institutional review board (IRB) approval number is 11500[Retro]

The data was collected and analysed from outpatient and inpatient records. The maternal factors considered are duration of disease, index presentation, gestational age, interventions required for EHPVO prenatally and during pregnancy, complications of upper gastrointestinal bleed, spontaneous bacterial peritonitis and ascites. Other factors considered were, the mode of delivery (lower segment caesarean section, vaginal delivery, instrumental delivery), neonatal outcomes, postpartum complications such as haemorrhage, ICU admission, requirement of blood and blood products.

Case definition

EHPVO: Asian Pacific Association for Study of Liver diseases defines EHPVO as a vascular disorder of liver, characterised by obliteration of extra-hepatic portion of portal-vein. This condition may or may not be linked with involvement of intra-hepatic portal vein radicles, splenic or superior mesenteric veins.[6]

Thrombocytopenia: In this study thrombocytopenia is taken as platelet value less than 100,000 platelets per cubic mm of blood.

Preterm: Birth before 37 completed weeks of gestation.

Abortion: Loss of pregnancy prior to 24 weeks of gestation.

Stillbirth: Birth after 24 weeks of pregnancy-with no signs of life.

Depressed at birth: Included in the study as APGAR ≤7 at 1 minute of-life

Early neonatal death: Death of a live born within first week-of life.

Good outcome: is defined as pregnancy beyond 28 completed weeks with live born baby with no complications requiring ICU care for mother.

Postpartum haemorrhage: Blood loss more than 500 ml in vaginal delivery and >1000 ml in LSCS within first 24 hours of delivery.

Intrauterine growth restriction (IUGR): If estimated weight of foetus is below 10th percentile for its gestational age.

Anaemia: Haemoglobin level less than 11 gm/dl (Mild anaemia- 9–10.9 gm/dl, moderate anaemia 7–8.9 gm/dl, severe anaemia : less than 7 gm/dl).

Results

Total of the 28 pregnancies with EHPVO were retrospectively studied.

The duration from diagnosis was less than five years for 17 (60.7%) of the women. The index presentation was variceal bleed in 14 (50%) of women. In 9 (32%) of the women it was diagnosed incidentally during ultrasonographic examination and blood investigation. In 25 (89.3%) women the diagnosis of EHPVO was made prior to pregnancy, as seen in Table 1. Two women were diagnosed during pregnancy and one postpartum. The mean age of diagnosis was 18.5 years. While most of the women were of 24.3 years of age. Out of these 11 were primigravidae.

Both obstetric and neonatal outcomes and complications related to portal vein hypertension are mentioned in detail.

Obstetric outcomes

Among 28 pregnancies, there were two abortions (7.1%), one IUD which occurred at 36 weeks. LSCS was required in 14 (50%) patients, 12 (42.8%) patients were delivered vaginally. All LSCS were done for obstetric reasons. One patient who underwent LSCS had PPH. Blood or blood products were required in 7 (25%) of women as tabulated in Table 2. Four women required ICU care.

Neonatal outcomes

Totally, 25 (89.3%) out of 28 pregnancies were live births. Preterm deliveries were seen in 10 (35.7%, n = 28) of the study population. Birth weight was <2.5 kg in 10 (35.7%, n = 28), NICU admission in 10 (40%) out of 25 live births. APGAR ≤7 at 1 minute of birth was seen in 3 (12%) out of 25 live births.

Portal hypertension related complications

Of the 28 pregnancies, one woman underwent primary EVL elsewhere during antenatal period, and one woman had variceal bleeding which was managed conservatively. Prenatally, portal hypertension related complications of variceal bleeding was index presentation in (14) 50% of the patients. Ascites and jaundice were seen in three and one women respectively; however, none of them had renal complications or encephalopathy.

Totally, 14 women required specific treatment modalities before pregnancy. Endoscopic variceal ligation (EVL) in 5 (17.8%), endoscopic sclerotherapy (EST) in 2 (7.1%), 4 (14.3%) had both EST and EVL. Three women (10.8%) underwent shunt surgery of which one underwent splenectomy as well. 19 (67.8%) of the women were on medical management with Propranolol.

Table 1: Baseline characteristics

	n (%)
Maternal characteristics	
Primigravidae	11 (39.28%)
Multi-gravidae	17 (60.71%)
Age of patients (mean)	24.28 yrs
Mean age of diagnosis	18.46 yrs
Index presentation	
Presentation	
Variceal bleed	14 (50)
Epistaxis	1 (3.6)
Incidental	9 (32)
Others[a]	4 (14.3)
Timing of diagnosis in relation to pregnancy	
Before pregnancy	25 (89.3)
After pregnancy	1 (3.6)
During pregnancy	2 (7.1)
Duration from diagnosis to pregnancy (in years)	
<5	17 (60.7)
5-10	0
>10	10 (35.7)
Undiagnosed[b]	1 (3.6)

Treatment modality	Before pregnancy	During pregnancy
EVL	5 (17.8)	1 (3.6)
EST	2 (7.1)	-
EVL + EST	4 (14.28)	-
Shunt surgery	2 (7.2)	-
Splenectomy + shunt surgery	1 (3.6)	-
Propranolol prophylaxis	19 (67.8)	
Disease associated conditions		
Ascites	3 (10.7)	
Jaundice	1(3.6)	
Splenomegaly	5 (17.8)	
Splenomegaly with thrombocytopenia	17 (60.7)	
Anemia	8 (28.5) Mild -3, Moderate-3, Severe-2	
Average antenatal OPD visits	10	

[a]Gum bleed with splenomegaly-1, pedal edema-1, jaundice-1, ascites-1. [b]One patient was diagnosed postpartum

There was splenomegaly in 22 (78.5%) of patients and associated thrombocytopenia was seen in 17 (60.7%) patients. Varying degrees of anaemia was found in 28.5% of patients.

Discussion

Considering all patients with portal hypertension (PHT), EHPVO is the cause of PHT in one third of them. It constitutes 30% of variceal bleeds in developing countries and nearly 5-10% in the west[6] The etiological origin in children is mainly intra-abdominal infection or umbilical sepsis or catheterization and congenital defects related. In-adults it is often occult and underlying prothrombotic states are frequently reported in west than in Asian patients, though the data are inadequate.[7] Other factors imposed are intra-abdominal inflammation and trauma. In adults, EHPVO presentation may be acute or chronic, the differentiation may be difficult.

Table 2: Obstetric outcomes

Outcome of pregnancy	*n* (%)
Abortions	2 (7.1)
Previous abortions	11 (39.2)
Delivery>37 wks GA	16 (57.1)
Delivery	
<37 wks GA	10 (35.7)
<28 wks	1
28 to 32 wks	2
23 to 36 wks	4
36 to 36+6 wks	3
Still birth	1 (3.6)
Onset of labor	SOL[‡]-6 IOL[§]-7
Mode of delivery	
Vaginal delivery	10 (35.7)
Instrumental delivery-2	
Vacuum extraction -1	2 (7.1)
Outlet forceps delivery -1	
LSCS	14 (50)
Anaesthesia for LSCS	
SAB	11 (78.6%, *n*=14))
(Platelet count <50000/cu mm in SAB)	Nil
GA	3 (21.4%, *n*=14))
PPH	1 (3.6)
Blood and blood product usage	
Used	7 (25) Blood alone 4 Blood and blood products 1 Blood products alone 2
SICU admission	4
HELLP	2
SPE, sepsis	1
Cellulitis, sepsis	1
Not used	21
Birth weight	
< 2.5 kg	10 (35.7)
>2.5 kg	16 (57.1)
IUGR	9(34.6, *n*=26)
APGAR <1 at 1 min of birth	3
Reasons for NICU admissions (10 of 25 livebirths)	
Depressed at birth	2
Prematurity	5
Low birth weight	2
Maternal reason	1

TOP=termination of pregnancy, [‡]SOL=spontaneous onset of labor, [§]IOL=induction of labor

In acute scenario they may report with febrile illness, associated with abdominal pain and in chronic patients, the presentation is variceal bleeding and hypersplenism. Other manifestations are ascites and jaundice. Portal biliopathy is seen in 80% of the patients but most of the patients are asymptomatic.[6]-In Indian population inherited thrombophilia are not very frequent-basis of-portal vein thrombosis.[6,8] Ascites is seen in 13–21% of the patients.[4]

The study by Keepanasseril *et al.* in south India showed variceal bleeding complicating 25% of pregnancies in women with non–cirrhotic PHT.[9] However, in this study, EHPVO-related complications of variceal bleed as index presentation was seen

in 50% of the patients, but during pregnancy only one patient had variceal bleeding which was managed conservatively and one patient had primary EVL done elsewhere. There were three patients with ascites and one with jaundice. Splenomegaly was observed in 78.5% of the patients, of which associated thrombocytopenia was seen in 60.7%. There was no EHPVO-related renal dysfunction or hepatic encephalopathy. The study by Mandal *et al.* found majority of patients to be having anaemia (70.8%). In this study, 28.5% of the patients were found to be anaemic.

Patients with EHPVO generally have no stigmata of liver disease.[3] Since liver function is preserved, the prognosis is better when compared to patients with cirrhotic liver disease. Long-term studies show almost no mortality post endotherapy.[10] Pregnancy in women with liver cirrhosis has high maternal and foetal morbidity.[11] Mortality can be as high as 50% in pregnant women with liver cirrhosis compared to 2–6% in non–cirrhotic.[12]

There is limited data on pregnancy outcomes with EHPVO. In pregnant women from developing countries, portal hypertension is frequently due to viral and autoimmune-related cirrhosis.[10] The physiological changes in pregnancy resulting in increased blood flow which predispose these patients for enhanced risk from variceal bleed. Figure 1 shows the physiological changes aggravating variceal bleed.[10,13]

Variceal bleed is the most dreaded complication. Oesophageal varices are seen in 90% and gastric varices are seen in 31–44% cases.[3,4] In the Indian population, approximately one third of variceal bleed is caused by EHPVO, but does not lead to

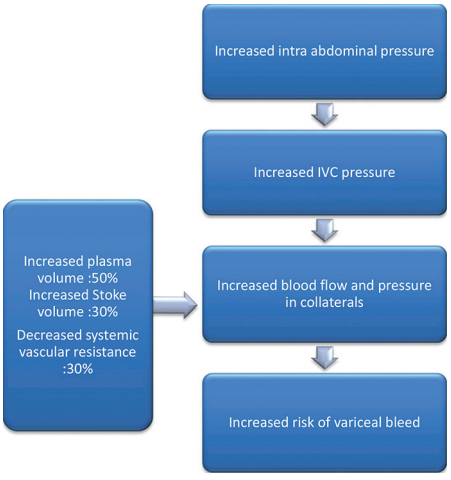

Figure 1: Physiological changes aggravating variceal bleed in pregnancy

mortality.[1,2] The risk is higher in patients with larger varices, undiagnosed, un-optimised patients, previous history of bleeding, severe liver disease, coagulopathy and endoscopic red signs. This study looks at the obstetric and neonatal outcome in patients with EHPVO. Table 3 is a tabulation of various studies of EHPVO in pregnancy.

Prenatally diagnosed and treated patients have nearly nil chances of variceal bleed.[14,15] In this study prenatal diagnosis of EHPVO was made in 89.3% of the patients. Prior to pregnancy, EVL or EST or both was required in 39.3% of women. There were two women requiring shunt surgery of which one had splenectomy also. Although EVL and EST both are regarded safe in pregnancy, Baveno V-consensus workshop.[15] recommends EVL for acute variceal bleed. Thrombocytopenia was seen in 17 (60.7%) patients. Study by Kilambi *et al.* showed that total platelet count ≤53,500 cells/mm^3 independently predicted significantly high portal pressure.[16]

Abortion rate was 23.8% in the study by Subbiah *et al.*[17] In our study, abortions were seen in 7.1% of the women although history of previous abortion was observed in 39.2% of the women.

Preterm deliveries were seen in 14–19% of the women [refer Table 3]. Totally, 35.7% of the women were delivered before 37 weeks of gestation of which only 3 (10.7%) were less than 32 weeks gestation. 10 (35.7%, n = 25) babies had birth weight <2.5 kg. Intrauterine growth restriction was seen in 9 (34.6%, n = 26) of babies. 19 (67.8%) of the women in the study group were on medical management with Propranolol which is FDA category C drug. Though concerns of growth restriction, cardiac anomalies, etc., have been found with beta blockers, the recent studies have shown them to be safe in pregnancy.[18,19] In this study comparing women with anaemia to women with normal haemoglobin, the rates of IUGR were 42.8 vs 31.6%. Also comparing IUGR in women who were on propranolol and those who were not, the rates of IUGR were 23.5 vs 55.55 % [Table 4]. Thus, IUGR was not significantly increased in anaemic women or women on treatment with propranolol. INASL-FOGSI statement, recommends continuation of Propranolol in pregnancy. It is safe to continue during breastfeeding as well.[20] Study by Mandal *et al.* showed that the perinatal morbidity and mortality associated with prematurity and less birth weight-was higher when the diagnosis was made in antenatal period. When prenatally diagnosed, the outcomes were better. In our study 25 patients were diagnosed to have EHPVO prenatally, 2 antenatally and

Table 3: Various studies on EHPVO in pregnancy

	Pregnancies/ patients	Abortion%	Preterm	Still birth	SGA	Thrombo cytopenia	PPH	Maternal Mortality (*n*)
Subbaiah *et al.*	21/12	23.8	18.7	0	12.5	61.9	0	0
Aggarwal *et al.* (EHPVO patients)	23/12	17.4	10.5	15.8	5.3	NA	NA	NA
D Mandal *et al.*	41/24	4.87	14.6	2.56	10.25	20.8	7.3	1

only one patient was diagnosed postpartum. There was only one still birth in this study.

12 (42.8%) women were delivered vaginally of which 2 (7.1%) were instrumental delivery. Instrumentation to cut short second stage of labour was required in only one patient. Induction of labour was required in 7 patients and spontaneous onset of labour was seen in 6 patients. The indications of LSCS were for obstetric reasons [Table 5]. Of the patients who had LSCS, 78.6% had subarachnoid block and 21.4% had general anaesthesia. None of the patients had variceal bleed in labour. Postpartum 4 patients required ICU admission. The reasons for ICU admission was not related to worsening of liver disease.

Blood and/or blood products were used in 7 (25%) of women. Three patients required pre-delivery transfusion for low haemoglobin. Preoperative correction of bleeding parameters was required in 3 patients [Table 6]. There was one patient with postpartum haemorrhage requiring transfusion. Maternal mortality is nil to <1% in the studies listed above. There was no maternal mortality in our study group. Good outcome (pregnancy beyond 28 completed weeks with live born baby with no complications requiring ICU care for mother) was seen in 71.4% women.

Table 4: Comparing rates of IUGR in women with anaemia and on Propranolol

	n (Excluding abortions)	IUGR	%
Women with anaemia	7	3	23.5
No anaemia	9	5	55.5
Women on propranolol	7	3	42.8
Not on propranolol	19	6	31.6

Table 5: Miscellaneous

Indications for LSCS[‖]	*n*
Deteriorating maternal condition	
Chorioamnionitis with ARDS[¶]	1
Severe pre ecclampsia/HELLP**	2
Cellulitis with sepsis	1
Previous LSCS not willing for VBAC[††]	2
Abnormal dopplers	1
Category II NRFS[‡‡]	2
Failed induction	1
Previous uterine perforation	1
SPE[‡] with unfavourable cervix	1

[‡]SPE= Severe pre ecclampsia. [¶]ARDS=Acute respiratory distress syndrome. **HELLP=Hemolysiselevated liver enzymes and low platelet count occurring in pregnancy. [††]VBAC=Vaginal birth after caesarean. [‖]LSCS=Lower segment Caesarean section. [‡‡]NRFS=Non reassuring foetal status

Table 6: Indications for blood transfusion

Indications for blood transfusion	
Pre delivery/termination low haemoglobin	3
PPH*	1
Preoperative deranged bleeding parameters (HELLP, Cellulitis with sepsis)	2
Postoperative deranged bleeding parameters (HELLP)	1

PPH*=Postpartum haemorrhage

Italian Association for the Study of the Liver (AISF) recommends that in chronic cases with stable and nonprogressive disease pattern, pregnancy can be planned.[21]

It is important to know the complications and the importance of multidisciplinary approach so that timely referral can be made not only in the antenatal period but also prenatally for risk stratification, optimisation and better outcome.

Conclusion

Disease optimisation is of prime importance in EHPVO. Under optimised conditions, the feto-maternal outcome with EHPVO is good. Anaemia should be corrected to prevent adverse outcomes with variceal bleed or postpartum haemorrhage. Prenatally, complete investigations to rule out low platelet counts, LFT, endoscopy for detection of GI varices should be done and the disease condition should be optimised by medical and surgical management of portal hypertension. Splenectomy or shunt surgery should be done when indicated. Vaginal delivery is preferred and LSCS is required only for obstetric indications. Management is better by multidisciplinary approach during the pregnancy and postpartum period in a tertiary care centre.

Key points

1. Normal physiological changes of pregnancy worsen portal hypertension.
2. However, the risk of variceal bleed is low in optimised conditions.
3. Prenatal and antenatal identification, risk stratification and disease optimisation is important for better maternal and neonatal outcome.
4. Antenatal management should be by a multidisciplinary approach in a tertiary care centre.
5. Blood and blood products should be kept ready for delivery.
6. Vaginal delivery is preferred and LSCS is for obstetric reasons only.
7. Non-selective beta blockers like Propranolol are safe in antenatal and lactating period.
8. Maternal mortality is nil to low, but management should be under vigilant look out from pre conceptional to postnatal period.

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Conflicts of interest

There are no conflicts of interest.

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