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" THE HEPATIC HIJACK:HOW PREGNANCY AFFECTS LIVER DISEASE: CASE SERIES "

Obstetrics & Gynaecology

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ABSTRACT

Liver diseases in pregnancy may be categorized into liver disorders that occur only in the setting of pregnancy and liver diseases that occur coincidentally with pregnancy. Out of all diseases Intra hepatic cholestasis of pregnancy is most commonly seen usually in third trimester and resolves post delivery with medication.Intrahepatic cholestasis of pregnancy (ICP) is a liver disease specific to pregnancy. ICP IS usually seen during the second or third trimester of pregnancy and improves automatically after delivery. ICP has been identified worldwide, but its prevalence varies considerably depending on country and ethnicity.The role of clinical suspicion, early diagnosis,variable presentation of patient,proper management and proper followup is being studied in this case series. **Methods :** This study was a retrospective observational study, carried out in the R L jalappa hospital and research centre kolar karnataka. Status of women who had liver diseases during their pregnancy.This was studied between December 2024 and February 2025 after taking exclusion and inclusion criteria into consideration. Following details were noted which included clinical history, examination, investigations and treatments including operative reports and management were reviewed and surgical outcomes were obtained. **Results:** 4 cases of liver diseases in pregnant females were identified from Dec 2024 to Feb 2025.4 patients were diagnosed as Intrahepatic cholestasis of pregnancy.All the 4 patients presented with complaints such as itching all over body more on palms and soles and pain in the right upper quadrant of abdomen.All the 4 patients were diagnosed by evaluating serum LFT and serum bile acids levels.All patients were treated by giving Tab.UDILIV 300MG Orally BD,Tab RIFAGUT 550 MG RT BD ,HEPAMER Q SACHETS orally TID along with intake of plenty of oral fluids.Usually by the end of 1 week or by 10 days of delivery of fetus which is either by vaginal delivery or caesarean section majority of the symptoms subsided. **Conclusion:** Intrahepatic cholestasis of pregnancy is a common hepatic disorder associated with pregnancy. Pruritus, developing most commonly in third trimester of pregnancy, is the most specific clinical symptom. The resolution of symptoms is seen most commonly after the delivery. Laboratory diagnosis is mainly based on elevated total Liver function tests especially ALT and serum bile acids levels in the maternal blood. The mainstay of therapeutic management consists in the reduction of maternal symptoms by using Urso deoxy cholic acid.In my study there is significant reduction of maternal symptoms after delivery of fetus and usuage of tablet ursodeoxy cholic acid. Maternal outcomes have good prognosis but fetal outcomes can be improved by timely and effective intervention which is usually possible in tertiary care centres as shown in my study.

KEYWORDS

Intrahepatic cholestasis,pregnancy related liver disorder,maternal pruritis,ursodeoxycholic acid therapy,feral outcome management

INTRODUCTION:

Liver dysfunction during pregnancy can be caused by conditions that are specific to pregnancy or by liver diseases that are not related to pregnancy itself[1].Liver diseases in pregnancy may be categorized into liver disorders that occur only in the setting of pregnancy and liver diseases that occur coincidentally with pregnancy. Hyperemesis gravidarum, preeclampsia/eclampsia, syndrome of hemolysis, elevated liver tests and low platelets (HELLP), acute fatty liver of pregnancy, and intrahepatic cholestasis of pregnancy are pregnancy-specific disorders that may cause elevations in liver tests and hepatic dysfunction. Out of all diseases Intra hepatic cholestasis of pregnancy is most commonly seen usually in thirs trimester and resolves post delivery with medication[2].They are caused by either a disorder that is unique to pregnancy or an acute or chronic liver disease that already exists or coincidentally develops as a comorbidity of pregnancy. Liver diseases unique to pregnancy include hyperemesis gravidarum; hypertensive disorders of pregnancy, such as pre-eclampsia/ eclampsia; hemolysis, elevated liver enzymes, and low platelet count syndrome; Intrahepatic cholestasis of pregnancy; and acute fatty liver of pregnancy[3].Pregnancy directly affects the physiology of the liver and hepatic disorders can adversely affect pregnancy outcomes. In developed countries, approximately 3% of pregnant women are affected by some form of liver disease during their pregnancy[4].Some of these conditions can be fatal for both the mother and fetus. It is, therefore, important to determine the underlying cause of abnormal liver function, enabling prompt management to reduce morbidity and mortality[5].Before considering the diagnosis of pregnancy-specific liver disorders, liver disorders that are not related to pregnancy must be excluded[6]. The aim of this article is to provide a systematic approach to pregnancy-specific liver disorders.Prompt diagnosis and management of liver diseases in pregnancy, while very challenging, is extremely important, as they might cause adverse maternal and fetal outcomes.

ICP typically appears in the third trimester of pregnancy, although it can present much earlier in some women. The most common symptom present is pruritus, which varies in intensity in each individual patient[7]. Other symptoms include pain in the right upper quadrant, pale stool, and dark urine. Elevated serum bile acids are used to make the diagnosis. Other cholestatic laboratory values may be elevated, including aspartate aminotransferase, alanine transaminase, alkaline phosphatase, gamma-glutamyl transferase, and bilirubin.ICP increases the risk of stillbirth for the baby, NICU care.In most women, pruritus resolves after delivery[8].Affected individuals have a defect involving the excretion of bile salts, which leads to increased serum bile acids. These are deposited within the skin, causing intense pruritus.The cause of ICP is unknown but is thought to be multiple factors with genetic, hormonal, and environmental involvement[9].The correlation of increased maternal serum bile acids concentrations with intrauterine fetal demise is consistently seen in retrospective studies of females with intrahepatic cholestasis of pregnancy. Most patients with ICP do not develop clinical jaundice.The liver function predominantly shows features of cholestasis. The most characteristic laboratory abnormality is high serum bile acid levels (≥10 µmol/L) which may be elevated up to 100- fold. Severe obstetric cholestasis is defined by levels >40 µmol/L. Other findings are conjugated hyperbilirubinemia, increase in serum ALP, gamma glutamyl transferase (GGT) and serum aminotransferases are normal or only minimally elevated[10]. The synthetic function of the liver and the liver architecture remains unaltered. ICP progresses until the time of delivery. Pruritus disappears within 24-48 hours postpartum, but biochemical and histological abnormalities may take weeks to months to resolve. ICP may reoccur in next pregnancies in 60-70%, although not necessarily as severe as the first episode.UDCA is the best available therapeutic agent which relives maternal symptoms[11].Managing these patients is of paramount importance to reduce the maternal and foetal morbidity and mortality. Non-pharmacological management includes keeping patients well-hydrated, use of cotton cool and wearing loose clothes and avoiding high-fat diet. Antihistamines are usually not effective[12].Ursodeoxycholic acid is currently the only effective medicine in dose of 10-15 mg/day in 2 to 3 doses to prevent maternal morbidity and mortality.Frequency of intrahepatic cholestasis of pregnancy . The drug should be given 2 to 3 weeks prior to delivery. Patient usually has relief within 2 weeks[13].

Case Series

Case 1: A 23 year old Primigravida with 32 weeks of gestation,

referred from District government Hospital in view of intrauterine demise with deranged LFT.Patient presented to RL Jalappa hospital with complaints of fatiguability since 2 days.Patient has history of fever and was treated conservatively.On arrival to casuality, her GCS was 9/15 , PR:108bpm,BP:120/80mmhg,SPO2: 97%on room air. Patient was pale, icteric with pedal edema. Relevant investigations done and reported Hb as 8.5gm, WBC- 77Th/mm3, PLT: 38th/mm3 ,urea: 147mg/dl, creat: 6mg/dl. Patient was shifted to ICU in view of drop in GCS with sepsis with MODS. Obstetric scan done and reported as Intrauterine fetal demise.Patient had a spontaneous preterm vaginal delivery of dead female baby of weight 1.56kg at 3:15pm on 12/03/2025. Physician opinion taken in view of sepsis and patient was started on higher antibiotics. Nephrology opinion taken in view of deranged RFT and strict I/O monitoring done. Blood culture and urine culture done and reported as no growth. Serial LFT,RFT monitoring was done and diagnosed as Intrahepatic cholestasis of pregnancy.Patient had one episode of GTCS type of convulsion associated with frothing and uprolling of eyes. Patient was resuscitated and MRI BRAIN was done and reported as metabolic encephalopathy with pituitary apololexy. Sodium bicarbonate IV correction was given in view of metabolic acidosis.6 platelets ,1 FFP, 2 PINTS PRBC TRANSFUSED. Patient had bilateral lower limb swelling for which venous Doppler was done and reported as normal. Patient was treated with Tab UDILIV 300MG Orally BDx 10 days,Tab RIFAGUT 550 MG RT BD X 12 DAYS ,HEPAMER Q SACHETS orally TID x 12 days.Regular vitals monitoring was done. Serial CBC, RFT , LFT monitoring done and patient improved symptomatically. Patient was shifted out of ICU on Post natal day 5. On PND 10 patient developed fever and fever profile was sent, urine routine and blood culture sent and reported as no growth of organisms. Regular vitals monitoring done and stable. Regular temperature monitoring done. Regular perineal care was given and wound was healthy.Patient was symptomatically better and discharged from the hospital on post natal day 15and advised for regular followup.

Case 2:
A 29 year old G3P1L1A1 with 36 weeks 2 days gestational age 9 months of amenorrhea appreciating fetal movements well came with itching all over the body with severity in palms and soles during night since 2 months.Relevant investigations sent and Hb reported as 10.1gm% and increased serum ALP and GGT levels seen along elevated serum bile acids .Physician opinion was taken in view of deranged LFT values and diagnosed as Intrahepatic cholestasis of pregnancy.Patient had a Misoprostol induced vaginal delivery of a single live term male baby of birth weight of 2.74kgs at 8:57 AM on 21/03/2025 .Baby cried after suction and stimulation.Meconium stained liquor noted. APGAR 1' 6/10 & 5'8/10 . Baby shifted to NICU in view of Respiratory distress. patient was treated with TAB.UDILIV 300 mg orally BD**.**Regular perineal care given, episiotomy wound healthy,Patient was stable and hence being discharged on post natal day 10 and advised for regular followup.

Case 3:
A 24 year-old G2P1L1 with 39 weeks of gestational age appreciating fetal moments well, came with complaints of Itching all over body severe in palms and soles since 1 month and pain in the right upper quadrant of abdomen since 3 days.Relevant investigations were sent and Hb was reported as 11.7 gm% and deranged LFT such as elevated ALT levels. Patient underwent Elective LSCS and Extracted by vertex a single live term Female baby of birth weight 2.96KGS at 6:34PM on 06/03/25 . Baby cried immediately after birth . Thick Meconium stained liquor noted .APGAR 1'6/10 & 5'8/10. Baby shifted to NICU in view of Respiratory distress.,Repeat LFT levels done and ALT levels remains elevated hence physician opinion taken and diagnoased as Intrahepatic cholestasis of pregnancy.Patient was treated with Tab UDILIV 300MG Orally BD,Tab RIFAGUT 550 MG RT BD. suture removal done on post operative day 13 wound healthy .Patient was symptomatically stabilized and hence being discharged and advised for regular followup.

Case:4
A 30 year old G2P1L1 with 9 months of amenorrhoea, appreciating fetal movements well came with complaints of intense itching all over body and more severe on palms and soles especially during nights.Patient has history of dark urine since since 15 days.On arrival patient vitals were stable. Patient was icteric with pedal edema. Relevant investigations were sent and hb reported as 9gm, WBC was 16Th/mm3, PLT: 158th/mm3 urea: 175mg/dl and creat: 4.6mg/dl. Investigations revealed deranged LFT. Obstetric scan done and reported as single live intrauterine gestation with 39 weeks 2days with AFI-11cm and EFW 2.9kgs.She had A Foleys and misoprostol Induced vaginal delivery of a single live male baby of birthweight 2.76kg at 5:35Am on 19/02/2025. Physician opinion was taken in view of deranged LFT and increased bilirubin levels and elevetaed bile acids levels and diagnosed as Intrahepatic cholestasis of pregnancy and started on higher antibiotics.Patient had 2 episodes of GTCS type of convulsions not associated with frothing and no uprolling of eyes. Patient was resuscitated and MRI BRAIN was done which reported as Posterior reversal encephalopathy syndrome. IV Mgso4 was given for 24 hours and then patient was started on antihypertensives in view of increased bp readings after delivery.Regular vitals monitoring done. Serial CBC, RFT , LFT monitoring done and patient improved symptomatically. Repeat LFT levels done and ALT levels remained elevated hence physician opinion taken and diagnosed as Intrahepatic cholestasis of pregnancy.Patient was given Tab UDILIV 300mg Orally BD,Tab RIFAGUT 550mg RT BD.Urine routine showed protein 3+ cells for which physician opinion was taken and advice was followed. Regular vitals monitoring done and stable.Strict bp monitoring done and antihypertensives tapered slowly. Regular perineal care given, episiotomy wound healthy,Patient is now stable and hence being discharged on post natal day 13 and advised for regular followup.

DISCUSSION:
Intrahepatic cholestasis of pregnancy is an obstetric cholestasis or jaundice of pregnancy. It frequently develops in late trimester of pregnancy in individuals who are predisposed and it is the most common pregnancy-related liver disorder[14]. ICP is a pregnancy specific liver disorder seen in third trimester of pregnancy and is associated with increased numbers of adverse neonatal outcomes. Though, maternal consequences of ICP are benign; however, clear association is seen amongst ICP and higher prevalence of fetal distress, premature delivery, and sudden intrauterine demise and maternal morbidity if left untreated.Most common symptom was pruritus and patients developed pruritus between 32weeks to 36 weeks of gestation[15] .A high rate of preeclampsia and convulsions was noted. In Intra hepatic cholestasis of pregnancy generalised pruritus is the first clinical symptom[16]. Pruritus can be mild and bearable for some females, but can also be very grave and unbearable. It may also lead to interfere the patient's sense of well-being by insomnia, mental sufferings and even increased suicidal tendencies[17]. Pruritus is more grave in later half of the day mostly in nights, more seen in the palms of the hands and soles of the fee.Moderately elevated levels of conjugated bilirubin occurs is 10- 15% patients presents as mild jaundice.Jaundice can sometimes be the initial symptom but usually develops one to four weeks after the onset of pruritus[18].Subclinical steatorrhea is usually seen in patients with poor fat absorption which can in turn cause vitamin K deficiency leading to prolonged PT (prothrombin time) and PPH (post-partum haemorrhage). Women with history of intrahepatic cholestasis of pregnancy, even in fist degree relatives tend to have higher chances of developing gall stones and cholecystitis.Increased levels of serum bile acids and serum aminotransferase levels are seen as most common biochemical derangements[19]. Serum total bile acids levels may be elevated by 10 folds.If womens fasting serum bile acid levels are more than 40 μmol/L it most commonly leads to fetal complications .In intrahepatic cholestatsis of pregnancy, cholic acid levels are more increased than chenodeoxcholic acid. Aminotransferases levels are also increases two –ten-fold more than the average in 26% of females with pruritus, and can exceed to 1000 U/L in rare circumstances. Serum aminotransferases help in better follow up of the patients once we start treatment with urssodeoxycholic acid rather with fasting serum bile acid levels (total) in patients which firstly are elevated secondary to elevated levels in serum urodeoxycholic acid (UDCA) levels[20]. Due to increased in levels of placenta isoenzyme, increased levels of serum alkaline phosphatase can be difficult to recognize.

In present study, all of the following patients had their symptom onset during the 32-36 weeks of gestation.Majority of symptoms occurred in the third trimester in 90% of the women presenting after 30 weeks of gestation[21].According to the statistics that the incidence of hyaline membrane disease leading to respiratory depression in neonates of mothers diagnosed with intrahepatic cholestasis of pregnancy is double than in neonates of normal population[22]. Respiratory depression in neonate can also be due to pre-term delivery, but based on study of fluid taken from bronchoalveolar lavage of newborn of mothers with intrahepatic cholestasis of pregnancy it demonstrates that respiratory

depression is specifically associated with ICP[23] . It has been postulated that increased levels of serum bile a acids can lead to depletion of surfactant in the alveoli of lungs of fetus. The chances of fetal affection in ICP is more than that of normal population. In our study 1 patient had intrauterine fetal demise[24].Lately management of intra hepatic cholestasis of pregnancy is induction of labor at 36–38 weeks period of gestational age, mostly used for patients with serum bile acids 40 μmol/L had higher fetal risk of premature delivery, birth asphyxia, meconium staining of liquor amnii, and patients with serum bile acids ranging from 10–39 μmol/L had decreased risk[25] .

In this study, no clinical or biochemical predictors association with increased fetal affection were significant enough. This can be due to contrast in basic practice, where we essentially terminate pregnancy in females diagnosed ICP at approx. 37 weeks gestational age[26].

RESULTS:

ICP is frequent cause of hepatic deterioration in pregnancy. Maternal morbidity is increased in terms of fetal distress and fetal demise and discomfort due to pruritus. Maternal cholestasis is transient with resolved after delivery.ICP is associated with adverse perinatal outcome. There is higher risk of meconium stained liquor, birth asphyxia, and sudden intrauterine demise at term as evidenced in this study.

CONCLUSION:

Intrahepatic cholestasis of pregnancy is a common hepatic disorder associated with pregnancy. Pruritus, developing most commonly in third trimester of pregnancy, is the most specific clinical symptom. The resolution of symptoms is seen most commonly after the delivery. Laboratory diagnosis is mainly based on elevated total Liver function tests especially ALT and serum bile acids levels in the maternal blood. The mainstay of therapeutic management consists in the reduction of maternal symptoms by using Urso deoxy cholic acid.In my study there is significant reduction of maternal symptoms after delivery of fetus and usuage of tablet ursodeoxy cholic acid**.** Maternal outcomes have good prognosis but fetal outcomes can be improved by timely and effective intervention.

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