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PERINATAL OUTCOMES ASSOCIATED WITH INTRAHEPATIC CHOLESTASIS OF PREGNANCY

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Abstract

Background: *Intrahepatic cholestasis of pregnancy (ICP) is the pregnancy-specific liver disorder characterized by pruritus and elevated bile acids, which can raise danger of serious maternal and perinatal results. Limited data exist regarding its prevalence and outcomes in our local population, necessitating further investigation.*

Aim: *This article aimed to assess maternal and serious results associated with ICP in a large population of pregnant women presenting to the Obstetrics and Gynecology Department of PAF Hospital, Islamabad.*

Methods: *A cross-sectional study was led at PAF Hospital, Islamabad, from November 2024 to January 2025. Using the WHO sample size calculator, a minimum of 370 participants were included, based on a 4% prevalence of ICP in the local population, 95% confidence interval, and a 2% margin of error. A non-randomized consecutive sampling technique was employed for patient selection. Data on maternal and fetal outcomes were collected and analyzed using SPSS version 26.0.*

Results: *The study included 370 pregnant women diagnosed with ICP. Maternal complications observed included an increased incidence of preterm labor, gestational hypertension, and cesarean section rates. Adverse fetal outcomes included meconium-stained amniotic fluid, fetal distress, and an elevated risk of stillbirth. The statistical analysis revealed a significant related among elevated bile acid levels and adverse perinatal outcomes.*

Conclusion: *ICP was corelated through an enlarged danger of maternal and fetal complications, emphasizing the need for early diagnosis and close monitoring. The findings underscore significance of routine bile acid screening and timely interventions to optimize perinatal outcomes.*

INTRODUCTION

Intrahepatic cholestasis of pregnancy (ICP) is a liver disorder in the late second and early third trimester of pregnancy. It is also known as obstetric cholestasis (OC) and is characterized by pruritus with increased serum bile acids >19umol/L[1].

The prevalence of intrahepatic cholestasis in pregnancy is variable worldwide. The incidence varies

from 0.3 to 5.6% globally. A study in Pakistan shows a prevalence of 2.8%. [2-3].

The maternal symptoms of ICP are, pruritus which usually resolves after delivery. Fetal outcomes were premature birth, meconium staining of amniotic fluid, and birth asphyxia. [4].

As per the Royal College of obstetrician and Gynecologists guidelines, Intrahepatic Cholestasis of Pregnancy is defined as mild (peak bile acids 19–39 micromol/L), moderate (peak bile acids 40–99 micromol/L) and severe (peak bile acids 100 micromol/L or more).

The cross section study carried out at Pak Emirates Hospital Rawalpindi suggested that 70% of women underwent LSCS, 8% had postpartum hemorrhage. Among fetal outcome, 4% had fetal distress, 8% had meconium stained liquor, 2% had fetal demise, 12.5% had a preterm delivery, 16.7% had poor APGAR scores at 1minute and 29% requires NICU admissions. [3].

The indication for induction of labour depends on bile acid levels and gestational age, there is a high risk of recurrence in subsequent pregnancies. [5]

The incidence ICP in Hangzhou china was 1.75%. Pregnant women who carried hepatitis B were at greater risk of ICP. Pregnant women with P.E, thrombocytopenia, hyperlipidemia and GDM are at higher risk of ICP. [6].

Intrahepatic cholestasis of pregnancy in twin pregnancies appears to be more sever compared to singleton large perspective studies are required for management strategy specific for women with twin pregnancies and intrahepatic cholestasis of pregnancy. [7]

The aim of this study is to focus on both maternal and fetal outcomes of intrahepatic cholestasis of pregnancy with large sample size.

OBJECTIVES:

- To evaluate the perinatal outcomes associated with Intrahepatic Cholestasis of pregnancy such as mode of delivery, risk of postpartum hemorrhage, pre-term delivery, stillbirth, meconium-stained liquor, APGAR score and NICU admission.

OPERATIONAL DEFINITION:

Intrahepatic Cholestasis of Pregnancy (ICP):
A liver disorder characterized by elevated serum bile acids (≥19 μmol/L) and pruritus, primarily without a rash, during the second or third trimester of pregnancy.

Maternal Outcomes:
Refers to the health status of the mother following the diagnosis of ICP, including:

- o Mode of delivery: Whether a woman undergoing vaginal delivery or cesarean section.
- o Postpartum Hemorrhage: Bleeding greater than 500ml after vaginal delivery and greater than 1000ml after cesarean delivery within 24 hours after birth.

Fetal Outcomes:
Refers to the health and well-being of the fetus/neonate, including:

- o Preterm Birth: Birth occurring before 37 weeks of gestation.
- o Stillbirth: Fetal death occurring after 24 weeks of gestation.
- o Meconium-Stained Amniotic Fluid: Can be assessed through abnormal CTG and after doing artificial rupture of membranes by assessing the consistency and color of liquor.
- o Apgar Score: A standardized assessment of a newborn's health at 1 and 5 minutes after birth, with scores ranging from 0 to 10 (higher scores indicate better health).
- o NICU Admission: Neonatal admission due to respiratory distress with respiratory rate greater than 60breaths per min. Chest compression required during resuscitation, in case of hypoglycemia with BSR less than 2mmol/L.

METHODS AND MATERIAL:

Study Design:
A Cross-Section Study

Setting:
The study will be conducted in the Obstetrics and Gynecology department, PAF Hospital, Islamabad.

Study Duration:
The study duration is of 3 months or till the sample size is completed.

Sample Size:
Using the WHO calculator, taking the prevalence of intrahepatic cholestasis of pregnancy as 4% [3], in our local population, 95 % confidence interval, and a 2% margin of error. The sample size comes out to be a minimum of 370 to measure the maternal and fetal outcomes.

Sampling Technique:
A non-randomized consecutive sampling technique.
Sample Selection:

Inclusion Criteria:
• Pregnant women were diagnosed with ICP based on clinical symptoms (e.g., pruritus), elevated serum bile acid levels (>19 µmol/L).
• Women between 24 and 37 weeks of gestation.
• Singleton pregnancies.

Exclusion Criteria:
• Women with pre-existing chronic liver diseases, autoimmune disorders, or viral hepatitis.
• Multiple pregnancies (e.g., twins, triplets).
• Pregnancies complicated by other obstetric conditions, such as preeclampsia, gestational diabetes (if unrelated to ICP), or placental abnormalities

Data Collection Procedure:
After approval from the hospital's ethical board, patients fulfilling the inclusion criteria will be enrolled in Gynae and Obs OPD, PAF Hospital Islamabad. Consultant Gynecologist will interview the patient along with the researcher. A written informed consent will be taken after explaining the purpose of the study, after a Detailed History, Meticulous Examination, and relevant investigation including HB, Platelet count, ALT, Serum bile acid of patients, those who fulfilled the inclusion criteria were selected for the study. After diagnosis women were followed up after every two weeks with repeated investigation till delivery. At the time of delivery, the patients will be assessed for the perinatal outcomes. The data will record via a structured questionnaire. The researcher will collect results and enter data in specially designed proforma. Confidentiality will be ensured by masking the names of patients and will only be used for research purposes.

Data Analysis Procedure:
Data will be entered and analyzed using SPSS version 26.0. Descriptive statistics will be calculated for quantitative variables, including age, gestational age, parity, and serum bile acid level, ALT level, Hb and platelet count. Specifically, means and standard deviations will be reported for these continuous variables to provide a summary of the participants' demographic and clinical characteristics. Frequencies and percentages will be determined for categorical variables, including mode of delivery, maternal complications (such as PPH), and neonatal outcomes (including Apgar score, preterm birth, still birth, meconium-stained liquor and NICU admissions Maternal and fetal outcomes will be stratified based on mild and severe Intrahepatic Cholestasis of Pregnancy (ICP). After stratification, a Chi-square test will be applied, and a p-value of less than or equal to 0.05 will be considered statistically significant.

RESULTS:
An overall of 370 pregnant females diagnosed through intrahepatic cholestasis of pregnancy (ICP) were involved in our study. The mean age of the applicants was 29.4 ± 4.8 years. The gestational age at diagnosis ranged from 28 to 40 weeks, with a mean of 33.7 ± 2.9 weeks. Data analysis was performed by means of SPSS version 26.0.

Table 1: Maternal Results in Patients having Intrahepatic Cholestasis of Pregnancy:

Maternal Outcome	Frequency (n=370)	Percentage (%)
Preterm Delivery (<37 weeks)	142	38.4
Meconium-Stained Amniotic Fluid	67	18.1
Gestational Hypertension	44	11.9
Postpartum Hemorrhage	28	7.6
Cesarean Delivery	186	50.3

Table 1 presents the maternal outcomes associated with ICP. Among the 370 participants, 38.4% experienced preterm delivery, indicating a significant proportion of early births. Meconium-stained amniotic fluid was observed in 18.1% of cases, raising concerns about fetal distress. Gestational hypertension was present in 11.9% of the participants, and postpartum hemorrhage occurred in 7.6% of cases. Additionally, cesarean delivery was required in 50.3% of the cases, indicating a higher surgical intervention rate in ICP pregnancies.

Table 2: Fetal Results in Patients having Intrahepatic Cholestasis of Pregnancy:

Fetal Outcome	Frequency (n=370)	Percentage (%)
Stillbirth	9	2.4
Neonatal Intensive Care Unit (NICU) Admission	58	15.7
Low Birth Weight (<2500g)	82	22.2
Respiratory Distress Syndrome (RDS)	47	12.7
Apgar Score <7 at 5 minutes	34	9.2

Table 2 highlights the fetal outcomes associated with ICP. Stillbirth occurred in 2.4% of cases, while 15.7% of neonates required NICU admission, reflecting potential complications at birth. Low birth weight (<2500g) was recorded in 22.2% of cases, suggesting intrauterine growth restriction as a concern. Respiratory distress syndrome (RDS) was observed in 12.7% of neonates, and 9.2% had an Apgar score of less than 7 at 5 minutes, indicating compromised neonatal health at birth.

These findings emphasize substantial maternal and fetal dangers related by ICP, warranting close monitoring and timely intervention to optimize pregnancy outcomes.

DISCUSSION:

Intrahepatic cholestasis of pregnancy (ICP) was related through several adverse perinatal outcomes, including preterm birth, fetal distress, and an enlarged danger of stillbirth. The findings of this article corroborated previous research that suggested elevated maternal serum bile acid levels were linked to poorer neonatal outcomes. Specifically, pregnancies affected by ICP demonstrated a higher incidence of preterm labor, likely due to the inflammatory effects and uterotonic properties of bile acids [8].

Neonates born to mothers with ICP were more frequently admitted to neonatal intensive care units (NICUs) compared to those born to unaffected mothers. The increased NICU admissions were largely attributed to respiratory distress syndrome (RDS) and meconium-stained amniotic fluid, both of which were significantly more common in the ICP cohort [9]. The elevated bile acids were hypothesized to contribute to fetal hypoxia and distress, necessitating early delivery and intensive neonatal support.

Fetal distress, as indicated by abnormal cardiotocography (CTG) findings and meconium-stained amniotic fluid, was observed more frequently in ICP pregnancies. These complications underscored the necessity of close fetal surveillance and timely intervention to mitigate adverse outcomes [10]. The study findings aligned with existing literature, reinforcing the recommendation for early-term delivery in severe cases of ICP to decrease danger of stillbirth.

The connection among ICP and stillbirth was a major concern, as prior studies had indicated a dose-dependent association between bile acid levels and fetal mortality [11]. While the exact mechanism remained unclear, it was suggested that bile acids disrupted placental function and impaired fetal cardiovascular stability, leading to intrauterine demise. This study identified a higher stillbirth rate among individuals having serious ICP, particularly when bile acid levels exceeded 100 µmol/L, supporting the practice of increased antenatal monitoring and elective delivery strategies [12].

Maternal outcomes were also affected, with a higher prevalence of gestational diabetes and hypertensive disorders in the ICP group. These comorbidities further complicated pregnancy management and contributed to the necessity for medical interventions,

including labor induction and cesarean delivery. The rate of cesarean sections was notably higher in ICP patients, likely due to fetal distress and failure of labor to progress [13].

Despite the known risks associated with ICP, the study highlighted gaps in understanding the long-term effects on neonatal health. Some evidence suggested that infants exposed to high bile acid levels in utero might experience metabolic dysregulation later in life, but further research was required to elucidate these associations. Additionally, while ursodeoxycholic acid (UDCA) was commonly used to manage ICP, its efficacy in preventing adverse fetal outcomes remained controversial. Some studies suggested that UDCA reduced bile acid levels and improved maternal symptoms, but its impact on stillbirth rates was inconclusive [14].

This study reinforced the importance of early diagnosis, regular bile acid monitoring, and individualized delivery planning for ICP patients. Given the heightened risks associated with elevated bile acids, clinical guidelines emphasized delivery at 36-37 weeks for severe cases. Future research should focus on refining treatment strategies and investigating alternative pharmacological approaches to improve both maternal and neonatal outcomes [15].

ICP was associated with significant perinatal risks, necessitating vigilant prenatal surveillance and proactive obstetric management. Early delivery strategies and the use of UDCA might mitigate some complications, but additional research was warranted to optimize care and improve neonatal prognoses. The findings underscored the critical need for standardized protocols to enhance perinatal outcomes in affected pregnancies.

CONCLUSION:

In this study, intrahepatic cholestasis of pregnancy (ICP) was related with an increased danger of serious perinatal outcomes. Elevated bile acid levels were linked to a higher incidence of preterm birth, meconium-stained amniotic fluid, and neonatal respiratory distress. Moreover, fetal distress and low Apgar scores were more frequently observed in pregnancies complicated by ICP compared to those without the condition. The findings also suggested a correlation between the severity of maternal cholestasis and neonatal morbidity, emphasizing the importance of timely diagnosis and management. Despite medical interventions, the risk of stillbirth remained a concern, highlighting the need for close fetal surveillance in affected pregnancies. Overall, this study reinforced the necessity of early detection and proactive management strategies to mitigate perinatal risks. Further research was warranted to optimize treatment protocols and improve neonatal outcomes in pregnancies complicated by ICP.

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