Taiwanese Journal of Obstetrics & Gynecology 54 (2015) 394–397

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Extrahepatic portal-vein obstruction in pregnancy

Murali Subbaiah*, Sunesh Kumar, Kallol Kumar Roy, Jai Bhagwan Sharma, Neeta Singh

Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi, India

ARTICLE INFO

Article history:
Accepted 11 November 2013

Keywords:
endoscopic sclerotherapy
endoscopic variceal ligation
extrahepatic portal-vein obstruction
pregnancy outcome
variceal bleed

ABSTRACT

Background: Extrahepatic portal-vein obstruction (EHPVO) is a common cause of portal hypertension in developing countries. The main risk in pregnant women with this condition is variceal bleeding, which may be life-threatening. The objective of our study was to assess the outcome of pregnancy in women with EHPVO.

Materials and Methods: A retrospective analysis of 21 pregnancies in 12 women with EHPVO was carried out at a tertiary hospital in India.

Results: The mean age of pregnant women with EHPVO was 25.3 years, and the mean duration of disease since diagnosis was 6.1 ± 1.2 years. All the patients had chronic EHPVO, and two patients were diagnosed in the index pregnancy. The incidence of abortion, preterm deliveries, and small for gestational age fetus was 23.8%, 18.7%, and 12.5%, respectively. Thrombocytopenia was found to complicate 61.9% of the pregnancies, while anemia was detected in 40% of the pregnancies. Variceal bleeding occurred in one woman, who was diagnosed during pregnancy and was managed successfully with endoscopic sclerotherapy. None of the patients who were diagnosed prenatally had variceal bleeding during pregnancy. The outcome in nine pregnancies, in which prenatal endoscopic variceal ligation was done, was compared with eight pregnancies, in which endoscopic sclerotherapy was done. No significant difference between the two groups in terms of pregnancy outcome and complications was found. There were no stillbirths or maternal mortality.

Conclusion: Women with EHPVO who have been diagnosed and treated prenatally have a good pregnancy outcome. They should be managed in a tertiary care center with a multidisciplinary approach.

Introduction

Extrahepatic portal-vein obstruction (EHPVO) is defined as obstruction of the extrahepatic portal vein with or without the involvement of the intrahepatic portal veins or splenic or superior mesenteric veins [1]. In developing countries, it is a common cause of portal hypertension, accounting for up to 30% of all variceal bleeders [2]. In Western countries, only 5–10% of variceal bleeders are due to this condition [3]. Adult-onset EHPVO is a heterogeneous entity with regard to etiology, but is frequently associated with one or several risk factors for thrombosis, like myeloproliferative disorders, or deficiencies of protein C and protein S [4]. However, these risk factors have not been adequately studied in Asian patients.

In pregnancy, the increased blood volume and cardiac output increase portal flow and aggravate portal hypertension in these patients. This increases the risk of variceal bleeding in pregnant EHPVO patients, which can compromise the perinatal outcome [5]. Prenatal obliteration of high-risk varices by endoscopic sclerotherapy (EST) or endoscopic variceal ligation (EVL) reduces the risk of variceal bleeding, and can improve the pregnancy outcome in these women [6].

We report our experience with 21 pregnancies in 12 women with EHPVO. We assessed the clinical profile, risk factors, and fetomaternal outcome in pregnant women with EHPVO.

Materials and methods

In a retrospective study, we observed the maternal and perinatal outcome of 21 pregnancies in 12 women with EHPVO who were managed at a tertiary care hospital in India during the years 2006–2012. The diagnosis of EHPVO was made on the basis of Doppler ultrasonographic findings (replacement of portal vein by venous collaterals—portal cavernoma) and by the presence of other features of portal hypertension, like splenomegaly and endoscopic

* Corresponding author. Department of Obstetrics and Gynecology, Room Number 254, I Main Road, 12th Block, 2nd Stage, Nagarbhavi, Bangalore 560072, India.
E-mail address: muralidraiims@gmail.com (M. Subbaiah).

http://dx.doi.org/10.1016/j.tjog.2013.11.012

evidence of upper gastrointestinal varices. Women with liver cirrhosis and noncirrhotic portal fibrosis, and those positive for hepatitis B and C were excluded from the study.

Details regarding clinical presentation, duration of the disease, treatment received, and obstetric history were noted. Laboratory investigations, including complete blood count, liver function test, and coagulation profile of the patients, were recorded in detail. These women were managed under the joint supervision of obstetricians and gastroenterologists.

They were regularly seen in antenatal clinic every 2 weeks, until 28 weeks, and thereafter, weekly until delivery. Patients with thrombocytopenia were admitted at term. An upper gastrointestinal endoscopy (UGIE) was performed at the first visit, if indicated. High-grade varices, with or without bleeding, were managed by endoscopic interventions (EST or EVL). In the presence of upper gastrointestinal bleeding, EST using absolute alcohol or EVL using a multiple band applicator was done. Cesarean sections and induction of labor were done only for obstetric indications.

The incidence of antenatal complications, medical complications (anemia, thrombocytopenia, variceal bleeding, and jaundice), and perinatal outcome (Apgar score, birth weight, preterm delivery, and stillbirth) was noted. The women were divided into two groups: patients with EHPVO who had undergone EST in the past and patients with EHPVO who had undergone EVL. The aforementioned determinants were compared between these two groups. The categorical variables between the two groups were compared using Fisher's exact test with $p < 0.05$ being considered statistically significant.

Results

A total of 21 pregnancies in 12 women with EHPVO were analyzed. The mean age of the women was 25.3 ± 2.1 years, and the mean duration of disease since diagnosis was 6.1 ± 1.2 years (Table 1). Two patients were diagnosed during pregnancy: presenting with abdominal lump in one and variceal bleed in the other. Both presented at 4 months of pregnancy with Grade 3 varices, and underwent EVL and EST, respectively. All the patients had chronic EHPVO. Two patients were previously operated (splenorenal shunt and splenectomy); five patients had undergone EVL and three patients had undergone EST in the past (Table 2). None of the patients were found to have underlying prothrombotic state.

Thrombocytopenia was the most common disease-associated complication, being seen in 61.9% of the pregnancies (Table 3). Severe thrombocytopenia (<50,000/mm^3) was present in 28.6% of the pregnancies, while anemia (hemoglobin <11 g/dL) complicated 40% of the pregnancies. There was no variceal bleed in any of the pregnancies, in which the diagnosis was made prenatally ($n = 19$). UGIE was done in eight of these pregnancies, and residual varices were found to complicate two of them. These Grade 1 residual varices were not treated further. High-grade varices were not found in any of these patients. In the rest of the pregnancies, UGIE was not done, as they had undergone the procedure shortly before conceiving. Among the two patients who were diagnosed during pregnancy, one presented with variceal bleed and underwent EST. The other patient presented with splenomegaly, and on UGIE was found to have Grade 3 varices and underwent prophylactic EVL. Both of these patients tolerated the procedure well, and had no further variceal bleed and went on to deliver at term. None of the pregnancies were complicated by jaundice, ascites, and pancytopenia, and there was no maternal mortality.

The incidence of abortion was 23.8%, and the majority of these (four out of five) were first-trimester abortions. One patient had preeclampsia and another had gestational diabetes mellitus. Abruptio placentae did not complicate any pregnancy. The gestational age at delivery was 37.4 ± 1.4 weeks. Out of a total of 16 live births, 12 were vaginal deliveries and four were delivered by caesarean section. All the cesareans were done for obstetric indications. One patient had postpartum hemorrhage (atonic), which was controlled with an oxytocin drip.

The mean birth weight was 2.6 ± 0.4 kg, and the incidence of preterm delivery and small for gestational age fetus was 18.7% and 12.5%, respectively (Table 4). There were no stillbirths, neonatal deaths, or any congenital anomaly. For two babies, the Apgar scores at 5 minutes was less than 8. Both required admission to the neonatal intensive care unit and were eventually discharged.

We compared the outcome in nine pregnancies, in which prenatal EVL was done with eight pregnancies, in which prenatal EST was done. Thrombocytopenia complicated 75% of pregnancies with prenatal EST compared with 66.7% in pregnancies with prenatal EVL ($p > 0.05$). The incidence of residual varices, preterm delivery, and low birth weight was found to be similar in both groups. None of the patients in either group had variceal bleed in any of the pregnancies.

Table 1
Baseline characteristics of patients with extrahepatic portal-vein obstruction ($n = 12$).

Maternal characteristics	Number (%)
Age of the patients (y)[a]	
Mean ± SD	25.3 ± 2.1
Obstetric history	
Primigravida	6 (50%)
Time since diagnosis (y)	
Mean	6.1 ± 1.2
During pregnancy	2 (16.7%)
Presenting complaint	
Variceal bleeding	8 (66.6%)
Abdominal lump	2 (16.7%)
Epistaxis[b]	2 (16.7%)

SD = standard deviation.
[a] At the time of last pregnancy.
[b] Due to thrombocytopenia.

Table 2
Details of the therapeutic interventions performed.

Therapy ($n = 12$)	No. (%)
Therapy prior to pregnancy	10 (83.3%)
EVL	5
EST	3
Shunt surgery with splenectomy	2
Therapy during pregnancy	2 (16.7%)
EST	1
EVL	1

EST = endoscopic sclerotherapy; EVL = endoscopic variceal ligation.

Table 3
Maternal complications in 21 pregnancies in women with EHPVO.

Maternal complications[a]	No. (%)
Disease-associated complications	
Variceal bleeding	1 (4.7%)
Thrombocytopenia (<1.5 × 10^5/mm^3)	13 (61.9%)
Ascites	0
Jaundice	0
Residual varices	2 (9.5%)
Mortality	0
Obstetric complications	
Abortion	5 (23.8%)
Gestational diabetes	1 (4.7%)
Preeclampsia	1 (4.7%)
Abruption	0
Postpartum hemorrhage	1 (4.7%)

EHPVO = extrahepatic portal-vein obstruction.
[a] In 21 pregnancies.

Table 4
Perinatal outcome in pregnant women with EHPVO.

Perinatal outcome[a]	No. (%)
Total newborns	16
Live born	16
Stillbirth	0
Preterm births	3 (18.7%)
Mean age of gestation (wk)	37.4 ± 1.4
Mean birth weight (kg)	2.6 ± 0.4
Birth weight <2.5 kg	5 (31.2%)
Intrauterine fetal complications	
Intrauterine growth restriction	2 (12.5%)
Oligohydramnios	0
Newborn with Apgar < 8	2 (12.5%)

EHPVO = extrahepatic portal-vein obstruction.
[a] In 16 pregnancies, which continued beyond 20 weeks of gestation.

Discussion

In developing countries, like India, EHPVO is the most common cause of portal hypertension, unlike Western countries, where portal hypertension is usually due to cirrhosis [7]. Also, these women with EHPVO have normal fertility, unlike women with cirrhosis who have reduced fertility and up to 40% fetal-loss rate [8]. However, data regarding the pregnancy outcome and complications in patients with EHPVO are sparse, and there is a lack of large case studies.

Pregnancy aggravates portal hypertension in these patients. This is because of the increased blood volume, increased cardiac output, and mesenteric vasodilatation [9]. Increasing intra-abdominal pressure in the second and third trimesters also contributes to portal hypertension by increasing the inferior vena cava pressure [10]. This results in rerouting of blood via gastroesophageal collaterals, and increases the risk of variceal bleeding.

The presentation could be either acute (recent) or chronic EHPVO. Patients with acute EHPVO usually present with abdominal pain, ascites, jaundice, or fever [2]. In these patients, there is no evidence of portosystemic collaterals and portal cavernoma. The majority of patients with chronic EHPVO present with repeated bleeding episodes from esophageal varices. In our study, all the patients had chronic EHPVO, and eight of the 12 patients presented with variceal bleeding. Two patients presented with epistaxis, and on workup, were found to have thrombocytopenia due to splenomegaly and EHPVO.

The underlying hypercoagulable and prothrombotic state is thought to be an important risk factor for the development of EHPVO [4,11]. Investigations to detect an underlying myeloproliferative disorder; factor V Leiden mutation; G20210 A prothrombin gene mutation; and levels of protein C, S, and antithrombin III need to be conducted in all patients with EHPVO. However, these investigations are more likely to be rewarding in Western patients than in Asian patients [2]. Aggarwal et al [12] retrospectively analyzed 26 pregnancies in 14 women with EHPVO, and found an underlying hypercoagulable state in 21% of the women. However, Mandal et al [6], who studied 41 pregnancies in 24 women with EHPVO, did not find any underlying hypercoagulable state in any of their patients. In our study, we also did not find any prothrombotic state in any of our patients.

The incidence of variceal bleeding in pregnancy in patients with EHPVO has been reported to range from 20% to 34% [5,13]. However, it is generally agreed that patients with a prenatal diagnosis of EHPVO have a much lower incidence of variceal bleeding compared to those who are diagnosed during pregnancy [6]. Aggarwal et al [12] reported that none of their 14 patients had new onset variceal bleeding during the course of index pregnancy. In our study, none of the patients who were diagnosed prenatally had variceal bleeding during pregnancy. This was probably because all these patients had undergone prenatal endoscopic obliteration of varices, or had undergone prior splenectomy with shunt surgery. However, two of these patients were found to have residual varices during pregnancy. Both of these residual varices were Grade 1, and these varices were not treated. Although it is generally recommended that all varices detected during pregnancy should be treated [2], the efficacy of this treatment in low-grade varices is not known. More studies are needed to address this issue. Only one patient in our study had variceal bleeding. In this patient, the diagnosis of EHPVO was made at 4 months of pregnancy when the patient presented with variceal bleed and splenomegaly. She underwent UGIE, which detected Grade 3 varices, and EST was done.

For the control of acute variceal bleeding and for secondary prophylaxis of variceal bleeding, endoscopic therapy is effective and EVL is preferred [1,2]. Primary prophylaxis by EVL is recommended for high-risk varices before pregnancy. Either beta-blockers or endoscopic therapy can be used for primary prophylaxis of variceal bleeding in patients not planning pregnancy [2,14]. Beta-blockers reduce the portal pressure by reducing the cardiac output and by causing splanchnic vasoconstriction [9]. However, if used during pregnancy, they can cause fetal bradycardia and growth retardation [15]. Further, there are no studies, which have evaluated the safety and efficacy of beta-blockers in pregnant patients with EHPVO. Patients not responding to EST or EVL require definitive surgery.

According to the report of the Baveno V consensus workshop, EVL is the recommended form of therapy for acute variceal bleeding, although the safety of EST in pregnancy has also been established [1]. However, there are no studies that have compared pregnancy complications in patients who underwent either of the two techniques prenatally. In our study, we compared the outcome in nine pregnancies, in which prenatal EVL was done with eight pregnancies, in which EST was done. We did not find any significant difference between the two groups in terms of pregnancy outcome and complications. As this finding was limited by the small sample size, a larger study is needed to confirm this.

Thrombocytopenia due to splenomegaly is one of the major complications in these patients and has to be corrected before delivery. Aggarwal et al [12] reported that 50% of their 14 patients received platelet transfusion intrapartum. In our study, platelet transfusion was given in 30% of the patients during delivery. However, 61.9% of the pregnancies were complicated by thrombocytopenia, making it the most common complication in pregnancy.

The obstetric outcome of our patients with EHPVO was almost similar as that in general population, except for increased incidence of abortion (23.8%). Prenatal detection and treatment of these patients were probably responsible for this good outcome. In a retrospective study, Sumana et al [13], who studied 12 pregnancies in five women with noncirrhotic portal hypertension, reported no preterm delivery or stillbirth. However, four babies (44%) were small for gestational age. Mandal et al [6] found a higher incidence of preterm delivery, low birth weight, and stillbirth among pregnant women who were diagnosed for the first time in pregnancy and presented with variceal bleed.

Prenatal evaluation and optimization of women with EHPVO is the key to improve pregnancy outcome in them. Investigations to find out any underlying prothrombotic condition and other baseline investigations, like complete blood count, liver function test, and UGIE, should be done in all these patients. Endoscopic therapy of the varices in the form of either EST or EVL should be done before conception, and patients not responding to them should undergo decompression surgery. Splenectomy without shunt surgery

should not be performed [2]. The role of anticoagulant therapy in chronic EHPVO is not clear. However, in patients with documented prothrombotic disorders, lifelong thromboprophylaxis is recommended [1]. Repeat endoscopic evaluation is usually done during pregnancy, and either EST or EVL may be used to obliterate the residual varices.

Cesarean delivery is reserved only for obstetric indications. The delivery should be monitored closely, and second stage of labor may be cut short by operative vaginal delivery in patients who are at risk [2]. Intravenous fluids should not be administered overzealously because of the risk of volume overload and variceal bleeding. Platelet transfusion is required intrapartum if the count is less than 50,000/mm^3.

In conclusion, women with EHPVO would have a good pregnancy outcome if they were managed in a tertiary care center with a multidisciplinary approach.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

References

[1] De Franchis R, Faculty Baveno V. Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol 2010;53:762–8.
[2] Sarin SK, Sollano JD, Chawla YK, Amarapurkar D, Hamid S, Hashizume M, et al. Consensus on extra-hepatic portal vein obstruction. Liver Int 2006;26:512–9.
[3] Valla DC, Condat B, Lebrec D. Spectrum of portal vein thrombosis in the West. J Gastroenterol Hepatol 2002;17(Suppl. 3):S224–7.
[4] Primignani M, Martinelli I, Bucciarelli P, Battaglioli T, Reati R, Fabris F, et al. Risk factors for thrombophilia in extrahepatic portal vein obstruction. Hepatology 2005;41:603–8.
[5] Aggarwal N, Sawhney H, Vasishta K, Dhiman RK, Chawla Y. Non-cirrhotic portal hypertension in pregnancy. Int J Gynaecol Obstet 2001;72:1–7.
[6] Mandal D, Dattaray C, Sarkar R, Mandal S, Choudhary A, Maity TK. Is pregnancy safe with extrahepatic portal vein obstruction? An analysis. Singapore Med J 2012;53:676–80.
[7] Dilawari JB, Chawla YK. Extrahepatic portal venous obstruction. Gut 1988;29:554–5.
[8] Kochhar R, Kumar S, Goel RC, Sriram PV, Goenka MK, Singh K. Pregnancy and its outcome in patients with non-cirrhotic portal hypertension. Dig Dis Sci 1999;44:1356–61.
[9] Mendez EL, Escobedo LA. Pregnancy and portal hypertension a pathology view of physiologic changes. Ann Hepatol 2006;5:219–23.
[10] Scott D, Kerr M. Inferior vena caval pressure in late pregnancy. Br J Obstet Gynaecol 1963;24:305–8.
[11] Jain P, Nijhawa S. Portal vein thrombosis: etiology and clinical outcome of cirrhosis and malignancy-related non-cirrhotic, non-tumoral extrahepatic portal venous obstruction. World J Gastroenterol 2007;13:5288–9.
[12] Aggarwal N, Chopra S, Raveendran A, Suri V, Dhiman RK, Chawla YK. Extra hepatic portal vein obstruction and pregnancy outcome: largest reported experience. J Obstet Gynaecol Res 2011;37:575–80.
[13] Sumana G, Dadhwal V, Deka D, Mittal S. Non-cirrhotic portal hypertension and pregnancy outcome. J Obstet Gynaecol Res 2008;34:801–4.
[14] Sarin SK, Lamba GS, Kumar M, Misra A, Murthy NS. Comparison of endoscopic ligation and propranolol for the primary prevention of variceal bleeding. N Engl J Med 1999;340:988–93.
[15] Meidahl PK, Jimenez SE, Andersen JT, Petersen M, Brødbæk K, Køber L, et al. β-Blocker treatment during pregnancy and adverse pregnancy outcomes: a nationwide population-based cohort study. BMJ Open 2012;2:e001185.