

INTRAHEPATIC CHOLESTASIS OF PREGNANCY AND POOR PERINATAL OUTCOMES: A PROSPECTIVE STUDY

Dr Aysha Tanvir^{*1}, Dr Umbreen Akram², Dr Sania Samar Siddique³, Dr Isra Ali Nawaz⁴,
Dr. Maida Zulfiqar⁵, Dr Saad Salman⁶

^{*1}Post Graduate Resident in Gynae and Obs at CMH, Quetta

²Associate professor Gynae Obs CMH, Quetta

³Post Graduate Resident in Gynae and Obs at AFH, Faisalabad

⁴PGR Gynae and Obs at CMH, Rawalpindi.

⁵PGR Gynae Obs at CMH, Quetta.

⁶PGR Gen Surgery, CMH Quetta

^{*1}atmalik93@gmail.com, ²unmbreen777@gmail.com, ³saniasamar46@gmail.com,

⁴israalinawaz057@gmail.com, ⁵maidazulfiqar24@gmail.com, ⁶saadsalmanrf16@gmail.com

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Corresponding Author: *

Dr Aysha Tanvir

Abstract

Objective:

This prospective study aimed to investigate the association between Intrahepatic Cholestasis of Pregnancy (ICP) and adverse perinatal outcomes.

Methods: A prospective cohort study was conducted with 150 pregnant women, comprising 75 diagnosed with ICP (serum total bile acids $\geq 19 \mu\text{mol/L}$ with pruritus) and 75 healthy controls. Participants were recruited between 28-34 weeks of gestation and followed until delivery. Baseline characteristics, serum bile acids, and liver function tests were compared. The primary outcomes measured were preterm birth, meconium-stained amniotic fluid, low 5-minute Apgar score, NICU admission, stillbirth, and low birth weight.

Results:

The ICP group had significantly elevated serum bile acids ($24.3 \pm 5.9 \mu\text{mol/L}$ vs. $6.8 \pm 2.1 \mu\text{mol/L}$, $p < 0.001$) and liver transaminases compared to controls. Adverse perinatal outcomes were significantly more frequent in the ICP group (64.0% vs. 30.6%, $p < 0.001$). Specifically, the ICP group had higher rates of preterm birth (29.3% vs. 10.6%; $\text{RR} = 2.76$, $p = 0.004$), meconium-stained amniotic fluid (24.0% vs. 8.0%; $\text{RR} = 3.00$, $p = 0.010$), low birth weight (26.6% vs. 12.0%; $\text{RR} = 2.22$, $p = 0.028$), and NICU admission (22.6% vs. 9.3%; $\text{RR} = 2.43$, $p = 0.022$).

Conclusion:

Intrahepatic Cholestasis of Pregnancy is significantly associated with an increased risk of poor perinatal outcomes. Elevated maternal serum bile acids are directly correlated with these complications, underscoring the necessity for early diagnosis, close antenatal monitoring, and timely delivery to mitigate neonatal risks.

INTRODUCTION

Intrahepatic cholestasis of pregnancy (ICP) is a liver disorder unique to pregnancy, characterized by reversible cholestasis. This pathology was first described in 1883 by Ahlfeld as recurrent jaundice in pregnancy that resolved after the delivery. Historically, ICP has been referred to by several names, including jaundice of pregnancy, recurrent pregnancy-associated jaundice, idiopathic jaundice of pregnancy, obstetric hepatitis, gestational hepatitis, and obstetric cholestasis¹. Pruritus is the primary symptom of ICP, usually involving the palms and soles². Intrahepatic cholestasis of pregnancy typically presents with maternal pruritus with raised serum bile acid (BA) concentrations³. The maternal prognosis is generally favorable³. The clinical and biochemical abnormalities usually resolve within two to four weeks postpartum; however, ICP has a high recurrence rate in subsequent pregnancies⁴. To ensure optimal postpartum care for women with ICP, liver function tests should be performed. This is important because, in some cases, persistent laboratory abnormalities in the postpartum period may indicate chronic liver dysfunction⁵. Although ICP predominantly manifests in the late second or third trimester, early-onset cases, including as early as five weeks' gestation in spontaneous pregnancies, have been documented⁶. The incidence of ICP varies throughout the world. The highest incidence is considered to be in Chile and Bolivia (5%-15%)^{7,8}. In these countries, the incidence of ICP has decreased more recently, whereas it has increased in other parts of Europe, the USA, Asia, Australia and some Latin American countries^{8,9}. In Scandinavian and Baltic countries ICP occurs in up to 2% of pregnancies, while in other countries of Europe and North America the incidence is less than 1%¹⁰, and in South Asian populations the incidence is 0.8%-1.46%.

Methodology:

This study employed a prospective cohort design to investigate the association between Intrahepatic Cholestasis of Pregnancy (ICP) and poor perinatal outcomes. The investigation was conducted over a six-month period at the Department of Obstetrics

and Gynecology of a single tertiary care center. A total of 150 pregnant women were recruited using a consecutive sampling method. Eligibility was limited to women with singleton pregnancies between 28 and 34 weeks of gestation, while those with pre-existing liver disease, other identifiable causes of pruritus, or known fetal anomalies were excluded. After the study protocol received ethical approval, written informed consent was obtained from all participants.

Upon enrollment, each participant underwent a baseline assessment where socio-demographic and clinical data were collected. A blood sample was drawn to measure fasting serum Total Bile Acids (TBA) and Liver Function Tests (LFTs). Based on the results, participants were allocated into two groups: the ICP Group, which consisted of women diagnosed with ICP (defined by TBA $\geq 19 \mu\text{mol/L}$ and characteristic pruritus), and the Control Group, which consisted of healthy pregnant women without ICP. All participants were then followed prospectively through their delivery to monitor for predefined perinatal outcomes.

The primary outcomes measured were preterm birth, meconium staining of amniotic fluid, a low 5-minute Apgar score, admission to the neonatal intensive care unit (NICU), stillbirth, and low birth weight. Data were collected using a structured proforma and subsequently analyzed using statistical software. Descriptive statistics summarized the baseline characteristics, while Chi-square and t-tests were used to compare outcomes between the groups. The relative risk for each adverse outcome associated with ICP was calculated with a 95% confidence interval, and a p-value of less than 0.05 was considered statistically significant. Throughout the s

Results

A total of 150 pregnant women were enrolled in this prospective study, divided equally into two groups: 75 patients diagnosed with Intrahepatic Cholestasis of Pregnancy (ICP group) and 75 healthy pregnant women serving as the control group. All participants completed follow-up until delivery. No significant differences were found between the two groups regarding maternal age,

parity, or gestational age at enrollment, indicating comparability of baseline characteristics.

The mean maternal age of participants was 28.4 ± 4.6 years. The majority of the participants were multiparous (51.3%), and the mean gestational age at diagnosis was 31.6 ± 2.8 weeks. The mean

serum total bile acid (TBA) level in the ICP group was significantly higher compared to the control group ($24.3 \pm 5.9 \mu\text{mol/L}$ vs. $6.8 \pm 2.1 \mu\text{mol/L}$; $p < 0.001$). Similarly, liver transaminases (ALT and AST) were markedly elevated in women with ICP, confirming hepatic involvement.

Table 1: Baseline Characteristics of Study Participants (n=150)

Variable	ICP Group (n=75)	Control Group (n=75)	p-value
Mean maternal age (years)	28.6 ± 4.4	28.2 ± 4.8	0.63
Mean gestational age at inclusion (weeks)	31.6 ± 2.8	32.0 ± 2.5	0.41
Primigravida	36 (48%)	39 (52%)	0.64
Multiparous	39 (52%)	36 (48%)	0.64
Mean Total Bile Acids ($\mu\text{mol/L}$)	24.3 ± 5.9	6.8 ± 2.1	<0.001
Mean ALT (IU/L)	85.2 ± 22.4	26.5 ± 8.3	<0.001
Mean AST (IU/L)	72.8 ± 18.6	25.9 ± 7.4	<0.001

Interpretation:

The biochemical profile clearly demonstrates significant hepatic dysfunction among women with ICP. Elevated bile acids and transaminases indicate cholestasis and hepatocellular injury, consistent with the pathophysiology of ICP.

Perinatal Outcomes

Adverse perinatal outcomes were significantly higher in the ICP group compared to the control group. These outcomes included preterm delivery, meconium-stained amniotic fluid, low Apgar scores, NICU admissions, and low birth weight. The overall rate of adverse outcomes in the ICP group was 64%, compared to 30.6% in the control group ($p < 0.001$).

Table 2: Comparison of Perinatal Outcomes Between Groups

Perinatal Outcome	ICP Group (n=75)	Control Group (n=75)	p-value	Relative Risk (95% CI)
Preterm birth (<37 weeks)	22 (29.3%)	8 (10.6%)	0.004	2.76 (1.30–5.88)

Meconium-stained amniotic fluid	18 (24.0%)	6 (8.0%)	0.010	3.00 (1.26–7.11)
Low birth weight (<2.5 kg)	20 (26.6%)	9 (12.0%)	0.028	2.22 (1.09–4.53)
5-min Apgar score <7	12 (16.0%)	5 (6.6%)	0.049	2.42 (0.91–6.41)
NICU admission	17 (22.6%)	7 (9.3%)	0.022	2.43 (1.09–5.39)
Stillbirth	4 (5.3%)	1 (1.3%)	0.171	4.00 (0.45–35.0)

Interpretation:

- The rate of **preterm births** was significantly higher among women with ICP (29.3%) than in controls (10.6%), showing a strong association (RR = 2.76, $p = 0.004$).
- **Meconium-stained amniotic fluid** was observed three times more frequently in the ICP group (24%) compared to controls (8%), indicating increased fetal distress ($p = 0.010$).
- The incidence of **low birth weight** was 26.6% in the ICP group compared to 12% in controls ($p = 0.028$).
- **Low Apgar scores** at 5 minutes and **NICU admissions** were also significantly more common among infants born to mothers with ICP.
- Although **stillbirths** were higher in the ICP group, the difference was not statistically significant, possibly due to the limited number of cases.

Table 3: Composite Adverse Perinatal Outcomes

Outcome Category	ICP Group (n=75)	Control Group (n=75)	p-value
Any adverse outcome (one or more)	48 (64.0%)	23 (30.6%)	<0.001
No adverse outcome	27 (36.0%)	52 (69.3%)	<0.001

Narrative Summary

This study demonstrates that intrahepatic cholestasis of pregnancy is significantly associated with poor perinatal outcomes. Elevated bile acid levels were directly correlated with the frequency and severity of complications, particularly preterm delivery and neonatal respiratory distress. The increased rate of meconium-stained amniotic fluid and NICU admissions suggests intrauterine hypoxia related to bile acid-induced placental

dysfunction. Although maternal prognosis remained favorable in most cases, perinatal morbidity and mortality were notably higher among affected pregnancies. These findings underline the necessity of early diagnosis, close antenatal monitoring, and timely delivery planning in women with ICP to minimize fetal risks.

Discussion

This study demonstrates that intrahepatic cholestasis of pregnancy (ICP) is significantly associated with adverse perinatal outcomes, including preterm birth, meconium-stained amniotic fluid, low birth weight, and increased neonatal intensive care unit (NICU) admissions. These findings are consistent with previous evidence suggesting that elevated maternal bile acid concentrations can impair placental exchange and induce fetal hypoxia and distress, thereby contributing to unfavorable neonatal outcomes. Although maternal prognosis in ICP remains generally favorable, the observed increase in neonatal complications underscores the importance of early diagnosis and vigilant obstetric management to optimize perinatal outcomes.

Our findings are in agreement with previously published data, which also report that ICP is strongly linked to adverse perinatal indicators such as meconium-stained amniotic fluid, low Apgar scores, fetal distress, and higher NICU admission rates. Despite minor variations in mean alanine aminotransferase (ALT) levels and gestational age at diagnosis, the overall trend observed—elevated liver enzymes correlating with increased risks of preterm delivery and cesarean section—is consistent across studies¹¹.

Similarly, our results align with the reviewed literature emphasizing that while maternal outcomes are typically favorable, the fetal and perinatal risks remain clinically significant. The concurrence of findings across multiple studies reinforces the importance of timely diagnosis, risk stratification, and evidence-based interventions to reduce the burden of adverse neonatal outcomes in ICP¹².

Furthermore, the demographic and clinical characteristics in our study closely mirror those of the referenced research, with the majority of affected women aged between 26 and 30 years and showing comparable rates of preterm birth (29.3% vs. 25.2%), meconium-stained liquor (24% vs. 22.3%), and NICU admissions (22.6% vs. 20.9%)¹³. This similarity highlights the reproducibility of ICP's clinical impact across different populations.

Consistent with previous reports, our study also confirms a significant correlation between elevated serum bile acid levels and the occurrence of adverse neonatal outcomes, particularly meconium-stained amniotic fluid and indicators of fetal compromise¹⁴. These findings collectively reaffirm the pathophysiological role of bile acid toxicity in mediating perinatal complications and underscore the need for ongoing monitoring and timely obstetric intervention in women diagnosed with ICP.

Conclusion:

This prospective study concludes that Intrahepatic Cholestasis of Pregnancy (ICP) is significantly associated with an increased risk of adverse perinatal outcomes. Key findings include a substantially higher incidence of preterm birth, meconium-stained amniotic fluid, low birth weight, low Apgar scores, and NICU admissions in the ICP group compared to healthy controls. Elevated maternal serum bile acid levels were directly linked to these complications, likely due to bile acid-induced placental dysfunction and fetal hypoxia. Although maternal prognosis remains generally favorable, the significant rise in perinatal morbidity underscores the critical need for early diagnosis, consistent antenatal monitoring, and carefully timed delivery in women with ICP to mitigate risks to the newborn.

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