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INTRAHEPATIC CHOLESTASIS OF PREGNANCY: A STUDY TO IDENTIFY THE CONTRIBUTING FACTORS AND FETOMATERNAL OUTCOME

COLESTASE INTRA-HEPÁTICA DA GRAVIDEZ: UM ESTUDO PARA IDENTIFICAR OS FATORES CONTRIBUINTES E O DESFASE FETOMATERNAL

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The authors declare that there is no conflict of interest

Abstract
Objective: To determine the contributing factors and evaluate the fetomaternal outcomes in patients with intrahepatic cholestasis of pregnancy. Study Design: Descriptive case series. Place and Duration of Study: Department of Obstetrics & Gynecology, University of Lahore Teaching Hospital, Lahore, in collaboration with Social Security Hospital, Multan Road, Lahore, from October 2025 to February 2026. Methodology: A total of 105 pregnant women diagnosed with intrahepatic cholestasis of pregnancy were included using non-probability consecutive sampling. Women aged 18–45 years, parity <5, and gestational age >24 weeks were enrolled. Patients with other causes of cholestasis were excluded. Data regarding demographic variables, clinical features, and contributing factors including gestational diabetes, hypertension, hyperlipidemia, multiple pregnancy, previous and family history of ICP were recorded. Fetomaternal outcomes including preterm delivery, cesarean section, postpartum hemorrhage, poor Apgar score, low birth weight, and intrauterine fetal death were assessed. Data were analyzed using SPSS version 25. Results:

Resumo
Objetivo: Determinar os fatores contribuintes e avaliar os resultados fetomaternos em pacientes com colestase intra-hepática da gravidez. Desenho do estudo: Série de casos descritiva. Local e duração do estudo: Departamento de Obstetrícia e Ginecologia, Hospital Universitário de Lahore, Lahore, em colaboração com o Hospital da Previdência Social, Multan Road, Lahore, de outubro de 2025 a fevereiro de 2026. Metodologia: Um total de 105 mulheres grávidas diagnosticadas com colestase intra-hepática da gravidez foram incluídas por meio de amostragem consecutiva não probabilística. Foram incluídas mulheres com idade entre 18 e 45 anos, paridade <5 e idade gestacional >24 semanas. Pacientes com outras causas de colestase foram excluídas. Foram registrados dados relativos a variáveis demográficas, características clínicas e fatores contribuintes, incluindo diabetes gestacional, hipertensão, hiperlipidemia, gravidez múltipla, histórico prévio e familiar de CIP. Foram avaliados os desfechos fetomaternos, incluindo parto prematuro, cesariana, hemorragia pós-parto, baixo índice de Apgar, baixo peso ao nascer e morte fetal intrauterina. Os dados

The mean age of patients was 30.8 ± 7.2 years, and the mean gestational age was 32.4 ± 4.1 weeks. Common contributing factors included hyperlipidemia (44.8%), gestational diabetes (39.0%), hypertension (34.3%), and previous history of ICP (30.5%). Preterm delivery was observed in 43.8% of cases, cesarean section in 49.5%, low birth weight in 36.2%, poor Apgar score in 32.4%, postpartum hemorrhage in 20.0%, and intrauterine fetal death in 10.5%. Significant associations were found between preterm delivery and gestational diabetes, hypertension, hyperlipidemia, multiple pregnancy, and previous history of ICP ($p \leq 0.05$). Conclusion: Intrahepatic cholestasis of pregnancy is associated with multiple metabolic and obstetric risk factors and leads to significant adverse fetomaternal outcomes.

Keywords: Intrahepatic Cholestasis of Pregnancy. Fetomaternal Outcome. Gestational Diabetes. Hyperlipidemia. Preterm Delivery.

foram analisados utilizando o SPSS versão 25. Resultados: A idade média das pacientes foi de 30,8 ± 7,2 anos, e a idade gestacional média foi de 32,4 ± 4,1 semanas. Fatores contribuintes comuns incluíram hiperlipidemia (44,8%), diabetes gestacional (39,0%), hipertensão (34,3%) e histórico prévio de CIP (30,5%). O parto prematuro foi observado em 43,8% dos casos, a cesariana em 49,5%, o baixo peso ao nascer em 36,2%, o baixo índice de Apgar em 32,4%, a hemorragia pós-parto em 20,0% e a morte fetal intrauterina em 10,5%. Foram encontradas associações significativas entre parto prematuro e diabetes gestacional, hipertensão, hiperlipidemia, gravidez múltipla e histórico prévio de CIP ($p \leq 0,05$). Conclusão: A colestase intra-hepática da gravidez está associada a múltiplos fatores de risco metabólicos e obstétricos e leva a resultados feto-maternos adversos significativos.

Palavras-chave: *Colestase Intra-Hepática da Gravidez. Desfecho Fetomaterno. Diabetes Gestacional. Hiperlipidemia. Parto Prematuro.*

1 INTRODUCTION

ICP is a common pregnancy related hepatic disorder where the woman experiences itching on seemingly normal skin and elevated peak random levels of total bile acid of [?]19 umol/L [1]. ICP is common among multiethnic populations in the UK, with a prevalence rate of 0.7% compared to women of Pakistani and Indian descent with a prevalence rate of between 1.2 and 1.5% [2,3]. ICP is also both maternal and fetal complication-associated, as well as quality of life impacting on the mother [4]. Patients tend to appear after the 34th week of pregnancy. The occasional instances of ICP have, however, been reported as well in earlier pregnancy in the past few years [5]. Intrahepatic cholestasis of pregnancy is the cause of 60 perinatal and 14% maternal mortality [6,7]. ICP may be linked with malabsorption of vitamin K, which may lead to an increased risk of post-partum bleeding [8]. It may cause NICU hospitalization because of its adverse effects on the newborn as well as fetus, such as higher chances of the neonate and fetus having an increased risk of meconium staining the amniotic fluid before delivery, and fetal distress resulting in fetal death and fetal bradycardia [9,10]. Li et al. noted that there

are several factors that are observed to increase the risk of ICP, such as multiple pregnancy (7.67%), family history of ICP (3.33%), gestational hypertension (8%), gestational diabetes (13.33%), and hyperlipidemia (10%) [11]. Das et al. had found that in females having ICP, pregnancy complicated by low Apgar score at 5 min < 7, and intrauterine fetal death was observed in (10.5%), and (1.31%), respectively [12]. In a study of ICP, postpartum haemorrhage, preterm birth and low Apgar score, Upreti et al. found that 33.2% of these were done by cesarean section [13]. It is because of these complications that early detection of this condition, an improved treatment format, and an earlier delivery schedule, should there be a need, are highly significant.

2 OBJECTIVES

1) To identify the frequency of contributing factors leading to intrahepatic cholestasis of pregnancy in pregnant women attending a tertiary care hospital.
2) To assess the frequency of adverse feto-maternal outcomes in women with intrahepatic cholestasis of pregnancy.

3 METHODOLOGY

This descriptive case series was conducted at the Department of Obstetrics & Gynecology, University of Lahore Teaching Hospital, Lahore, in collaboration with Social Security Hospital, Multan Road, Lahore from October 2025 to February 2026. A total of 105 cases were included. The sample size was calculated using the WHO sample size calculator with a 95% confidence interval, a 5% margin of error, and an expected proportion of IVF-ET in females with intrahepatic cholestasis of pregnancy of 7.33%. A non-probability consecutive sampling technique was used to recruit participants. Pregnant women aged 18–45 years, with parity less than 5, gestational age greater than 24 weeks, and diagnosed with intrahepatic cholestasis of pregnancy as per the operational definition were included in the study. Patients with pruritic skin lesions not related to intrahepatic cholestasis of pregnancy, viral hepatitis, hemolytic anaemia, autoimmune liver disease, coagulopathies (prothrombin time >15 seconds), thrombocytopenia (platelet count

<150,000/µL), gallstones, and cholestasis due to other causes documented in medical records were excluded.

4 DATA COLLECTION

After obtaining approval from the ethical review board, a total of 105 pregnant females were enrolled from the outpatient department. Informed consent was obtained in writing from all participants before enrolment. Demographic data were collected on age, gestational age, parity, body mass index, dietary habits, and history of nausea and vomiting. The diagnosis was confirmed by measuring bile acid levels in the serum. The participants were assessed on the factors that contributed to intrahepatic cholestasis of pregnancy by assessing their history of gestational diabetes mellitus (oral glucose tolerance test >186 mg/dl), gestational hypertension (blood pressure ≤140/90 mmHg), hyperlipidemia (total cholesterol >200mg/dl), multiple pregnancy, a history of intrahepatic cholestasis of pregnancy, and family history of the disease. Ultrasound examinations for fetal surveillance were performed on all participants. Cases where the fetus did not show any cardiac activity or movements were identified as intrauterine fetal death. The patients in the outpatient department were followed up until delivery. Gestational age at delivery was recorded, and preterm delivery was predetermined as a birth before =37 weeks of gestation. The delivery mode was also documented. Patients were then moved to the postnatal ward after delivery, where they were observed for 4 hours to assess blood loss. If it was per the operational definition, postpartum haemorrhage was registered. At birth, the neonates were observed in relation to the Apgar score and weight at birth. According to operational definitions, poor Apgar scores and low birth weight were observed.

5 DATA ANALYSIS

Data were entered and analysed using Statistical Package for the Social Sciences (SPSS) version 25. Quantitative variables such as age, gestational age, body mass index, and serum bile acid levels were presented as mean ± standard deviation. Qualitative variables such as parity, dietary habits, nausea and vomiting, contributory factors

(multiple pregnancy, prior history of intrahepatic pregnancy-related cholestasis, family history, gestational hypertension, gestational diabetes, and hyperlipidemia), and fetomaternal outcomes (preterm, cesarean section, postpartum bleeding, low Apgar, low birth weight and intra uterine fetal death) were displayed in frequencies and percentages. Stratification was used to control for effect modifiers, including age, body mass index, gestational age, dietary habits, and parity. The chi-square test was applied to determine the relationship between contributing factors and fetomaternal outcomes after stratification. A p-value of ≤0.05 was considered statistically significant.

6 RESULTS

Data were collected from 105 patients; the mean age was 30.8 ± 7.2 years, and the mean gestational age was 32.4 ± 4.1 weeks. Most participants had parity 0–2 (64.8%), while 35.2% had parity 3–4. The mean BMI was 26.7 ± 4.3 kg/m². Regarding dietary habits, 36.2% had a normal diet, 34.3% consumed a high-fat diet, and 29.5% had a low-nutrient diet. Nausea and vomiting were reported in 56.2% of patients. The mean bile acid level was 54.6 ± 21.3 µmol/L. Among contributing factors, gestational diabetes was present in 39.0%, hypertension in 34.3%, and hyperlipidemia in 44.8% of cases.

Table 1

Demographic and Clinical Characteristics (n = 105)

Variable	Category	Total (n = 105)
Age (years)	Mean ± SD	30.8 ± 7.2
Gestational Age (weeks)	Mean ± SD	32.4 ± 4.1
Parity	0–2	68 (64.8%)
	3–4	37 (35.2%)
BMI (kg/m²)	Mean ± SD	26.7 ± 4.3
Diet Habits	Normal	38 (36.2%)
	High Fat	36 (34.3%)
	Low Nutrition	31 (29.5%)
Nausea & Vomiting	Yes	59 (56.2%)
	No	46 (43.8%)

Bile Acid Level (µmol/L)	Mean ± SD	54.6 ± 21.3
Gestational Diabetes	Yes	41 (39.0%)
	No	64 (61.0%)
Hypertension	Yes	36 (34.3%)
	No	69 (65.7%)
Hyperlipidemia	Yes	47 (44.8%)
	No	58 (55.2%)
Multiple Pregnancy	Yes	28 (26.7%)
	No	77 (73.3%)
Previous History of ICP	Yes	32 (30.5%)
	No	73 (69.5%)
Family History of ICP	Yes	29 (27.6%)
	No	76 (72.4%)

Regarding fetomaternal outcomes, 43.8% of patients had preterm delivery, while 56.2% delivered at term. The mode of delivery was nearly equally distributed, with cesarean section in 49.5% and vaginal delivery in 50.5% of cases. Postpartum haemorrhage occurred in 20.0% of patients. Neonatal outcomes showed that 32.4% of newborns had poor APGAR scores, and 36.2% had low birth weight.

Table 2

Fetomaternal Outcomes (n = 105)

Outcome	**Category**	**Total (n = 105)**
Preterm Delivery	Yes	46 (43.8%)
	No	59 (56.2%)
Mode of Delivery	Cesarean Section	52 (49.5%)
	Vaginal Delivery	53 (50.5%)
Postpartum Hemorrhage	Yes	21 (20.0%)
	No	84 (80.0%)
Poor APGAR Score	Yes	34 (32.4%)
	No	71 (67.6%)

Low Birth Weight	Yes	38 (36.2%)
	No	67 (63.8%)
Intrauterine Fetal Death	Yes	11 (10.5%)
	No	94 (89.5%)

Preterm delivery was more frequent among patients with gestational diabetes (54.3% vs 27.1%, p=0.003), hypertension (45.6% vs 25.4%, p=0.02), hyperlipidemia (56.5% vs 35.6%, p=0.03), multiple pregnancy (41.3% vs 15.3%, p=0.001), and previous history of ICP (43.4% vs 20.3%, p=0.01), indicating these as significant predictors of preterm birth.

Table 3

Association of Risk Factors with Preterm Delivery

Variable	Category	Preterm Yes (n=46)	Preterm No (n=59)	p-value
Gestational Diabetes	Yes	25 (54.3%)	16 (27.1%)	0.003
	No	21 (45.7%)	43 (72.9%)	
Hypertension	Yes	21 (45.6%)	15 (25.4%)	0.02
	No	25 (54.4%)	44 (74.6%)	
Hyperlipidemia	Yes	26 (56.5%)	21 (35.6%)	0.03
	No	20 (43.5%)	38 (64.4%)	
Multiple Pregnancy	Yes	19 (41.3%)	9 (15.3%)	0.001
	No	27 (58.7%)	50 (84.7%)	
Previous ICP	Yes	20 (43.4%)	12 (20.3%)	0.01
	No	26 (56.6%)	47 (79.7%)	

Low birth weight was significantly associated with several risk factors. It was more common in patients with gestational diabetes (52.6% vs 31.3%, p=0.02), hypertension (44.7% vs 28.4%, p=0.04), hyperlipidemia (57.9% vs 37.3%, p=0.03), and multiple pregnancy (42.1% vs 17.9%, p=0.006).

Table 4

Association of Risk Factors with Low Birth Weight

Variable	Category	LBW Yes (n=38)	LBW No (n=67)	p-value
Gestational Diabetes	Yes	20 (52.6%)	21 (31.3%)	0.02
	No	18 (47.4%)	46 (68.7%)	
Hypertension	Yes	17 (44.7%)	19 (28.4%)	0.04
	No	21 (55.3%)	48 (71.6%)	
Hyperlipidemia	Yes	22 (57.9%)	25 (37.3%)	0.03
	No	16 (42.1%)	42 (62.7%)	
Multiple Pregnancy	Yes	16 (42.1%)	12 (17.9%)	0.006
	No	22 (57.9%)	55 (82.1%)	
Previous ICP	Yes	15 (39.5%)	17 (25.4%)	0.09
	No	23 (60.5%)	50 (74.6%)	

Poor APGAR score was also significantly associated with certain maternal risk factors. It was more frequent in patients with gestational diabetes (52.9% vs 32.4%, p=0.03), hypertension (47.1% vs 28.2%, p=0.04), and multiple pregnancy (41.2% vs 19.7%, p=0.01). Hyperlipidemia (p=0.08) and previous history of ICP (p=0.20) did not show statistically significant associations with poor APGAR score.

Table 5

Association of Risk Factors with Poor APGAR Score

Variable	Category	Poor APGAR Yes (n=34)	Poor APGAR No (n=71)	p-value
Gestational Diabetes	Yes	18 (52.9%)	23 (32.4%)	0.03
	No	16 (47.1%)	48 (67.6%)	
Hypertension	Yes	16 (47.1%)	20 (28.2%)	0.04
	No	18 (52.9%)	51 (71.8%)	
Hyperlipidemia	Yes	19 (55.9%)	28 (39.4%)	0.08
	No	15 (44.1%)	43 (60.6%)	
Multiple Pregnancy	Yes	14 (41.2%)	14 (19.7%)	0.01
	No	20 (58.8%)	57 (80.3%)	

Previous ICP	Yes	13 (38.2%)	19 (26.8%)	0.20
	No	21 (61.8%)	52 (73.2%)	

7 DISCUSSION

This investigation was conducted to determine contributing factors and evaluate fetomaternal outcomes in intrahepatic cholestasis of pregnancy. These results showed that ICP is linked with a significant burden of maternal and neonatal complications, which has clinical importance in obstetric practice. The average age of the participants in the current study was 30.8 ± 7.2 years, and most of the women were multiparous. These results are in tandem with earlier studies, which stated that ICP is more commonly seen in women during their late reproductive age and in women with high parity. The average gestational age at presentation was 32.4±4.1 weeks, consistent with the clinical course of ICP, which typically occurs in the late second or third trimester due to increased hormone levels [14].

The most common of these factors included hyperlipidemia (44.8%), and gestational diabetes (39.0%). Other studies have also reported similar results, with metabolic imbalances identified as a major cause of ICP. This relationship between ICP and gestational diabetes can be attributed in part to overlapping pathways related to insulin resistance and bile acid metabolism [15]. A significant percentage of patients (34.3) also had hypertension, confirming earlier results that vascular and metabolic dysfunction can co-exist in such patients. The history of ICP was reported in 30.5% of cases, whereas 27.6% had a positive family history, indicating a genetic predisposition. The recurrent nature of ICP and the role of genetic factors in its occurrence, particularly mutations in bile acid transport, have always been emphasised in previous studies. Multiple pregnancy was detected in 26.7% of the cases, which is consistent with previous research that pointed to a higher risk because of higher levels of estrogen in twin pregnancies [16].

As to fetomaternal outcomes, 43.8% of the cases were associated with preterm delivery, which is not dissimilar to prior studies indicating higher rates of spontaneous and iatrogenic preterm birth in ICP. The reason behind the high rate of cesarean section

(49.5) in the study could be attributed to more obstetric interventions because of fetal distress or fear of negative results, which previous studies have already indicated [17]. Neonatal complications were also highly reported with low birth weight at 36.2% and poor Apgar score at 32.4%. The results can be compared with earlier studies, which show that high amounts of bile acids in the mother negatively impact fetal health, potentially by impairing placental viability and causing fetal hypoxia [18]. Intrauterine fetal death rates were 10.5%; this is not very high when compared with some previous studies, but it is still a serious issue of concern and makes close attention to the fetus a priority. The stratification analysis indicated that preterm delivery was significantly related to various risk factors such as gestational diabetes, hypertension, hyperlipidemia, multiple pregnancy and history of ICP beforehand delivery ($p<0.05$). The findings are like those of previous studies, which have found these factors to be significant predictors of poor outcomes. In like manner, low birth weight and low Apgar were found to be strongly linked with metabolic and obstetric risk factors, especially gestational diabetes and multiple pregnancy [19,20].

8 LIMITATIONS

This study had several limitations that should be considered while interpreting the findings. As a descriptive case series lacking a control group, it failed to permit causal conclusions about risk factors and fetomaternal outcomes. The research was conducted in small tertiary care units using non-probability consecutive sampling, which could limit the generalisability of the findings and introduce selection bias. The sample size was also relatively small (although sufficient) to identify less common outcomes like intrauterine fetal death and postpartum haemorrhage. Others, such as dietary habits and clinical history, were self-reported by the patients, which implies their susceptibility to recall and reporting bias. Moreover, no further biochemical and genetic studies were conducted and so the mechanism of the disease could not be fully understood. Follow-up was limited to delivery and postpartum immediate results, and thus long-term maternal and neonatal outcomes were not evaluated.

9 CONCLUSION

Intrahepatic cholestasis of pregnancy was found to be associated with multiple contributing factors, particularly metabolic and obstetric conditions such as hyperlipidemia, gestational diabetes, hypertension, multiple pregnancy, and a previous history of ICP. The condition demonstrated a significant impact on fetomaternal outcomes, with increased frequencies of preterm delivery, cesarean section, low birth weight, poor Apgar score, and intrauterine fetal death. Significant associations were observed between key risk factors and adverse outcomes, highlighting their role in disease severity and prognosis.

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Authors' Contribution

All authors contributed equally to the development of this article.

Data availability

All datasets relevant to this study's findings are fully available within the article.

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