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ORIGINAL ARTICLE

Fetomaternal Outcomes in Pregnant Women with Intrahepatic Cholestasis of Pregnancy in Third Trimester

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ABSTRACT

Objective: To determine the fetal outcome in pregnant women with intrahepatic cholestasis in the third trimester.
Methodology: Patients aged 18 to 45, with a gestational age of at least 24 weeks and a diagnosis of intrahepatic cholestasis of pregnancy, were included. Exclusion criteria included having cholelithiasis or choledocholithiasis on ultrasonography, having a shrunken or echogenic liver on ultrasonography, having a platelet count of less than 100,000/microlitre at study enrollment, having a diagnosis of PIH or pre-eclampsia, or not knowing their LMP. Under the guidance of a specialist gynaecologist with at least three years of post-fellowship experience, the researcher herself evaluated each participant every two weeks and monitored them till birth.
Results: Preterm delivery in 38 (25.33%), NICU admission in 23 (15.33%), meconium-stained liquor in 13 (8.67%), cesarean delivery in 85 (56.67%), postpartum hemorrhage in 53 (35.33%), and perinatal death in 11 (7.33%) were the fetomaternal outcomes in this study among pregnant women with intrahepatic cholestasis of pregnancy in the third trimester.
Conclusion: IHCP is linked to negative outcomes for both the mother and the fetus (preterm, NICU admission, and perinatal death).
Keywords: Intrahepatic cholestasis, NICU, Outcome, Perinatal death, Preterm Outcome

Authors' Contribution:
[1,2]Conception; Literature research; manuscript design and drafting; [1,2]Critical analysis and manuscript review; [1,2]Data analysis; Manuscript Editing.

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Article info:
Received: February 24, 2026
Accepted: May 25, 2026

Cite this article. Akhter A, Ikram M. Fetomaternal Outcomes in Pregnant Women with Intrahepatic Cholestasis of Pregnancy in Third Trimester. J Islamabad Med Dental Coll. 2026; 15(2): 129-134. *DOI: https://doi.org/10.35787/jimdc.v15i2.1505*

Funding Source: Nil
Conflict of interest: Nil

Introduction

One common pregnancy-related disease is intrahepatic cholestasis of pregnancy (ICP). It is typified by abnormal liver function tests that usually go away in the postpartum phase, as well as maternal pruritus and elevated serum bile acid levels that cause maternal pruritus. Preterm birth, fetal distress, stillbirth, and neonatal hospitalization are all linked to intrahepatic cholestasis during pregnancy, according to earlier research.[1,2]

Problems arise when maternal bile acids build up in the amniotic fluid after being transferred to the fetus via the placenta. Women with ICP are also more likely to experience premature labor, which may be linked to bile acid buildup in the uterine myometrium that causes an increase in uterine activity.[3] The most worrisome consequence of ICP is sudden fetal mortality, which may be related to the harmful effects of bile acids on the fetal heart, which can result in arrhythmias and chorionic vasospasm, which deprives the fetus of oxygenated blood from the mother, causing hypoxia. The risk of fetal death

rises as bile acid levels rise, and it is much higher when bile acid levels exceed 100 micromole/L.[4-8]

Research on the local contextual factors in ICP in relation to feto-maternal outcomes is scarce in poor nations. To create effective therapeutic, diagnostic, and prevention plans, research should be done. Our study's justification is to assess feto-maternal outcomes in ICP. In order to lessen the strain on the already limited resources, my study will draw attention to the burden of those complications in the index population, particularly in relation to the severity of ICP. It may also aid in the development of guidelines for the management of ICP cases.

Methodology

This case series study was carried out in the obstetrics and gynaecology department of Shaikh Zayed Hospital in Lahore between January and June of 2025. The ethical review board of the hospital approved it. A sample size of 150 with a 95% confidence level, an 8% margin of error, and a 40.0%8 premature delivery rate in intrahepatic cholestasis of pregnancy was determined using the WHO calculator for single proportion. Patients of aged 18 to 45, with a gestational age of at least 24 weeks and a diagnosis of intra-hepatic cholestasis of pregnancy (serum bile acid level ≥ 10 mmol/L, at least 1.5 times elevated from the upper limit of normal serum aspartate transferase (AST) (normal upper limit is 40 IU/ml), negative viral hepatitis serology for HAV, HBV, HCV, and HEV (measured using the ELISA method), and normal abdominal ultrasound for liver). Exclusion criteria included having a cholelithiasis or choledocholithiasis on ultrasonography, having a shrunken or echogenic liver on ultrasonography, having a platelet count of less than 100,000/microliter at study enrolment, having a diagnosis of PIH or pre-eclampsia, or not knowing their LMP.

Each participant's informed consent was obtained. Participants received assurances regarding anonymity and the fact that there was no patient risk associated with this study. The researcher herself inquired about age, LMP, parity, and gestational age. The hospital's central laboratory conducted a liver function test and measured the serum bile acid level. Both gestational hyperglycemia and intrahepatic cholestasis were diagnosed. In every instance, viral hepatitis serology was examined. A hospital consultant radiologist with at least three years of post-fellowship experience performed the liver ultrasonography. Under the guidance of a specialist gynecologist with at least three years of post-fellowship experience, the researcher herself evaluated each participant every two weeks and monitored them till birth. Ursodeoxycholic acid (cap. Urso 500mg per-oral BID) was prescribed to the participants. In order to relieve pruritis, chlorpheniramine (Tab. Piriton 4m HS) will also be given in all ICP instances. Every two weeks, the researcher followed up with each woman until delivery, overseen by a consultant gynecologist with at least two years of post-fellowship experience. LMP scheduled the delivery for weeks 37–38 of pregnancy. A consultant paediatrician also evaluated all delivered new-borns at birth, and the researcher herself monitored the parameters listed in the fetal outcome factors. A freshly created proforma was used to record all of the data.

SPSS-24 was used to enter and analyze the data. The data's normality was evaluated using the Shapiro-Wilks Normality Test. For quantitative variables such maternal age and the mother's serum bile acid level at enrollment, mean and standard deviation or median and IQR were computed. For the fetal outcome variables (perinatal neonatal death, preterm delivery, and neonatal unit admission) and ICP severity,

frequencies and percentages were computed. Age groups, parity, the severity of ICP, gestational age at delivery, gestational diabetes, and post-stratification using the chi square test were used to stratify the fetal outcome variables, and a p-value of less than 0.05 was deemed significant.

Ethical approval of the study was taken from Shaikh Zayed Hospital, Lahore (Ref No. TERC/NHRC-SZH-INT-SC-825) dated.29.07.2025.

Results

The study's participants ranged in age from 18 to 45, with a mean age of 28.87 ± 4.16 years. Ninety-two (61.33%) of the patients were in the 18–30 age range. An average gestational age of 28.87 ± 4.41 weeks was recorded. 3.17 ± 0.88 was the mean parity. Table I displays the distribution of patients with additional confounding variables.

Table I: Distribution of patients with other confounding variables (n=150)

		No. of Patients	Percentage
Age (in years)	**18-30**	92	61.33
	31-45	58	38.67
Gestational age (weeks)	**24-32**	98	65.33
	>32	52	34.67
Parity	**0-3**	100	66.67
	4-5	50	33.33
Gestational diabetes mellitus	**Yes**	60	40.0
	No	90	60.0
Severity of ICP	**Mild**	33	22.0
	Moderate	71	47.33
	Severe	46	30.67

Table II: Fetomaternal outcome in pregnant women with intrahepatic cholestasis of pregnancy in third trimester

Fetomaternal outcome	**Frequency (%)**	
	yes	no
Cesarean section	85 (56.67%)	65 (43.33%)
Postpartum hemorrhage	53 (35.33%)	97 (64.67%)
Meconium-stained liquor	13 (8.67%)	137 (91.33%)
5-minute apgar score <7	28 (18.67%)	122 (81.33%)
Preterm birth	38 (25.33%)	112 (74.67%)
NICU admission	23 (15.33%)	127 (84.67%)
Perinatal death	11 (7.33%)	139 (92.67%)

Table III: Stratification of the fetomaternal outcome with respect to age.

		18-30 (n=135)	**31-45 (n=82)**	**P-value**
Cesarean section	Yes	95	57	**0.894**
	No	40	25	
Postpartum hemorrhage	Yes	39	14	**0.049**
	No	96	68	
Meconium-stained liquor	Yes	12	01	**0.021**
	No	123	81	
5-minute apgar score <7	Yes	18	10	**0.808**
	No	117	72	
Preterm birth	Yes	29	09	**0.048**
	No	106	73	
NICU admission	Yes	16	07	**0.442**
	No	119	75	
Perinatal death	Yes	06	05	**0.590**
	No	129	77	

Table IV: Stratification of the fetomaternal outcome with respect to gestational age.				
		24-32 weeks (n=98)	>32 weeks (n=52)	P-value
Cesarean section	Yes	57	28	**0.612**
	No	41	24	
Postpartum hemorrhage	Yes	31	22	**0.193**
	No	67	30	
Meconium stained liquor	Yes	10	03	**0.358**
	No	88	49	
5 minute apgar score <7	Yes	17	11	**0.569**
	No	81	41	
Preterm birth	Yes	23	15	**0.390**
	No	75	35	
NICU admission	Yes	19	04	**0.058**
	No	79	48	
Perinatal death	Yes	07	04	**0.902**
	No	91	48	

Preterm delivery in 38 (25.33%), NICU admission in 23 (15.33%), meconium-stained liquor in 13 (8.67%), cesarean delivery in 85 (56.67%), postpartum hemorrhage in 53 (35.33%), and perinatal death in 11 (7.33%) were the fetomaternal outcomes in this study among pregnant women with intrahepatic cholestasis of pregnancy in the third trimester. Tables III and IV respectively, illustrate the stratification of the fetomaternal outcome by age, gestational age, and parity. Table VI and VII, respectively, illustrate the stratification of the fetomaternal outcome according to the severity of ICP and GDM.

Discussion

The liver condition known as intrahepatic cholestasis of pregnancy (IHCP), which usually manifests in the second or third trimester, is characterized by pruritus and increased bile acids. Increased risks of stillbirth, meconium-stained amniotic fluid, and premature birth are linked to the disorder. Bile acid levels, which have a direct impact on fetal-maternal outcomes, are used to categorize IHCP severity as mild, moderate, or severe. IHCP prevalence ranges from 0.2% to 15% worldwide, with South Asian communities reporting greater rates. There is insufficient local data to stratify outcomes by disease severity, despite its clinical significance. To inform evidence-based care in our context, this study compares the fetal outcomes of mild, moderate, and severe IHCP.

Preterm delivery in 38 (25.33%), NICU admission in 23 (15.33%), meconium-stained liquor in 13 (8.67%), cesarean delivery in 85 (56.67%), postpartum hemorrhage in 53 (35.33%), and perinatal death in 11 (7.33%) were the fetomaternal outcomes in our study of pregnant women with intrahepatic cholestasis of pregnancy in the third trimester. Rook M. et al. conducted research at San Francisco General Hospital on 101 ICP cases, 33% of births had fetal problems. Fetal distress, meconium staining of the amniotic fluid, and respiratory distress were the most frequent perinatal problems. None of the patients experienced fetal death. Five out of eighteen patients in the TBA <10 group (28%), ten out of thirty-four patients in the TBA 10–40 group (29%), three out of sixteen in the TBA 40–100 group (19%), and three out of five in the TBA >100 group (60%) experienced fetal complications.[5]

Another study by Glantz A et al. indicated that for every micromol/L of serum bile acid, the likelihood of fetal problems (spontaneous preterm births, asphyxial episodes, and meconium staining of amniotic fluid, placenta, and membranes) increased by 1% to 2%. Fetal problems did not appear until bile acid levels were > or = 40 micromol/L, according to

complementary investigations. In total, 24% of ICP cohorts had meconium staining, and 0.4% had intrauterine fetal death.[6]

Seventy consecutive women who gave birth at Ataturk University Hospital between January 2012 and December 2017 were the subject of another study. 61 (87%) of the women had high liver transaminases. The preterm delivery rate was 40% (28 women gave birth spontaneously at ≤36 weeks gestation), and the median week of delivery was 37 (range, 26–42). There were eight (11%) women with preeclampsia. Neither neonatal death nor stillbirth occurred.[8]

Although there are some variations in absolute rates, these results generally agree with the regional and international literature. Higher rates of preterm birth (71.1%), low birth weight (56.6%), and cesarean delivery (63.2%) were reported by Jamsheed et al. (2024). Our NICU admission rates were somewhat higher (15.33% vs. 7.9%), our preterm rate was lower (25.33%), and our stillbirth rates (7.33%) were similar to those of 5.3%.[9]

In comparison to our cohort, Shafqat et al. (2022) reported a 1.6% prevalence of obstetric cholestasis, with greater rates of fetal distress (48%) and meconium-stained liquor (40%), but similar rates of IUD (4%) and NICU stay (14%).[10] Our results (PPH 35.33%, NICU 15.33%) are mostly consistent with those of Rehman et al. (2024), who reported PPH in 11.7%, low birth weight in 20.8%, and NICU admission in 23.3%.[11] In agreement with our finding that higher IHCP severity was associated with higher preterm birth and IUGR, Fawad (2016) reported preterm delivery in 25% of cases, meconium-stained liquor in 25% of cases, and a direct association with poor outcomes with higher ALT and pruritus grade.[12] Preterm birth rates of 22.3% and 24.1%, meconium-stained liquor rates of 31.5% and 31.9%, and IUD rates of 6.1% and 7.8% were reported in earlier studies by Rehman et al. (2023) and Akram et al. (2022). These findings are in good agreement with our preterm (25.22%), meconium (8.67%), and IUD (7.33%) rates.[13] Our results of gestational age 28.87 ± 4.41 weeks and PPH 15.4% are similar to Singh et al. (2024), who reported 5.03% IHCP prevalence, mean gestational age 37.25 weeks, and PPH of 8.3%.[14]

In line with our observed unfavorable fetal outcomes, Nasir et al. (2025) reported preterm delivery in 20.51%, emergency cesarean in 38.46%, and fetal death in 6.41%.[15] Lastly, Akram et al. (2022) observed meconium-stained liquid in 31.91%, IUD in 7.8%, and premature birth in 24.11%, all of which closely matched our findings.[16]

According to one study, preterm delivery (20.51%) and emergency caesarean section (38.46%) were the most frequent pregnancy complications. Five cases (6.41%) of intrapartum fetal death, one stillbirth (2.5%), and seven cases (8.97%) of spontaneous premature delivery were reported. 13.7% of participants in a local study experienced IHCP, with mild, moderate, and severe cases making up 69.2%, 23.1%, and 7.7% of the total. Of IHCP instances, 69.2% had fetal problems and 46.2% had maternal difficulties. The more severe IHCP, the higher the rate of preterm birth and NICU admissions. According to recent studies, women with ICP are far more likely than women with normal pregnancies to use IUDs.[17-21]

All things considered, our results are consistent with previous research showing that IHCP is linked to a higher risk of maternal and perinatal problems, specifically preterm birth, meconium staining, and NICU admissions, and that the risk increases as biochemical severity increases. Studies varied in their absolute rates, most likely as a result of variations in patient demographics, management practices, and sample sizes. Nonetheless, the patterns and trends found in our investigation align with those documented in earlier research.

This study fills a research vacuum in Pakistan by offering local data on foetomaternal outcomes across various IHCP severities. It allows for a more transparent risk assessment by classifying outcomes according to mild, moderate, and severe disease. The findings are given more legitimacy by the

prospective design. However, the study's generalizability is limited because it was only carried out at one location. Despite being sufficient, the sample size was tiny in comparison to research conducted internationally. Variations in laboratories and diagnostics may also have an impact on how results are interpreted.

Conclusion

IHCP is linked to negative outcomes for both the mother and the fetus (preterm, NICU admission, perinatal death). One of the most common causes of hepatic impairment during pregnancy, hence prompt and effective care is necessary to avoid negative consequences.

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