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Maternal and fetal outcome in pregnancy with liver disorders

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Abstract
Aims: To determine the maternal and perinatal outcome among pregnant woman with DLFT.
Materials and Methods: A prospective study was conducted in the Department of Obstetrics and Gynaecology, Tertiary care institute in West Bengal ESI-PGIMSR JOKA over a period of one year (January to December 2023). All pregnant woman with DLFT were included in the study.
Results and Analysis: Incidence of DLFT in our hospital was 4.88%, among 1923 deliveries, 94 were diagnosed to have deranged liver function out of which 90.4% were obstetric cholestasis, 6.38% severe pre-eclampsia, 2.12% Hepatitis B, 1.06% leptospira. 71.2% were primigravida, Gestational Diabetes Mellitus associated in 28.7%, Gestational hypertension in pregnancy in 15.9% and few with hypothyroidism, Bronchial asthma. Most of the patients were delivered by cesarean section for various reasons, 26.5% were preterm, 20 admitted to NICU.
Conclusion: Early diagnosis and management is necessary to decrease maternal and perinatal mortality and morbidity.

Keywords: DLFT, pregnancy, liver disorders, viral hepatitis, cesarean section, preterm deliveries

Introduction

Liver disease during pregnancy is rare but can lead to serious complications. It is more prevalent in developing countries than in developed ones. Liver diseases that complicate pregnancy are classified into three general categories. The first includes those specifically related to pregnancy that resolve either spontaneously or following delivery, The most common causes are Hyperemesis gravidarum not responding to medical management, severe pre-eclampsia, HELLP syndrome, intrahepatic cholestasis and AFLP. The second category involves acute hepatic disorders that are coincidental to pregnancy, such as acute viral hepatitis. The third category includes chronic liver diseases that predate pregnancy, such as chronic hepatitis, cirrhosis, or esophageal varices [1]. The overall incidence of liver disease in pregnancy is 3% [2].

Intrahepatic cholestasis is the most common presentation among liver disorders in pregnancy. The literature reports an incidence of ICP ranging from 0.1% -15.6% with a wide variability based on ethnicity and geographic location [3].

ICP is hepatic dysfunction characterized by jaundice, pruritis, elevated aminotransferases, and bile acid levels with insidious onset in the late second or third trimester of pregnancy when hormonal influences are at their peak and resolving completely after delivery [4]. ICP is associated with maternal and fetal complications. It is also named as icterus gravidarum, recurrent jaundice of pregnancy, cholestatic hepatosis. The exact etiology is still unclear. However current research focuses on the numerous mutations in many genes that control hepatocellular transport systems. Examples include mutations of ABCB4 gene, which encodes multidrug resistance protein 3 (MDR3) associated with progressive familial intrahepatic cholestasis, and errors of the ABCB11 gene, which encodes a bile-salt export pump [5]. Other potential gene products are the farnesoid X receptor and transporting ATPase encoded by ATP8B1 [6]. Some drugs that similarly decrease canalicular transport of bile acids aggravate the disorder. Risk factors include family history, maternal age>35 years, multiple pregnancies, and previous history of ICP, more common in winter months. Common symptoms are pruritis (Mostly on the palms, and soles) worsens at night with the

absence of rash other than excoriations, nausea, vomiting, jaundice, and steatorrhea [7].

Methodology

Study type: Hospital based prospective observational study.

Study setting: The study was conducted in the Department of Obstetrics and Gynaecology, Tertiary care institute in West Bengal ESI-PGIMSR JOKA.

Place of study: Both the antenatal out-patient clinic, Labour ward, Labour room of the Department of Obstetrics and Gynaecology, Tertiary care institute in West Bengal ESI-PGIMSR JOKA.

Study duration: The study was conducted over a period of one year (January 2023- December 2023).

Study population: All pregnant women diagnosed with deranged liver function test (2-3 fold raise in aminotransferase, bile acid levels > 10 umol/L) in late second and third trimester.

Statistics

Table 1: Incidence of DLFT in the study population

Total deliveries	Total DLFT	Percentage
1923	94	4.88%

In our study, out of 1923 total number of deliveries, the incidence of DLFT was 4.88%.

Table 2: Distribution of DLFT according to maternal age

Age group (Years)	Number	Percentage
15-20	09	9.57%
21-25	33	35.1%
26-30	32	34.0%
31-35	17	18.0%
36-40	03	3.19%
Total	94	

In our study, the maximum number of patients were in the age group of 21-25years that is 35%.

Table 3: Incidence of DLFT according to gravida

Gravida	Number	Percentage
Primigravida	67	71.2%
Multigravida	27	28.7%
Total	94	

In our study primigravida were 71.2% and multigravida 27%.

Table 4: Distribution according to gestational age at delivery.

Gestational age at delivery	Number	Percentage
< 34 weeks	03	3.19%
34-36 weeks	05	5.31%
36-37 weeks	15	15.9%
>37 weeks	71	75.5%
Total	94	

In our study, the majority delivered at term, and 24.4% delivered before 37 weeks POG.

Table 5: Distribution based on associated maternal co-morbidities.

Co-morbidity	Number	Percentage
Gestational diabetes mellitus	27	28.7%
Hypertensive disorders	15	15.9%
Overt diabetes mellitus	02	2.12%
Hypothyroidism	11	11.7%
Bronchial Asthma	02	2.12%
Anaemia	02	2.12%
Hepatitis B	02	2.12%
Leptospirosis	01	1.06%

In our study, 27 patients (28.7%) were associated with gestational diabetes mellitus, with 2 cases of overt diabetes, 15.9% cases of hypertensive disorders in pregnancy, and 11.7% of hypothyroidism.

Table 6: Causes of deranged liver enzymes in our study.

Causes	Number	Percentage
Obstetric cholestasis	85	90.4%
Severe pre-eclampsia	06	6.38%
Hepatitis-B	02	2.12%
Leptospira	01	1.06%
Total	94	

Out of 94 patients with deranged liver function, 90.4% were associated with intrahepatic cholestasis.

Table 7: Distribution according to mode of delivery.

Mode of delivery	Number	Percentage
Vaginal delivery	23	24.46%
LSCS	71	75.54%
Total	94	

In our study around 75.5% underwent LSCS and 24.4% delivered vaginally.

Table 8: Indication of cesarean section.

Indication for LSCS	Number	Percentage
Induction failure	21	29.57%
Previous LSCS	13	18.30%
Thick MSL with fetal distress	12	16.90%
PPROM with poor Bishops score	08	11.26%
Severe pre-eclampsia	03	04.22%
Severe oligohydramnios	03	04.22%
IUGR with deranged Doppler study	03	04.22%
NPOL	03	04.22%
Twins	02	02.81%
Breech in early labor	02	02.81%
CPD with short stature	01	01.40%
Total	71	

In our study around 29.57% underwent LSCS due to induction failure, 18.30% due to previous LSCS, 16.90% with thick MSL.

Table 9: Based on birth weight

Birth weight	Number	Percentage
<2.5 kgs	22	22.9%
>2.5 kgs	74	77.0%
Total	96 (Twins -2)	

In our study, birth weight was more than 2.5 kgs in around 77% of the cases, with 22.9% having low birth weight.

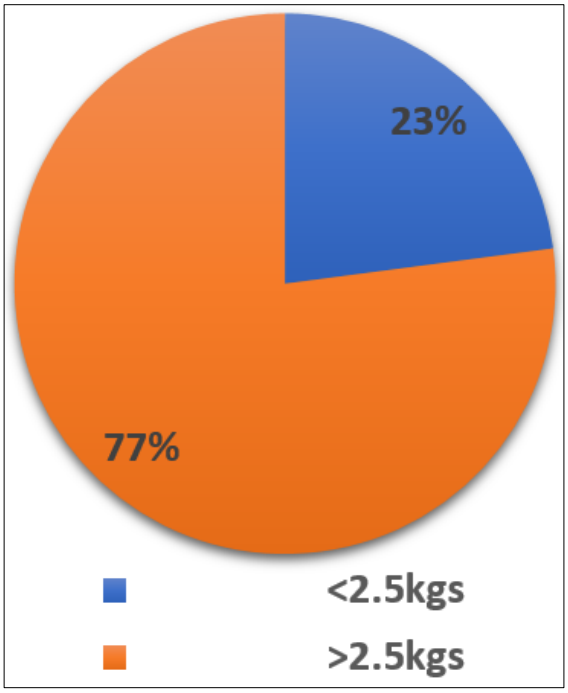

Fig 1: Birth Weight

Table 10: Neonatal outcome in women with deranged liver enzymes

Fetal outcome	Number	Percentage
Hyperbilirubinemia requiring phototherapy	17	17.7%
Transient tachypnea of newborn	08	8.33%
Hypoglycemia	08	8.33%
Meconium aspiration	04	4.16%
Respiratory distress syndrome	03	3.12%
Neonatal sepsis	03	3.12%
Birth asphyxia	01	1.04%
IUFD	02	2.08%

In our study around 17.7% of neonates required phototherapy for hyperbilirubinemia, 8.33% with TTN, 8.33% with hypoglycemia and there was no neonatal mortality.

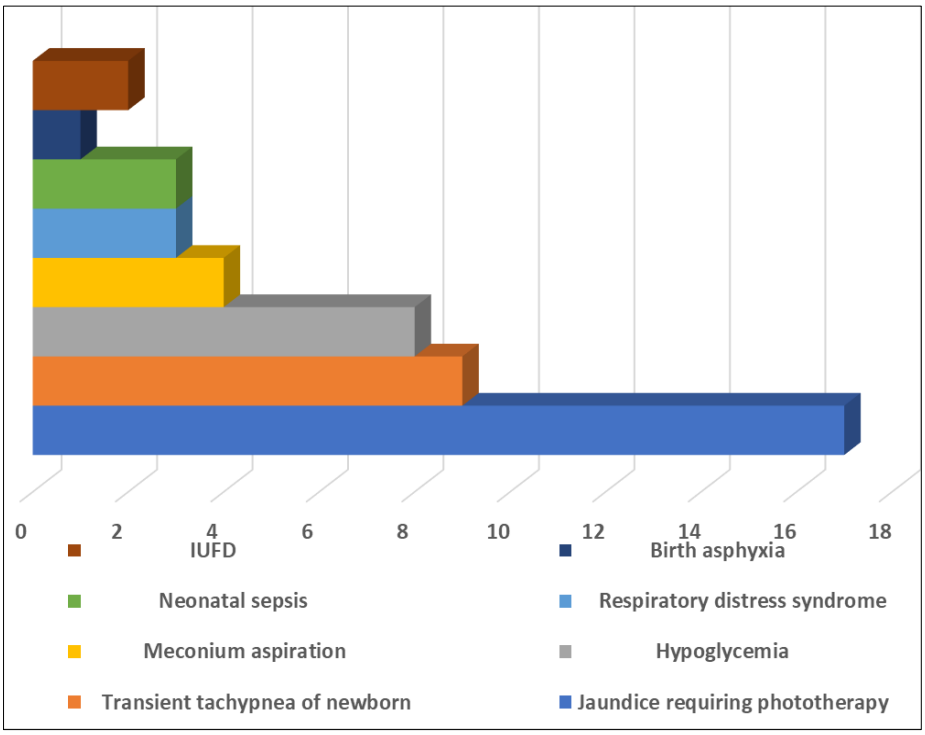

Fig 2: Neonatal outcome of woman with deranged liver enzymes

Discussion

The first case of DLFT in pregnancy was reported in 1883, the disease was renamed as 'unnamed' until the mid-1950s. In 1998, Shornick introduced the term ICP [8]. During pregnancy as there is an increased blood volume usually associated with changes in hematological and biochemical markers. The liver is an organ that moulds itself physiologically according to the growing fetus.

The frequency of ICP varies widely in different populations. We found ICP in 4.88% of pregnancies at our centre, this may be an underestimation.

A majority of the patients in our study were in the age group of 21-25 years and 26-30 years with a mean age of 25 years. The above results were consistent with Alokananda *et al*., mean age in their study was 24.7 years [9] similarly, Padmaja *et al*., found the mean age to be 28.7 years [10].

The mean gestational age in our study was in the late third trimester, Mishra *et al*., in their study found that most of the patients had an onset of symptoms after 28 weeks, about 87.5% of patients in the third trimester [11].

In our study, pregnancy-specific liver diseases were seen in 91 patients (96.42%) and co-incidental and chronic liver disorders in 3 (3.58%). 28.7% of the pregnant women in our study were diagnosed with gestational diabetes mellitus, Glucose metabolism is altered due to increased gluconeogenesis and altered sensitivity to insulin, and there are changes in the maternal lipid metabolism due to increased insulin resistance.

The overall rate of cesarean section in our study was higher than vaginal delivery (75.54 vs. 24.46%), as compared with Padmaja *et al*., whose cesarean section rate was 93%.(10) 29.57% of mothers with ICP had induction failure, 16.90% had thick MSL with fetal distress, 11.26% with PPROM, and 4.22% with IUGR & severe oligohydramnios each.

Increased bile acids can cause vasoconstriction of chorionic vessels of the placenta leading to oxygen deprivation which can result in fetal death, they also stimulate prostaglandin release which leads to myometrial contraction causing preterm labor. In our study preterm deliveries were 24.4% the mechanism for preterm deliveries is the action of bile salts at the placental level as mentioned above [12-14].

The IUFD rate in our study was 2.12%, while 17.7% required phototherapy for jaundice, 9.37% of term neonates had TTN, and 8.33% neonates of GDM mothers suffered hypoglycemia.

The management includes weekly fetal and biochemical surveillance in the form of fetal CTG, and LFT. Pharmacological management with Ursodeoxycholic acid 300mg twice a day for 3days; provides symptomatic relief and reduces the risk to the fetus. Kong *et al*., concluded that when compared with control groups, Ursodeoxycholic acid also mitigated pruritus. Walker *et al*., found that although Ursodeoxycholic acid likely diminishes the pruritis of ICP, the overall effect is minimal. The guidelines of the Royal College of Obstetricians and Gynaecologists include a recommendation to induce premature delivery in ICP-complicated pregnancies in patients with severe biochemical disorders at 37+0 weeks [15].

Due to the lack of recommendations based on randomized studies, the optimum management consists of inducing delivery at 36-37 weeks if total bile acid levels exceed 40 mmol/L. The likelihood of intrahepatic cholestasis of pregnancy recurring during a subsequent pregnancy is about 60% [16].

Our study found that there were no neonatal adverse events recorded and none of the patients showed signs of chronic liver disease.

Conclusion

Intrahepatic cholestasis is one of the most common liver diseases during pregnancy usually associated with adverse maternal and fetal outcomes, hence early diagnosis with a proper clinical history and examination, if necessary biochemical tests are to be done. Decision of obstetric intervention to be taken as and when required to improve maternal and fetal outcome.

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