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Maternal and Perinatal Outcomes in Intrahepatic Cholestasis of Pregnancy: A Prospective Observational Study from a Tertiary Care Centre

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Abstract

Background: Intrahepatic cholestasis of pregnancy (IHCP) is the most common pregnancy-specific liver disorder, characterized by pruritus and elevated serum bile acids, and is associated with adverse maternal and perinatal outcomes. Despite increasing recognition, regional data regarding its clinical spectrum and outcomes remain limited. This study aimed to evaluate maternal complications and perinatal outcomes in antenatal women diagnosed with IHCP at a tertiary care centre.

Methods: A prospective observational study was conducted over 18 months [January 2024 – June 2025] at T.S. Misra Medical College and Hospital, Lucknow. A total of 100 antenatal women diagnosed with IHCP based on clinical features and biochemical parameters (serum bile acids >10 µmol/L and/or abnormal liver enzymes) were included. Ethical approval was obtained from the Institutional Ethics Committee, and the study adhered to the Declaration of Helsinki. All patients received ursodeoxycholic acid and were monitored with fetal surveillance protocols including cardiotocography and biophysical profile. Data were analyzed using SPSS version 29.0, with statistical significance set at $p<0.05$.

Results: The mean maternal age was 30.53 ± 5.46 years, with 59% primigravida. Pruritus was the most common symptom (86%). Higher serum bile acid levels (>60 µmol/L) were significantly associated with adverse outcomes, including meconium-stained amniotic fluid (81.8%), fetal distress (81.8%), respiratory distress syndrome (72.7%), preterm delivery (54.5%), NICU admission (100%), and intrauterine death (27.3%) ($p\leq0.031$). Mean birth weight was significantly lower in the high bile acid group ($p=0.017$).

Conclusion: IHCP is associated with significant maternal and perinatal morbidity, especially at higher serum bile acid levels. Serum bile acids serve as a reliable predictor of adverse outcomes, emphasizing the need for early diagnosis, close monitoring, and timely intervention.

Keywords: Intrahepatic cholestasis of pregnancy, serum bile acids, pruritus, perinatal outcomes, preterm delivery, fetal distress

Introduction

Intrahepatic cholestasis of pregnancy (IHCP), also referred to as obstetric cholestasis, is a reversible liver disorder unique to pregnancy, typically presenting in the late second or third trimester [1]. It is characterized clinically by generalized pruritus and biochemically by elevated serum bile acids and liver enzymes [2]. Although maternal prognosis is generally favorable with resolution after delivery, IHCP poses significant risks to the fetus, including preterm birth, fetal distress, meconium-stained amniotic fluid, and intrauterine fetal death [3-6].

The liver plays a central role in metabolism, detoxification, bile production, and protein synthesis. Physiological changes during pregnancy alter hepatic function and laboratory parameters, making interpretation of liver function tests challenging. However, elevations in transaminases or bile acids beyond normal pregnancy ranges indicate pathology requiring further evaluation [2].

The etiology of IHCP is multifactorial, involving genetic predisposition, hormonal influences (particularly estrogen and progesterone), and environmental factors. Elevated hormone levels during pregnancy impair bile acid transport mechanisms, leading to accumulation of bile acids in maternal circulation. Genetic mutations affecting hepatobiliary transport proteins further contribute to disease pathogenesis [4].

Globally, the incidence of IHCP varies widely, ranging from 0.2% to 2% of pregnancies, with higher rates reported in certain populations [3]. In India, prevalence ranges from 1–5%, reflecting geographic and ethnic variability [7].

Despite increasing awareness, there remains variability in reported outcomes due to differences in diagnostic criteria, sample sizes, and management strategies. Furthermore, the relationship between serum bile acid levels and adverse outcomes is not fully elucidated in all populations [5,6].

Aim

To study maternal and perinatal outcomes in antenatal women with intrahepatic cholestasis of pregnancy.

Objectives

1. To evaluate maternal complications associated with IHCP.
2. To assess perinatal outcomes including neonatal morbidity and mortality.

Materials and Methods

Study Design and Setting

This was a prospective observational study conducted in the Department of Obstetrics and Gynaecology at T.S. Misra Medical College and Hospital, Lucknow, over a period of 18 months (January 2024–July 2025).

Study Population

A total of 100 antenatal women diagnosed with IHCP were included.

Inclusion Criteria

- Pregnant women with pruritus
- Elevated serum bile acids (>10 μmol/L) and/or abnormal liver function tests

Exclusion Criteria

- Pre-existing liver disease
- Other causes of liver dysfunction in pregnancy

Ethical Considerations

The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants. The study adhered to the principles of the Declaration of Helsinki [9].

Data Collection

Detailed clinical history, obstetric profile, and laboratory investigations including liver function tests and serum bile acid levels were recorded. Patients were followed until delivery.

Management Protocol

All patients received ursodeoxycholic acid (10–15 mg/kg/day) [9,10]. Vitamin K was administered during delivery. Fetal monitoring included:

- Daily fetal movement count
- Cardiotocography
- Biophysical profile

Outcome Measures

Maternal Outcomes

- Pruritus severity
- Time and mode of delivery
- Incidence of pre-eclampsia and gestational diabetes mellitus

Perinatal Outcomes

- Preterm birth
- Fetal distress
- NICU admission
- Birth weight
- Intrauterine death

Statistical Analysis

Data were analyzed using SPSS version 29.0. Chi-square test and t-test were applied. A p-value <0.05 was considered statistically significant.

Results

Demographic Profile

The mean maternal age was 30.53 ± 5.46 years. Majority (59%) were primigravida.

Clinical Features

Pruritus was present in 86% of patients, with nocturnal aggravation in 79% and sleep disturbance in 70%.

Biochemical Findings

Serum bile acid levels increased significantly with advancing gestational age ($p<0.001$).

Maternal Outcomes

Higher bile acid levels were associated with increased maternal complications, although pruritus remained the predominant symptom.

Perinatal Outcomes

Adverse outcomes were significantly higher in patients with serum bile acid levels >60 µmol/L:

- Meconium-stained amniotic fluid: 81.8%
- Fetal distress: 81.8%
- Respiratory distress syndrome: 72.7%

- Preterm delivery: 54.5%
- NICU admission: 100%
- Intrauterine death: 27.3%

All associations were statistically significant ($p \leq 0.031$).

Birth Weight

Mean birth weight was lowest in the high bile acid group (2.55 ± 0.43 kg), showing significant association ($p=0.017$).

Discussion

This study highlights the significant impact of intrahepatic cholestasis of pregnancy (IHCP) on maternal and perinatal outcomes, emphasizing serum bile acid levels as a key determinant of fetal risk.

Pruritus was the predominant presenting symptom (86%), consistent with existing literature identifying it as the hallmark feature of IHCP, particularly with nocturnal aggravation [1]. The associated sleep disturbance (70%) reflects the considerable impact on maternal quality of life.

The study population showed a higher proportion of primigravida (59%). While some studies report increased recurrence in multigravida due to genetic predisposition, global evidence remains inconsistent, likely reflecting variations in population characteristics and healthcare access.

A key finding of this study is the strong association between elevated serum bile acid levels and adverse perinatal outcomes. Patients with bile acid levels >60 µmol/L had significantly higher rates of meconium-stained amniotic fluid (81.8%), fetal distress (81.8%), respiratory distress syndrome (72.7%), preterm delivery (54.5%), and NICU admission (100%), indicating that bile acids act as active contributors to fetal compromise rather than merely biochemical markers [5,6].

The pathophysiological basis of these outcomes likely involves transplacental transfer of bile acids, leading to fetal cardiotoxicity and arrhythmias, along with placental vasoconstriction resulting in fetal hypoxia. These mechanisms are supported by international studies demonstrating increased fetal complications with rising bile acid concentrations [4-6].

The findings are consistent with global evidence, where bile acid levels ≥40 µmol/L are associated with increased risk of preterm birth and meconium-stained liquor, and levels ≥100 µmol/L significantly increase stillbirth risk [5,12]. Although this study used a threshold of >60 µmol/L, the overall trend remains comparable, reinforcing serum bile acids as a reliable prognostic marker.

The high incidence of preterm delivery (54.5%) aligns with international data, reflecting both spontaneous onset and iatrogenic early delivery to prevent fetal complications [13,14]. Similarly, the high rate of NICU admission (100%) and respiratory distress syndrome (72.7%) highlights the substantial neonatal morbidity associated with IHCP, likely due to prematurity and direct effects of bile acids on fetal lung function [15].

A significant reduction in mean birth weight (2.55 ± 0.43 kg) was observed in patients with higher bile acid levels, suggesting impaired fetal growth or early delivery. This finding is consistent with global literature reporting low birth weight in IHCP pregnancies [13].

The occurrence of intrauterine death (27.3%) in the high bile acid group underscores the severity of fetal risk in IHCP. Variations in rates compared to international studies may be attributed to differences in disease severity and referral patterns in tertiary care settings.

Clinically, these findings highlight the importance of early diagnosis and routine monitoring of serum bile acid levels in pregnant women presenting with pruritus. Risk stratification based on bile acid levels allows timely intervention and improved outcomes. Ursodeoxycholic acid remains the standard treatment for

symptomatic and biochemical improvement, although its impact on perinatal mortality is still under evaluation [9,10].

The study also emphasizes the need for individualized timing of delivery. While international guidelines suggest planned delivery around 37 weeks, management should be guided by disease severity and fetal condition [9]. Continuous fetal surveillance using cardiotocography and biophysical profile is essential in high-risk cases.

Multidisciplinary management involving obstetricians, neonatologists, and hepatologists is crucial for optimizing outcomes. Adequate patient counseling regarding risks, monitoring, and delivery planning is equally important.

In summary, this study reinforces that IHCP is associated with significant perinatal morbidity, with serum bile acid levels serving as both diagnostic and prognostic markers, guiding clinical management and improving outcomes.

Conclusions

Intrahepatic cholestasis of pregnancy is associated with significant maternal and perinatal morbidity. Elevated serum bile acid levels, particularly above 60 μmol/L, are strongly associated with adverse outcomes including preterm birth, fetal distress, NICU admission, and intrauterine death [5,6].

Serum bile acids serve as a reliable predictor of disease severity and fetal risk. Early diagnosis, regular monitoring, and timely delivery are essential to improve outcomes.

Future research should focus on optimizing management protocols and identifying additional predictive markers for risk stratification.

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Tables

Table 1: Distribution of the studied IHCP patients on the basis of their Age and Educational status

		Frequency (n=100)	Percentage
Age in years	**≤25**	16	16.0%
	26-30	40	40.0%
	31-35	24	24.0%
	>35	20	20.0%
	Mean Age	30.53±5.46 (20-48 years)	
Educational Status	**Up to primary education and above**	76	76.0%
	Below primary education	24	24.0%

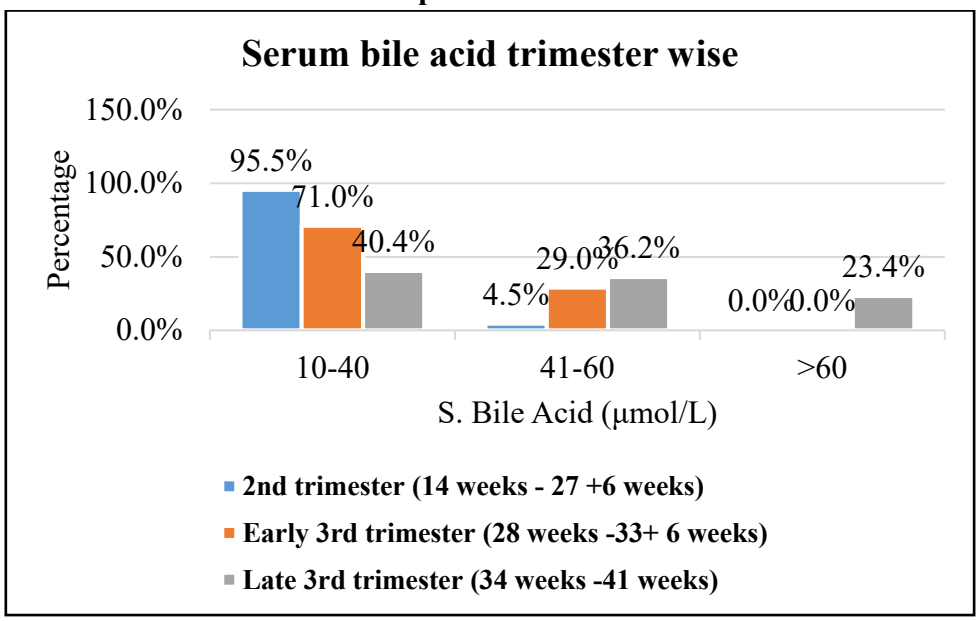
In the studied IHCP patients (n=100), the largest proportion belonged to the 26–30-year age group, comprising 40 patients (40.0%). This was followed by 24 patients (24.0%) aged 31–35 years and 20 patients (20.0%) aged above 35 years, while the youngest group (≤25 years) included 16 patients (16.0%). The overall mean age of the cohort was 30.53 ± 5.46 years, with ages ranging from 20 to 48 years.

Table 2: Distribution of the studied IHCP patients on the basis of Serum bile acid trimester wise

Serum Bile Acid (µmol/L)	2nd trimester (14 weeks - 27 +6 weeks)	Early 3rd trimester (28 weeks -33+ 6 weeks)	Late 3rd trimester (34 weeks -41 weeks)	P value
10-40	21 (95.5%)	22 (71.0%)	19 (40.4%)	<0.001

41-60	1 (4.5%)	9 (29.0%)	17 (36.2%)	
>60	0 (0.0%)	0 (0.0%)	11 (23.4%)	

Figure 1: Distribution of the studied IHCP patients on the basis of Serum bile acid trimester wise

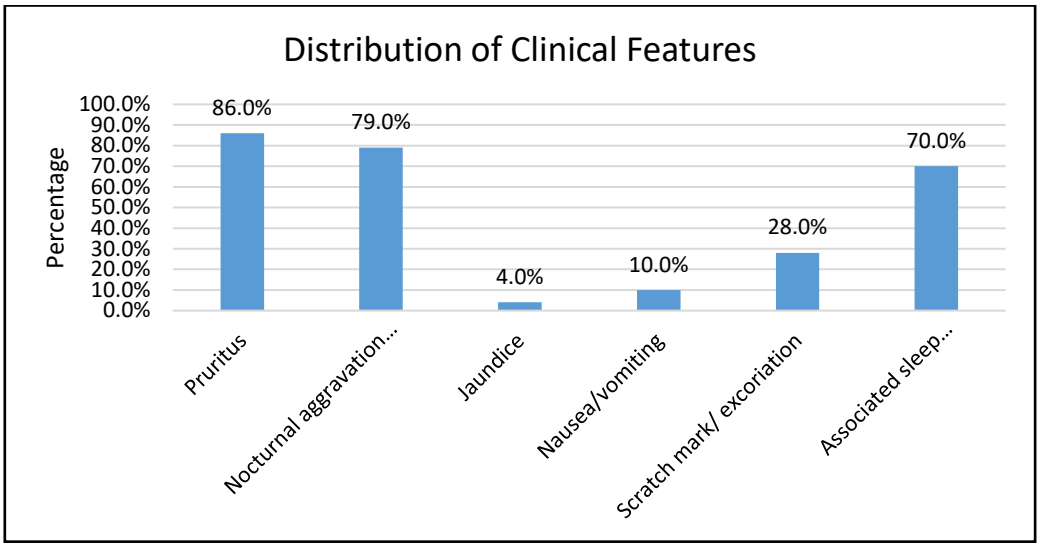


In the studied IHCP patients, serum bile acid distribution showed a significant trimester-wise variation ($p < 0.001$). During the second trimester, nearly all patients (95.5%) had bile acid levels within 10–40 µmol/L, with only a small fraction (4.5%) in the 41–60 µmol/L range and none exceeding 60 µmol/L. In the early third trimester, the majority (71.0%) remained within 10–40 µmol/L, though 29.0% had levels between 41–60 µmol/L, and none crossed 60 µmol/L. By the late third trimester, however, the distribution shifted markedly, with only 40.4% in the 10–40 µmol/L range, 36.2% in the 41–60 µmol/L range, and a notable 23.4% exceeding 60 µmol/L, highlighting a progressive rise in bile acid levels as gestation advanced.

Table 3: Distribution of the studied IHCP patients on the basis of clinical features

Clinical Features	Frequency (n=100)	Percentage
Pruritus	86	86.0%
Nocturnal aggravation of Pruritus	79	79.0%
Jaundice	4	4.0%
Nausea/vomiting	10	10.0%
Scratch mark/ excoriation	28	28.0%
Associated sleep disturbance	70	70.0%

Figure 2: Distribution of the studied IHCP patients on the basis of clinical features



Among the 100 studied patients with intrahepatic cholestasis of pregnancy (IHCP), pruritus was the predominant clinical feature, observed in 86% of cases, with nocturnal aggravation reported in 79%. Sleep disturbance was also common, affecting 70% of patients, while scratch marks or excoriations due to itching were noted in 28%. Less frequent manifestations included nausea and vomiting in 10% and jaundice in only 4% of cases.

Table 4 :LFT parameters distribution of the studied IHCP patient's trimester wise

LFT Parameters	2nd trimester (14 weeks -27+6 weeks)	Early 3rd trimester (28 weeks -33+6 weeks)	Late 3rd trimester (≥34 weeks)	P value
ALP (IU/L)	261.73±114.63	280.29±104.80	300.47±129.28	0.435
AST (IU/L)	165.55±79.13	185.68±84.37	257.32±122.04	**0.001**
ALT (IU/L)	158.27±75.83	171.94±63.03	224.74±78.47	**0.001**
Total Bilirubin (mg/dl)	0.92±0.34	0.95±0.39	1.08±0.65	0.367

In the studied IHCP patients, liver function test parameters demonstrated trimester-wise variation. Alkaline phosphatase (ALP) levels showed a gradual rise from the second trimester (261.73 ± 114.63 U/L) to the late third trimester (300.47 ± 129.28 U/L), though this increase was not statistically significant ($p = 0.435$). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, however, rose significantly across trimesters, with AST increasing from 165.55 ± 79.13 U/L in the second trimester to 257.32 ± 122.04 U/L in the late third trimester ($p = 0.001$), and ALT rising from 158.27 ± 75.83 U/L to 224.74 ± 78.47 U/L ($p = 0.001$). Total bilirubin levels showed a mild increase from 0.92 ± 0.34 mg/dL in the second trimester to 1.08 ± 0.65 mg/dL in the late third trimester, but this change was not statistically significant ($p = 0.367$).

Table 5: Distribution of the studied patients on the basis of indication of labour , mode of delivery, and parity and its association with serum bile acid

Outcome		Serum Bile Acid (µmol/L)			p-value
		10-40 (n=62)	40-60 (n=27)	>60 (n=11)	
Parity	Primigravida	32 (51.6)	17 (63.0)	10 (90.9)	**0.045**
	Multigravida	30 (48.4)	10 (27.0)	1 (9.1)	
Induction of labour	Yes	32 (51.6)	18 (66.7)	3 (27.3)	0.082
	No	30 (48.4)	9 (33.3)	8 (72.7)	
Mode of delivery	Vaginal	26 (41.9)	12 (44.4)	3 (27.3)	0.603
	Cesarean	36 (58.1)	15 (55.6)	8 (72.7)	

Figure 3: Indication and mode of delivery associated with serum bile acid level in IHCP cases

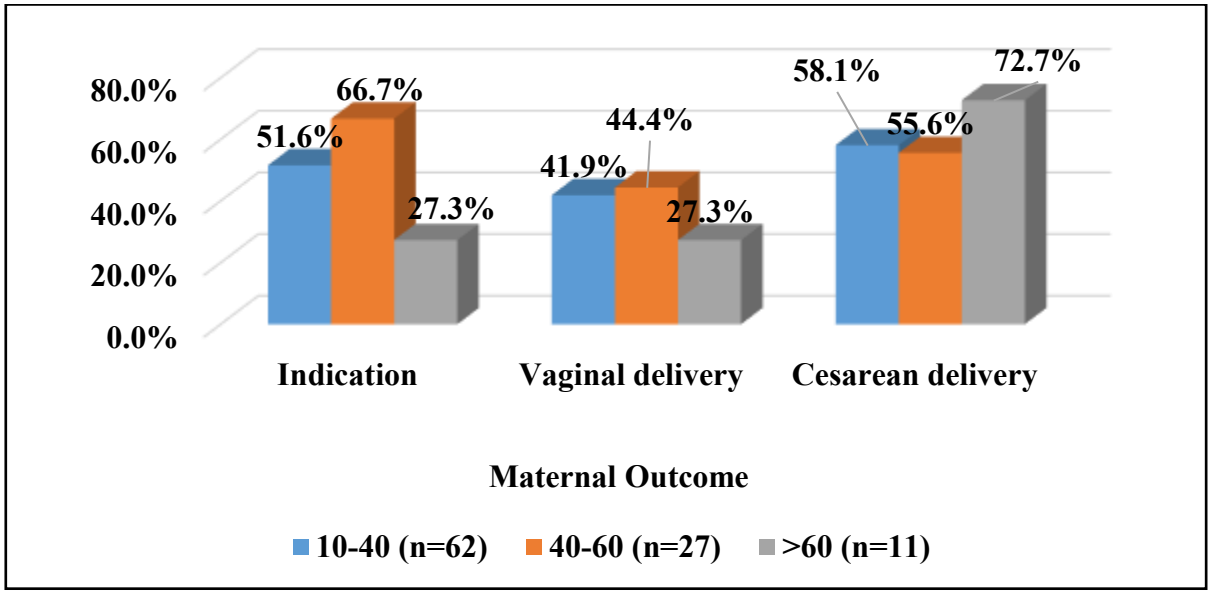
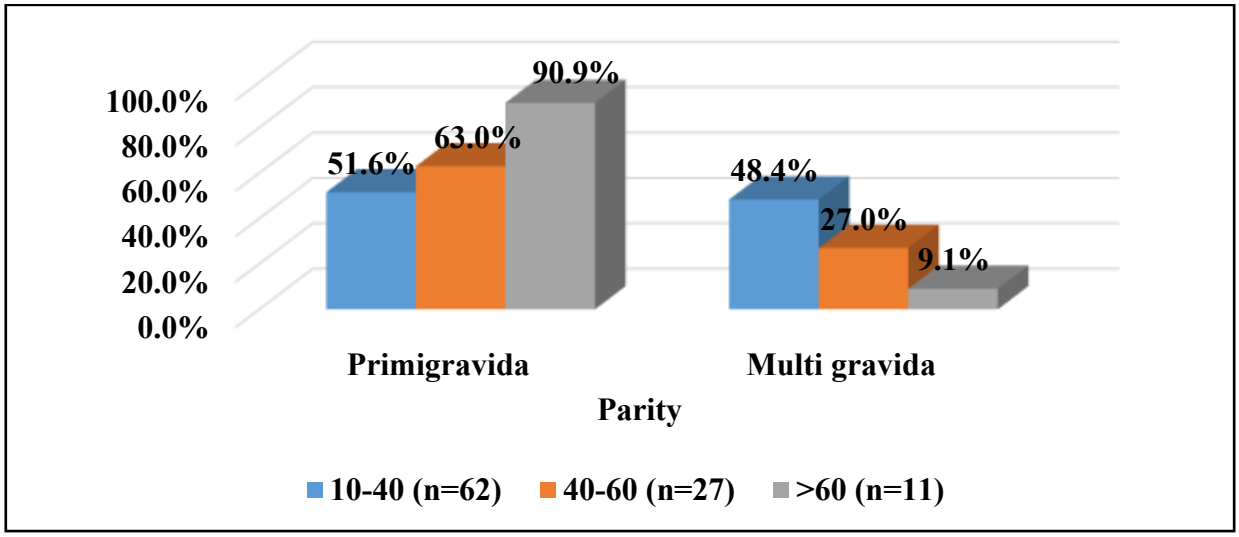


Figure 4: Parity associated with Serum bile acid level



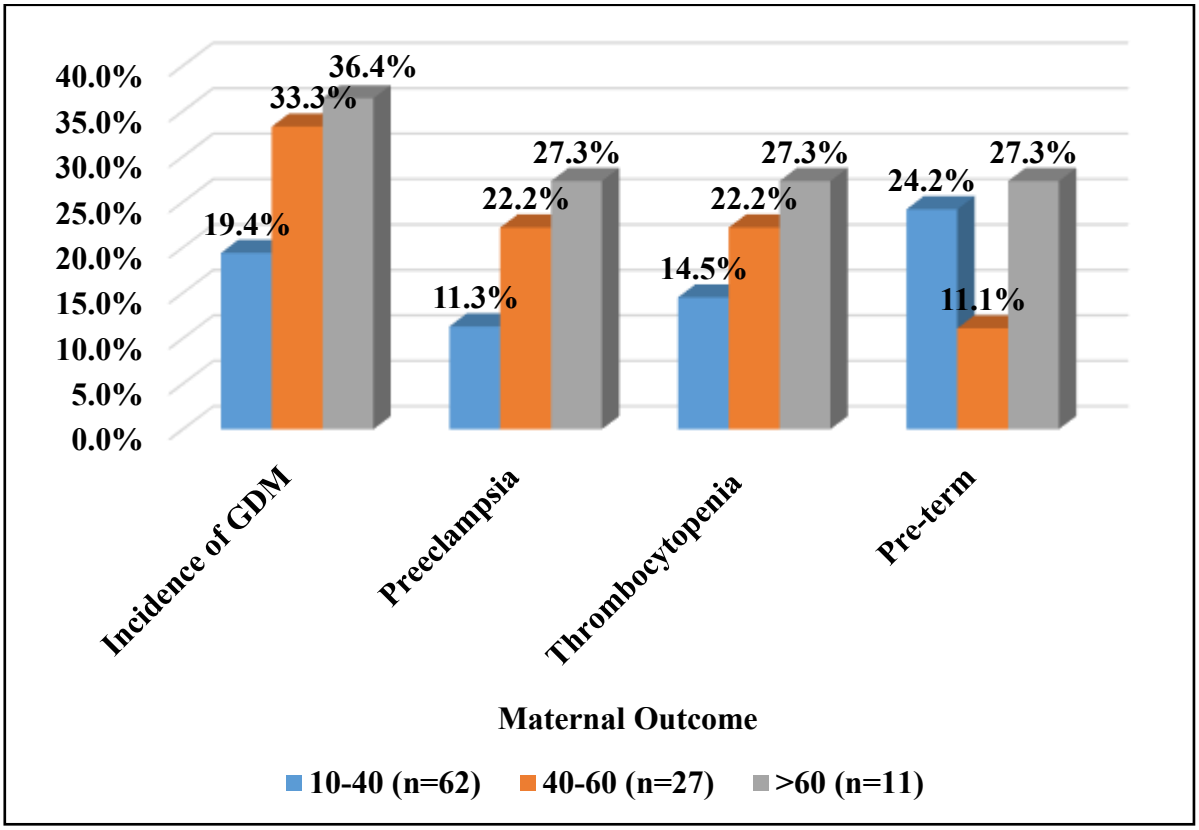
In the studied IHCP patients, the association of serum bile acid levels with induction and mode of delivery did not reach statistical significance. Induction was performed in 32 patients (51.6%) with serum bile acid 10–40 µmol/L, 18 patients (66.7%) with serum bile acid 41–60 µmol/L, and 3 patients (27.3%) with serum bile acid >60 µmol/L, compared to non-induction rates of 48.4%, 33.3%, and 72.7% respectively (p=0.082). Regarding mode of delivery, vaginal births were recorded in 26 patients (41.9%), 12 patients (44.4%), and 3 patients (27.3%) across the respective serum bile acid groups, while cesarean sections accounted for 58.1%, 55.6%, and 72.7% (p=0.603).

Among primigravida women, 67 (58.3%) had bile acid levels between 10–40 µmol/L, 45 (75.0%) between 41–60 µmol/L, and 19 (76.0%) exceeding 60 µmol/L. In contrast, multigravida patients accounted for 48 (41.7%), 15 (25.0%), and 6 (24.0%) in the respective categories. Serum bile acid levels showed a significant association with parity (p=0.043).

Table 6: Association of Serum Bile Acid with Maternal Complications

Outcome	Serum Bile Acid (µmol/L)			p-value
	10-40 (n=62)	40-60 (n=27)	>60 (n=11)	
Gestational Diabetes Mellitus	12 (19.4)	9 (33.3)	4 (36.4%)	0.245
Preeclampsia	7 (11.3)	6 (22.2)	3 (27.3%)	0.242
Thrombocytopenia	9 (14.5)	6 (22.2)	3 (27.3%)	0.478
Pre-term	15 (24.2)	3 (11.1)	3 (27.3%)	0.327

Figure 5: Association of Serum Bile Acid with Maternal Complications

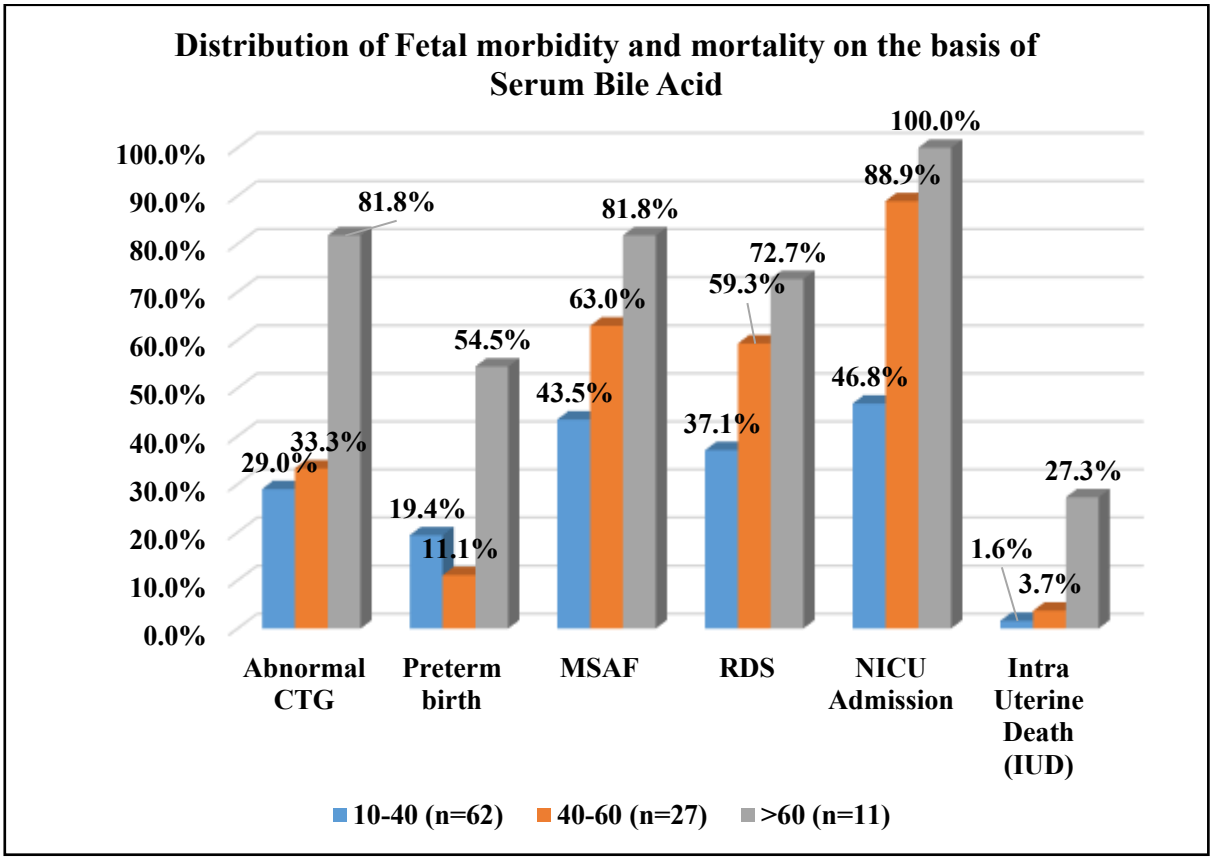


The incidence of gestational diabetes mellitus (GDM) rose from 19.4% in patients with serum bile acid 10–40 µmol/L to 33.3% in those with 40–60 µmol/L and 36.4% in those exceeding 60 µmol/L (p = 0.245). Similarly, preeclampsia was observed in 11.3% of patients with serum bile acid 10–40 µmol/L, increasing to 22.2% and 27.3% in the 40–60 µmol/L and >60 µmol/L groups, respectively (p = 0.242). Thrombocytopenia also showed a rising trend (14.5%, 22.2%, and 27.3% across the three serum bile acid categories (p = 0.478). Preterm delivery occurred in 24.2% of patients with serum bile acid 10–40 µmol/L, 11.1% with 40–60 µmol/L, and 27.3% with >60 µmol/L (p = 0.327).

Table 7: Distribution of Fetal morbidity and mortality on the basis of Serum Bile Acid

Fetal Outcome	Serum Bile Acid (µmol/L)			p-value
	10-40 (n=62)	40-60 (n=27)	>60 (n=11)	
Abnormal CTG	18 (29.0)	9 (33.3)	9 (81.8)	**0.003**
Preterm birth	12 (19.4)	3 (11.1)	6 (54.5)	0.010
Meconium Stained Amniotic Fluid	27 (43.5)	17 (63.0)	9 (81.8)	**0.031**
Respiratory Distress Syndrome	23 (37.1)	16 (59.3)	8 (72.7)	0.030
NICU Admission	27 (46.8)	24 (88.9)	11 (100.0)	**<0.001**
Intra Uterine Death (IUD)	1 (1.6)	1 (3.7)	3 (27.3)	0.003

Figure 6: Distribution of Fetal morbidity and mortality on the basis of Serum Bile Acid



As serum bile acid concentrations rise from 10–40 µmol/L to >60 µmol/L, the incidence of meconium-stained amniotic fluid (43.5% vs. 81.8%, p=0.031), respiratory distress syndrome (37.1% vs. 72.7%,

p=0.030), preterm delivery (19.4% vs. 54.5%, p=0.010), fetal distress (29.0% vs. 81.8%, p=0.003), and NICU admission (46.8% vs. 100%, p<0.001) increases significantly. Importantly, intrauterine death also shows a marked rise with higher bile acid levels (1.6% vs. 27.3%, p=0.003). These findings highlight that elevated maternal serum bile acids are strongly associated with worsening fetal outcomes, underscoring their prognostic value in predicting morbidity and mortality.