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Study of Maternal and Perinatal Outcome in Pregnancy Complicated By Non –Cirrhotic Portal Hypertension

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Abstract
Objectives: *The aim of the study iwas to evaluate complications during pregnancy and pregnancy outcomes in women with Non-Cirrhotic Portal HTN.*
Methods: *22 women were retroscpectivelyanalysed with the diagnosis of NCPH in pregnancy. The study was conducted at Gandhi Hospital/Medical College, Secunderabad, Telangana from Augest 2018-July 2019. Records were reviewed for data.*
Results: *In this study 18 patients were diagnosed prior to pregnancy, 4 patients were diagnosed during present pregnancy for evaluation of anemia, thrombocytopenia and sleenomegaly. 10 patients had thrombocytopenia, out of which 2 patients had severe thrombocytopenia (<50000) requiring platelet transfusion. 15 patients had documented spleenomegaly. 13 vaginal deliveries, 7 cesareum deliveries and 2 ongoing pregnancys. 3 patients had PPH and managed medically. Cesareum sections were done with obstetric indications (ie, prev. LSCS, MSL, CPD). 1 patient developed ascitis and pleural effusion, treated medically on PND-1. 1maternal death due to hypertensive encephalopathy observed (due to Antepartum Ecclampsia , not related to complications of portal HTN). 5 preterm deliveries and 3 NICU admssions were observed, 2neonates had prolonged stay, discharged healthy. 8 patients had grade 1-2 esophageal varices which did not require banding.*
Conclusion: *fertility and pregnancy without serious complications in patients with Non-Cirrhotic Portal Hypertension is allowed and can be mnanagedsucessfully even with variceal bleeding (medically/surgically). Preterm and small for gestational age are noted . No elective indications for LSCS were observed.*

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I. Introduction

Non-cirrhotic portal hypertension can be seen without 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.

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. 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.

Objectives : The aim of the study iwas to evaluate complications during pregnancy and pregnancy outcomes in women with Non-Cirrhotic Portal HTN.

II. Methodology

This is an observational study carried out at Gandhi hospital over a period of 2 years. It is a tertiary care hospital and a major referral centre for high risk obstetrics in Telangana State.
SOURCE OF DATA: Gandhi Hospital/Medical College, Secunderabad, Telangana
SAMPLE SIZE: 22
STUDY DESIGN: Prospective observational study
STUDY DURATION: Augest 2018 - July 2018.

III. Results

In this study 18 patients were diagnosed prior to pregnancy, 4 patients were diagnosed during present pregnancy for evaluation of anemia, thrombocytopenia and sleenomegaly. 10 patients had thrombocytopenia, out of which 2 patients had severe thrombocytopenia (<50000) requiring platelet transfusion. 15 patients had documented spleenomegaly. 13 vaginal deliveries, 7 cesareum deliveries and 2 ongoing pregnancys. 3 patients had PPH and managed medically. Cesareum sections were done with obstetric indications (ie, prev. LSCS, MSL, CPD). 1 patient developed ascitis and pleural effusion, treated medically on PND-1. 1maternal death due to hypertensive encephalopathy observed (due to Antepartum Ecclampsia , not related to complications of portal HTN). 5 preterm deliveries and 3 NICU admssions were observed, 2neonates had prolonged stay, discharged healthy. 8 patients had grade 1-2 esophageal varices which did not require banding. 7 patients had developed Grade 1-2 esophageal varices, out of which 3 patient had variceal banding pre conceptionally, managed conservatively.

TABLE 1. AGE WISE DISTRIBUTION:

S.no	Age of the patient	Number of patients	Percentage%
1	<20 Years	10	45.4%
2	20-25 Years	5	22.7%
3	26-30 Years	2	9%
4	30 Years	5	22.7%

TABLE 2. DISTRUBUTION BY GRABIDITY

S.no	Grabidity	Number of patients	Percentage%
1	Primipara	10	45.4%
2	Multipara	12	54.5%

TABLE 3. INCIDENCES OF ABNORMALLITIES IN BLOOD INDICES

S.no	Investigations	Number of patients	Percentage%
1	Hemoglobin(<6gm/dl)	7	31.8%
2	Platelets(<1.5lakhs)	10	45.45%
3	Leucopenia(<4000)	8	36.36%
4	Pancytopenia	4	18.1%
5	Altered coagulation(INR>1.5)	2	9%

TABLE 4. ABNORMAL ULTTRASONOGRAPHIC FINDINGS

S.no	USG Abdomen	Number of patients	Percentage%
1	Spleenomelgaly	8	36.3%
2	Ascitis	1	4.5%

TABL 5. MODE OF DELIVERY

S.no	Status of delivery	Number of patients	Percentage%
1	Cecaream section	8	36.36%
2	Vaginal Birth	13	59%
3	Undelivered	1	4.5%

TABLE 6. OBSTETRIC COMPLICATIONS

S.no	Maternal complicatons	Number of patients	Percentage%
1	Spontanous abortion	2	9%
2	Induced termination(fetal anomaly)	1	4.5%
	Pregnancy induced hypertension		
3	Preterm labour	4	18.1%
4	Post preterm hemoglobin	5	22.7%
5	Maternal Death (hypertensive	3	13.6%
6	encephalopathy due to antepartum eclampsia)	1	4.5%

TABLE 6. FETAL OUTCOME

S.no	Fetal outcome	Number of patients	Percentage%
1	Live births	18	81.8%
2	Preterm births	5	22.7%
3	Small for gestationalage	6	27.2%
4	NICU admissions	3	13.6%
5	Neonatal deaths	0	--
6	Still birth	0	--

IV. Discussion

Role of Pre conceptionalcounselling : Extensive and detailed pre-conceptional counseling, evaluation and antenatal and perinatal monitoring is needed in patients with portal hypertension with or without cirrhosis planning for pregnancy. A complete medical history, detailed examination, lab investigations and imaging studies need to be completed to undertand the cause of the disease and its status.

Screening endoscopy should be done in the pre-conceptional period. Varices should be treated prior to planning a pregnancy, endoscopic variceal ligation is the preferred therapy and non-responders should be offered surgery in the form of shunt procedure or splenectomy.

Drugs should be reviewed for adverse effects on the fetus and alternative safe drugs to be changed, and also dose needs to be tapered. Prednisolone and azathioprine, if needed, can be continued in the minimum effective doses. Selective β blockers can be continued as their benefits are more than risks. Spironolactone should preferably be discontinued.

Since variceal bleed is the single important complication linked with poor pregnancy outcome, the basic aim is to prevent it and that can be done by assessment and treating the varices prior to conception.

Antenatal management :The principles of management include anticipation, early dignosis and management of the antenatal complications associated with portal hypertension. Maternal and fetal prognosis is dependent on the cause of underlying liver disease and its clinical condition at the time of conception. Pregnancy is not a contra-indication if the disease is well compensated.Anemia should be prevented and if present treated accordingly as anemia itself also leads to cardiac compromise in addition to being a risk factor for pre- term labor, low birth weight. Liver function and hematological assessment should be done 4 weekly, fetal growth needs to be monitored carefully and effects of the drugs need to be watched. Upper gastrointestinal endoscopy is found safe during pregnancy,[53] the main risk is fetal hypoxia due to sedation or positioning. Risk of variceal hemorrhage is higher in patients with grade 3 and grade 4 esophageal varices.There are no definite guidelines on primary prophylaxis for varices during pregnancy, the opinion is extrapolated from the studies from non-pregnant patients. Current American Association for the Study of Liver Disease (AASLD) recommendations include screening endoscopy in the second trimester as that is the time of maximum increase in the portal pressure.[54] The treatment options in presence of esophageal varices are both medical and surgical. There are no definite recommended guidelines of varices during pregnancy, these are based on the best guess experience extrapolated from the non- pregnant state.

Though non-selective beta blockers used to reduce portal pressure also reduce the risk of first bleed by half but the principal risk of using them in pregnancy is fetal growth restriction and fetal bradycardia. EVL of the large varices can also be done during pregnancy to prevent variceal bleeding. Current literature (Baveno V consensus workshop) recommends EVL for acute esophageal variceal bleed, although, endoscopic sclerotherapy may be used if banding is technically difficult.[17] In case of failure to control bleeding endoscopically by EVL or endoscopic sclerotherapy, emergency transjugular intrahepatic portosystemic stent shunt procedure may be required.

Pregnancy can be allowed to go to term if the disease is well compensated. Early termination of pregnancy may be expected in case of any obstetrical indication or progressive liver failure. In case of planned termination before 34 weeks, antenatal corticosteroids can be administered for fetal lung maturity. There are no

recommendations as to the preferred mode of delivery- vaginal vs caesarean section in patients with portal hypertension. The Asian Pacific Association for the Study of the Liver (APASL) has developed consensus statement on various aspects of extra-hepatic portal vein obstruction (EHPVO) including pregnancy and recommended that vaginal delivery can be anticipated in most of these women.[57] Cesarean is usually done for the obstetrical indications.

Peripartummanagement : The management during labor reserving and arranging adequate amount of blood and plasma and measures for balloon tamponade for the variceal bleed if needed. While carrying out delivery in such patients, obstetricians must take care of blood loss and fluid overload, coagulation disorders, raised intra-abdominal pressure, and drugs administered. Intravenous labor analgesia or epidural analgesia can be given if there is no coagulopathy. Spinal anesthesia may lead to hypotension and also may be contra-indicated due to thrombocytopenia. Drugs used in general anesthesia may precipitate encephalopathy. Epidural analgesia, in fact, is the preferred choice as it can also work in case caesarean is required. Delivery should be conducted under supervision of the senior obstetrician. Second stage of labor may be shortened prophylactically to avoid overstraining by the mother.[58] The third stage should be managed actively; methergin should not be used as oxytocics. Postpartum hemorrhage should be anticipated and managed effectively.Platelet transfusion may be needed in the intra-partum period in cases of hypersplenism. Antibiotics use needs to be individualized. Caesarean delivery is usually carried out in case of obstetric indications and vascular surgeon may be needed to stop the bleeding from ectopic varices in the operative field.

Maternal complications :The complications of portal hypertension in pregnancy include multiple risks to the mother and the fetus. In pregnancies with portal hypertension 30%–50% of pregnancy suffer from portal hypertension associated complications, mainly by variceal bleed and hepatic failure. 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 hepatic failure and renal failure, hepatic encephalopathy, splenic artery aneurysm rupture, ascites, spontaneous bacterial peritonitis, and post-partum hemorrhage. 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 increased blood volume andhyperdynamic circulation during pregnancy. Predictors of variceal bleed during pregnancy associated with portal hypertension are large varices, presence of endoscopic red signs and history of pre conceptionalvariceal bleed and untreated or undiagnosed varices.[16] . The serious complication of active variceal bleeding canoccur 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.

These patients are at a high risk of post-partum hemorrhage which occurs in 7%–10% of cases. Post-partum hemorrhage may be due tothrombocytopenia due to hypersplenism associated with portal hypertension and associated coagulopathy as a result of liver dysfunction. The treatment remains the same, these patients require blood and coagulation factors along with uterine contractile agents such as oxytocin. Active management of third stage of labor is the mainstay of management.

Perinatal complication : The incidence of spontaneous abortion, premature birth, still births and perinatal death are increased in women with portal hypertension. There is 10%–66% fetal wastage in patients of liver cirrhosis and spontaneous abortion rate of about 20% first trimester abortion.[47,48] Patients with causes like extrahepatic portal venous obstruction not associated with cirrhosis have portal hypertension with preserved liver function and have similar rates of spontaneous abortion as in the general population of 3%–6%, these patients also have better fertility than the patients with liver cirrhosis.[49] In patients with portal hypertension perinatal mortality is increased to 11–18%

Post partummanagement : The postpartum management includes strict monitoring for postpartum hemorrhage. Antibiotics should be given in the postpartum period. Spontaneous bacterial peritonitis is a specific complication which is seen in puerperium especially in the presence of ascites. Puerperal fever should be investigated and treated with appropriate antibiotics.

Breast feeding is usually not contra-indicated in these women unless she is on some FDA category D or X drugs. American College of Obstetrics and Gynecology (ACOG) guidelines recommend breast feeding for mothers with hepatitis C and B though in cases of hepatitis B, it should be started after immunoglobulin administration to the neonate.

V. Conclusion

Fertility and pregnancy without serious complications in patients with Non-Cirrhotic Portal Hypertension is allowed and can be mnanagedsucessfully even with variceal bleeding (medically/surgically). Preterm and small for gestational age are noted . No elective indications for LSCS were observed.

Pregnancy in a patient with portal hypertension requires a multispecialty team approach including expert obstetrician, hepatologist, neonatologist and anesthesiologist in a tertiary care center with facilities and expertise for gastrointestinal endoscopy, portal vascular surgery, high-risk pregnancy unit, perinatal and adult intensive care unit.

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