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Frequency of Obstetric Intrahepatic Cholestasis and Its Maternal and Neonatal Outcomes: A Descriptive Cross-Sectional Study at Aga Khan University Hospital

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Author`s Contribution
[1]Conceptualized the study, curated the data, visualization, investigations, and methodology, analysed the data and did the writing of the original draft, [2]Supervised the project

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ABSTRACT

Objective: To determine the frequency of intrahepatic cholestasis of pregnancy and to describe maternal and neonatal outcomes among affected women in a tertiary care setting in Karachi.

Methodology: This descriptive cross-sectional study was conducted in the Department of Obstetrics and Gynaecology, Aga Khan University Hospital, Karachi, and included 162 pregnant women with biochemically confirmed intrahepatic cholestasis of pregnancy (total bile acids ≥19 µmol/L). Data on maternal and neonatal outcomes such as preterm birth, meconium-stained liquor, and NICU admission were collected using a structured proforma. Statistical analysis was performed using SPSS version 26.0, applying Chi-square with $p \leq 0.05$ considered significant.

Results: Among the total 2569 deliveries during the study period, ICP was diagnosed in 162 women (6.31%). The mean maternal age among affected women was 30.09±4.58 years, and 59.9% were multigravida. Caesarean delivery occurred in 48.1%, gestational diabetes mellitus in 50.6%, and postpartum haemorrhage in 15.4%. Foetal outcomes included preterm birth (29.6%), low birth weight (17.9%), and NICU admission (13.6%). Small-for-gestational-age infants and intrapartum foetal distress each occurred in 11.1% of cases, whereas respiratory distress syndrome was observed in 9.3%.

Conclusion: Intrahepatic cholestasis of pregnancy demonstrated a considerable frequency of maternal and neonatal complications in this tertiary care setting. The most frequent maternal outcomes included gestational diabetes, caesarean delivery, and postpartum haemorrhage, while preterm birth, low birth weight, and NICU admission were the predominant neonatal outcomes. Early diagnosis, close biochemical monitoring, and timely obstetric intervention may help improve perinatal outcomes and reduce complications among affected Pakistani women.

Key words: Intrahepatic Cholestasis of Pregnancy, Maternal Outcomes, Neonatal Outcomes, Pregnancy Complications, Liver

Introduction

Intrahepatic cholestasis of pregnancy (ICP) is a hepatobiliary disorder that typically occurs in the second or third trimester and is characterized by severe itching (especially on the palms and soles), elevated bile acids, and liver enzymes, posing significant risks to the foetus (such as preterm birth and stillbirth) and causing considerable maternal discomfort.[1-3]

The prevalence of intrahepatic cholestasis of pregnancy (ICP) exhibits significant variability across geographical regions and diverse ethnic populations. On the international level, it is known to impact between 0.2% to 2% of all pregnancies, with greater prevalence being reported in women of the South Asian and South American descent.[4,5] Since the prevalence of ICP is relatively high in the Pakistani population, some hospital-based studies have been conducted to show a range of 2-3 percent.[6,7]

The exact cause of ICP is not fully understood, but it appears to be the result of multiple interacting factors. Hormonal changes during pregnancy, especially increased levels of estrogen and progesterone, can interfere with bile acid transport. Genetic factors also play a role, as mutations in certain transporter genes such as ABCB4 (MDR3), ABCB11, and ATP8B1 have been linked to a higher risk of developing the condition.[8,9] Environmental influences and dietary deficiencies may further contribute to its occurrence in genetically predisposed women.[10]

Clinically, ICP occurs with irritating itching with the potential of a major impact on sleep and quality of life. Mild jaundice may also develop in some women. Maternal outcome is generally favourable; however, ICP also involves various complications of the infant; preterm delivery, meconium-contaminated amniotic fluid, low Apgar readings and still birth.[11] There is a risk of stillbirth in case the level of maternal serum bile acid exceeds 100 µmol/L.[4,12]

Despite ongoing research, information about the burden and outcomes of intrahepatic cholestasis of pregnancy in Pakistan remains limited. Most local studies have been small, hospital-based reports and have not comprehensively evaluated both maternal and neonatal outcomes in a tertiary care setting [6,7,13]. Moreover, treatment patterns particularly the utilization of ursodeoxycholic acid (UDCA), the recommended first-line therapy and their potential

influence on perinatal outcomes have not been adequately explored in the local context.

Consequently, the present study was designed to determine the frequency of intrahepatic cholestasis of pregnancy and to describe maternal and neonatal outcomes among affected women in a tertiary healthcare setting. The findings are intended to provide local data that may support improved clinical monitoring and management of this condition in similar healthcare environments.

Methodology

This descriptive cross-sectional study was conducted in the Obstetrics and Gynaecology Department of the AKUH in Karachi. The study was conducted over a minimum duration of six months following institutional ethical approval. Eligible participants were pregnant women aged 18–40 years with singleton gestations at ≥20 weeks. Potential ICP cases were initially identified based on pruritus in pregnancy with either elevated maternal bile acids exceeding 19 µmol/L or abnormal liver function tests (ALT levels greater than 35 IU/L). Subsequently, the final analysis was restricted to the 162 women who had confirmed elevated total bile acids (≥19 µmol/L), thereby excluding cases identified solely on the basis of ALT elevation. Maternal outcomes included postpartum haemorrhage (PPH) and mode of labour/delivery and neonatal outcomes were recorded as preterm birth, stillbirth, meconium-stained liquor/aspiration, intrapartum foetal distress, Apgar score less than 7 at 5 minutes, neonatal respiratory distress syndrome (RDS), and neonatal intensive care unit (NICU) admission within 48 hours. A non-probability consecutive sampling technique was used, and all eligible cases presenting during the study period were included. As this was a descriptive study, no formal a priori power calculation was performed. This descriptive cross-sectional study has been reported in accordance with the STROBE checklist. The completed STROBE checklist, including items 12 (statistical methods), 13 (participants), 14 (descriptive data), and 15 (outcome data), is provided as a supplementary file.

Exclusion criteria included multiple gestation; chronic hepatic diseases (hepatitis B/C, biliary cirrhosis, primary sclerosing cholangitis); symptomatic gallstone disease or cholecystitis; autoimmune hepatitis; acute hepatic infections; preeclampsia or eclampsia; shock or ischemic hepatitis; congestive hepatopathy; haemolytic anaemia; use of hepatotoxic or cholestasis-inducing medications (e.g., statins, acetaminophen, valproate, phenytoin, amiodarone); and malignancy.

Written informed consent was obtained from all participants, after which data were collected using a predesigned proforma. Variables included demographic characteristics, maternal age gestational age, clinical presentation (pruritus/jaundice), laboratory parameters (ALT, AST, total/direct bilirubin, total bile acids), and predefined maternal and neonatal outcomes. Maternal outcomes included postpartum haemorrhage (PPH) and mode of labour/delivery, while neonatal outcomes included preterm birth, stillbirth, meconium-stained liquor/aspiration, intrapartum foetal distress, Apgar score <7 at 5 minutes, neonatal respiratory distress syndrome (RDS), and neonatal intensive care unit (NICU) admission within 48 hours. Potential confounders (maternal age, gestational age, BMI, and comorbid diabetes/hypertension) were also documented.

Data were analyzed using SPSS version 26.0. Descriptive statistics were calculated as frequencies and percentages for categorical variables. Comparisons were assessed using the Chi-square test, with $p < 0.05$ considered statistically significant.

Results

A total of 162 women with intrahepatic cholestasis of pregnancy (ICP) were included. The mean maternal age was 30.14 ± 4.52 years, and 59.9% of participants were multigravida. The demographic and baseline clinical characteristics, including gestational age, BMI, previous history of ICP, treatment received, causes of postpartum haemorrhage, and maternal complications, are presented in Table I.

Regarding fetomaternal outcomes, spontaneous vaginal delivery was the most common mode of delivery (48.8%), followed by caesarean section (48.1%). Preterm birth occurred in 29.6% of pregnancies, while low birth weight and small-for-gestational-age infants accounted for 17.9% and 14.2%, respectively. Intrapartum fetal distress was observed in 17.3% of cases, and 13.6% of neonates required NICU admission. Respiratory distress syndrome occurred in 8.6% of neonates, while meconium aspiration syndrome was reported in 4.9%. The complete distribution of maternal and neonatal outcomes is shown in Table II.

When fetomaternal outcomes were compared between women aged 19–30 years and those aged >30 years, no statistically significant differences were observed for the assessed outcomes (all $p>0.05$). The age-group comparison is presented in Table III.

Table I: Demographic Characteristics of the ICP patients .(n=162)			
Characteristics		Mean ± SD/N	Range/%
Age (Years)		30.14±4.52	Range: 19-40
Age Groups (Years)			
19-30		89	54.9%
>30		73	45.1%
Gestational age at admission		31.74±5.01	Range: 20-38
Gestational age		36.75±1.65	Range: 29-39
Height (cm)		158.96±4.87	Range: 145-173
Weight (kg)		70.65±10.61	Range: 44-106
BMI (kg/m^2)		28.04±4.58	Range: 18.8-43.4
BMI Category			
Normal		40	24.7%
Overweight		73	45.1%
Obese		49	30.2%
Gravida			
Primigravida		65	40.1%
Multigravida		97	59.9%
Previous History of ICP		32	19.8%
ICP treatment	Ursodeoxycholic Acid	129	79.6%
	Antihistamines	28	17.3%
	No Treated	5	2.70%
Causes of PPH	Uterine Atony	23	92%
	Retained Tissue	2	8%
Maternal Complications			
Gestational Diabetic Mellitus (GDM)		82	50.6%
Chronic Hypertension		2	1.2%
Pregnancy-Induced Hypertension		12	7.4%
Hypothyroidism		9	5.6%
Anaemia		6	3.7%
Postpartum Haemorrhage (PPH)		25	15.4%
Meconium-Stained Liquor (MSL)		6	3.7%

Table II: Distribution of Fetomaternal Outcomes in Obstetric Cholestasis (n=162)			
Maternal Outcomes		N	%
Mode of Delivery			
Caesarean Section	Elective	25	15.4%
	Emergency	53	32.7%
Instrumental Delivery		5	3.1%
Spontaneous Vaginal Delivery		79	48.8%
Type of Labour (n=128)			
Induced		84	65.6%
Spontaneous		44	34.4%
Foetal Outcomes			
Preterm (GA<37 weeks)		48	29.6%
Meconium Aspiration (MAS)		01	0.6%
Low Birth Weight (<2.5kg)		29	17.9%
Small for gestational age (SGA)		18	11.1%
Intrapartum Foetal Distress (IFD)		18	11.1%
Apgar score <7 at 1min		03	1.9%
Apgar score <7 at 5min		02	1.2%
NICU Admission		22	13.6%
Neonatal RDS		15	9.3%

Table III: Comparison of Fetomaternal Outcomes with Age Group (n=162)				
Maternal Outcomes		Age Group		P-Value
		19-30 n=89	>30 n=73	
Caesarean Section	Elective	10 (11.2)	15 (20.5)	0.323
	Emergency	28 (31.5)	25 (34.2)	
Instrumental Delivery		3 (3.4)	2 (2.7)	
Spontaneous Vaginal Delivery		48 (53.9)	31 (42.5)	
Type of Labour (n=128)	Induced	51 (68)	33 (62.3)	0.501
	Spontaneous	24 (32)	20 (37.7)	
Foetal Outcomes				
Preterm (GA<37 weeks)		23 (25.8)	25 (34.2)	0.224
Meconium Aspiration (MAS)		0 (0)	1 (1.4)	0.451
Low Birth Weight (<2.5kg)		17 (19.1)	12 (16.4)	0.660
Small for gestational age (SGA)		9 (10.1)	9 (12.3)	0.655
LBW+SGA		20(22.5%)	15(20.5%)	0.767
Intrapartum Foetal Distress (IFD)		10 (11.2)	8 (11)	0.955
Apgar score <7 at 1min		2 (2.2)	1 (1.4)	0.99
Apgar score <7 at 5min		2 (2.2)	0 (0)	0.502
NICU Admission		11 (12.4)	11 (15.1)	0.651
Neonatal RDS		8 (9)	7 (9.6)	0.99

Discussion

The present study evaluated the maternal and neonatal outcomes in women diagnosed with intrahepatic cholestasis of pregnancy (ICP) at a tertiary care hospital in Karachi. The results demonstrate a substantial frequency of maternal morbidity and adverse perinatal outcomes among women diagnosed with ICP, findings that are consistent with both local and international literature. The mean maternal age in this study was 30.09 ± 4.58 years, with most women being multigravida (60.2%). This finding concurs with the results of Shafqat et al.[1] and Smith and Rood[2], who observed that ICP commonly affects women in their late twenties to early thirties and tends to recur in subsequent pregnancies. The predominance of multigravidity may be attributed to cumulative hormonal exposure and hepatic sensitivity to oestrogen and progesterone during successive pregnancies.[3] The mean gestational age at admission and delivery in this study, 31 and 37 weeks respectively, closely aligns with previously reported ranges.[1,4,6] Ovadia et al.[4] demonstrated that ICP typically presents during the late second or third trimester when oestrogen levels peak, which is consistent with our findings. Similarly, Hafeez et al. [6]

in Punjab reported that most cases of ICP are diagnosed between 30 and 36 weeks of gestation, emphasizing the hormonal basis of the disease. Biochemical abnormalities were common in this cohort, with elevated ALT in 93.5% of patients; all 162 women in the final cohort had confirmed elevated bile acids (≥19 µmol/L), as this was a prerequisite for inclusion in the analysis. These results are consistent with the hepatic dysfunction pattern described by Geenes and Williamson[3] and Reyes and Sjövall[5], who noted that increased bile acids and transaminases are hallmark features of ICP. Glantz et al.[14] and Brouwers et al.[15] also reported that elevated bile acid concentrations are directly related to adverse perinatal outcomes. Our findings reinforce this biochemical pattern and suggest that even moderate elevations in bile acids warrant close foetal surveillance. Although international guidelines recommend elevated fasting total bile acids as the diagnostic gold standard for intrahepatic cholestasis of pregnancy, ALT elevation was used as part of the initial case identification process due to limited availability and delayed reporting of bile acid assays in the local setting. However, the final analysis was restricted to the 162 women with biochemically confirmed elevated bile acids (≥19 µmol/L), thereby minimising the risk of misclassification. This two-step approach reflects pragmatic clinical practice in resource-constrained settings while preserving diagnostic specificity. In terms of treatment practices, the majority of women in this cohort (79.6%) received ursodeoxycholic acid (UDCA), while 17.3%were managed with antihistamines. Recent guidelines from the Royal College of Obstetricians and Gynaecologists (2022) and the Society for Maternal-Foetal Medicine (2021) endorse UDCA as first-line therapy for reducing pruritus and improving liver biochemistry.[12,16] Geenes et al. and Chappell et al. reported UDCA use exceeding 70–90% in Western populations[3,14], whereas antihistamines provide only symptomatic relief without improving bile acid levels.[15] The relatively high utilization of UDCA in our cohort reflects adherence to contemporary management guidelines in this tertiary care setting. However, variations in timing of initiation, dosage optimization, and underlying disease severity may still have influenced the observed maternal and neonatal outcomes. Therefore, treatment-related factors should be considered when interpreting the findings. Among maternal outcomes, caesarean section was the predominant mode of delivery (48.1%). This observation is in agreement with Akram et al.[7] and Kenyon et al.[17] who reported high caesarean rates in ICP. Gestational diabetes mellitus was present in 50.6%, similar to the findings of Hafeez et al.[6], and may reflect metabolic dysregulation influenced by hormonal and genetic interactions.[8,9] Postpartum haemorrhage occurred in 16.7% of participants, consistent with frequencies between 14% and 20% reported by Akram et al.[7] and Kenyon et al.[17] This may be attributed to impaired vitamin K absorption and coagulation disturbances in cholestatic pregnancies.[10] Foetal outcomes such as preterm birth (29.6%), low birth weight (17.9%), and NICU admission (13.6%) were comparable to findings from Rook et al.[11] and Brouwers et al.[15] Ovadia et al.[4] demonstrated that increasing maternal bile acid concentrations correlate with adverse neonatal outcomes including spontaneous preterm labour and foetal distress. Jamsheed et al.[13] similarly reported preterm birth in 31% and NICU admissions in 17% of ICP pregnancies. Collectively, the findings of this study indicate that ICP remains an important obstetric condition characterized by notable maternal and neonatal complications. Compared with Western populations, the relatively higher adverse outcome rates observed in South Asian settings may be attributed to genetic predisposition, nutritional factors, and delayed access to specialized care.[6,13] This study has several limitations. First, the absence of a comparison group precludes causal inference or estimation of relative risk, and the findings should therefore be interpreted descriptively. Second, although the final analysis was restricted to women with confirmed elevated bile acids, the initial identification process included ALT elevation as an additional criterion; any cases that may have been missed during initial screening due to reliance on ALT

alone could not be captured. Third, multivariable regression analysis was not performed to adjust for potential confounders such as BMI, gestational age, and comorbidities. Finally, treatment variability, including differences in timing and optimisation of UDCA therapy, may have influenced the observed outcomes.

Conclusion

Intrahepatic cholestasis of pregnancy demonstrated a considerable frequency of maternal and neonatal complications in this tertiary care setting. The most frequent maternal outcomes included gestational diabetes, caesarean delivery, and postpartum haemorrhage, while preterm birth, low birth weight, and NICU admission were the predominant neonatal outcomes. Early diagnosis, close biochemical monitoring, and timely obstetric intervention are essential to improve perinatal outcomes and reduce complications among affected Pakistani women.

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