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Transamnitis and hepato-splenomegaly in pregnancy with normal feto-maternal outcome: A case report

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Abstract
Abnormal values of liver function tests can be seen in 3-5% of pregnancies. Most of the abnormal liver tests in pregnancy are a result of 5 liver diseases unique to pregnancy- heyperemesis gravidarum (HG), intra hepatic cholestasis of pregnancy (ICP), pre-eclampsia, HELLP syndrome and Acute Fatty Liver of Pregnancy (AFLP). This is a case report of 30 year nulligravida who conceived spontaneously after being treated for Poly cystic ovaries. Pre-conceptionaly the patient's metabolic parameters were within normal range, her BMI was 23.4Kg/m^2 at the time of conception. Patient had developed mild COVID related illness and was not on any antibiotics, antivirals or steroids. Patient developed nausea and vomiting of pregnancy at around 8 weeks of gestation. She developed intractable vomiting and was admitted at 15 weeks of gestation with hyperemesis gravidarum and treated accordingly. Patient had elevated liver enzymes at this point of time with her AST = 106 U/L and ALT 94 U/L. Ultrasound upper abdomen showed no gall stones, no organomegaly. Her serum bile acids remained <10µmol/L throughout the pregnancy. She never developed any pruritus either, but her transaminases were consistently raised. She was started on ursodeoxycholic acid which decreased the values but even after this treatment she had transamnitis ultrasound at 24 weeks gestation showed increased liver span and splenomegaly (12cm) but no gall stones. Her viral markers were also negative. She was given steroid cover. Patient went into spontaneous labor and delivered a healthy female child with no post natal complications.

Keywords: Transamnitis, hepatomegaly, splenomegaly, ICP, hyperemesis gravidarum

Introduction
Most of the pregnant females are young and healthy, and physiological changes in pregnancy should not be mistaken for liver dysfunction (table1) [1]. Abnormal values of liver function tests can be seen in 3%-5% of pregnancies, with many potential reasons. (table2) Any liver disease can occur in a pregnant female or pregnancy can occur in women who have underlying liver diseases. Most of the abnormal liver tests in pregnancy are a result of 5 liver diseases unique to pregnancy- heyperemesis gravidarum (HG), intra hepatic cholestasis of pregnancy (ICP), pre-eclampsia, HELLP syndrome and Acute Fatty Liver of Pregnancy (AFLP). These disorders are a consequence of pregnancy.

Table 1: physiological changes in liver tests during pregnancy

	First trimester	Second trimester	Third trimester	Term
AST	4-40	10-33	4-32	5-103
ALT	1-32	2-34	2-32	5-115
ALP	17-88	39-105	46-228	48-249
Total Bilirubin	0.05-1.3	0.1-1.0	0.1-1.2	0.1-1.1
Total bile acids	1.7-9.1	1.3-6.7	1.3-8.7	1.8-8.2
LDH	78-433	80-447	82-524	-

Table 2: liver diseases in pregnancy categories

Coincidental to pregnancy	Underlying chronic liver disease	Unique to pregnancy
Viral hepatitis	Chronic hepatitis B or C	Hyperemesis gravidarum
gallstones	Autoimmune hepatitis	Intrahepatic cholestasis of pregnancy
Drugs	Primary sclerosing cholangitis	Preeclampsia
Sepsis	Wilsons disease	HELLP syndrome
Budd-chiari	Cirrhosis	Acute Fatty Liver of Pregnancy

Hyperemesis Gravidarum (HG)

HG complicates 0.3% of pregnancies. It is intractable vomiting in first trimester of pregnancy necessitating hospitalization and intravenous hydration. Etiology of HG includes hormonal, immunological and psychological effects of pregnancy. Coexistent factors like hyperthyroidism, molar pregnancy, multiple pregnancy, and preexisting diabetes may abet the symptoms [2, 3].

Liver dysfunction occurs in 50% of patients with aminotranferases upto 20 times increased above their upper limit [2]. Viral hepatitis must be ruled out, hepatic histology shows cholestasis. Hospitalization is necessary for rehydration.

Intrahepatic cholestasis of pregnancy

ICP is pruritus and elevated bile acids which appear in second half of pregnancy and disappear after delivery. It is a cause of jaundice in pregnancy. It is associated with abnormal biliary transport across the canalicular membrane. It is associated with hormone levels in third trimester, increased incidence with multiple pregnancies, and precipitation by exogenous progesterone [4].

There is familial predisposition which points towards genetic predisposition to ICP. MDR3 mutations are responsible for 15% cases of ICP [5, 6, 7, 8]. Foetal complications in ICP are placental insufficiency, Preterm labor and sudden foetal death because of increased bile acid levels. Bile acids have a predisposition to bind with collagen, which when present in foetal circulation bind to the foetal SA node and cause sudden foetal demise.

The diagnosis of ICP is made by pruritus which typically starts around 25-32 weeks of gestation and occasionally earlier even in first trimester. It affects all body parts, more effect at the palms and soles and is typically worse at night. Aminotransferase levels vary from mild to 10 to 20 fold increase. Bilirubin is usually less than 5mg/dL. ALP will be increased. Most specific and sensitive marker is serum Bile acid levels of greater than 10µmol/L.

Management of ICP is 2-fold: symptomatic therapy and close monitoring and early delivery of fetus. Pruritus and liver dysfunction resolve immediately post-partum. Vitamin K being a fat soluble vitamin, its supplementation may be needed in severe cases with steatorrhoea. Withdrawal of exogenous progesterone may cause remission before delivery. Ursodeoxycholic acid (UCDA) 10-15mg/kg is the treatment of choice. It reduces abnormal foetal and maternal BA levels and is safe for the fetus [9, 10].

Preeclampsia

Preeclampsia is a triad of hypertension, edema and proteinuria in third trimester of pregnancy. It complicates 5-10% of all pregnancies. Liver involvement indicates severe preeclampsia with perinatal mortality and morbidity. Aminotransferases are 10-20 fold increased, bilirubin is usually less than 5mg/dL. It is an indiactor of severity of preeclampsia with need for immediate delivery to avoid eclampsia, hepatic rupture or necrosis.

HELLP syndrome

HELLP syndrome is characterized by hemolysis (H), elevated liver enzymes (EL) and low platelet count (LP) [11, 12]. It is microangiopathic hemolytic anemia associated with vascular endothelial injury, fibrin deposition in blood vessels, and platelet consumption. Patients present with upper abdominal pain and tenderness, nausea and vomiting, malaise, headache, edema, hypertension and protienuria. Treatment includes early delivery. Occasionally DIC may be present.

Table 3: Diagnostic criteria for HELLP

Hemolysis	Elevated liver enzymes	Low platelets
Abnormal blood smear	AST>70U/L	<150,000
LDH> 600U/L		
Increased indirect bilirubin		

Acute fatty liver of pregnancy

AFLP is an illness occurring in third trimester of pregnancy, where microvesicular fatty infiltration results in encephalopathy and hepatic failure [13, 14]. It carries significant perinatal and maternal mortality. Increased incidence is seen in twin pregnancies [13, 14]. AFLP occurs between 28-40 weeks of pregnancy. It might also present as jaundice in the post-partum period. Presentation can vary from asymptomatic to fulminant liver failure. In AFLP aminotransferases vary from near-normal to 1000. Bilirubin is less than 5mg/dL but higher in severe or complicated disease. Management consists of early diagnosis and immediate termination of pregnancy with intensive supportive care.

Case Report

This is a case report of 30 year nulligravida who conceived spontaneously after being treated for Poly cystic ovaries. Pre-conceptionaly the patients metabolic parameters were within normal range, her BMI was 23.4Kg/m^2 at the time of conception. The patient contracted COVID 19 at around 5 weeks overdue at which time her urine pregnancy test came positive. Patient had developed mild COVID related illness and was not on any antibiotics, antivirals or steroids. Patient developed nausea and vomiting of pregnancy at around 8 weeks of gestation. At this time, her CBC, LFT, RFT parameters were within normal range. Patient had mild dehydration for which she was put on Tablet Doxylamine and H_2 blockers. Patient improved but symptoms did not subside entirely. Her ultrasound for upper abdomen was normal. Patient underwent foetal ultrasound for nasal bone and nuchal translucency which were within normal limits. She developed intractable vomiting and was admitted at 15 weeks of gestation with hyperemesis gravidarum and treated accordingly. Patient had elevated liver enzymes at this point of time with her AST = 106 U/L and ALT 94 U/L. Her thyroid profile was within normal limits. S. fasting bile acids were tested and came out to be <10 µmol/l. Ultrasound upper abdomen showed no gall stones, no organomegaly. Patient was discharged on 4th day of admission on oral doxylamine and fluids. Patients vomiting subsided at 18 weeks of gestation. Her ultrasound for foetal target scan showed no foetal anomalies. Her liver function tests were repeated routinely at 22 weeks of gestation and were found to be markedly elevated. Her total serum bilirubin was 0.8mg/dL. AST = 457, ALT = 450. Bile acids were less than 10µmol/l. Patient was started on tablet ursodeoxycholic acid at a dose of 150mg 8 hourly. Her serial LFTs were repeated every week and showed very little improvement at which point of time dose of UDCA was increased to 300 mg TDS. Patient was negative for Hepatitis B, Hepatitis C, Hepatitis A and Hepatitis E. ultrasound at 24 weeks gestation showed increased liver span and

splenomegaly (12cm). Patient had no pruritus. Her bleeding and clotting time were also within normal range. Patient had no symptoms. Her LFTs were repeated fortnightly and were consistently found to be increased. UDCA dose was further increased to 600mg thrice a day. At a daily dose of 1800mg of UDCA, patients AST and ALT were 208 and 267 respectively. The patient was administered Injection Dexamethasone 6 mg intramuscularly 4 doses 12 hours apart for foetal lung maturity. Patient was also given a prophylactic course of Vitamin K. The foetal ultrasound showed normal growth parameters and the foetal BPP score was also perfect. Patient was asked to maintain a daily foetal movement count chart and was planned for termination of pregnancy at 37 completed weeks. At 37 weeks 2 days, patient went into spontaneous labor which was uneventful and resulted in the delivery of a healthy female child of birth weight 2.9 kg. Post-partum period was uneventful. Patient was called at 6 weeks post-partum for evaluation of liver function and ultrasound abdomen. Liver function tests were in normal range at this time, she had borderline hepatomegaly and splenomegaly had subsided.

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