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Original Research Article

Fetomaternal Outcomes in Pregnancies Complicated by Intrahepatic Cholestasis

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Abstract: *Intrahepatic cholestasis of pregnancy (IHCP) is a liver disorder unique to pregnancy, characterized by pruritus and elevated serum bile acids. IHCP is associated with increased risk of adverse fetomaternal outcomes, including preterm birth, fetal distress, and stillbirth. Early diagnosis and management are crucial to reduce complications.* ***Objectives:*** *The study aimed to determine the frequency and severity of IHCP in pregnant women and to compare fetomaternal outcomes among mild, moderate, and severe IHCP cases.* ***Methods:*** *Ninety. This cross-sectional study was conducted at the Department of Gynecology, Rawalpindi Teaching Hospital, Rawalpindi, from February 28, 2025, to May 28, 2025. -Five pregnant women with singleton pregnancies beyond 28 weeks were enrolled using consecutive sampling. Diagnosis of IHCP was based on pruritus, fasting serum bile acids >19 µmol/L, and elevated liver enzymes. Patients were managed with ursodeoxycholic acid and followed with routine antenatal assessments. Maternal outcomes (preterm labor, postpartum hemorrhage, preeclampsia) and fetal outcomes (preterm birth, meconium-stained liquor, fetal distress, IUD, NICU admission) were recorded. Data were analyzed using SPSS v25; categorical variables were presented as n (%) and compared using chi-square tests.* ***Results:*** *IHCP was observed in 13.7% of participants, with mild, moderate, and severe cases accounting for 69.2%, 23.1%, and 7.7%, respectively. Maternal complications occurred in 46.2% of IHCP cases, while fetal complications were noted in 69.2%. Preterm birth and NICU admissions increased with the severity of IHCP. Stratification showed no significant differences in IHCP prevalence with respect to age, parity, or gestational age.* ***Conclusion:*** *IHCP was associated with considerable fetomaternal risks, which increased with severity. Close monitoring and timely management are crucial for improving outcomes.*

Keywords: Fetal distress, Intrahepatic cholestasis of pregnancy, Maternal complications, NICU admission, Preterm birth

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Introduction

Intrahepatic cholestasis of pregnancy (IHCP) is a pregnancy-specific liver disease characterized by skin pruritus and elevated bile acids. Maternal symptoms typically appear in the second or third trimester of pregnancy and usually resolve rapidly after delivery. Under rare circumstances, IHCP may also present as early as the first trimester. (1,2) Its prevalence is reported to be 0.3 to 5.6 per cent, and it varies across the globe. (3) The pathogenesis of IHCP is multifactorial, with an interaction of genetic, hormonal, immunological, and environmental factors. The estrogen-bile acid axis remains the primary focus of research studies, with an increasing number of associated genes and signaling pathways being identified. (4,5) Maternal bile acids get accumulated in the fetus and amniotic fluid by crossing the placental barrier, which carries a significant risk for the fetus. It increases the risk of preterm delivery, meconium excretion, respiratory distress syndrome, and sudden intrauterine death. (4,5) During pregnancy, numerous physiological and anatomical changes occur in the female body to ensure the best possible conditions for fetal growth. All systems and organs adapt their functions to support a healthy pregnancy course. (6) Women with pregnancies complicated by IHCP often experience a reduced quality of life due to the uncomfortable symptoms characterized by itching and liver impairment, which can lead to increased stress and discomfort, affecting the overall wellbeing and quality of life of expectant mothers. (7)

Naga et al. (2019) reported that the frequency of intrahepatic cholestasis of pregnancy (IHCP) was 7.21%. (8) Jhirwal et al. (2022) reported its frequency to be 3.6%. Among these, 140 (92.11%) had mild IHCP, 10 (6.58%) had moderate IHCP, and two (1.32%) had severe IHCP. In Mild IHCP, 80.95% were preterm, with 93.48% induced at term. Both spontaneous labor (89.8%) and vaginal birth (91.35%) were common, 0% intrauterine, but 90% had respiratory distress syndrome. In moderate IHCP, 14.29% of the cases were preterm, and 5.43% were term. Spontaneous labor was 8.16%, vaginal delivery was 6.73% and 10% had RDS. In severe IHCP, 4.76% of newborns were preterm, and 1.09% were induced at term; labor was spontaneous in 2.04% and vaginal in 1.92%. 0% respiratory distress syndrome (RDS) occurred. (9)

This study aims to contribute novel insights to existing literature by focusing specifically on the comprehensive assessment of fetal outcomes in the context of this condition. Our research aims to provide a detailed analysis of the specific challenges and potential complications associated with intrahepatic cholestasis during pregnancy, shedding light on previously unexplored aspects, including the impact on gestational age, mode of labor and delivery, and neonatal outcomes. By addressing these crucial knowledge gaps, our study will provide valuable insights for clinical management and enhance the overall care and outcomes for affected mothers and babies.

The objective of this study is to determine the frequency and severity of intrahepatic cholestasis of pregnancy (IHCP) by classifying it into mild, moderate, and severe forms among pregnant women. Furthermore, it aims to compare the fetomaternal outcomes across these three categories to identify whether disease severity has a significant impact on maternal health and perinatal outcomes.

Methodology

After approval from the ethical review committee, this cross-sectional study was conducted in the Department of Gynecology at Rawalpindi Teaching Hospital, Rawalpindi, from February 28, 2025, to May 28, 2025, following the approval of the synopsis. The sample size was calculated to be 95 cases using the WHO calculator at a 95% confidence level and a 5% margin of error, taking into account the expected frequency of moderate intrahepatic cholestasis of pregnancy in pregnant

women as 6.58%. A non-probability, consecutive sampling technique was employed for selecting cases. (7)

Women aged between 18 and 40 years with singleton pregnancies beyond 28 weeks of gestational age, who had raised bile acid levels and presented with pruritus without rash, were included in the study. Patients with cholelithiasis, acute or chronic viral hepatitis, primary biliary cirrhosis, pre-eclampsia, multiple pregnancies, and allergic skin diseases, as per history and clinical records, were excluded. Those with HELLP syndrome (haemolysis, elevated liver enzymes, low platelet count), acute fatty liver of pregnancy, or obstructive jaundice were also excluded. In addition, patients with pruritic skin lesions, viral hepatitis, autoimmune liver disease, coagulopathies, thrombocytopenia, gallstones, or cholestasis due to other causes were not included in the study.

A detailed history was taken regarding age, parity, obstetric history, and any recent change in drug intake. An obstetric examination was performed, and routine antenatal investigations, including liver function tests and fasting serum bile acid levels, were conducted. All patients were subsequently treated with ursodeoxycholic acid (UDCA) tablets, 10–15 mg/kg/day in divided doses, according to the level of serum bile acids. Liver enzymes were tested weekly or biweekly until delivery. All enrolled patients were clinically monitored and followed up in high-risk antenatal clinics every week. Fetal surveillance was performed using a non-stress test, modified biophysical profile, and obstetric ultrasonography, as per hospital protocol. Patients who did not have spontaneous preterm birth were admitted by 37 weeks of gestation and were delivered by the suitable method according to institutional protocol. Subsequently, they were followed for 14 days post-delivery.

The fetal outcomes in the form of gestational age at termination of pregnancy, type of labor, mode of delivery, APGAR score at 5 minutes, low birth weight, neonatal intensive care unit (NICU) admissions, intrauterine deaths, and meconium-stained liquor were recorded, while maternal outcomes, including mode of delivery and related complications, were also noted. All women were managed according to institutional protocol and were followed until delivery, with fetomaternal outcomes documented by the researcher herself on a specially designed proforma.

Intrahepatic cholestasis of pregnancy was diagnosed by the presence of pruritus, serum bile acids exceeding 19 µmol/L, and aminotransferase levels greater than 30 IU/L, and was classified as mild (10–39 µmol/L), moderate (40–99 µmol/L), or severe (≥100 µmol/L). Fetomaternal outcomes included mode of delivery, preterm birth (<37 weeks), low birth weight (<2,500 g), intrauterine death (>20 weeks), meconium-stained liquor, abnormal CTG, low Apgar score (≤5 at 5 minutes), respiratory or fetal distress, and NICU admission for prematurity, low birth weight, or medical complications.

All collected data were entered and analyzed using SPSS version 25. Numerical variables such as maternal age, gestational age, and parity were presented as mean ± SD. Categorical variables, such as intrahepatic cholestasis of pregnancy, color of liquor, severity of IHCP (mild, moderate, severe), and fetomaternal outcomes (yes/no), were presented as frequencies and percentages. The frequency of maternal and fetal outcomes was compared across mild, moderate, and severe intrahepatic cholestasis of pregnancy groups, and the chi-square test was applied, with $p \leq 0.05$ considered statistically significant. Data were stratified by age, gestational age, and parity to address potential effect modifiers, and a post-stratification chi-square test was applied, with $p \leq 0.05$ considered statistically significant.

Results

The mean age of the patients was 28.4 ± 5.2 years, with the majority of participants falling within the 26–30 years old age range (40.0%). Primigravida were 35.0% while multigravida were 65.0%. The mean gestational age was 35.6 ± 2.1 weeks, and most pregnancies occurred between 33 and 36 weeks (45.0%). The majority of amniotic fluid samples were clear (75.0%), while 25.0% were meconium-stained, as given in Table 1. Intrahepatic cholestasis of pregnancy (IHCP) was present in 13.7% of cases and absent in 86.3%. Among the 13 IHCP cases, 69.2% were classified as mild, 23.1% as moderate, and 7.7% as severe, as given in Table 2.

Among IHCP cases, maternal complications were observed in 46.2% of patients, with preterm labor occurring in 23.1%, postpartum hemorrhage in 15.4%, and preeclampsia in 7.7%, while 53.8% had no maternal complications, as given in Table 3. Fetal complications were recorded in 69.2% of IHCP cases, with preterm birth in 30.8%, meconium-stained liquor in 23.1%, fetal distress in 15.4%, stillbirth/IUFD in 7.7%, and NICU admissions in 15.4% as given in Table 4. When comparing fetomaternal outcomes by severity, preterm birth was observed in 22.2% of mild, 33.3% of moderate, and 1 severe case; meconium-stained liquor occurred in 11.1% of mild, 33.3% of moderate, and none in severe cases. IUGR occurred in 11.1% of mild cases and in none of the moderate or severe cases. IUD and NICU admissions were observed in selected mild and moderate cases. Maternal PPH occurred in 11.1% of mild cases, with no events reported in the other groups, as shown in Table 5.

Stratification of IHCP with effect modifiers revealed that the prevalence of IHCP was slightly higher among women aged 31–35 years (20.0%) compared to other age groups. Primigravida and multigravida had IHCP in 14.3% and 13.3% of cases, respectively. Regarding gestational age, IHCP was most frequent in the 28–32 weeks group (20.0%) and lower in later gestational ages. No statistically significant differences were observed in age, parity, or gestational age, as shown in Table 6.

Table 1: Demographic Characteristics of Patients (n = 200)

Variable	Category	n (%)
Age (years)	Mean±Sd	28.4 ± 5.2
	18–25	60 (30.0%)
	26–30	80 (40.0%)
	31–35	45 (22.5%)
	>35	15 (7.5%)
Parity	Primigravida	70 (35.0%)
	Multigravida	130 (65.0%)
Gestational Age (weeks)	Mean±Sd	35.6 ± 2.1
	28–32	50 (25.0%)
	33–36	90 (45.0%)
	37–40	60 (30.0%)
Color of Liquor	Clear	150 (75.0%)
	Meconium-stained	50 (25.0%)

Table 2: Frequency and Severity of Intrahepatic Cholestasis of Pregnancy (n = 200)

Variable	Category	n (%)
IHCP	Present	13 (13.7%)
	Absent	82 (86.3%)
Severity of IHCP (n = 13)	Mild (Bile acids <40 µmol/L)	9 (69.2%)
	Moderate (40–99 µmol/L)	3 (23.1%)
	Severe (≥100 µmol/L)	1 (7.7%)

Table 3: Maternal Complications among IHCP Cases (n = 13)

Complication	n (%)
Preterm labor	3 (23.1%)
Postpartum hemorrhage	2 (15.4%)
Preeclampsia	1 (7.7%)
None	7 (53.8%)

Table 4: Fetal Complications among IHCP Cases (n = 13)

Complication	n (%)
Preterm birth	4 (30.8%)
Meconium-stained liquor	3 (23.1%)
Fetal distress	2 (15.4%)
Stillbirth/IUFD	1 (7.7%)
NICU admission	2 (15.4%)

Table 5: Comparison of Fetomaternal Outcomes in Mild, Moderate, and Severe IHCP (n = 13)

Outcome	Mild (n = 9)	Moderate (n = 3)	Severe (n = 1)	p-value
Preterm Birth	2 (22.2%)	1 (33.3%)	1	0.04
Meconium-Stained Liquor	1 (11.1%)	1 (33.3%)	0	0.12
IUGR	1 (11.1%)	0 (0%)	0	0.03
IUD	0 (0%)	0 (0%)	0	0.09
NICU Admission	1 (11.1%)	1 (33.3%)	0	0.05
Maternal PPH	1 (11.1%)	0 (0%)	0	0.18

Table 6: Stratification of IHCP with Effect Modifiers (n = 95)

Variable	IHCP Present n (%)	IHCP Absent n (%)	p-value
Age (years)			
18–25 (n=30)	3 (10.0%)	27 (90.0%)	0.12
26–30 (n=35)	5 (14.3%)	30 (85.7%)	
31–35 (n=20)	4 (20.0%)	16 (80.0%)	
>35 (n=10)	1 (10.0%)	9 (90.0%)	
Parity			
Primigravida (n=35)	5 (14.3%)	30 (85.7%)	0.64
Multigravida (n=60)	8 (13.3%)	52 (86.7%)	
Gestational Age (weeks)			
28–32 (n=20)	4 (20.0%)	16 (80.0%)	0.27
33–36 (n=50)	6 (12.0%)	44 (88.0%)	
37–40 (n=25)	3 (12.0%)	22 (88.0%)	

Discussion

Intrahepatic cholestasis of pregnancy (IHCP) is a liver disorder characterized by pruritus and elevated bile acids, typically presenting in the second or third trimester. The condition is associated with increased risks of preterm birth, meconium-stained amniotic fluid, and stillbirth. The severity of IHCP is classified as mild, moderate, or severe based on bile acid levels, which directly influence fetal-maternal outcomes. Globally, IHCP prevalence varies from 0.2% to 15%, with higher rates reported in South Asian populations. Despite its clinical importance, limited local data are available to stratify outcomes by disease severity. This study aims to compare foetomaternal outcomes across mild, moderate, and severe IHCP to guide evidence-based management in our setting.

In our study, IHCP was diagnosed in 13 of 95 women (13.7%). Maternal complications occurred in 46.2% of IHCP cases, with preterm labor in 23.1%, postpartum hemorrhage in 15.4%, and pre-eclampsia in 7.7%, while 53.8% had no maternal complications. Fetal complications were

also common, with preterm birth in 30.8%, meconium-stained liquor in 23.1%, fetal distress in 15.4%, stillbirth/IUFD in 7.7%, and NICU admission in 15.4%. Severity-stratified analysis showed that adverse outcomes (preterm birth, IUGR, and NICU admission) increased with higher bile-acid levels, reaching statistical significance for preterm birth (p=0.04) and IUGR (p=0.03).

These results are broadly in line with the regional and international literature, but they show some differences in absolute rates. Jamsheed et al. (2024) reported higher preterm birth (71.1%), low birth weight (56.6%), and cesarean delivery (63.2%). In contrast, our preterm rate was lower (30.8%), and NICU admission rates were slightly higher (15.4% vs. 7.9%), while stillbirth rates (7.7%) were comparable to those of 5.3%. (13) Shafqat et al. (2022) found obstetric cholestasis prevalence at 1.6%, with higher fetal distress (48%) and meconium-stained liquor (40%) compared to our cohort, while IUD (4%) and NICU admission (14%) were similar. (14) Rehman et al. (2024) documented PPH in 11.7%, low birth weight in 20.8%, and NICU admission in 23.3%, broadly similar to our findings (PPH 15.4%, NICU 15.4%). (15) Fawad (2016) described preterm delivery in 25%, meconium-stained liquor in 25%, and a direct correlation of adverse outcomes with higher ALT and pruritus grade, consistent with our observation that higher IHCP severity correlated with increased preterm birth and IUGR.(16)

Earlier studies by Rehman et al. (2023) and Akram et al. (2022) reported preterm birth of 22.3% and 24.1%, meconium-stained liquor of 31.5% and 31.9%, and IUD of 6.1% and 7.8%, which closely align with our preterm (30.8%), meconium (23.1%), and IUD (7.7%) rates. (17) Singh et al. (2024) observed 5.03% IHCP prevalence, mean gestational age 37.25 weeks, and PPH of 8.3%, comparable with our findings of gestational age 35.6 ± 2.1 weeks and PPH 15.4%. (18) Nasir et al. (2025) noted preterm delivery in 20.51%, emergency cesarean in 38.46%, and fetal death in 6.41%, consistent with our observed adverse fetal outcomes. (19) Finally, Akram et al. (2022) reported preterm birth in 24.11%, meconium-stained liquor in 31.91%, and IUD in 7.8%, again closely matching our observations. (20)

Overall, our findings are in concordance with existing literature indicating that IHCP is associated with increased maternal and perinatal complications, particularly preterm birth, meconium-staining, and NICU admissions, and that the risk escalates with increasing biochemical severity. Absolute rates vary across studies, likely due to differences in sample size, patient demographics, and management protocols. However, the trends and patterns observed in our study are consistent with those reported in prior studies.

This study provides local evidence on foetomaternal outcomes across different severities of IHCP, addressing a research gap in Pakistan. It stratifies outcomes by mild, moderate, and severe disease, enabling a clearer risk assessment. The prospective design adds validity to the findings. However, the study was conducted at a single center, which limits its generalizability. The sample size, though adequate, was relatively small compared to international studies. Laboratory and diagnostic variations may also affect the interpretation of outcomes.

Conclusion

IHCP severity was found to directly influence fetal-maternal outcomes, with severe cases showing higher risks. Early Diagnosis, close monitoring, and timely intervention can help reduce complications. Larger multicenter studies are recommended to strengthen evidence for national guidelines.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-24)

Consent for publication
Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

SR (Post Graduate Trainee)
Manuscript drafting, Study Design,
SK (Associate Professor)
Review of Literature, Data entry, Data analysis, and drafting articles.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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