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Original Research Article

A Prospective Observational Study of Feto-Maternal Outcome in Patients Presenting with Intrahepatic Cholestasis of Pregnancy

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ABSTRACT

Background; Intrahepatic cholestasis of pregnancy is a pregnancy-specific liver disorder characterized by pruritus and elevated serum bile acid levels, primarily occurring in the third trimester. ICP is associated with significant maternal morbidity and adverse fetal outcomes, including preterm birth, low birth weight, fetal distress, and intrauterine fetal demise. Data from rural populations remain limited. This study aimed to evaluate maternal and fetal outcomes in patients diagnosed with ICP in a tertiary care rural hospital.

Methods; This prospective observational study was conducted in the Department of Obstetrics and Gynaecology at Burdwan Medical College & Hospital from June 2023 to December 2024. A total of 100 pregnant women (34 weeks gestation to delivery) with confirmed ICP (Intrahepatic Cholestasis of Pregnancy) (serum bile acid ≥10 µmol/L) were enrolled. Patients with other hepatic disorders were excluded. Maternal complications, mode of delivery, laboratory parameters, neonatal outcomes, APGAR scores, birth weight, and SNCU admissions were recorded. Statistical analysis was performed using SPSS version 23, with $p < 0.05$ considered significant.

Results; Among 100 patients, 77% had no maternal complications, while 16% developed postpartum haemorrhage and 7% developed disseminated intravascular coagulation. Sixty percent underwent induced vaginal delivery and 24% required caesarean section. The mean bile acid level was 68.54 µmol/L. Elevated bile acid, SGPT, SGOT, and bilirubin levels were significantly associated with maternal complications ($p \leq 0.05$). Neonatal mean birth weight was 2.727 kg. 41% of neonates required SNCU admission. Significant associations with SNCU admission ($p < 0.001$) were found for lower gestational age, elevated maternal bile acid levels, abnormal liver enzymes, lower birth weight, and low APGAR scores.

Conclusion; ICP is associated with significant maternal and neonatal morbidity, particularly in rural settings. Elevated bile acid and liver enzyme levels strongly predict adverse outcomes. Early diagnosis, close monitoring, and timely intervention are crucial to improving feto-maternal outcomes.

Keywords*: Intrahepatic Cholestasis of Pregnancy, Bile Acids, Maternal Complications, Neonatal Outcomes, SNCU Admission, Postpartum Haemorrhage.*

INTRODUCTION

Intrahepatic cholestasis of pregnancy, also known as obstetric cholestasis or prurigogravidarum, is a pregnancy-specific liver disorder characterized by pruritus and elevated serum bile acid levels, typically occurring in the second or third trimester.[1] It is one of the most common liver disorders unique to pregnancy, with a prevalence ranging from 0.2% to 2% in most populations, though higher rates are reported among South Asians and Scandinavians.[2,3] ICP is associated

with significant maternal discomfort and serious fetal risks, including preterm birth, fetal distress, meconium-stained amniotic fluid, and IUFD (Intra-Uterine Fetal Demise).[4,5]

Pruritus, especially involving the palms and soles, is the hallmark symptom and occurs without an accompanying rash.[6,7] Jaundice is uncommon, occurring in fewer than 10% of cases.[8] The pathogenesis of ICP is multifactorial, involving genetic, hormonal, and environmental factors. Mutations in hepatobiliary transport proteins such as ABCB4 and ABCB[11] suggest a genetic predisposition.[9,10] Elevated estrogen and progesterone levels during pregnancy impair bile acid transport and secretion, contributing to cholestasis.[11]Diagnosis is based on elevated serum bile acid levels (>10 µmol/L), with levels above 40 µmol/L strongly associated with adverse fetal outcomes.[10,12] Liver transaminases (ALT and AST) are often elevated but are less specific 5. Maternal complications include postpartum haemorrhage due to vitamin K deficiency and coagulopathy, as well as spontaneous preterm labor.[9,11] Fetal complications include preterm birth, IUGR, meconium aspiration syndrome, and stillbirth.[2,3] The risk of stillbirth correlates strongly with rising bile acid levels.[4]

Management focuses on symptomatic relief and close fetal monitoring. UDCA (Ursodeoxycholic Acid) is the first-line therapy to reduce bile acid levels and pruritus,[5] while antihistamines and emollients offer limited benefit.[7] Early delivery at 37–38 weeks is often recommended to reduce stillbirth risk.[8]

Despite advances in understanding ICP, data from rural and low-resource settings remain limited.[9,10] This study aims to evaluate maternal and fetal outcomes of ICP in a rural Indian population to improve clinical management strategies.

AIMS AND OBJECTIVES

The study aimed to evaluate the maternal and fetal outcomes in patients diagnosed with ICP (Intrahepatic Cholestasis of Pregnancy). The objectives were to assess maternal outcomes, particularly the occurrence of complications such as bleeding disorders including DIC (Disseminated Intravascular Coagulation), PPH (Post-Partum Haemorrhage), and maternal death, and to evaluate fetal outcomes including preterm birth, IUGR (Intra-Uterine Growth Restriction), admission to the SNCU (Special Newborn Care Unit), and IUFD (Intra-Uterine Fetal Demise).

MATERIALS AND METHODS

Study Design

This study was designed as a prospective observational clinical study conducted in the Department of Obstetrics and Gynaecology at Burdwan Medical College & Hospital, PurbaBardhaman, from June 2023 to December 2024. The study aimed to evaluate maternal and fetal outcomes in patients diagnosed with ICP, a condition associated with significant perinatal morbidity and mortality. The study population included pregnant women with a gestational age between 34 weeks and delivery who either attended the antenatal OPD (Outpatient Department) or were admitted to the antenatal ward or labour room during the study period.

Inclusion and Exclusion Criteria

The study included pregnant women aged 18 to 40 years with a single live fetus and a gestational age between 34 weeks and delivery. Exclusion criteria were applied to eliminate confounding factors and included patients with viral hepatitis (A, B, C, D, E, or G); acute fatty liver of pregnancy; liver damage secondary to severe preeclampsia, eclampsia, or HELLP syndrome; hepatic damage due to hyperemesis gravidarum; and those whose complications were attributable to alternative obstetric causes such as placental abruption, uterine atony, or preeclampsia. During the study period, no patient received UDCA, as per institutional protocol; therefore, all maternal and fetal outcomes observed reflect the natural course of intrahepatic cholestasis of pregnancy without pharmacological intervention, ensuring uniformity in management and eliminating treatment-related bias.

Sample Size Calculation

Thesamplesizewasdeterminedusingtheformulaforestimatingproportionsinapopulation:

$$N = \frac{Z^2 pq}{d^2}$$

$$N = \frac{Z^2(1-p)}{d^2}$$

Where:

- Z=1.96(corresponding to a 95% confidence level),
- p=0.18(expected prevalence of ICP based on prior studies),

- q=0.82 =(1 -p),
- d=0.075(precision or margin of error).

The calculated sample size was 100 participants, ensuring adequate statistical power to detect significant associations. Participants were selected using a serial sampling technique, wherein consecutive patients meeting the inclusion criteria were enrolled until the target sample size was achieved.

Data Collection Tools

A structured, pre-designed, and pre-tested data collection schedule was used to systematically record patient information. Clinical assessment included monitoring of vital signs such as pulse, blood pressure, and temperature using a BP apparatus and stethoscope. Laboratory investigations comprised hemogram, blood group typing, RBS (Random Blood Sugar), and viral markers (HIV, HBsAg, Anti-HCV, VDRL), along with TSH (Thyroid Function Tests) and HPLC (High-Performance Liquid Chromatography) for haemoglobin analysis. Obstetric evaluation included USG (Ultrasonography) for FPP (Fetal Biophysical Profile) and AFI (Amniotic Fluid Index), as well as routine urine examination. Biochemical investigations included measurement of total bilirubin (conjugated and unconjugated), SGPT (Serum Glutamic-Pyruvic Transaminase), SGOT (Serum Glutamic-Oxaloacetic Transaminase), and serum bile acid levels. Fetal monitoring was performed using CTG (Cardiotocography) to assess fetal heart rate patterns. Relevant clinical information was documented using OPD tickets and BHTS indoor records from the Department of Obstetrics & Gynaecology and Critical Care Units (CCU & HDU).

Data Collection Procedure

A comprehensive history was obtained from each participant, including menstrual history (cycle regularity, length, and last menstrual period), obstetric history (gravidity, parity, and previous pregnancy outcomes), personal and medical history (cardiovascular, respiratory, gastrointestinal, endocrine, and coagulation disorders), as well as current medications, allergies, and history of sexually transmitted diseases. Baseline vital signs were recorded and monitored during follow-up visits, and a detailed general and systemic examination was performed to assess overall clinical status. Written informed consent was obtained after explaining the study objectives and procedures. All participants underwent routine antenatal investigations, including hemogram, blood group and Rh typing (with anti-D prophylaxis for Rh-negative mothers), random blood sugar for gestational diabetes screening, viral markers (HIV, HBsAg, Anti-HCV, VDRL), TSH (Thyroid Function Tests), and HPLC (High-Performance Liquid Chromatography) for haemoglobin analysis. Obstetric evaluation included ultrasonography to assess fetal growth, amniotic fluid index, and placental status, along with routine urine examination. Biochemical investigations included estimation of total bilirubin (conjugated and unconjugated), SGPT (Serum Glutamic-Pyruvic Transaminase), SGOT (Serum Glutamic-Oxaloacetic Transaminase), and serum bile acid levels to confirm the diagnosis of intrahepatic cholestasis of pregnancy and determine disease severity.

Statistical Analysis

The collected data were tabulated using Microsoft Excel and subsequently analyzed using SPSS version 23. Descriptive statistics were applied to summarize demographic and clinical variables, which were presented as means and standard deviations for continuous variables and as frequencies and percentages for categorical variables. Inferential statistical methods were used to evaluate the associations between maternal and fetal outcomes and relevant laboratory parameters. The Pearson chi-Square test was applied for categorical variables, and the independent sample t-test was used for comparison of continuous variables, depending on the distribution of data. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1: Maternal Complications in ICP

Maternal Outcome	Frequency	Percentage (%)
No Complication	77	77%
DIC	7	7%
PPH	16	16%
Total	**100**	**100%**

Table 1 illustrates the distribution of maternal complications among women diagnosed with ICP. The majority (77%) had no complications. However, 16% developed PPH (Post-Partum Haemorrhage () and 7% developed DIC (Disseminated Intravascular Coagulation). No maternal mortality was reported.

Table 2: Mode of Delivery

Mode of Delivery	Frequency	Percentage (%)
Induced Vaginal Delivery	60	60%
Spontaneous Vaginal Delivery	16	16%

LSCS	24	24%
Total	**100**	**100%**

Table 2 shows the distribution of mode of delivery. Induction of labour was the most common mode (60%), reflecting proactive obstetric management in ICP cases. Caesarean section was performed in 24% of patients.

Table 3: APGAR Score Distribution (1 min and 5 min)

APGAR Score at 1 Minute		
Score	**Frequency**	**Percentage (%)**
3–5	21	21%
6–7	35	35%
8–9	44	44%
APGAR Score at 5 Minutes		
Score	**Frequency**	**Percentage (%)**
5–6	11	11%
7	10	10%
8–9	79	79%

Table 3 demonstrates significant improvement in neonatal condition from 1 minute to 5 minutes. While 21% had low APGAR scores (≤5) at 1 minute, 79% achieved reassuring scores (8–9) at 5 minutes, indicating effective neonatal resuscitation.

Table 4: SNCU Admission

SNCU Admission	**Frequency**	**Percentage (%)**
Yes	41	41%
No	59	59%
Total	**100**	**100%**

Table 4 highlights that 41% of neonates required SNCU (Special Newborn Care Unit) admission, indicating substantial neonatal morbidity in ICP pregnancies.

Table 5: Descriptive Statistics of Maternal and Neonatal Parameters

Parameter	**Mean**	**SD**	**Minimum**	**Maximum**
Maternal Age (years)	29.07	2.08	25	35
Gestational Age (weeks)	36.10	1.54	34	39
Bile Acid (µmol/L)	68.54	30.93	33	132
SGPT (U/L)	87.44	32.98	48	160
SGOT (U/L)	96.30	36.23	55	175
Total Bilirubin (mg/dL)	1.66	0.75	0.8	3.5

Table 5 summarizes key clinical and laboratory parameters. The mean bile acid level was markedly elevated (68.54 µmol/L), reflecting moderate to severe ICP. The mean birth weight (2.727 kg) suggests increased prevalence of low birth weight neonates.

Table 6: Independent Sample t-test (SNCU Admission as Grouping Variable)

Variable	**p-value**	**Significance**
Maternal Age	0.003	Significant
Gestational Age	<0.001	Highly Significant
Bile Acid Level	<0.001	Highly Significant
SGPT	<0.001	Highly Significant
SGOT	<0.001	Highly Significant
Total Bilirubin	<0.001	Highly Significant
Birth Weight	<0.001	Highly Significant
APGAR 1 min	<0.001	Highly Significant
APGAR 5 min	<0.001	Highly Significant
Maternal Complications	<0.001	Highly Significant
Mode of Delivery	<0.001	Highly Significant

Table 6 reveals strong statistical associations between elevated bile acids, liver enzyme abnormalities, earlier gestational age, lower birth weight, and SNCU admission. These findings confirm that disease severity significantly impacts neonatal outcomes.

Table 7: Association between Maternal Laboratory Parameters and Maternal Complications (Chi-Square Test)

Parameter	Chi-Square Value	df	p-value	Significance
Bile Acid Level	128.371	86	0.002	Significant
SGPT	103.899	62	0.001	Significant
SGOT	94.670	74	0.053	Borderline
Total Bilirubin	105.821	52	<0.001	Highly Significant

Table 7 indicates that elevated bile acid levels, SGPT, and bilirubin are significantly associated with maternal complications such as PPH and DIC. SGOT showed a borderline association.

DISCUSSION

The present study provides important insights into the maternal and fetal outcomes associated with ICP in a rural tertiary care setting. The findings both align with and expand upon existing literature, while also highlighting the distinct challenges faced in resource-limited populations.

In the current study, 77% of women with ICP did not experience maternal complications, which is consistent with previous studies reporting generally favourable maternal outcomes when timely monitoring and intervention are implemented.[13] However, maternal morbidity was still significant, with 7% developing DIC (Disseminated Intravascular Coagulation) and 16% experiencing PPH. These findings reinforce the established association between cholestasis severity and coagulation abnormalities.[14]Glantz et al. demonstrated that women with severe ICP (bile acids >40 μmol/L) have a higher risk of PPH, likely secondary to vitamin K deficiency and impaired hepatic synthesis of clotting factors.[15] Importantly, no maternal deaths were observed in this study, which may reflect effective intrapartum surveillance and prompt obstetric management.[16]

The high rate of induced vaginal deliveries (60%) observed in this study reflects current obstetric practice aimed at minimizing fetal risks in ICP pregnancies. Induction at 37–38 weeks is widely recommended to reduce the risk of stillbirth. Ovadia et al. (2019) demonstrated that planned delivery in women with severe ICP significantly reduces adverse perinatal outcomes.[17] The caesarean section rate of 24% in this study is comparable to previously reported rates, where operative delivery is often necessitated by non-reassuring fetal status or failed induction.[18]

A significant association was observed between elevated total bilirubin levels and maternal complications ($p < 0.001$), supporting earlier findings that the biochemical severity of cholestasis correlates with adverse maternal outcomes.[19] Similarly, elevated SGPT levels were significantly associated with complications ($p = 0.001$), underscoring the role of hepatocellular dysfunction in the development of coagulopathy and haemorrhage.[5] Although SGOT demonstrated only a borderline significant association ($p = 0.053$), this may still suggest a clinically relevant relationship requiring further investigation.[20]

Neonatal outcomes in this study revealed important findings. Although APGAR scores improved significantly between 1 and 5 minutes, 21% of neonates had low APGAR scores (3–5) at 1 minute, which is consistent with literature documenting increased rates of perinatal asphyxia in ICP pregnancies.[11] The mean birth weight of 2.727 kg indicates a higher prevalence of LBW (Low Birth Weight) and small-for-gestational-age (SGA) neonates compared to global averages.[9]Geenes et al. (2011) similarly reported that elevated maternal bile acid levels are associated with impaired fetal growth and LBW.[19]

The SNCU admission rate of 41% in this study is relatively high compared to some international reports but is comparable to findings from resource-limited settings. Neonates requiring SNCU admission were significantly associated with elevated maternal bile acid levels, earlier gestational age at delivery, lower birth weights, and reduced APGAR scores. These findings are consistent with previous studies demonstrating that increasing bile acid levels directly correlate with neonatal morbidity.[13] Brouwers et al. (2014) reported that neonates born to mothers with severe ICP (bile acids ≥100 μmol/L) had higher rates of respiratory distress and intensive care admission.[5]

The prevalence of preterm birth and low birth weight observed in this study mirrors findings from other low-resource settings, where delayed diagnosis and limited access to specialized care may worsen outcomes.[16] In contrast, studies from high-income countries such as the Netherlands and the UAE report comparatively lower adverse outcome rates, likely due to earlier detection, standardized monitoring protocols, and widespread use of ursodeoxycholic acid.[5,11]

The strong association between elevated bile acid levels and adverse maternal and neonatal outcomes in this study supports the conclusions of Ovadia et al. (2019), who demonstrated that bile acid levels >40 µmol/L significantly increase the risk of stillbirth, preterm birth, and neonatal morbidity.[17] Notably, this study also emphasizes the predictive value of liver enzyme abnormalities, particularly SGPT and bilirubin levels, which are less frequently highlighted in large cohort analyses. These findings suggest that comprehensive liver function assessment, beyond bile acid estimation alone, may enhance risk stratification in ICP patients.

Clinical Implications

The findings underscore the importance of early diagnosis, serial bile acid monitoring, and timely delivery planning in ICP pregnancies. Elevated bile acids, abnormal liver enzymes, and reduced gestational age at delivery were strongly associated with adverse outcomes. These parameters should be incorporated into clinical decision-making algorithms to optimize maternal and neonatal care.

STRENGTHS AND LIMITATIONS

A major strength of this study is its focus on a rural population, which remains under-represented in the global literature on ICP. By evaluating outcomes in a resource-constrained environment, the study provides valuable insights into real-world challenges in managing ICP. However, limitations include the relatively small sample size and single-center design, which may restrict generalizability. Larger, multi-center studies are warranted to validate these findings and refine risk prediction strategies.

CONCLUSION

This study highlights the substantial maternal and fetal risks associated with ICP, particularly in rural populations where access to timely diagnosis and specialized care may be limited. Elevated maternal bile acid levels, abnormal liver enzyme parameters, and preterm delivery emerged as key determinants of adverse outcomes. These findings emphasize that early diagnosis, vigilant antenatal surveillance, and appropriately timed obstetric intervention are essential to reducing morbidity in both mother and neonate. Furthermore, the results underscore the urgent need to strengthen awareness, improve diagnostic facilities, and enhance clinical management protocols for ICP in low-resource settings. Additional large-scale studies are warranted to further elucidate the predictive value of liver function tests in identifying patients at increased risk of complications and to optimize evidence-based management strategies.

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