Pregnancy with Portal Hypertension

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Even though pregnancy is rare with cirrhosis and advanced liver disease, but it may co-exist in the setting of non-cirrhotic portal hypertension as liver function is preserved but whenever encountered together is a complex clinical dilemma. Pregnancy in a patient with portal hypertension presents a special challenge to the obstetrician as so-called physiological hemodynamic changes associated with pregnancy, needed for meeting demands of the growing fetus, worsen the portal hypertension thereby putting mother at risk of potentially life-threatening complications like variceal hemorrhage. Risks of variceal bleed and hepatic decompensation increase many fold during pregnancy. Optimal management revolves round managing the portal hypertension and its complications. Thus management of such cases requires multi-speciality approach involving obstetricians experienced in dealing with high risk cases, hepatologists, anesthetists and neonatologists. With advancement in medical field, pregnancy is not contra-indicated in these women, as was previously believed. This article focuses on the different aspects of pregnancy with portal hypertension with special emphasis on specific cause wise treatment options to decrease the variceal bleed and hepatic decompensation. Based on extensive review of literature, management from pre-conceptional period to postpartum is outlined in order to have optimal maternal and perinatal outcomes. (J Clin Exp Hepatol 2014;4:163–171)

Pregnancy associated with liver diseases is an infrequent situation, but when seen together, presents a complicated clinical situation. Portal hypertension develops as a result of number of etiologies. In the west, cirrhosis is the commonest cause of portal hypertension. In the setting of cirrhotic portal hypertension, pregnancy is very rare due to hepatocellular damage leading to amenorrhea and infertility, the incidence of cirrhosis in pregnancy has been reported as 1 in 5950 pregnancies.[1] Cirrhosis may get exacerbated during pregnancy and has significant adverse effects on the mother and the baby.[2–4] In the developing countries, other causes like extrahepatic portal vein obstruction contribute significantly to non-cirrhotic portal hypertension (NCPH). Mostly liver function is much better preserved in women with NCPH and pregnancy is spontaneous in these women. Portal hypertension associated with pregnancy is a high risk situation as both pregnancy and portal hypertension share some of the hemodynamic changes. The physiological changes, in adaptation to the pregnancy and fetal needs, worsen the portal hypertension resulting in potentially life- threatening variceal bleed and other complications. Pregnancy is a potential hazard for occurrence of recurrent variceal bleed due to its hyperdynamic state causing increase in flow to the collaterals.[5–7] Therefore management in pregnancy requires knowledge of both the effects of changes during pregnancy on portal hemodynamics and the effects of portal hypertension and its cause on both mother and fetus, hepatotoxicity of the drugs used, management of portal hypertension so as to have an optimal pregnancy outcome. This review deals with various aspects of pregnancy with portal hypertension including cirrhotic as well as non-cirrhotic causes and focuses on the treatment options.

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Abbreviations: ACOG: American College of Obstetrics and Gynecology; EHPVO: extrahepatic portal vein obstruction; EST: endoscopic sclerotherapy; EVL: endoscopic variceal ligation; FDA: Food & Drug Association of America; HVPG: hepatic vein pressure gradient; NCPF: non-cirrhotic portal fibrosis; NCPH: non-cirrhotic portal hypertension; PPH: postpartum hemorrhage; PVT: portal vein thrombosis
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PHYSIOLOGICAL CHANGES OF PREGNANCY

Numerous hemodynamic and physiological changes occur during pregnancy as an adaptation to the needs of the growing fetus.[8,9] These changes start as early as six weeks and peak around 32 weeks. These changes are summarized in Table 1.

One of the earliest changes is an increase in plasma output by 40–50%. Maternal cardiac output increases by 30–50% due to increase in stroke volume and the heart rate. There is decline in systemic vascular resistance as a

Table 1 Normal Physiological Changes During Pregnancy.

1.	↑ Maternal blood volume
2.	↑ Maternal heart rate
3.	↑ Maternal blood volume
4.	↓ Systemic vascular resistance and blood pressure
5.	Peripheral vasodilatation & placental bed circulation.

result of progesterone effect and development of placental vascular bed. As a result of all of these changes, there is a profound alteration in systemic hemodynamics resulting in a hyperdynamic state with increased pulse pressure. These changes can worsen the portal hypertension in pregnant patients with portal hypertension and markedly increase the risks of variceal hemorrhage.[9] In patients suffering from liver cirrhosis, splanchnic arterial vasodilatation occurs, due to an increased local release of nitric oxide and other vasodilators related to portal hypertension, resulting in severely impaired circulatory function.[10,11] Consequently compensatory mechanisms essential in maintenance of arterial pressure in cirrhotic patients, unfortunately result in development of marked hemodynamic disturbances known as hyperdynamic syndrome. The pregnant woman has a 20–27% chance of esophageal bleed which increases markedly in case she has demonstrable varices.[9]

Pathophysiology of Portal Hypertension

Portal hypertension most commonly results from cirrhosis. Due to irreversible progressive damage in cirrhosis, these women usually have amenorrhea and infertility. Noncirrhotic portal hypertension can be encountered without evidence of liver disease. The first known mechanism of portal hypertension is an increase in intrahepatic resistance to blood flow. Hepatic damage thus caused results in shunting of hepatic blood, development of extrahepatic collaterals and elevated pressure in the portal venous system.[12] The normal portal pressure is 4–8 mm of mercury. Hepatic venous pressure gradient (HVPG = wedge hepatic pressure- free hepatic pressure) is used as a reflection of the portal pressure, and considered to be the gold standard for measuring portal pressure. It helps to guide therapy and prognosis in cirrhotic patients who have had a previous history of variceal bleed. Normal values of HVPG are between 1 and 5 mmHg, portal hypertension is defined as the pathologic increase in portal pressure expressed as HVPG. An HVPG>10 mmHg is needed for development of esophageal varices and HVPG >12 mmHg for them to bleed (Table 2).[13,14]

Variceal bleeding, ascites, encephalopathy and hepatorenal syndrome are the various clinical manifestations of the portal hypertension. Esophageal varices are seen in >40% of patients with liver cirrhosis at the time of diagnosis. Other manifestations of portal hypertension are splenomegaly and hypersplenism (Figure 1).

Table 2 Pathophysiological Effects of Portal Hypertension.

HPVG (mm Hg)	Clinical features	Stage of cirrhosis
1–5	Normal, non-cirrhotic	–
6–10	Compensated cirrhosis	1
>10	Compensated cirrhosis with development of varices	2
>12	Decompensated cirrhosis with ascites, variceal bleed, hepatic encephalopathy	3–4

Effect of Portal Hypertension on Pregnancy

In pregnant women, alcoholic cirrhosis is uncommon while viral or autoimmune related cirrhosis is more common in developing countries. The non-cirrhotic causes of portal hypertension include extra-hepatic portal vein obstruction, non cirrhotic portal fibrosis, portal vein thrombosis, Budd–Chiari syndrome, infection or congenital hepatic fibrosis.[15]

Maternal Complications

The complications of portal hypertension in pregnancy pose multiple risks to the mother and the fetus. In pregnancies with portal hypertension 30%–50% of pregnancy suffer from portal hypertension associated complications, resulting mainly because of variceal bleed and hepatic failure.[15] The severity of complications depends on the cause of portal hypertension and disease severity. These include variceal bleed, severe anemia, hepatic decompensation leading to progressive liver and renal failure, hepatic encephalopathy, splenic artery aneurysm rupture, ascites, spontaneous bacterial peritonitis, and post-partum hemorrhage.

Esophageal Varices

Gastro-intestinal hemorrhage remains the most catastrophic complication of portal hypertension during pregnancy. Variceal bleed has been reported in 18–32% of pregnant patients with cirrhosis and in 50% with a known portal hypertension. About 75% of patients with varices bleed during pregnancy which is one of the most serious consequences.[16] This is due to increased flow and pressure transmitted to collaterals due to hyperdynamic circulation during pregnancy. The dreaded complication of active variceal bleeding may occur at all stages of the pregnancy though second and third trimester and second stage of labor are the time of greatest risks of variceal bleed. Predictors of variceal bleed during pregnancy associated with portal hypertension are large varices, presence of endoscopic red signs and