

LIVER DISEASES IN PREGNANCY

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ABSTRACT

Three to five percent of pregnancies show abnormal liver tests which includes coincidental liver diseases like viral hepatitis or gallstones, previous (underline) chronic liver diseases or aggravated by pregnancy state. Liver diseases in pregnancy cause remarkable morbidity and mortality in women (pregnant) as well as in their infants. Liver diseases in pregnancy are divided into two categories, Preeclampsia related (the hemolysis, elevated liver tests and low platelet count, (HELLP) syndrome, acute fatty liver of pregnancy) and unrelated to preeclampsia (hyperemesis gravidarum and intrahepatic cholestasis of pregnancy). Only fifty percent of hyperemesis gravidarum patients have liver dysfunction, which occurs in 1st trimester of pregnancy. 2nd half of pregnancy with pruritus, jaundice (less than 5mg/dl), elevated liver enzymes are characteristic features of intrahepatic cholestasis of pregnancy (ICP). Prompt delivery is recommended for HELLP syndrome. Acute fatty liver of pregnancy (AFLP) occurs in 3rd trimester.

KEYWORDS: AFLP Acute fatty liver of pregnancy, ICP Intrahepatic cholestasis of pregnancy, HG Hyperemesis gravidarum, HELLP.

INTRODUCTION

Approximately 3%, of pregnancies are associated with liver disease, severe episode associated with high morbidity and mortality in mother and baby.^{[1],[2],[3]} Rapid diagnosis is required for liver disease whether related to pregnancy or unrelated. High yield point is that, disease is present during pregnancy as denovo, related to pregnancy or pre-existing disease occurring in pregnancy. Table 1 shows classification of liver diseases in pregnancy. Severity of liver disease in pregnancy ranges from: Mild asymptomatic to fatal Irreversible deterioration in liver functions, associated with high mortality and morbidity. With the advancement of medical science morbidity and mortality during pregnancy related to liver disease are reduced, but still has high numbers. We tried our best to discuss various liver diseases during pregnancy and their outcomes and management. Physiological changes during pregnancy, as we know, pregnancy is a hyperdynamic state (due to hyper-estrogen). Few signs are commonly seen in pregnancy like palmar erythema and multiple spider naevi nearly 70%^[4] which are quite often seen in chronic liver disease. There is increase in cardiac output (co) upto 45%. There is increase in plasma volume with decrease in peripheral vascular resistance. Blood flow during pregnancy is unchanged. There is decreased in motility of gall bladder as well as increase in the secretion of cholesterol during pregnancy especially during second and third trimester. Liver tests usually

remains normal during pregnancy, however changes are only observed in alpha fetoprotein and alkaline phosphatase due to secretion from placenta. Moreover, changes in albumin and hemoglobin are due to hemodilution. During pregnancy, there is increase in the hepatic synthesis of coagulation factors like 7,8,10 and fibrinogen. No changes are noted during pregnancy in prothrombin time (PT) and activated partial thromboplastin time (APTT). Any change in PT is considered as an early reliable marker of synthesis dysfunction of liver.

Table 1: Classification of Liver Disease In Pregnancy

Pregnancy associated acute liver disease

- Pre-eclampsia/eclampsia with liver infarction.
- HELLP syndrome.
- Acute fatty liver of pregnancy (AFLP).

Exacerbated by pregnant state

- Viral hepatitis.
- Budd–Chiari syndrome.
- Gallstone disease.

Unrelated to pregnant state

- Drug-induced liver disease
- Toxins/mushroom poisoning
- Shock
- Trauma

- Decompensation of pre-existent liver disease.

Hyperemesis Gravidarum

Hyperemesis Gravidarum (HG) complicated around 0.2-2% pregnancies.^{[5], [6]} Defined as an intractable vomiting which leads to dehydration, weight loss occurs in 5% due to severe dehydration which needs hospitalization. Cause of HG is unclear but it is thought that there is high levels of HCG in first trimester which activates TSH receptors and causes suppression of TSH and increase in T₄. This inter-correlation has been suggested in some studies.^{[7], [8]} HCG levels are more elevated in molar and twin pregnancies which are associated with high incidence of HG. Nearly, 60% cases shows transient hyperthyroidism, this type of gestational hyperthyroidism are not related with complications, so does not require treatment.

HG is not related to liver disease, but it is seen that 50% can present with rise in enzyme levels (mild to 20 folds increase) and jaundice rarely present. Common biochemical abnormalities are hyponatremia, hypokalemia, hypomagnesaemia are secondary to dehydration due to vomiting and reduced oral intake. Immediately, treatment is important. As per the census there is one maternal mortality is seen every year in UK due to HG related complications. During treatment, B₆ and B₆ with doxylamine is safe and effective, as a first line treatment for HG.^{[9], [10]} Perinorm (Metoclopramide which is a dopamine antagonist) can be used as second line. Emeset (ondansetron) and glucocorticoids can be used for refractory cases. HG is a reversible disease with no permanent impact on liver, but it is seen that it is commonly seen in subsequent pregnancies.

Intrahepatic Cholestasis of Pregnancy

Incidence usually ranges between three to five percent pregnancies and high in subsequent pregnancies. ICP is the most common cause of cholestasis during pregnancy. As we know, pregnancy is cholestatic condition so, not always ICP during pregnancy, chronic liver disease are uncovered during pregnancy must be considered before reaching the diagnosis. ICP is a reversible form of cholestasis after delivery usually 6 weeks.^[11] Itching (Pruritis) is the main symptom and severe at night which usually occurs at palms and soles, sometimes whole body. Only ten percent of cases develop jaundice which occurs after the pruritis and jaundice is < 5mg/dl. There are elevated fasting and post prandial bile acid levels in ICP and comes to normal after 6 weeks of delivery. Elevated fasting bile acid level is usually >10 umol/L and is considered as a key test for diagnosis, but unfortunately not available at all centers. Liver enzymes SGOT/SGPT usually increases two-ten times but may be elevated upto 20 times. GGT usually not raises in ICP, it is considered as marker for CLD. During diagnosis three important point should be considered: 1) Second trimester, Severe itching, Use of contraceptive pills. 2) Exclude of other causes (viral/drug). 3) Spontaneous recovery after delivery.

Ursodeoxycholic acid (UDCA) is the drug of choice for treatment of ICP. The usual dose of UDCA is 10-15 mg/Kg/Day and it is safe for both mother and fetus which improves symptoms nearly 75%.^{[12], [13]} Atarax (Hydroxyzine) can be used for relief of itching. Dose is 25 mg/day. Local application is also available in the form of 1% Methanol. One most important point, with these types of treatment steatorrhea worsens, reason is fat soluble vitamins deficiencies. Many studies added S-adenosyl Methionine (SAM) with UDCA which gave good results. Early delivery is usually preferred (Not beyond 38 weeks).

Pre- Eclampsia/ HELLP Syndrome

Pre-Eclampsia is defined as denovo hypertension and proteinuria after 80 weeks of pregnancy to 48 hours of delivery. Multi system involvement which complicates ten percent of pregnancies but liver involvement is noticed in twenty to thirty percent cases. Previous pregnancy Pre-eclampsia, hypertension, chronic renal disease, autoimmune diseases, diabetes mellitus are the risk factors for Pre-eclampsia.^[14] Symptoms of pre-eclampsia are RUQ pain (hepatic tenderness), visual changes, light headache and vomiting, but these are usually absent at the time of antenatal care. Treatment of Pre-eclampsia is supportive. Prompt Delivery Should be done if fetal age is beyond 34 weeks. If it is less than 34 weeks then glucocorticoids should be given, for lung maturity.

HELLP It comprises 3 components, Hemolysis, Elevated liver enzymes and Low platelet counts. It is severe form of Pre-eclampsia which complicates around two to twelve percent cases of Pre- eclampsia.^[15] Endothelial injury and fibrin deposition which leads to micro angiopathic haemolytic anemia with platelet activation and consumption. Areas of hemorrhage and necrosis is noted around zone one which eventually leads to capsular tears and large hematomas (less commonly). Most patients present in 3rd trimester. Nearly thirty percent cases occur in PPP (Post partum period). There are no particular signs or symptoms that can differentiate HELLP from Pre-eclampsia. However it is seen that RUQ pain or mid-epigastric pain is the mostly presenting symptom only five percent cases present with nausea, headache. Jaundice and vomiting.^[16] Immediate (prompt) delivery is the main treatment in HELLP syndrome. Immediate delivery is effective, at or after thirty four weeks with evidence of dysfunction (Multi-organ) or features of DIC (Disseminated intravascular coagulation) or fetal distress. Only five percent cases present with severe hepatic complications like liver infarction, Hepatic Failure, Intraparenchymal hemorrhage and hepatic rupture.

Acute Fatty Liver of Pregnancy

Rare, seen in/20,000 deliveries. Also known by various names like acute yellow atrophy or acute fatty metamorphosis. It is the most common cause of Acute liver failure during Pregnancy as well life threatening

condition which is characterized by microvesicular fatty infiltration which ultimately leads to hepatic failure. It occurs in 3rd trimester and median age of gestation around 36 weeks. The exact cause is unknown but it is thought that there is abnormality in fatty acid oxidation, due to accumulation of chain metabolites of fatty acid in maternal circulation and deposited in liver cells (hepatocytes) leads to Hepatotoxicity. Nausea, vomiting and abdominal pain are the presenting symptoms (non-specific). There are high elevations of liver enzymes with increase bilirubin Hepatic failure can manifest in the form of coagulopathy, hypoglycemia or encephalopathy. Renal failure and /or pancreatitis are the commonest findings seen in AFLP.^[17] Diagnosis can be made on clinical grounds and with the help of Swansea criteria (Table 2). In Swansea criteria six or more features should be present in the absence of other explanation. Polyuria and polydipsia are specifically characteristic symptoms but it is seen only in five percent cases. It is seen, high male fetus ratio in affected individuals.^[18]

Table 2: Swansea criteria for diagnosis of acute fatty liver of pregnancy.

- _ Vomiting
- _ Abdominal pain
- _ Polydipsia and/or polyuria
- _ Encephalopathy
- _ High bilirubin (>14 mmol/L)
- _ Hypoglycemia (<4 mmol/L)
- _ High uric acid (>340 mmol/L)
- _ High TLC (>11000)
- _ Ascites or bright liver(ultrasound)
- _ High AST/ALT (>42 IU/L)
- _ High ammonia (>47 mmol/L)
- _ Renal impairment (creatinine >150 mmol/L)
- _ Coagulopathy (PT >14 s or aPTT >34 s)
- _ Microvesicular steatosis on liver biopsy

Most patients present in 3rd trimester, nearly thirty percent cases occur in Post Partum Period. There are elevations in liver enzymes (SGOT/SGPT) usually 300-500 times, but not as high as in viral hepatitis. Jaundice is always present (more than 5mg/dl). In extreme cases prothrombin time (PT) is elevated whereas, hypoalbuminemia and low cholesterol are commonly noticed. In late pregnancy if low platelet counts are noticed, immediate liver function tests (LFT) should be done. Hypoglycemia is the characteristic feature of AFLP, also presents as a poor prognostic indicator. Immediate delivery should be considered, usually by cesarean section after correction of prothrombin time (PT). Hospitalization should be needed with correction of prothrombin time and other parameters. Normal delivery should be considered only when INR less than 1.5 and platelets counts more than fifty thousand. Usually recovery is seen after one to four weeks, but cholestasis persists for longer period. As per the old records and new studies does not showed any improvement.

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Competing interest

No conflicts of interest for this article.

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