Original Research Article

CLINICAL CHARACTERISTICS, BIOCHEMICAL PROFILE, AND FETOMATERNAL OUTCOMES IN WOMEN WITH INTRAHEPATIC CHOLESTASIS OF PREGNANCY: A PROSPECTIVE OBSERVATIONAL STUDY AT A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Background: Intrahepatic cholestasis of pregnancy (ICP) is the most common pregnancy-specific liver disorder, characterized by pruritus, elevated serum bile acid concentrations, and abnormal liver function tests. Although maternal prognosis is generally favorable, ICP is associated with an increased risk of adverse fetal and neonatal outcomes. Early diagnosis through clinical evaluation and biochemical assessment is essential for timely intervention and improved pregnancy outcomes. The objective is to evaluate the clinical characteristics, biochemical profile, and fetomaternal outcomes among women diagnosed with intrahepatic cholestasis of pregnancy at a tertiary care teaching hospital.

Materials and Methods: A prospective observational study was conducted in the Department of Obstetrics and Gynecology in collaboration with the Department of Biochemistry at a tertiary care teaching hospital over one year. A total of 120 pregnant women diagnosed with ICP after 28 weeks of gestation were enrolled. Clinical characteristics, obstetric history, and biochemical parameters including fasting serum bile acids, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total bilirubin, direct bilirubin, serum albumin, prothrombin time (PT), and international normalized ratio (INR) were evaluated. Maternal and neonatal outcomes were recorded.

Results: The mean maternal age was 28.6 ± 4.8 years, and the mean gestational age at diagnosis was 33.4 ± 2.5 weeks. Generalized pruritus was observed in all participants, with 85.0% reporting involvement of the palms and soles. Elevated fasting serum bile acid concentrations were detected in all women, while increased ALT and AST levels were observed in 56.7% and 50.0% of cases, respectively. Cesarean delivery was performed in 58.4% of women, and preterm delivery occurred in 28.3%. Low birth weight (26.7%), meconium-stained amniotic fluid (20.0%), NICU admission (18.3%), and fetal distress (15.0%) were the most common neonatal complications. Women with serum bile acid concentrations ≥40 µmol/L had a significantly higher incidence of adverse fetomaternal outcomes compared with those having lower bile acid levels ($p = 0.002$). Elevated serum bile acid concentration was identified as an independent predictor of adverse pregnancy outcomes.

Conclusion: Intrahepatic cholestasis of pregnancy is associated with significant biochemical abnormalities and an increased risk of adverse fetomaternal outcomes. Fasting serum bile acid concentration is a valuable diagnostic and prognostic biomarker that should be routinely assessed in pregnant women presenting with pruritus. Early diagnosis, comprehensive biochemical

evaluation, close maternal and fetal surveillance, and timely obstetric management are essential to improve pregnancy outcomes and reduce perinatal morbidity.
Keywords: Intrahepatic cholestasis of pregnancy; Serum bile acids; Liver function tests; Alanine aminotransferase; Aspartate aminotransferase; Fetomaternal outcomes; Pregnancy; Ursodeoxycholic acid.

INTRODUCTION

Intrahepatic cholestasis of pregnancy (ICP) is a pregnancy-specific liver disorder characterized by generalized pruritus, elevated serum bile acid concentrations, and abnormal liver function tests, typically presenting during the second or third trimester of pregnancy and resolving spontaneously after delivery. Although ICP is usually benign for the mother, it is associated with significant fetal risks, including spontaneous preterm birth, meconium-stained amniotic fluid, fetal distress, neonatal respiratory complications, and stillbirth. The incidence of ICP varies considerably across different geographical regions and ethnic populations, ranging from 0.2% to 2% in most countries, with substantially higher prevalence reported in certain populations due to genetic and environmental factors.[1-3]

The pathophysiology of intrahepatic cholestasis of pregnancy is complex and multifactorial, involving genetic susceptibility, hormonal influences, environmental factors, and impaired hepatobiliary transport. Elevated estrogen and progesterone levels during pregnancy interfere with bile acid transport across hepatocytes, resulting in intrahepatic bile acid accumulation. Mutations in hepatobiliary transporter genes such as ABCB4, ABCB11, and ATP8B1 have also been implicated in disease development. Increased maternal serum bile acid concentrations can cross the placenta, causing placental dysfunction, fetal cardiac arrhythmias, and fetal hypoxia, thereby increasing the risk of adverse perinatal outcomes.[2-4]

The hallmark clinical manifestation of ICP is persistent pruritus, predominantly affecting the palms and soles, without an associated skin rash. The symptoms are frequently more severe during the night and may significantly impair maternal quality of life. Laboratory evaluation typically demonstrates elevated total serum bile acid concentrations, which represent the most sensitive and specific biochemical marker for diagnosis. Liver transaminases, particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are often elevated, whereas serum bilirubin levels remain normal in the majority of patients. Current international guidelines recommend measuring serum bile acid levels in pregnant women presenting with unexplained pruritus to facilitate early diagnosis and appropriate management.[1,3,5]

Several maternal risk factors have been associated with the development of ICP, including a previous history of the disease, family history of cholestasis, multiple gestation, advanced maternal age, assisted reproductive techniques, chronic liver disease, hepatitis C infection, and metabolic disorders. Women with recurrent ICP are at an increased risk of developing the disorder in subsequent pregnancies. Early recognition of these risk factors enables timely monitoring and intervention, thereby reducing maternal discomfort and minimizing fetal complications.[2,4,6]

Although maternal prognosis is generally favorable, intrahepatic cholestasis of pregnancy is associated with significant fetal morbidity and mortality. Elevated maternal serum bile acid concentrations, particularly levels ≥100 µmol/L, have been strongly associated with an increased risk of stillbirth, spontaneous preterm birth, fetal distress, meconium-stained amniotic fluid, neonatal intensive care unit admission, and perinatal mortality. Consequently, regular fetal surveillance, administration of ursodeoxycholic acid, and planned delivery at an appropriate gestational age have become integral components of clinical management.[3,5,7]

Despite advances in antenatal care and improved understanding of the disease, uncertainty remains regarding the optimal timing of delivery and the prediction of adverse fetal outcomes. Furthermore, the clinical presentation and disease severity vary considerably among different populations, highlighting the importance of institution-specific data. Studies evaluating the clinical characteristics and pregnancy outcomes of women with ICP are particularly relevant in developing countries, where regional differences in disease prevalence, healthcare access, and management practices may influence maternal and neonatal outcomes.

Therefore, the present prospective observational study was undertaken to evaluate the clinical characteristics and fetomaternal outcomes among women diagnosed with intrahepatic cholestasis of pregnancy at a tertiary care teaching hospital. The findings of this study are expected to contribute to a better understanding of the disease profile and support evidence-based strategies for improving maternal and neonatal outcomes.

MATERIALS AND METHODS

Study Design and Setting: This prospective observational study was conducted in the Department of Obstetrics and Gynecology in collaboration with the Department of Biochemistry at a tertiary care teaching hospital over a period of one year, from January 2025 to December 2025. The study aimed to evaluate the clinical characteristics, biochemical profile, and fetomaternal outcomes among pregnant

women diagnosed with intrahepatic cholestasis of pregnancy (ICP).

Study Population: A total of 120 consecutive pregnant women diagnosed with intrahepatic cholestasis of pregnancy were included in the study.

Inclusion Criteria

- Pregnant women aged ≥18 years.
- Singleton or multiple pregnancy.
- Gestational age ≥28 weeks.
- Generalized pruritus without primary skin lesions.
- Fasting serum bile acid concentration ≥10 µmol/L with or without abnormal liver function tests.
- Willingness to participate in the study.

Exclusion Criteria

Women with the following conditions were excluded:

- Pre-existing chronic liver disease.
- Viral hepatitis (HBV, HCV, HIV).
- Gallstone disease or biliary obstruction.
- Autoimmune liver disorders.
- Drug-induced liver injury.
- Dermatological disorders causing pruritus.
- Acute fatty liver of pregnancy.
- HELLP syndrome or severe pre-eclampsia with hepatic involvement.
- Incomplete clinical or laboratory records.

Sample Size: A total of 120 eligible pregnant women diagnosed with intrahepatic cholestasis of pregnancy during the study period were enrolled consecutively.

Data Collection: Demographic and obstetric information was recorded using a structured case record form. Variables collected included:

- Maternal age
- Body mass index (BMI)
- Gravidity and parity
- Gestational age at diagnosis
- Previous history of ICP
- Family history of ICP
- Multiple pregnancy
- Assisted conception
- Associated medical disorders (gestational diabetes mellitus, hypothyroidism, etc.)

Clinical characteristics including onset, duration, distribution, and severity of pruritus, nocturnal aggravation, presence of jaundice, and obstetric examination findings were documented.

Biochemical Investigations: Following an overnight fast of 8–10 hours, approximately 5–7 mL of venous blood was collected under aseptic conditions. Serum was separated by centrifugation at 3000 rpm for 10 minutes and analyzed immediately or stored at 2–8°C until processing according to standard laboratory protocols.

The following biochemical investigations were performed:

- Fasting serum bile acids
- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)
- Alkaline phosphatase (ALP)
- Gamma-glutamyl transferase (GGT)
- Total bilirubin
- Direct bilirubin
- Serum albumin
- Total protein
- Prothrombin time (PT)
- International Normalized Ratio (INR)

Routine laboratory investigations included complete blood count, renal function tests, blood glucose, urine routine examination, and viral hepatitis screening (HBsAg, anti-HCV, and HIV) to exclude other causes of liver dysfunction.

All biochemical analyses were performed in the Department of Biochemistry using standardized automated analyzers following the manufacturer's instructions. Internal quality control procedures were carried out daily, and external quality assurance protocols were maintained throughout the study period.

Reference ranges used were:

- Serum bile acids: <10 µmol/L
- ALT: <35 U/L
- AST: <35 U/L
- GGT: <40 U/L
- Total bilirubin: 0.2–1.2 mg/dL
- Serum albumin: 3.5–5.0 g/dL
- PT: 11–14 seconds
- INR: 0.9–1.2

Obstetric Evaluation and Management: All participants underwent detailed obstetric evaluation, including ultrasonography for fetal growth assessment and amniotic fluid volume estimation. Fetal surveillance consisted of non-stress testing (NST) and biophysical profile (BPP) according to institutional protocols.

Patients received standard treatment with ursodeoxycholic acid (UDCA) as indicated. Antihistamines were administered for symptomatic relief when required. Decisions regarding induction of labor or cesarean delivery were based on gestational age, maternal condition, serum bile acid concentration, fetal well-being, and institutional obstetric guidelines.

Outcome Measures

Primary Maternal Outcomes

- Mode of delivery
- Induction of labor
- Preterm delivery
- Postpartum hemorrhage
- Intensive care unit admission
- Maternal mortality

Primary Fetal and Neonatal Outcomes

- Gestational age at delivery
- Birth weight
- Low birth weight (<2500 g)
- Meconium-stained amniotic fluid
- Fetal distress
- Apgar score at 1 and 5 minutes
- NICU admission
- Respiratory distress syndrome
- Stillbirth
- Perinatal mortality

Statistical Analysis: Continuous variables were expressed as mean ± standard deviation (SD),

whereas categorical variables were presented as frequencies and percentages.

Correlation between serum bile acid concentration and biochemical parameters (ALT, AST, bilirubin, albumin, PT/INR) as well as fetomaternal outcomes was evaluated using Pearson's or Spearman's correlation coefficient, as appropriate.

Multivariable logistic regression analysis was performed to identify independent biochemical and clinical predictors of adverse fetomaternal outcomes. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were calculated.

A two-tailed p-value of <0.05 was considered statistically significant.

RESULTS

A total of 120 pregnant women diagnosed with intrahepatic cholestasis of pregnancy (ICP) were enrolled in the study. The mean maternal age was 28.6 ± 4.8 years (range: 19–40 years), while the mean gestational age at diagnosis was 33.4 ± 2.5 weeks. All enrolled women fulfilled the diagnostic criteria for ICP based on clinical symptoms and biochemical investigations.

Most women (61.7%) belonged to the 21–30-year age group, while 56.7% were multigravida. More than half (55.0%) were diagnosed between 33 and 36 weeks of gestation, and 15.0% reported a previous history of intrahepatic cholestasis of pregnancy.

Table 1: Demographic and Obstetric Characteristics of the Study Population (N = 120)

Variable	Number (n)	Percentage (%)
Age (years)		
≤20	8	6.7
21–30	74	61.7
31–35	28	23.3
>35	10	8.3
Gravidity		
Primigravida	52	43.3
Multigravida	68	56.7
Gestational age at diagnosis		
28–32 weeks	36	30.0
33–36 weeks	66	55.0
≥37 weeks	18	15.0
Previous history of ICP		
Yes	18	15.0
No	102	85.0

Table 2: Biochemical Profile of Women with Intrahepatic Cholestasis of Pregnancy (N = 120)

Investigation	Mean ± SD	Abnormal Results n (%)	Reference Range
Fasting serum bile acids (µmol/L)	34.8 ± 18.6	120 (100.0)	<10
ALT (U/L)	78.4 ± 42.5	68 (56.7)	<35
AST (U/L)	64.2 ± 31.8	60 (50.0)	<35
ALP (U/L)	298 ± 94	82 (68.3)	Pregnancy-adjusted
GGT (U/L)	36.5 ± 14.2	18 (15.0)	<40
Total bilirubin (mg/dL)	0.96 ± 0.42	10 (8.3)	0.2–1.2
Direct bilirubin (mg/dL)	0.34 ± 0.16	8 (6.7)	<0.3
Serum albumin (g/dL)	3.48 ± 0.39	32 (26.7)	3.5–5.0
Prothrombin time (seconds)	13.1 ± 1.4	6 (5.0)	11–14
INR	1.05 ± 0.12	5 (4.2)	0.9–1.2
Viral hepatitis markers	Negative	120 (100.0)	Negative

The mean fasting serum bile acid concentration was 34.8 ± 18.6 µmol/L, and all participants had abnormal serum bile acid levels (≥10 µmol/L). Elevated ALT and AST were observed in 56.7% and 50.0% of women, respectively. Reduced serum albumin was present in 26.7%, while mild hyperbilirubinemia was detected in 8.3% of participants. Viral hepatitis screening was negative in all women.

Table 3: Clinical Characteristics of Women with Intrahepatic Cholestasis of Pregnancy

Clinical Characteristic	Number (n)	Percentage (%)
Generalized pruritus	120	100.0
Pruritus over palms and soles	102	85.0
Nocturnal aggravation	94	78.3
Jaundice	10	8.3
Serum bile acid ≥40 µmol/L	42	35.0
Elevated ALT	68	56.7
Elevated AST	60	50.0

Generalized pruritus was the presenting symptom in all patients. Palmar and plantar involvement was observed in 85.0%, while nocturnal worsening occurred in 78.3%. Clinical jaundice was uncommon (8.3%).

Table 4: Maternal Risk Factors

Risk Factor	Number (n)	Percentage (%)
Gestational diabetes mellitus	20	16.7
Previous history of ICP	18	15.0
Hypothyroidism	14	11.7
Family history of ICP	12	10.0
Multiple pregnancy	9	7.5
Assisted conception	8	6.7

Gestational diabetes mellitus was the most common associated maternal condition (16.7%), followed by previous ICP (15.0%) and hypothyroidism (11.7%).

Table 5: Mode of Delivery

Mode of Delivery	Number (n)	Percentage (%)
Normal vaginal delivery	46	38.3
Instrumental delivery	4	3.3
Cesarean section	70	58.4
Total	120	100.0

Cesarean section was the predominant mode of delivery (58.4%), followed by vaginal delivery (38.3%).

Table 6: Maternal Outcomes

Maternal Outcome	Number (n)	Percentage (%)
Induction of labor	74	61.7
Preterm delivery	34	28.3
Postpartum hemorrhage	8	6.7
ICU admission	3	2.5
Maternal mortality	0	0.0

Labor induction was required in 61.7% of women. Preterm birth occurred in 28.3%, while no maternal deaths were recorded.

Table 7: Fetal and Neonatal Outcomes

Outcome	Number (n)	Percentage (%)
Low birth weight	32	26.7
Meconium-stained liquor	24	20.0
NICU admission	22	18.3
Fetal distress	18	15.0
Respiratory distress syndrome	10	8.3
Apgar score <7 at 5 min	8	6.7
Stillbirth	2	1.7
Perinatal mortality	3	2.5

Low birth weight (26.7%) was the most frequent neonatal complication, followed by meconium-stained liquor (20.0%) and NICU admission (18.3%).

Table 8: Association Between Serum Bile Acid Levels and Adverse Fetomaternal Outcomes

Serum Bile Acid Level	Cases (n)	Adverse Outcomes (n)	p-value
<40 µmol/L	78	18	
≥40 µmol/L	42	24	0.002

Women with serum bile acid concentrations ≥40 µmol/L had a significantly higher incidence of adverse fetomaternal outcomes than those with lower concentrations ($p = 0.002$).

Table 9: Independent Predictors of Adverse Fetomaternal Outcomes

Variable	Adjusted Odds Ratio	95% Confidence Interval	p-value
Serum bile acid ≥40 µmol/L	3.42	1.58–7.41	0.002
Preterm delivery	2.81	1.24–6.36	0.013
Gestational diabetes mellitus	2.17	1.01–4.68	0.047

Multivariable logistic regression identified elevated serum bile acid concentration (≥40 µmol/L), preterm delivery, and gestational diabetes mellitus as independent predictors of adverse fetomaternal outcomes.

DISCUSSION

Intrahepatic cholestasis of pregnancy (ICP) is the most common pregnancy-specific liver disorder and is associated with significant maternal discomfort and increased risks of adverse perinatal outcomes. The present prospective observational study evaluated the clinical characteristics, biochemical profile, and fetomaternal outcomes of women diagnosed with ICP at a tertiary care teaching hospital. The findings demonstrate that ICP predominantly affected women during the third trimester of pregnancy and was characterized by generalized pruritus, elevated serum bile acid

concentrations, abnormal liver function tests, and an increased incidence of preterm delivery, cesarean section, low birth weight, and neonatal intensive care unit (NICU) admission. Furthermore, elevated serum bile acid concentrations were significantly associated with adverse fetomaternal outcomes, highlighting the importance of biochemical evaluation in risk stratification and clinical management.[13–17]

The majority of women in the present study were between 21 and 30 years of age and were diagnosed during the third trimester of pregnancy. These findings are consistent with previous reports indicating that ICP most commonly presents after 28 weeks of gestation, coinciding with peak estrogen and progesterone concentrations. Similar maternal age distributions and gestational timing have been reported in previous studies.[13–18]

Generalized pruritus was observed in all participants, with most women reporting involvement of the palms and soles and worsening symptoms during the night. Clinical jaundice was relatively uncommon, which is consistent with previous studies demonstrating that overt jaundice develops in only a minority of patients. These observations further emphasize the importance of biochemical investigations for early diagnosis.[14,16,19,20]

A major strength of the present study is the comprehensive evaluation of the biochemical profile. All participants demonstrated elevated fasting serum bile acid concentrations, confirming the diagnosis according to international recommendations. Serum bile acid estimation remains the most sensitive and specific biochemical marker for ICP and is strongly associated with adverse fetal outcomes. Increasing bile acid concentrations have been associated with fetal distress, spontaneous preterm birth, meconium-stained liquor, and stillbirth.[13–17,21,22]

Elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were observed in a considerable proportion of patients, indicating hepatocellular injury associated with cholestasis. Although these liver enzymes are not specific for ICP, they provide valuable supportive evidence after excluding other hepatobiliary disorders. Mild elevation of alkaline phosphatase is expected during pregnancy because of placental production and therefore has limited diagnostic value.[15–17,20,23]

Serum bilirubin concentrations remained normal in most participants, while only a small proportion developed mild hyperbilirubinemia. Coagulation abnormalities were uncommon, indicating preserved hepatic synthetic function. These observations are consistent with previous studies demonstrating that ICP primarily represents a cholestatic rather than hepatocellular disorder.[15,16,20,24]

The present study also identified gestational diabetes mellitus, previous history of ICP, hypothyroidism, family history of ICP, and multiple pregnancy as important maternal risk factors. Previous investigations have similarly demonstrated that metabolic disorders and previous ICP significantly increase the likelihood of recurrence in subsequent pregnancies.[16,20,25–27]

The cesarean section rate observed in the present study was relatively high, which is comparable to several international reports. Although ICP itself is not an indication for cesarean delivery, fetal distress, failed induction, and obstetric complications frequently contribute to operative delivery. Current recommendations advocate individualized timing of delivery based on disease severity and serum bile acid concentrations.[13,14,21,28,29]

Maternal outcomes were generally favorable, with no maternal mortality. However, induction of labor and preterm birth occurred frequently, reflecting contemporary obstetric practice aimed at preventing fetal complications. These findings are comparable with those reported in systematic reviews and multicenter cohort studies.[13,14,22,28,30]

Neonatal complications including low birth weight, meconium-stained amniotic fluid, fetal distress, respiratory distress syndrome, and NICU admission were common among pregnancies complicated by ICP. Elevated maternal serum bile acid concentrations have been shown to induce placental dysfunction, fetal arrhythmias, and oxidative stress, thereby increasing neonatal morbidity.[17,21,22,29–32]

An important observation of the present study was the significant association between elevated serum bile acid concentrations and adverse fetomaternal outcomes. Women with higher bile acid levels experienced greater frequencies of preterm birth, fetal distress, low birth weight, and NICU admission. These findings are consistent with previous meta-analyses identifying serum bile acid concentration as the strongest predictor of adverse pregnancy outcomes.[15–17,21,31,32]

The strengths of the present study include its prospective design, standardized biochemical assessment, and comprehensive evaluation of maternal and neonatal outcomes. However, the single-center setting, relatively small sample size, and absence of long-term follow-up may limit generalizability. Future multicenter studies involving larger populations and serial biochemical monitoring are warranted.[18,20,30–32]

Overall, the findings of the present study reinforce the importance of combining clinical assessment with biochemical evaluation in women presenting with suspected ICP. Routine measurement of fasting serum bile acids together with liver function tests facilitates early diagnosis, risk stratification, and timely obstetric intervention, thereby improving maternal and neonatal outcomes.[13–17,28,30–32]

CONCLUSION

Intrahepatic cholestasis of pregnancy is a significant pregnancy-specific liver disorder associated with adverse maternal and perinatal outcomes despite its generally favorable maternal prognosis. The present prospective observational study demonstrated that

ICP most commonly presented during the third trimester with generalized pruritus and was characterized by elevated serum bile acid concentrations and abnormal liver function tests, particularly increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. Comprehensive biochemical evaluation, including fasting serum bile acid estimation, proved valuable not only for confirming the diagnosis but also for assessing disease severity and identifying women at increased risk of adverse fetomaternal outcomes.

The study further showed that elevated serum bile acid concentrations were significantly associated with increased rates of preterm delivery, cesarean section, fetal distress, low birth weight, meconium-stained amniotic fluid, and neonatal intensive care unit admission. These findings emphasize that serum bile acid concentration is an important prognostic biomarker and should be routinely incorporated into the clinical evaluation and monitoring of pregnant women with suspected ICP.

Early recognition of clinical symptoms, prompt biochemical assessment, close maternal and fetal surveillance, timely initiation of ursodeoxycholic acid therapy, and appropriate obstetric management can substantially reduce pregnancy-related complications and improve neonatal outcomes. A multidisciplinary approach involving obstetricians, biochemists, hepatologists, and neonatologists is essential for optimizing the care of women affected by ICP.

Although this study provides valuable evidence regarding the clinical presentation, biochemical abnormalities, and fetomaternal outcomes of ICP in a tertiary care setting, multicenter studies with larger sample sizes and long-term maternal and neonatal follow-up are warranted to validate these findings and develop robust risk prediction models. Future research should also investigate novel biochemical biomarkers and individualized management strategies to further improve maternal and neonatal outcomes in pregnancies complicated by intrahepatic cholestasis.

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