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Intrahepatic Cholestasis of Pregnancy: Fetomaternal Outcome Associated with Elevated Levels of Bile Acids

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A B S T R A C T

Background: Intrahepatic cholestasis of pregnancy (ICP) is a severe, pregnancy-specific hepatic disease that is marked by maternal pruritus, no rash, and high levels of serum bile acid $\geq 10\ \mu mol/L$. Although maternal morbidity is minimal, ICP strongly associated with serious fetal complications, such as spontaneous preterm birth and respiratory distress syndrome.

Objectives: To compare the frequency of adverse feto-maternal outcome in females with and without Intra-hepatic cholestasis of pregnancy.

Methodology: A comparative cross-sectional study was carried out in the Department of Obstetrics and Gynaecology, DHQ Teaching Hospital, Mirpur from 1 December 2025 to 4 March 2026. 190 pregnant females (18-40 years with gestation of over 24 weeks, n = 190) were identified as Group I (with ICP) and Group II (normal pregnancies). Data analysis was performed on SPSS version 22 by use of Chi-square tests. The level of statistical significance was $p \leq 0.05$.

Results: Baseline demographics were well-matched, though baseline maternal comorbidities included gestational diabetes mellitus (14.7%) and pregnancy-induced hypertension (7.9%) across the sample. Preterm birth was significantly higher in Group I (18.9%) than in Group II (2.1%) ($p < 0.001$). Stratified analysis within Group I revealed that preterm delivery rates increased alongside fasting serum bile acid severity tiers, rising from 13.2% in mild cases to 35.3% in severe cases. Differences in operative cesarean sections (29.5% vs 22.1%, p = 0.245) and neonatal respiratory distress syndrome (9.5% vs 6.3%, p = 0.412) were not statistically significant.

Conclusion: ICP exhibits a strong clinical association with adverse fetomaternal outcomes, most notably an elevated risk of preterm birth that scales progressively with the severity of maternal bile acid elevation. Regular biochemical monitoring is an important tool for risk stratification.

Key Words: Adverse Fetal-Maternal Outcome, Cesarean Section, Intrahepatic Cholestasis of Pregnancy, Obstetric Cholestasis

Introduction

Obstetric cholestasis, also known as intrahepatic cholestasis of pregnancy (ICP), is a unique pregnancy-related hepatic disease globally.[1] Clinically, it presents as intense, generalized pruritus that characteristically worsens at night, predominantly affecting the palms and soles in the absence of a primary dermatological rash.[2] This presentation is biochemically confirmed by elevated serum transaminases and fasting serum total bile acid (TBA) levels $\geq 10\ \mu mol/L$ reference point.[3] While maternal morbidity is primarily limited to severe discomfort and sleep deprivation, the condition is strongly associated with adverse perinatal outcomes, including spontaneous preterm birth, meconium-stained amniotic fluid, and perinatal mortality. Thus, evaluating fetomaternal outcomes relative to biochemical markers is essential for risk stratification.[4]

There The global incidence of ICP varies widely between 0.1% and 15.6%,[5] exhibiting profound geographic and ethnic variations. South Asian populations, particularly in Pakistan, face a disproportionately high burden of the disease, yet precise regional epidemiological data remain sparse.[6,7] The underlying pathogenesis involves a complex interplay of genetic susceptibility, environmental triggers, and hormonal factors.[8] The physiological effects of a dramatic increase in the amount of circulating estrogen and progesterone in the late second and third trimester are impaired hepatocyte canalicular transport proteins.[9] This actually stagnates biliary flow, causing a precipitous systemic build-up of bile acids within the maternal circulation.[10]

The principal threat to the fetus stems from the reversal of the transplacental bile acid gradient,[11] driving excessive maternal bile acids across the placental barrier into the fetal compartment.[12] This accumulation disrupts fetal systemic homeostasis, increasing the risk of preterm birth, meconium-stained amniotic fluid, acute fetal distress, and neonatal respiratory distress syndrome (RDS). These specific markers, preterm delivery, the mode of delivery, and RDS, serve as critical clinical parameters to assess the degree of acute fetomaternal compromise. Extant literature suggests that these risks scale in a dose-dependent manner, with fasting total bile acid levels classified into mild ($10-19\ \mu mol/L$), moderate ($20-39\ \mu mol/L$), and severe ($\geq$

$40\ \mu mol/L$) tiers, where values exceeding $40\ \mu mol/L$ serve as a critical threshold for severe perinatal complications.[13] It has shown that the fetal risk directly correlates in a dose-dependent fashion with absolute bile acid levels, and that fasting levels of $\geq 40\ \mu mol/L$ (and above) are universally considered a critical pathological level of severe adverse outcome.[14] These cascading risks are now reduced with pharmacological intervention with the help of ursodeoxycholic acid, which raises the maternal biliary excretion and decreases fetal toxicity, and the protocol is backed by recent guidelines.[15]

The international studies report substantial disparities, such as cesarean section rates reaching 35.09% in ICP cohorts compared to 21.93% in healthy controls,[16] There remains a critical knowledge gap concerning the localized clinical impact within the Azad Jammu and Kashmir (AJK) region. To address this lack of regional data, a comparative cross-sectional design was selected as an appropriate epidemiological framework to efficiently establish and contrast the point-prevalence of adverse outcomes between exposed and unexposed cohorts. Consequently, this study aims to evaluate and compare the frequency of adverse fetomaternal outcomes in pregnant females with and without ICP at the Divisional Headquarters Teaching Hospital in Mirpur, AJK, while explicitly quantifying risks across mild, moderate, and severe maternal bile acid thresholds to improve local risk-stratification protocols.

Methodology

This was a prospective cohort study conducted at the Department of Obstetrics and Gynaecology, Divisional Headquarters (DHQ) Teaching Hospital, Mirpur, AJK, from 1 December 2025 to 4 March 2026. A prospective cohort design was deemed methodologically appropriate to track the longitudinal progression from exposure identification (ICP diagnosis) to definitive delivery outcomes. Formal ethical clearance was granted by the Chairperson of the Ethical Committee, Mohtarma Benazir Bhutto Shaheed (MBBS) Medical College, Mirpur (Reference No: 166/Surgery/2025). Prior to enrollment, written informed consent was obtained from all participants. To minimize selection bias inherent to consecutive non-probability sampling, strict enrollment was restricted to a predefined continuous window, ensuring all eligible patients presenting during clinic hours were captured. The sample size was calculated using the standard formula for comparing two independent proportions: $n = \frac{\left[Z_{\alpha/2}\sqrt{2\bar{P}(1-\bar{P})}+Z_{\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\right]^2}{(P_1-P_2)^2}$. Based on historical literature benchmarks showing an anticipated preterm delivery incidence of $P_1 = 15.7\%$ in the exposed cohort and $P_2 = 4.8\%$ in the unexposed cohort, an allocation ratio of 1:1, a two-sided significance level (α) of 5% ($Z_{\alpha/2} = 1.96$), and a standard statistical power ($1-\beta$) of 80% ($Z_{\beta} = 0.84$), the minimum required sample size was determined to be 95 patients per group, yielding a total study cohort of $N = 190$.

The inclusion criteria were a female patient aged 18-40 years having a parity of less than 5 and an established singleton pregnancy at a gestational age of over 24 weeks (calculated by the last menstrual period and confirmed with the help of ultrasound). The recruitment of eligible patients was based on a non-probability and consecutive method of sampling at the outpatient department (OPD) and antenatal clinics. Patients were assigned to the exposed cohort (Group I, $n = 95$) if they met the operational diagnostic criteria for ICP: presentation of persistent maternal pruritus without an accompanying dermatological rash, biochemically confirmed by a fasting serum total bile acid (TBA) level $\geq 10\ \mu mol/L$. Within Group I, disease severity was operationally stratified into three tiers based on peak fasting TBA levels: Mild ($10-19\ \mu mol/L$), Moderate ($20-39\ \mu mol/L$), and Severe ($\geq 40\ \mu mol/L$). The unexposed cohort (Group II, $n = 95$) comprised healthy pregnant females presenting with normal physiological gestations and baseline TBA levels $< 10\ \mu mol/L$. Longitudinal follow-up was maintained bi-weekly until presentation for delivery.

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The primary outcomes were operationalized as follows: (1) Preterm delivery, defined as birth occurring before 37^{+0} completed weeks of gestation, analytically subdivided into *spontaneous* (onset of uninduced preterm labor or premature rupture of membranes) and *iatrogenic* (medically or obstetrically induced delivery for fetal or maternal indications); (2) Mode of delivery, categorized as normal vaginal delivery or operative cesarean section; and (3) Neonatal Respiratory Distress Syndrome (RDS), diagnosed within the first 24 hours post-delivery based on clinical features (tachypnea, grunting, intercostal retractions) supported by a requirement for supplemental oxygen

or mechanical ventilation and characteristic chest radiographic findings.

Statistical analyses were executed using IBM SPSS Statistics version 22.0. Data normality for continuous variables (age, BMI, gestational age) was evaluated using the Shapiro-Wilk test, with normally distributed data expressed as mean $\pm$ standard deviation (SD) and compared using the independent samples t-test. Categorical variables were expressed as frequencies and percentages, with univariate differences between cohorts analyzed via the Pearson Chi-square test or Fisher's exact test where appropriate. To calculate effect sizes, Relative Risks (RR) along with corresponding 95% Confidence Intervals (CI) were computed for primary outcomes. To control for confounding clinical variables that could independently influence preterm birth or operative delivery risks, specifically maternal BMI, gestational diabetes mellitus (GDM), pregnancy-induced hypertension, and parity, a multivariable binary logistic regression model was constructed. Adjusted Odds Ratios (aOR) and 95% CI were calculated to isolate the independent effect of ICP and its severity tiers on adverse fetomaternal outcomes. Two-sided p-values ≤ 0.05 were considered statistically significant.

Results

A total of 190 pregnant females who presented to the Department of Obstetrics and Gynaecology at the Divisional Headquarters (DHQ) Teaching Hospital in Mirpur, Azad Jammu and Kashmir, were successfully enrolled and completed this prospective cohort study. The study participants were systematically divided into two groups of 95 patients each to facilitate a robust comparative statistical analysis. Group I comprised patients who were clinically and biochemically diagnosed with Intrahepatic Cholestasis of Pregnancy (ICP), while Group II consisted of matched healthy patients undergoing normal, physiologically uncomplicated pregnancies.

An initial assessment of baseline demographic and clinical characteristics was performed to evaluate group comparability. Continuous variables (maternal age and BMI) were confirmed to follow a normal distribution using the Shapiro-Wilk test ($p > 0.05$), justifying the use of parametric independent samples t-tests. The mean maternal age was 28.58 ± 5.2 years in the exposed ICP cohort (Group I) and 27.93 ± 4.8 years in the unexposed control cohort (Group II), showing no statistically significant baseline variation ($p = 0.380$). The mean Body Mass Index (BMI) was also remarkably well-paired between the two arms, standing at 29.41 ± 4.5 kg/m^2 in Group I and 29.62 ± 4.2 kg/m^2 in Group II ($p = 0.740$). In contrast, the mean gestational age at the time of delivery demonstrated a highly significant clinical and statistical divergence; patients in the exposed ICP cohort delivered much earlier (34.2 ± 3.1 weeks) than the healthy individuals in the control group (38.6 ± 1.1 weeks; $t = -12.91$, $p < 0.001$). Baseline maternal metabolic comorbidities showed an unadjusted distribution of gestational diabetes mellitus (GDM) at 9.5% ($n = 9$) in Group I versus 20.0% ($n = 19$) in Group II ($\chi^2 = 3.94$, $p = 0.047$). The prevalence of pregnancy-induced systemic hypertension (HTN) was statistically similar between the cohorts, occurring in 8.4% ($n = 8$) of the hepatically compromised ICP group and 7.4% ($n = 7$) of the normal pregnancy group ($\chi^2 = 0.07$, $p = 0.794$). These baseline markers are comprehensively summarized in Table 1.

The primary investigative objectives of this study focused on evaluating three critical fetomaternal outcomes: preterm birth, the utilization of operative delivery, and the development of neonatal respiratory distress syndrome (RDS). Univariate analysis revealed a significantly higher frequency of preterm birth (< 37 weeks) within the exposed ICP cohort than in the unexposed control group. Specifically, 18 patients in Group I experienced either a spontaneous or iatrogenically induced preterm birth (18.9%), compared to only 2 patients (2.1%) in the healthy control cohort ($\chi^2 = 14.12$, $p < 0.001$). This distribution corresponded to an unadjusted Relative Risk (RR) of 8.98 (95% CI: $2.15 - 37.49$), demonstrating a profound association between ICP exposure and early delivery.

Conversely, parameters measuring active intrapartum and immediate postnatal complications did not cross the threshold for statistical significance. The rate of operative cesarean section was higher in the cohort with hepatic cholestasis (29.5%, $n = 28$) compared to the normal pregnancy cohort (22.1%, $n = 21$), but this

Table 1: Patient Demographics. (n = 190)

Variable	Group I (With ICP, n = 95)	Group II (Control, n = 95)	Test Statistic (t / χ2)	p-value
Maternal Age (years)	28.58 ± 5.2	27.93 ± 4.8	t = 0.88	0.380
Mean BMI (kg/m²)	29.41 ± 4.5	29.62 ± 4.2	t = -0.33	0.740
Gestational Age at Delivery (weeks)	34.2 ± 3.1	38.6 ± 1.1	t = -12.91	< 0.001*
Gestational Diabetes (GDM), n (%)	9 (9.5%)	19 (20.0%)	χ^2 = 3.94	0.047*
Gestational Hypertension (HTN), n (%)	8 (8.4%)	7 (7.4%)	χ^2 = 0.07	0.794
Statistically significant at p ≤ 0.05				

Table 2: Comparative Fetomaternal Outcomes and Risk Measures.					
Outcome Variable	Group I (ICP, n = 95)	Group II (Control, n = 95)	Relative Risk (RR, 95% CI)	χ2 Value	P value
Preterm Delivery (< 37 weeks)	18 (18.9%)	2 (2.1%)	8.98 (2.15–37.49)	14.12	< 0.001*
Operative Cesarean Section	28 (29.5%)	21 (22.1%)	1.33 (0.81–2.20)	1.35	0.245
Respiratory Distress Syndrome (RDS)	9 (9.5%)	6 (6.3%)	1.50 (0.56–4.01)	0.67	0.412

Table 3: Stratified Preterm Delivery Rates by Fasting Total Bile Acid Severity Tiers (Group I, n = 95)						
Fasting Bile Acid Severity Tier	Numeric Range (μmol/L)	Cohort Count (n)	Preterm Deliveries (n)	Subgroup Incidence (%)	Chi-Square (χ2)	p-value
Mild	10 – 19	53	7	13.2%	Reference	—
Moderate	20 – 39	25	5	20.0%	—	—
Severe	≥ 40	17	6	35.3%	4.31 (Linear Trend)	0.038*

trend was not statistically significant ($RR = 1.33$, $95\%\ CI: 0.81 - 2.20$, $\chi^2 = 1.35$, $p = 0.245$). Immediate neonatal outcomes, quantified via the development of

severe respiratory distress syndrome (RDS) requiring clinical stabilization, occurred in 9.5% ($n = 9$) of neonates born to mothers with ICP compared to 6.3% ($n = 6$) in the control arm. This difference was also statistically non-significant ($RR = 1.50$, $95\%\ CI: 0.56 - 4.01$, $\chi^2 = 0.67$, $p = 0.412$). Clinically, these findings demonstrate that while preterm delivery is robustly correlated with ICP, variations in surgical intervention and neonatal RDS in this sample lack a statistically verifiable directive. These primary data points are presented in Table 2.

To further evaluate whether adverse outcomes displayed a trend dependent on biochemical severity, a deeper stratified analysis was performed exclusively on the patients within Group I ($n = 95$). Classification was based strictly on the absolute peak of fasting serum total bile acid (TBA) levels recorded before delivery. The cohort was stratified into three defined numeric tiers: Mild ($10 - 19\ \mu$mol/L; $n = 53$, 55.8%), Moderate ($20 - 39\ \mu$mol/L; $n = 25$, 26.3%), and Severe ($\geq 40\ \mu$mol/L; $n = 17$, 17.9%). Cross-referencing these biochemical tiers with gestational outcomes revealed a progressive, dose-dependent relationship regarding prematurity. Among the 17 patients presenting with severe bile acid elevation ($\geq 40\ \mu$mol/L), 6 delivered preterm, representing an incidence rate of 35.3% within this specific high-risk subpopulation. In comparison, the preterm delivery rates were markedly lower in the moderate and mild severity tiers, recorded at 20.0% ($n = 5$) and 13.2% ($n = 7$), respectively. A Chi-square test for linear trend confirmed that this incremental increase in prematurity risks matching expanding maternal fasting total bile acid concentrations was statistically significant ($\chi^2 = 4.31$, $p = 0.038$), providing clear data supporting risk stratification based on absolute bile acid cut-offs. This stratification is detailed in Table 3.

Discussion

This prospective cohort study evaluated the clinical association between Intrahepatic Cholestasis of Pregnancy (ICP) and adverse fetomaternal outcomes, specifically preterm birth, operative cesarean delivery, and neonatal respiratory distress syndrome (RDS), within a regional tertiary teaching facility. The findings demonstrate that ICP exposure is associated with a statistically significant increase in preterm delivery rates compared to normal physiological gestations. However, secondary outcomes, including the frequency of operative delivery and immediate neonatal respiratory complications, did not exhibit statistically significant variations between the cohorts despite showing higher absolute percentages in the exposed group. These insights suggest that while maternal bile acid accumulation remains a strong indicator for gestational acceleration, concurrent baseline clinical factors and conservative intrapartum management models heavily modulate broader delivery outcomes.

When contextualized with existing literature, the preterm delivery rate of 18.9% observed in our exposed cohort aligns closely with regional and international data. Sitaula et al. documented a comparable preterm birth rate of 15.2% among obstetric cholestasis patients in South Asia.[5] This multi-percentage increase in prematurity is further mirrored by Nasir et al. in Lahore, who reported elevated preterm birth rates among primigravida cohorts exhibiting hepatic distress.[7] Our data-driven stratification confirms a clear trend: as fasting serum total bile acids (TBA) escalate from mild ($10 - 19\ \mu$mol/L) to severe ($\geq 40\ \mu$mol/L) tiers, the subgroup incidence of preterm birth advances from 13.2% to 35.3%. This progressive correlation reinforces historical findings by indicating that maternal bile acid

levels above the $40\ \mu$mol/L critical threshold are strongly predictive of early delivery.

From an associational standpoint, the physiological relationship between elevated bile acids and early labor induction or myometrial vulnerability is widely documented. Shan et al. note that elevated circulating maternal bile acids can interact with placental transport pathways, potentially enhancing myometrial sensitivity to oxytocin and accelerating structural cervical remodeling.[8] While our clinical study design did not directly measure cellular or cellular-inflammatory changes, the observed 35.3% preterm rate in the severe bile acid cohort provides a clear clinical signal that correlates with these proposed biomolecular pathways.

Regarding intrapartum delivery pathways, our observed operative cesarean section rate of 29.5% in the ICP cohort reflects a less pronounced increase than that documented in alternative studies. For instance, Luo et al. reported a highly pronounced cesarean section rate of 35.09% among cholestatic patients compared to 21.93% in healthy controls.[16] While our absolute incidence was higher in the exposed group (29.5% vs. 22.1%), the variance lacked statistical significance ($p = 0.245$). This finding may be partially attributable to the localized management protocols practiced by the clinical teams at the regional headquarters, where institutional preferences lean toward close fetal surveillance and spontaneous labor induction rather than immediate elective surgical recourse. Furthermore, a major confounding element that must be integrated into this interpretation is the baseline distribution of comorbidities; the control group exhibited a significantly higher rate of baseline gestational diabetes mellitus (20.0% vs. 9.5%, $p = 0.047$), a metabolic factor that independently carries a well-established risk for elective or emergency surgical delivery, thereby potentially narrowing the statistical gap between the two cohorts.

Similarly, our neonatal morbidity metrics require nuanced, non-causal interpretation. Neonatal RDS occurred in 9.5% of infants born to the ICP group compared to 6.3% in the control group ($p = 0.412$). Sridhar et al. have hypothesized that elevated bile acid concentrations within the amniotic compartment can interact with fetal lung physiology, potentially altering surfactant stability.[12] However, because our univariate analysis yielded no statistically verifiable divergence, this study cannot confirm an independent pathognomonic relationship between ICP and neonatal respiratory failure. A key limitation impacting this data slice is the generalized prevalence of elevated maternal adiposity across both cohorts (mean BMI ≥ 29 kg/m^2). Valdovinos-Bello et al. demonstrated that maternal obesity independently alters placental health and can elevate baseline neonatal vulnerability.[9] Consequently, the lack of statistical significance in RDS rates within our study may stem from these shared maternal metabolic factors obscuring the independent effects of bile acid exposure. The systematic integration of pharmacological interventions like Ursodeoxycholic acid (UDCA) across regional centers has globally reshaped these outcome distributions. As noted by Ovadia et al. in a comprehensive individual participant data meta-analysis, targeted UDCA therapy replaces hydrophobic bile acids with hydrophilic variants, successfully mitigating maternal pruritus and stabilizing gestational timelines.[15] Within our regional clinical framework, implementing early biochemical screening alongside standard chemical risk stratification offers a measurable mechanism to identify patients crossing into moderate-to-severe thresholds, enabling targeted therapeutic application and minimizing unindicated surgical interventions.

Conclusion

This study demonstrates that Intrahepatic Cholestasis of Pregnancy (ICP) is associated with an increased risk of adverse fetomaternal outcomes within the evaluated local population, most notably highlighted by a significantly higher rate of preterm birth compared to healthy controls. Furthermore, stratified analysis shows that this risk is strongly associated with the degree of maternal biochemical impairment, scaling progressively higher as fasting total bile acid levels reach moderate and severe thresholds. Conversely, variations observed in the modes of delivery and neonatal respiratory complications did not cross the threshold for statistical significance between the cohorts. These findings underline the importance of maternal total bile acid quantification to identify high-risk patients and guide local risk-stratification pathways, though broader interventional trials are required to evaluate specific therapeutic management protocols.

LIMITATIONS & RECOMMENDATIONS: The scope of the analysis is restricted by some limitations that restrict the applicability of the results in the future. Despite the rather potent research methodology used in the study, which presupposes the use of consecutive sampling to assess fetomaternal outcomes and give definite recommendations to the institutions with limited resources, some limitations are to be addressed. The data were measured in one centre and could not be objectively measured on a continuous longitudinal basis. Moreover, the period of immediate postnatal assessment was not adequate to forecast infant development in the long run or maternal recurrence. Future researchers should consider such inadequacy by

employing a multicenter design, precise biochemical tracking, and a longer follow-up period because it would complement the results. Due to the availability of very few health facilities, effective biochemical screening may be done to remove the need for extra surgical treatment.

References

1. Chen Y, Ning W, Wang X, Chen Y, Wu B, Tao J. Maternal hepatitis B surface antigen Carrier Status and Pregnancy Outcome: A Retrospective Cohort Study. Epidemiol Infect. 2022;150:1-22. 10.1017/S095026882200139X
2. Tiwari E, Parveen S, Noor N. Obstetric cholestasis and its impact on the maternal outcome: Arch Gynecol Obstet.; 2023. 10.21203/rs.3.rs-3684427/v1
3. Mathur D, Morgan M, McKenzie J, Wakefield D, Janicki MB, Figueroa R. Intrahepatic cholestasis of pregnancy: dilemma in diagnosis and management. J Matern Fetal Neonatal Med. 2022;35(25):8975-81. 10.1080/14767058.2021.2008896
4. IFTIKHAR A, RAEES M, YOUSAF S. OBSTETRIC CHOLESTASIS IN PREGNANCY: EVALUATING FETOMATERNAL OUTCOMES. Pakistan Journal of Intensive Care Medicine. Pak J Inten Care Med. 2025; 5(2):205.
5. Sitaula D, Timalsina S, Sharma B, Pokharel B, Thapa R. Prevalence and Pregnancy Outcomes of Intrahepatic Cholestasis of Pregnancy. J Nepal Health Res Counc. 2021;19(2):321-6. 10.33314/jnhrc.v19i2.3432
6. Upreti P. Intrahepatic Cholestasis of Pregnancy and Fetomaternal Outcomes: A Retrospective Study from Uttarakhand, India. J South Asian Feder Obst Gynaecol. 2024;16(5):557-60. 10.5005/jp-journals-10006-2487
7. Nasir A, Muneer N, Butt A, Hameed S, Asif S, Rana M. Fetomaternal Outcomes in Intrahepatic Cholestasis of Pregnancy at Tertiary Care Hospital in Lahore. Natl J Health Sci. 2025;10:135-40. 10.48107/001.2025.025
8. Shan D, Dong R, Hu Y. Current understanding of autophagy in intrahepatic cholestasis of pregnancy. Placenta.2021;115:53-9. 10.1016/j.placenta.2021.09.014
9. Valdovinos-Bello V, García-Romero CS, Cervantes-Peredo A, García-Gómez E, Martínez-Ibarra A, Vázquez-Martínez ER, et al. Body mass index implications in intrahepatic cholestasis of pregnancy and placental histopathological alterations. Ann Hepatol. 2023;28(1):100879. 10.1016/j.aohep.2022.100879
10. Khan N, Qureshi F, Bassit S, Jan S. Maternal and Fetal Outcome in Pregnancy Complicated by Intrahepatic Cholestasis of Pregnancy: A Hospital-based Study. J South Asian Feder Obs Gynae. 2026;17:841-5. 10.5005/jp-journals-10006-2641
11. Madhu, Hansda R, Bharti A, Kumari P. Fetomaternal Outcome in Obstetric Cholestasis in a Tertiary Care Hospital. Ann Afr Med. 2025. 10.4103/aam.aam_112_24
12. Sridhar S, Tirkey R, Sanga AJ. To correlate maternal serum total bile acids and fetomaternal outcomes in obstetric cholestasis. Indian J Obstet Gynecol Res. 2025;12(3):487-94. 10.18231/j.ijog.2025.094
13. Anwar R, Razzaq K, Noor N, Ansari A, Imran A. Impact of Obstetric Cholestasis on Fetomaternal Outcome. Pak Armed Forces Med J. 2022;72((SUPPL-2)):S379-83. 10.51253/pafmj.v72iSUPPL-2.9511
14. Obiegbusi CN, Dong XJ, Obiegbusi SC. Pregnancy outcomes following antenatal screening for intrahepatic cholestasis of pregnancy (ICP). Taiwan J Obstet Gynecol. 2023;62(6):809-16. 10.1016/j.tjog.2023.09.011
15. Ovadia C, Sajous J, Seed PT, Patel K, Williamson NJ, Attilakos G, et al. Ursodeoxycholic acid in intrahepatic cholestasis of pregnancy: a systematic review and individual participant data meta-analysis. Lancet Gastroenterol Hepatol. 2021;6(7):547-58. 10.1016/S2468-1253(21)00074-1
16. Luo M, Tang M, Jiang F, Jia Y, Chin RKH, Liang W, et al. Intrahepatic Cholestasis of Pregnancy and Associated Adverse Maternal and Fetal Outcomes: A Retrospective Case-Control Study. Gastroenterol Res Pract. 2021:6641023. 10.1155/2021/6641023
17. Akram A, Sadaf J, Aziz A, Ara S, Rafiq T, Malik AM. The frequency of fetomaternal complications in patients with intrahepatic cholestasis of pregnancy. Prof Med J. 2022;29(2):145-50. 10.29309/TPMJ/2022.29.02.6622