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Original Research Article

Fetomaternal Outcome in Pregnancies Complicated with Intrahepatic Cholestasis of Pregnancy (IHCP)

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Abstract

Background: The effects of Intrahepatic cholestasis of pregnancy (IHCP) on the foetus are significant. Preterm birth, meconium staining of the amniotic fluid, respiratory difficulties, foetal distress, and death are among the adverse foetal outcomes that are more likely to occur.

Methods: This research recruited 101 women who were diagnosed with ICP at Regional Institute of Medical Sciences, Imphal in India between January 2019 and March 2023. To evaluate the relationships between foetal problems and maternal clinical and biochemical indicators, single predictor logistic regression models were used. Age, race/ethnicity, gravidity, parity, history of liver or biliary illness, history of ICP in prior pregnancies, and induction were among the clinical variables examined. Serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total bilirubin, direct bilirubin, albumin, total protein, and total bile acids (TBA) were among the biochemical predictors examined.

Results: 1.9% of cases were ICP cases. Most were born by spontaneous vaginal birth (84%), and most had labour induced (87%). In 33% of the births, there were difficulties related to the foetus, most often respiratory distress. Clinical or biochemical variables that were statistically significant were not linked to a higher incidence of foetal problems. Until elevated TBA exceeded 100 mmoL/L, there was no correlation between elevated TBA and foetal difficulties, with 3 out of 5 cases reporting problems. Reduced risk of foetal problems was linked to ICP in prior pregnancies (OR 0.21, p = 0.046). No instances of late-term foetal death were reported.

Conclusions: Elevated TBA and other maternal clinical and laboratory characteristics did not seem to be significant predictors of foetal problems in ICP.

Keywords: Intrahepatic Cholestasis, Pregnancy, Complications

Introduction

Pregnancy-related intrahepatic cholestasis (ICP) is the most common liver disease. This reversible cholestatic disease is typically detected in the latter half of pregnancy and is characterised by pruritus, mostly on the palms and soles, elevated serum aminotransferase levels, and/or elevated serum bile acid levels (>or = 10micromol/L). Laboratory abnormalities and symptoms spontaneously resolve after delivery, but not more than a month after delivery [1, 2].

By definition, ICP is associated with pregnancy and the postpartum phase and is defined by ruling out all other causes of cholestasis. ICP often coexists with maternal symptoms and is linked to poor newborn outcomes, such as meconium-stained fluid amnii, early labour, and stillbirth [3]. For this reason, early detection and treatment are crucial.

Intrahepatic cholestasis during pregnancy has been seen in 0·1-2% of pregnant women [4-6]. It is identified in women who have high serum bile acids and generalised pruritus in the second and third trimesters. Complications include meconium-stained liquid amnii, early labour, and stillbirth [7].

A significant Swedish cohort research found that women who were pregnant and had serum bile acid concentrations of 40 μmol/L or higher. Premature labour, liquid amnii tinged with meconium, and newborn hypoxia were more likely to worsen these pregnancies [8].

An additional investigation involving a UK cohort indicated that the outcome of pregnancy in women with intrahepatic cholestasis during pregnancy and serum bile acids of 40 μmol/L or higher supported these conclusions and also showed a correlation with intrauterine foetal death (adjusted odds ratio = 3.05)

when compared to data from 2205 UK women who had singleton pregnancies without complications [3].

Retrospective investigations of pregnant women with intrahepatic cholestasis in the USA8 and Scandinavian nations [9] consistently show a connection between elevated maternal blood bile acid concentrations and intrauterine foetal death. According to the 2007 stillborn workshop [10], intrahepatic cholestasis during pregnancy is a medical condition characterised by an increased level of bile acid in the mother's blood, which may cause intrauterine foetal death in some pregnancies [1, 8, 11].

The majority of ICP patients do not have clinical jaundice. The liver function mostly exhibits cholestasis-related characteristics. Serum bile acid levels (≥10 μmol/L) are a typical laboratory anomaly that may increase up to 100 times. Levels more than 40 μmol/L are considered severe obstetric cholestasis. Conjugated hyperbilirubinemia, high serum ALP, normal or slightly raised serum aminotransferases, and gamma glutamyl transferase (GGT) are further findings. The architecture and synthetic function of the liver do not change. ICP continues to advance till delivery. After giving birth, pruritus goes away in 24 to 48 hours, but histological and biochemical abnormalities may take weeks or months to go away. Sixty to seventy percent of ICP cases may reoccur in later pregnancies, however they may not be as severe as the first episode [3].

Method

Patient Demographic

In this retrospective analysis, 101 women with clinical ICP diagnoses were included. When a patient with clinical pruritus symptoms who could not be attributed to any other cause reported to their obstetrician in the second or third trimester of pregnancy, the patient was diagnosed with clinical ICP. The following criteria were used to identify patients: having a doctor or certified nurse midwife (CNM) diagnose them with ICP; having the proper paperwork in their medical records; and experiencing pruritus in the second or third trimester of pregnancy. At the time of delivery, all individuals had ICD 9 diagnoses that were consistent with bile duct abnormalities.

The study's exclusion criteria included diagnosis of acute fatty liver of pregnancy (AFLP), HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), and chronic liver disease (hepatitis B, hepatitis C, primary biliary cirrhosis, primary sclerosing cholangitis, symptomatic cholelithiasis, cholecystitis, Wilson disease, alpha-1-antitrypsin deficiency, cyto-megalovirus, Epstein-Barr virus, or autoimmune hepatitis) that could not be differentiated from ICP at the time of delivery. The research included six women who had either hepatitis B or C since their presenting symptoms were compatible with ICP rather than being signs of infectious hepatitis. Between January 1, 2019, and March 1, 2023, all patients saw doctors in the Department of Obstetrics & Gynaecology at Regional Institute of Medical Sciences, Imphal in India.

Dimensions

All of the women who had been diagnosed with ICP throughout the research period were identified after the acquisition of IRB permission. Each patient participating in the research had data on certain maternal and foetal features gathered, and the individuals' medical records were extracted. The mother's age at delivery, race/ethnicity, delivery style, history of intrauterine pressure in a prior pregnancy, history of biliary or liver illness, spontaneous vs. induced labour, reasons for induction, gravidity, parity, weight (kg), and height (cm) were among the maternal data gathered. Based on pre-pregnancy weight and height, BMI was computed.

Maximum serum levels of albumin (ALB), total protein (TP), alkaline phosphatase (ALP), alanine aminotransferase (ALT), total bilirubin (TB), direct bilirubin (DB), cholic acid (cholic), deoxycholic acid (deoxy), and chenodeoxycholic acid (cheno) were among the values assessed. When more than one laboratory test was conducted, we used the maximum values measured for AST, ALT, TB, DB, ALP, TBA, cholic, deoxy, and cheno, and the minimum values for ALB, and TP. These values most likely correlate with hepatic dysfunction if they are abnormal. Serum laboratory tests were typically obtained at the time of presentation or delivery. The results of bile acid and serum biochemical testing were obtained using standard laboratory techniques.

A composite outcome of one or more foetal or neonatal problems was the main outcome examined in this research. Foetal discomfort, significant congenital abnormalities, hyperbilirubinemia, meconium staining of amniotic fluid at birth, meconium aspiration, pneumonia, respiratory distress, and sepsis were among the foetal problems. Foetal distress was characterised by late or severe decelerations that occurred repeatedly, or by bradycardia of fewer than 110 beats per minute that persisted for three minutes or more and necessitated emergency delivery. Any infant in need of intubation, continuous positive airway pressure (CPAP), or bag/mask ventilation was considered to be in respiratory distress. postpartum, pneumonia diagnosis, respiratory discomfort due to aspiration of meconium documented by a healthcare practitioner, or documentation based on physical examination. The estimated gestational age at delivery, the birth weight (in grammes), the 1-

minute and 5-minute Apgar scores, and other perinatal data were also gathered. Using a data abstraction form and a study of the patient's medical records, the clinical, biochemical, and pregnancy outcomes for each patient were retrieved. This information was then put into an Excel spreadsheet to generate the ICP database.

Analytical Statistics

For the purpose of our data analysis, the cohort was described using descriptive statistics. As applicable, the findings are presented as means +/- SD, medians, and interquartile ranges. For simplicity of interpretation, continuous predictor variables were dichotomized to binary variables. Ages above 35 during delivery were considered advanced maternal age. Based on the standardised normal values of our laboratory, the maximum values of AST, ALT, cholic, deoxy, and cheno were dichotomized into binary variables. Values above 40 IU/L were considered high for AST, 45 IU/L for ALT, 3.1 mmoL/L for cholic, 7.3 mmoL/L for deoxy, and 9.9 mmoL/L for cheno. The TBA was then divided into four groups: 100 Iu/L and above, less than 10 umoL/L, 10–40 umoL/L, and 40–100 umoL/L. "less than 10 umoL/L" used as the benchmark group for analysis. To evaluate the unadjusted correlations between clinical and biochemical predictors and respiratory distress and foetal problems, single-predictor logistic regression models were used. In order to account for a mother's history of hepatic and biliary illness, two predictor models were created. Odds ratios were used to express the results. STATA version 10 (Stata Corp, College Station, TX) was used for the statistical analysis. Two-sided p values are used in all reports, and a p-value of 0.05 was deemed statistically significant.

Results

ICP was diagnosed in 101/5,238 pregnant women from January 1, 2019, to March 1, 2023, for a prevalence of 1.9%. Table 1 presents the mother demographic characteristics of the intrahepatic cholestasis of pregnancy (ICP) group. The average age of mothers at the time of delivery was 27.5 years, with a standard deviation of 65.8. The range of maternal ages varied from 16 to 41 years.

Table 1: Maternal Demographics

Maternal Demographics.	
Age (years)	27.5+/25.8
Delivery Methods	
Vaginal	86
Cesarian section	15
History ICP	20
Liver/Biliary History	16
Induction	88
Induction Indications	
ICP	84
PROM	1
Diabetes	1
Oligohydramnios	1
Preeclampsia	3
Gravida n = 98	3+/21.4
Parity n = 98	1+/21.2
BMI n = 76	27.7+/26.1

The birth procedures used for women with intrahepatic cholestasis of pregnancy (ICP) included typical spontaneous vaginal delivery (84%), low transverse caesarean section (14.9%), and one patient had a vacuum-assisted delivery. The birth techniques used within the general population consisted of normal spontaneous vaginal delivery (74%), vacuum aided delivery (3.5%), forceps delivery (2%), and low transverse caesarean section (21%). Among the cohort of patients with intrahepatic cholestasis of pregnancy (ICP), it was found that 20 individuals had a prior history of ICP in their previous pregnancies. Additionally, 16 women had a history of other biliary or hepatic diseases, as shown in Table 2.

Table 2: Maternal Medical History

Maternal Medical History.	
Cholecystitis	2
Cholecystectomy	3
Cholelithiasis	5
Chorioamnionitis	1
Hepatitis A	1
Hepatitis B	3
Hepatitis C	3
Postpartum Hemorrhage	2
Spontaneous Abortion	2
*Perinatal Death	1
*Postnatal Death	1

The medical records indicated a notable prevalence of cholelithiasis in five individuals, cholecystitis in two individuals, cholecystectomy in three individuals, hepatitis A in one individual, hepatitis B in three individuals, and hepatitis C in three individuals. According to the available evidence, it was determined that none of the patients had active illness upon presentation with symptoms related with intracranial pressure (ICP). Table 2 displays instances of post-partum haemorrhage, spontaneous abortion, peri-natal foetal death, and postnatal infant mortality in prior pregnancies, as documented in the mother histories. The majority of patients in the ICP cohort were subjected to induction (87%), with the diagnosis of ICP being the prevailing indication (95.5%). Additional reasons for induction of labour are premature rupture of membranes (PROM), diabetes, oligohydramnios, and pre-eclampsia.

The mean pre-pregnancy body mass index (BMI) was determined to be 27.7, with a standard deviation of 66.1. During the second or third trimester, all patients had pruritus, whereas none of the patients displayed jaundice. Ursodeoxycholic acid (UDCA) was supplied to a subset of patients, namely 29% of the total population, as a therapeutic intervention for the management of pruritus.

Table 3 presents the median maximum laboratory results seen in the group of patients with intracranial pressure (ICP) prior to childbirth. Bile acid levels were quantified in 72% of the patient cohort. The median value for the maximum TBA was determined to be 23.4, while the interquartile range spanned from 10.6 to 42. Seventy-five percent of the patients who underwent TBA testing had elevated TBA levels above 10 mmoL/L. The concentrations of cholic acid, deoxycholic acid, and chenodeoxycholic acid were quantified in a cohort of 72 individuals. The serology of Hepatitis A was examined in a cohort of 45 individuals, out of which 43 patients had non-reactive titers. The test for Hepatitis B surface antigen was performed on a sample of 99 individuals, of whom 97 patients had non-reactive titers. Hepatitis B core antibody titers were measured in a cohort of 50 individuals, with 47 patients exhibiting non-reactive titers. The antibody titers for Hepatitis C were analysed in a sample of 55 individuals, of whom 52 patients exhibited non-reactive titers.

Table 3. Maternal Laboratory Values

Maternal Laboratory Values			
N		Median	Interquartile Range
AST (U/L)	99	44	30–89
ALT (U/L)	99	62	33–139
ALP (U/L)	71	251	192–329
TB (mg/dL)	81	0.5	0.4–0.8
DB (mg/dL)	77	0.2	0.1–0.3
ALB (g/dL)	73	3.5	3.4–3.7
TP (g/dL)	74	6.5	6.0–6.7
TBA (mmol/L)	73	23.4	10.6–42
Cholic (mmol/L)	72	12	3.8–25.0
Deoxy (mmol/L)	72	2.5	1.7–4.3
Cheno (mmol/L)	72	6.1	3.0–13.9

Table 4 presents a comprehensive description of neonatal features observed throughout the delivery process. The average estimated gestational age was 37 weeks, with a standard deviation of 61.2. Similarly, the average birth weight was 3,126.3 grammes, with a standard deviation of 6519.1. The

mean Apgar scores at one minute and five minutes were 8 (standard deviation [SD] = 61) and 9 (SD = 61), respectively. No 5-minute Apgar values below 7 were observed. Within the general cohort of pregnant women, it was observed that 3.8% of births had a 5 minute Apgar score below the threshold of 7. Foetal problems were seen in 33% of the births within the intrahepatic cholestasis of pregnancy (ICP) group.

Table 4: Fetal Characteristics at Birth

Fetal Characteristics at Birth.	
EGA (weeks)	37+/21.2
Birthweight (grams)	3126.3+/2519.1
1 minute APGAR	8+/21
5 minute APGAR	9+/21
Complications	33
Respiratory Distress	17
Meconium	9
Fetal Distress	5
Congenital Anomalies	2
Hyperbilirubinemia	2
Sepsis	2
Pneumonia	1

The perinatal problems seen in this study were respiratory difficulty, meconium staining of the amniotic fluid, and foetal discomfort. There was no occurrence of foetal demise seen in any of the individuals. Foetal complications were seen in 5 out of 18 patients (28%) in the TBA, 10 group, 10 out of 34 patients (29%) in the TBA 10-40 group, 3 out of 16 patients (19%) in the TBA 40-100 group, and 3 out of 5 patients (60%) in the TBA, .100 group.

The study used logistic regression analysis to assess the factors that might potentially predict foetal problems. The results of this analysis were summarised and presented in Table 5. The influence of advanced maternal age on risk may have a marginal effect, while the level of ambiguity around this relationship is substantial. The presence of hepatic or biliary illness in the mother's medical history, excluding intrahepatic cholestasis of pregnancy (ICP), was shown to have a potential association with an increased likelihood of foetal problems. However, it is important to note that this association did not reach statistical significance (odds ratio [OR] 2.10, 95% confidence interval [CI] 0.70, 6.28). The presence of a prior pregnancy with intrahepatic cholestasis of pregnancy (ICP) in the maternal history was shown to be linked to a significant reduction of 80% in the likelihood of experiencing a foetal problem in the present pregnancy (odds ratio [OR] 0.21, p = 0.046). Maternal elevation of the laboratory levels of AST and ALT during pregnancy did not exhibit a significant correlation with a notable increase in the likelihood of foetal problems.

Table 5: Predictors of Fetal Complications

Predictors of Fetal Complications.			
OR		P	95% CI
Advanced Maternal Age	1.20	0.80	0.28–5.17
Historyliver/biliary disease	2.10	0.19	0.70–6.28
ICP in previous pregnancy	0.21	0.05	0.05–0.97
Elevated ALT	0.82	0.66	0.34–1.97
Elevated AST	0.76	0.53	0.32–1.80
TBA (reference group ,10)			
TBA 10–40	1.08	0.90	0.30–3.85
TBA 40–100	0.60	0.54	0.12–3.05
TBA.100	3.90	0.20	0.49–30.76
Ursodiol use	1.34	0.53	0.53–3.38
Gravida	0.77	0.15	0.54–1.10
Parity	0.74	0.16	0.49–1.13
Induction	2.57	0.24	0.53–12.36

The concentration of TBA at 10 mmol/L did not demonstrate statistical significance in predicting foetal problems. This research posits that TBA.100 may be indicative of a significantly heightened risk; nevertheless, the confidence interval is sufficiently broad, hence limiting the strength of the data supporting this claim. There was no observed reduction in the likelihood of foetal problems (OR 1.34, p = 0.53) when ursodiol was used for the treatment of pruritus in pregnant individuals. A total of twenty-nine individuals had treatment with UDCA. The median total bile acid (TBA) level for those who were administered UDCA was found to be 23.4 (with an interquartile range of 12.8 to 31.7), whereas the median TBA level for those who did not receive UDCA was 21.9 (with an interquartile range of 8.3 to 42). However, it should be noted that this difference in TBA levels between the two groups was not shown to be statistically significant (p = 0.57, as determined by the Mann-Whitney test).

A majority of patients, namely four out of five, who were diagnosed with TBA.100 received treatment via the administration of ursodiol. There is a possibility that patients who had induction may have a higher likelihood of foetal problems (odds ratio = 2.57, p = 0.24). The statistical analysis did not find a significant relationship between the number of prior pregnancies and previous births and the occurrence of foetal difficulties. However, there is a noticeable pattern suggesting that greater values of gravidity and parity may be associated with a lower risk of foetal complications (gravidity odds ratio [OR] 0.77, p = 0.15; parity OR 0.74, p = 0.16). There were no discernible qualitative differences seen when accounting for the presence of hepatic or biliary illness in the maternal history within a two-predictor model.

Discussion

The available data on intrahepatic cholestasis of pregnancy (ICP) in the is notably scarce, considering the prevalence of this medical condition. The retrospective cohort of patients in this study revealed a prevalence rate of 1.9% for ICP, which aligns with previous findings reported in Central and Western Europe. The incidence rates in Chile and Bolivia are greater, ranging from 1.5% to 4% and 9% respectively [1, 10]. In this research, we examined a diverse study group to identify women with intrahepatic cholestasis of pregnancy (ICP).

While intrahepatic cholestasis of pregnancy (ICP) often poses little harm to the mother, it is recognised that pregnancies impacted by ICP have an elevated likelihood of foetal problems. The potential complications associated with this condition include heightened probabilities of meconium stained amniotic fluid, premature birth, foetal discomfort, and intrauterine foetal death (IUFD). This research revealed that a significant proportion of births, namely 33%, were accompanied by perinatal complications such as respiratory distress syndrome, meconium staining of amniotic fluid, foetal distress, congenital abnormalities, sepsis, hyperbilirubinemia, and pneumonia. There was a lack of occurrences of intrauterine foetal demise (IUFD). Prior research has shown that meconium staining occurs in 24% of intrahepatic cholestasis of pregnancy (ICP) cohorts, whereas intrauterine foetal death is seen in 0.4% of such cases [7]. The prevalence of meconium staining in the amniotic fluid among full-term pregnancies in a typical pregnant population ranges from 17% to 24%. At 37 weeks of gestational age, the prevalence drops to less than 5%. However, our research showed a higher incidence of 9% compared to previous studies [11, 12]. Respiratory distress was shown to be the cause of 52% of the reported problems occurring after childbirth.

According to reports, the prevalence of respiratory distress syndrome in neonates delivered to women with intrahepatic cholestasis of pregnancy (ICP) is twice as high as that seen in the general population [13, 14]. One possible explanation for this phenomenon is the very premature birth of infants affected by neonatal respiratory distress syndrome. However, it has been shown that there is a correlation between neonatal respiratory distress syndrome and intrahepatic cholestasis of pregnancy (ICP), as evidenced by the examination of bronchoalveolar lavage fluid from neonates delivered to women with ICP [14]. There exists a hypothesis suggesting that bile acids have the potential to induce surfactant depletion inside the alveoli [13, 14].

The presence of hyaline membranes was seen in rabbits after the administration of taurocholic acid by intratracheal instillation [15]. Upon administration of surfactant, the alveoli exhibited a suitable response, resulting in enhanced aeration [15]. In a separate investigation, bronchial alveolar lavage was conducted postmortem on a cohort of twelve newborns, revealing reduced phospholipid concentrations and elevated bile acid levels [16]. This finding implies a potential correlation between bile acids and surfactant, which may be facilitated by phospholipase A2, an enzyme responsible for surfactant synthesis in the lungs [16]. Additional information is required in order to ascertain the impact of bile acids on the maturation of the foetal lungs, the generation of surfactant, and the occurrence of respiratory distress.

The incidence of foetal morbidity and death in intrahepatic cholestasis of pregnancy (ICP) is elevated compared to that in the general population, as shown by previous studies [7, 17–20]. Although no occurrences of intrauterine foetal demise (IUFD) were seen in this investigation, the overall prevalence of complications remains a cause for worry. The present approach to managing intracranial pressure (ICP) involves initiating labour between 36 and 38

weeks of gestational age, irrespective of total bile acid (TBA) levels. Nonetheless, there have been proposals to perhaps explore a more conservative approach for individuals with TBA levels over 40 mmol/L [7].

According to the findings of Glantz et al, pregnancies in women with TBA levels of 40 mmol/L were associated with an elevated foetal risk of preterm delivery, asphyxia events, meconium staining of amniotic fluid, and green-staining of placenta and membranes. Conversely, women with TBA levels between 10-39 mmol/L exhibited minimal to no increased risk compared to women experiencing pruritus but with normal TBA levels. Consequently, it is suggested that the latter group of women could be managed expectantly, potentially leading to a reduction in healthcare costs. [21] The user did not provide any text to rewrite. However, the odds ratios for these direct comparisons were not provided, therefore making it unclear how comparable their findings are to ours. In the present investigation, we observed that there were no clinically or biochemically relevant predictors that demonstrated a statistically significant association with an elevated likelihood of foetal problems. This disparity may be attributed, at least in part, to variations in clinical protocols. In our clinical practise, we tend to deliver patients with diagnosed intracranial pressure (ICP) at a gestational age of 37 weeks.

However, in the research conducted by Glantz et al., obstetricians were not provided with any guidelines about the management of pregnancies or the optimal time of delivery. This observation may potentially provide an explanation for the variations seen in foetal demise, given that the majority of occurrences of intrauterine foetal death (IUFD) tend to occur during the latter stages of gestation, often after 36 weeks of gestation. In the present investigation, the only variable that demonstrated statistical significance was the preexisting history of intracranial pressure (ICP), which exhibited a connection with a reduced incidence of foetal complications. Although the statistical significance is not evident, a previous medical history including hepatic/biliary illness might potentially be associated with a significant increase in foetal problems. Individuals who have hepatic or biliary disorders may have an elevated likelihood of experiencing foetal problems.

The presence of a previous pregnancy with intrahepatic cholestasis of pregnancy (ICP) in the maternal lineage was associated with an estimated 80% reduction in the risk of complications. This finding implies that there may be an enhanced recognition of ICP among both patients and healthcare providers, potentially leading to increased foetal monitoring and earlier initiation of maternal obstetric care. These proactive measures have the potential to mitigate the likelihood of foetal complications. The average gestational age among individuals with a prior history of intrahepatic cholestasis of pregnancy (ICP) was found to be 37 weeks, with a range of 36 to 39 weeks. Similarly, the average gestational age among individuals without a history of ICP in previous pregnancies was similarly 37 weeks, with a range of 33 to 40 weeks. among individuals with a history of intrahepatic cholestasis of pregnancy (ICP), the percentage of births with a gestational age exceeding 37 weeks was found to be 35%. Conversely, among individuals without a history of ICP, the proportion of deliveries with a gestational age more than 37 weeks was observed to be 26%.

The present pharmacological intervention entails the administration of ursodeoxycholic acid (UDCA) after the diagnosis of intrahepatic cholestasis of pregnancy (ICP). The administration of S-adenosyl-L-methionine, dexamethasone, and cholestyramine has been shown to have potential benefits in the management of maternal pruritus, as well as in the improvement of total bile acids (TBA) levels and serum transaminase levels. In a randomised, double-blinded placebo-controlled experiment conducted by Glantz et al., the researchers discovered that UDCA exhibited greater efficacy compared to dexamethasone in alleviating pruritus and enhancing serum biochemical markers associated with intrahepatic cholestasis of pregnancy (ICP). However, neither UDCA nor dexamethasone shown any impact on foetal complication rates. The user's text does not contain any information to rewrite. The findings of our investigation indicate that the administration of UDCA did not result in any clinically meaningful impact on foetal problems, as seen in Table 5.

The TBA values were classified into four distinct categories: normal or less than 10 mmol/L, 10-40 mmol/L, 40–100 mmol/L, and more than 100 mmol/L. When comparing the TBA 10-40 group and the TBA 40–100 group to the reference group of normal (,10), no significant increase in foetal problems was seen. This implies that increased TBA levels up to 100 may not be a reliable indicator for assessing the risk of foetal difficulties. When the total bile acid (TBA) level exceeded 100 mmoL/L, 60% of the participants reported experiencing complications, resulting in an odds ratio (OR) of 3.90. However, it is important to note that the confidence range for this estimate was large, ranging from 0.49 to 30.76 at a 95% confidence level.

There were various limitations inherent in our investigation. Controlling for missing data and ensuring homogeneity of laboratory procedures scheduled within a cohort poses challenges in a retrospective analysis. A significant proportion of the patients had the testing of TBA, AST, and ALT. Nevertheless, a comprehensive evaluation for alternative aetiologies of hepatic disorders was not conducted on all female subjects. The highest concentration of total blood bile acids is often seen between 30 to 90 minutes after meals. However, it is unclear from the available

evidence if the total bile acid values provided were obtained from fasting individuals. It is probable that these samples were sent as a component of standard laboratory examinations conducted at the clinic appointment or upon the patient's admission for childbirth. The diagnostic criteria for intracranial pressure (ICP) are also prone to subjectivity, since there is currently a lack of standardised criteria for the diagnosis of ICP.

The majority of research studies employ elevated levels of serum bile acids or serum transaminases in conjunction with pruritus as diagnostic criteria for pregnancy-related conditions. However, it is important to note that serum bile acid levels may not always be elevated during a blood draw, as this can be influenced by factors such as fasting or non-fasting state. Additionally, there is evidence to suggest that serum bile acid levels tend to increase more significantly during the later stages of pregnancy. Furthermore, the duration for getting the laboratory findings may range from 1 to 2 weeks, posing challenges in terms of awaiting the outcome while making decisions on the initiation of labour induction in order to mitigate possible foetal problems, particularly foetal death.

Conclusion

In summary, in this cohort of ICP patients, 33% of the pregnancies resulted in perinatal complications, with respiratory distress being the most common complication. A history of liver and biliary disease and TBA greater than 100 may be clinically relevant, but our data were not conclusive. Our results suggest that it may be difficult to use maternal clinical and biochemical features to accurately predict fetal complications.

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