CASE SERIES

Correlation of Liver Function Test and Serum Bile Acid with Feto-Maternal Outcome in Patients with Intrahepatic Cholestasis of Pregnancy - Case Series

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ABSTRACT

Background: The incidence of intrahepatic cholestasis of pregnancy (IHCP) in India is 0.02–2.4% IHCP is the foremost liver disorder, presenting substantial risks and complications to maternal and fetal health. Characterized by pruritus and elevated bile acids and serum transaminases. **Materials and Methods:** The study focuses on profiling 6 patients of ICP understanding the correlations between liver function tests with serum bile acid and evaluating the impact of ursodeoxycholic acid (UDCA) treatment and also focus on various maternal and fetal outcome. **Results:** The study identified a predominance of primigravida (83%) of 26–30 years of age (66%), with maximum patients with moderate serum bile acid levels. IHCP diagnosis was commonly noted between 32 and 36.6 weeks GA (66.6%). The treatment with UDCA 300-BD (in 66% of patients) was providing relief to about 66% of participants within a week. Most deliveries occurred between 37 and 39 weeks GA, predominantly through vaginal Deleveries (83%). Post-partum hemorrhage was seen in 33% of patients. Fetal outcomes revealed a 66% incidence of meconium-stained liquor and about 33% neonatal intensive care unit admissions with no fetal mortality. Most participants (83%) had serum bile acid levels in the 10–40 µmoL/L range. **Conclusion:** Significant correlations were noted between serum glutamate oxaloacetate transaminase and serum glutamate pyruvate transaminase and with alkaline phosphatase and bile acid. In contrast, bilirubin showed no significant correlations. Higher UDCA dosages showed a dose-response relationship, implying their effectiveness in managing ICP.

Keywords: Intrahepatic cholestasis of pregnancy, serum bile acid, serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, ursodeoxycholic acid

INTRODUCTION

Pregnancy induces various physiological alterations that influence maternal health. These changes can interact with existing health predispositions, leading to complications specific to pregnancy.[1]

The incidence of IHCP in India is - 0.02–2.4%.[2]

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Obstetric cholestasis is a liver disorder unique to pregnancy, which typically presents with pruritus. However, pruritus is common in pregnancy and the diagnosis of obstetric cholestasis is confirmed by finding abnormal liver function.[2] Intrahepatic cholestasis of pregnancy or obstetric cholestasis is the most common pregnancy-related liver disorder and is characterized by pruritus, elevated serum-aminotransferases, and bile-acid levels with onset in the second or third trimester of pregnancy and spontaneous relief of symptoms within a 2nd or 3rd week after delivery. It typically presents with troublesome itching and can lead to complications for both mother and fetus.[3]

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A hallmark of ICP is the marked elevation in the serum bile acid level ICP.[1]

Further, it is common to observe serum aminotransferases at levels exceeding twice the normal range, along with increased alkaline phosphatase levels.[1]

The underlying causes of intrahepatic cholestasis of pregnancy (ICP) remain elusive, involving a complex interplay of genetic, hormonal, and environmental elements.[4]

It's hypothesized that genetic factors make some women more vulnerable to the condition, especially in cases where familial patterns or recurrence in subsequent pregnancies are observed.[5]

Hormonal influences, particularly the impact of elevated estrogen levels, have been consistently noted in various situations such as multiple pregnancies, ovarian hyper-stimulation, and ICP's typical emergence in the late second trimester, coinciding with peak estrogen levels.[6]

ICP is associated with several maternal complications including increased risks of severe pruritis, dyslipidemia, deranged Doppler, pre-term rupture of membranes, operative delivery, and post-partum hemorrhage.

Increased bile acids and other factors can lead to severe fetal complications, including sudden intrauterine death, pre-term birth, and meconium-stained amniotic fluid). The immediate treatment upon diagnosing ICP focuses on reducing perinatal morbidity and alleviating maternal discomfort. Ursodeoxycholic acid (UDCA) is the preferred treatment, known to correlate with improved maternal symptoms and fetal outcomes, and neonatal unit admission.[7,8]

Our study is thus strategically focused on scrutinizing the relationship between liver function tests (LFTs), serum bile acid levels, and their correlation with feto-maternal outcomes. By investigating the diagnostic patterns of LFTs and other biomarkers in light of variable manifestations of ICP, our research endeavors to enhance maternal and fetal health outcomes, mitigating the risks associated with undiagnosed or poorly managed ICP.

Aims and Objectives

Aim

To correlate LFTs and Serum Bile acid with feto-maternal outcome in patients with intrahepatic cholestasis of pregnancy (ICP).

Objectives

1. To correlate LFT and Serum bile acid in patients with intrahepatic cholestasis of pregnancy
2. To assess its effect on maternal morbidity and pregnancy outcome
3. To assess the perinatal morbidity and mortality associated with IHCP.

MATERIALS AND METHODS

Study Area

The present study has been conducted in antenatal care (ANC) and the labor ward of Smt. Kashibai Navale Medical College and general hospital Pune.

Study Population

All were diagnosed with IHCP attending an antenatal clinic or to be admitted in a hospital during the study period from January 2024 to January 2025.

Study Design

This study is a hospital-based prospective observational study.

Inclusion Criteria

All pregnant women (singleton/multiple gestations) diagnosed with intrahepatic cholestasis of pregnancy in antenatal ward and labor ward of Smt. Kashibai Navale Medical College and general hospital Pune.

Exclusion Criteria

- Pregnancy <24 weeks
- Dermatological lesion with pruritus
- Acute or chronic liver disease
- Infective hepatitis
- Any liver/gall bladder disorder before pregnancy.

Methodology

After ethical committee approval.

All antenatal patients who attended the antenatal clinic at Smt. Kashibai Navale Medical College and diagnosed with IHCP were included in the study after exclusion criteria were applied as previously mentioned and informed consent was obtained.

The diagnosis was based on clinical symptoms of persistent pruritus without a skin rash, coupled with biochemical evidence of cholestasis of pregnancy, such as elevated serum transaminases (alanine transaminase >40, aspartate transaminase >40 U/L), and Serum Bile acid levels exceeding 10 μmoL/L.

Patients were categorized as mild, moderate, and severe as per Serum bile acid level.

All the data were entered into a preformed pro forma, which included detailed history, such as presenting complaints,

obstetric history, menstrual history, past medical history (including previous IHCP or liver disorders), personal history, and family history. General physical examinations and obstetric examinations were conducted. A comprehensive set of ANC investigations, including complete blood count, blood typing and Rh grouping, blood sugar levels, viral markers (HIV, HBsAg,), venereal disease research laboratory, thyroid profile, LFTs, kidney function tests, and ultrasound scans with or without color Doppler, were performed. Fetal monitoring was done with non-stress tests and biophysical profile scores.

Patients diagnosed with IHCP were monitored with repeated LFT and Serum Bile acid tests after 1–2 weeks or as needed. UDCA was administered in divided doses to patients with IHCP based on the levels of LFT and Serum bile acid for the remainder of the antenatal period. Patient follow-up extended throughout the pregnancy until delivery, and their perinatal and maternal outcomes were analyzed based on LFT and Bile acid levels.

Statistical Analysis

We initiated our analysis with a thorough descriptive examination of the data. This involved summarizing the central tendencies and variability of LFT parameters and serum bile acid levels using appropriate measures such as means, medians, standard deviations, and interquartile ranges.

OBSERVATIONS AND RESULTS

In our study period total 1,703 deliveries took place out of that 6 cases were reported of IHCP and delivered this accounts for 0.35% study participants profile:

In terms of age distribution, the majority of the study population falls within the 26–30 years age group, accounting for 66%, followed by 31–35 years. The 18–25 years and >35 years age groups are less represented. This suggests a higher prevalence of IHCP among women in their late twenties to early thirties Table 1.

When examining parity, the data reveals a significant inclination toward first-time pregnancies, with 83% of the participants being primigravida than women in their second and third pregnancies indicating that ICP is more commonly diagnosed in first pregnancies.

Hypertensive disorders are slightly more prevalent according to the background characteristics. This higher percentage might reflect an increased risk of fetal distress or could be linked to other underlying conditions Table 2.

Regarding the diagnosis of ICP, it is predominantly diagnosed in the later stages of pregnancy. This timing emphasizes the importance of vigilant monitoring for ICP symptoms in late second to early third trimester.

Table 1: Frequency distribution of study participants by background characteristics - mother's profile

Background characteristics	Years	*n* (%)
Age groups	18–25	0
	26–30	4 (66)
	31–35	2 (33)
	>35	0
Parity	1	5 (83)
	2	1 (16.6)
	3	0
H/O OCP use	No	4 (66.6)
	Yes	2 (33)
Hormonal support	No	3 (50)
	Yes	3 (50)

Table 2: Frequency distribution of study participants by background characteristics - obstetric characteristics

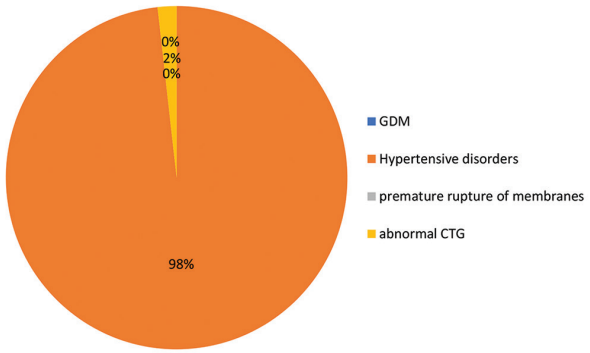

Table 3: Frequency distribution of study participants by background characteristics - IHCP allied

Background characteristics	*n* (%)
Gestational age at diagnosis IHCP (Weeks)	
28–31.6	0
32–36.6	4 (66.6)
37–39.6	2 (33.3)
>40 weeks	0
H/o IHCP in previous pregnancy	
No	5 (83)
Yes	1 (16.6)
Family history of IHCP	0

A history of ICP in previous pregnancies and a family history of IHCP are less commonly reported in the study sample Table 3.

In terms of treatment, the use of UDCA is predominant, with the 300-BD dosage being the most common,

Further, among study participants with intrahepatic cholestasis of pregnancy being treated with UDCA, experienced relief of symptoms within 1 week (66.6%) 33% reported symptom relief between 1 and 2 weeks Table 4.

The percentage of normal deliveries (83%) encountered was more as compared to LSCS or operative deliveries and post-partum hemorrhage was observed in (66%).

More cases of meconium-stained liquor were noted, no fetal death, fetal growth restriction or neonatal intensive care unit (NICU) admission noted.

LFTs

Serum bile acids	*n* (%)
<10 µmoL/L	1 (16.6)
10–40	5 (83.3)
40–100	0
>100	0
SGOT	
40–100 IU/L	5 (83.3)
100–200 IU/L	1 (16.6)
<200 IU/L	0
SGPT	
40–100 IU/L	6 (100)
100–200 IU/L	0
>200 IU/L	0

SGOT: Serum glutamate oxaloacetate transaminase, SGPT: Serum glutamate pyruvate transaminase

Most common range of serum bile acids were 10–40 µmoL/L (83%).

DISCUSSION

The incidence of IHCP in the Indian population is 0.02–2.4% and our study showed 0.35% consistent with Fathima *et al*. study.[2]

In the present research, we have explored the intricate relationship between LFT abnormalities and feto-maternal outcomes in cases of intrahepatic cholestasis of pregnancy (ICP).

Our objectives were threefold: To correlate LFTs and serum bile acid levels with ICP, to assess their effect on maternal morbidity and pregnancy outcomes, and to understand the perinatal morbidity and mortality associated with.

Our findings have shed light on significant correlations that not only align with existing literature but also provide novel insights into the clinical management of this condition.

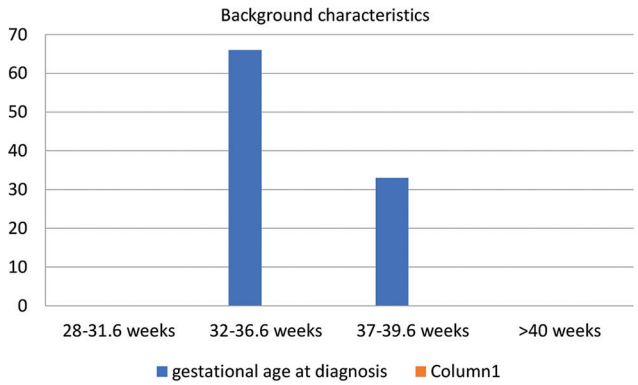

Table 4: Frequency distribution of study participants by background characteristics - UDCA treatment

Background characteristics	*n* (%)
UDCA	
150-TDS	2 (33.3)
300-BD	4 (66.6)
Onset of relief	
Within 1 week	4 (66.6)
1–2 weeks	2 (33.3)
More than 2 weeks	0

UDCA: Ursodeoxycholic acid

The percentage of primigravida was found to be (68.6%) in our study as compared to the study of Kant *et al*. was found to be (79%), which was close to the percentage in our study.[3]

In our study, the maximum percentage of age group was noted between 26 and 30 years of age (47.1%) which was found close to the percentage noted in Gupta *et al*. study, which was (66%).[9]

83% cases of mild IHCP were recorded in our study which was consistent with Jhirwal *et al*. study where mild IHCP (83%) was noted.[10]

The treatment with UDCA 300-BD provided relief to (72.9%) of patients within a week in Gupta *et al*. study which was consistent with our study where 75% of patients received relief.[9]

In our study, 66% of patients had meconium staining of liquor which was comparatively higher than Jhirwal *et al*. where 12.5% was noted.[10]

Fetal death was not seen in our study which resonated with Kant *et al*. study.[3]

Which is in line with our observation of increased bile acid levels in the later gestational period (37–39.6 weeks) Table 5.

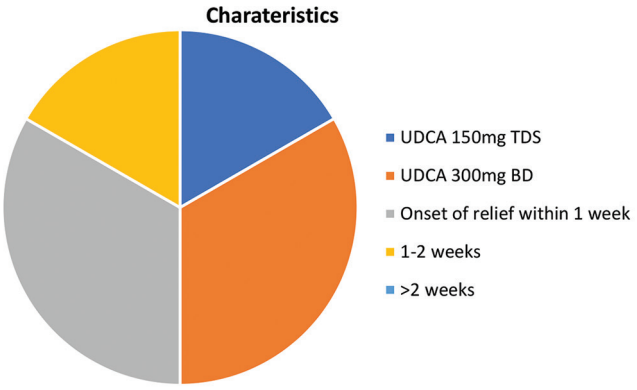

Table 5: Frequency distribution of study participants by background characteristics - maternal outcomes

Background characteristics	*n* (%)
Gestational age at delivery	No.
28–31.6	0
32–36.6	3 (50)
37–39.6	3 (50)
≥40	0
Mode of delivery	No.
Normal vaginal delivery	5 (83.3)
LSCS	1 (16.6)
Assisted vaginal delivery	0
Post-partum hemorrhage	No.
No	4 (66.6)
Yes	2 (33.3)

Table 6: Frequency distribution of study participants by background characteristics - fetal outcomes

Background characteristics	n (%)
APGAR <7 at birth	No 5 (83.3)
	Yes 1 (16.6)
APGAR <7 at 5 min	No 6 (100)
	Yes 0
NICU admission	No 4 (66)
	Yes 2 (33.3)
Fetal growth restriction	No 6 (100)
	Yes 0
Meconium stained liquor	No 2 (33.3)
	Yes 4 (66)
Fetal death	No 6 (100)
	Yes 0

NICU: Neonatal intensive care unit

Elevated bile acids, a hallmark of ICP, have been implicated in various adverse outcomes. Bile acids are known to play a critical role in fetal development and maternal health. When their levels rise, as evidenced in our study, they can induce oxidative stress and inflammation in the liver, leading to cellular damage. This mechanism aligns with the findings of Geenes and Williamson (2004),[11] which suggested that elevated bile acids can disrupt the normal physiological functions of the liver, thereby contributing to the pathogenesis of ICP.

The incidence and demographics of ICP in our study, primarily diagnosed in the third trimester and notably among primiparous women, resonate with the findings of and the incidence rates reported by Jhirwal *et al*. (2022).[10]

Our study also established that in most of the subjects, symptoms disappear after delivery or within 1 week of delivery.

CONCLUSION AND SUMMARY

Summary

Intrahepatic cholestasis of pregnancy (ICP) is the foremost liver disorder in pregnancies, presenting substantial risks and complications to maternal and fetal health. Characterized by symptoms, such as pruritus and elevated bile acids and Serum transaminases.

The study focuses on profiling 6 patients of ICP, evaluating the impact of UDCA treatment, and understanding the correlations between LFTs with Serum bile acid and various maternal and treatment factors, to improve surveillance and intervention.

The study identified a predominance of primigravida (83%) women of 26–30 years of age (66%), often needing hormonal support (33%), with maximum patient with moderate serum bile acid levels. IHCP diagnosis was commonly noted between 32 and 36.6 weeks GA (66%). The treatment with UDCA 300-BD (66%) was notably effective, providing relief to about 66% of participants within a week. Most deliveries occurred between 37 and 39 weeks (70%) GA, predominantly through, vaginal deliveries (83%). Post-partum hemorrhage was seen in patients. Fetal outcomes revealed a 66% incidence of meconium-stained liquor and about 33% NICU admissions with no fetal mortality Table 6.

The study emphasizes the importance of monitoring serum bile acid levels due to their direct correlation with adverse maternal and fetal outcomes, advocating for enhanced surveillance and timely interventions. It provides a comprehensive understanding of ICP, the efficacy of UDCA treatment, and the critical role of liver function monitoring in improving outcomes. The findings pave the way for future research and clinical practices, aiming to optimize ICP management for safer pregnancies and healthier feto-maternal outcomes.

Conclusion

The research presented in this study offers a comprehensive examination of the correlation between LFTs and feto-maternal outcomes in intrahepatic cholestasis of pregnancy (ICP). Thorough meticulous analysis and interpretation, this study illuminates the critical role of LFTs, specifically serum bile acid, serum glutamate oxaloacetate transaminase, and serum glutamate pyruvate transaminase levels, in predicting and managing the complexities of ICP.

The study found a significant association between elevated LFTs and various adverse maternal and fetal outcomes, including the necessity for surgical intervention in delivery, the presence of meconium-stained liquor indicating fetal distress, and poor/lower APGAR scores signifying immediate neonatal care requirements.

The findings advocate for a proactive and individualized approach to managing ICP, emphasizing the need for regular LFT monitoring and tailored care plans. The study highlights the potential of LFTs to serve as valuable indicators for clinical decision-making, from determining the mode of delivery to preparing for potential neonatal intensive care.

In conclusion, this research underscores the complex interplay between maternal liver function and feto-maternal health in ICP.

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