Original Article

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Maternal and Perinatal Outcome in Cholestasis of Pregnancy

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Abstract

Background: Intrahepatic cholestasis of pregnancy has been associated with adverse perinatal outcomes but mechanisms are poorly understood and optimal management is uncertain. Intrahepatic cholestasis of pregnancy or obstetric cholestasis is the most common pregnancy related liver disorder. Hence; the present study was planned for assessing the maternal and perinatal outcome in cholestasis of pregnancy. **Subjects and Methods:** A total of 50 subjects were enrolled in the present study. Out of these 50 subjects, 25 were of pregnant women with confirmed diagnosis of Intrahepatic cholestasis of pregnancy (IHCP), while the remaining 25 were healthy pregnant women (taken as control). Diagnosis of IHCP was done on the basis of presence of unexplained pruritus in addition to increased bile acids and/or transaminases during the late second and third trimester of pregnancy. Complete demographic details of all the patients were obtained. Clinical examination of all the patients was done and haematological profile was obtained. Regular follow-up and check-up of all patients was done throughout the pregnancy extending upto a time period to 3 weeks postpartum. Complications, if any, were recorded separately. **Results:** Mean serum bilirubin, SGOT and SGPT levels of the subjects of the IHCP group were found to be significantly higher in comparison to the subjects of the control group. Pre-term deliveries were found to be present in 5 subjects of the IHCP group, while they were present in 2 subjects of the control group. While comparing the intra-partum complications in between the two study groups, non-significant results were obtained. NICU stay was found to be present in 4 neonates of the IHCP group while it was present in 1 neonate of the control group. Mean birth weight was found to be 3.45 Kg in the IHCP group while it was found to be 3.19 Kg in the control group. Morbidity was absent in both the study groups. **Conclusion:** Pregnant women with IHCP are at a higher risk for having pre-term delivery. Although, no significant difference was observed in terms of complications, still these subjects are slightly higher risk of adverse events.

Keywords: Intrahepatic Cholestasis of Pregnancy, Pregnant Women.

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Introduction

Intrahepatic cholestasis of pregnancy has been associated with adverse perinatal outcomes but mechanisms are poorly understood and optimal management is uncertain. Cholestasis of pregnancy complicates 0.2–2% of pregnancies; the incidence is higher in multiple gestations and among certain ethnic populations, particularly Latina women. The disease is multifactorial; genetic, hormonal, and environmental factors may play a role. Cholestasis characteristically involves maternal pruritus without a rash after 30 weeks gestation and elevated serum bile acid levels. Although pruritus is medically benign, cholestasis of pregnancy has been associated with morbid complications including stillbirth, particularly as gestation advances.[1–3]

Obstetric cholestasis is a liver disorder unique to pregnancy, which typically presents with pruritus. However, pruritus is common in pregnancy and the diagnosis of obstetric cholestasis is confirmed by finding abnormal liver function. Intrahepatic cholestasis of pregnancy or obstetric cholestasis is the most common pregnancy related liver disorder and is characterized by pruritus, elevated serum-aminotransferases and bile-acid level with onset in second or third trimester of pregnancy and spontaneous relief of symptoms within second or third week after delivery.[4–6] Hence; the present study was planned for assessing the maternal and perinatal outcome in cholestasis of pregnancy.

Subjects and Methods

The present study was conducted in the department of Gynaecology, Patna Medical College and Hospital, Patna, Bihar (India) and it included assessment of maternal and perinatal outcome in cholestasis of pregnancy. Ethical approval was obtained from institutional ethical committee after explain-

ing in detail the entire research protocol. A total of50 subjects were enrolled in the present study. Out of these50 subjects, 25 were of pregnant women with confirmed diagnosis of IHCP, while the remaining 25were healthy pregnant women (taken as control). Diagnosis of IHCP was done on the basis of presence of unexplained pruritus in addition to increased bile acids and/or transaminases during the late second and third trimester of pregnancy. Complete demographic details of all the patients were obtained. Clinical examination of all the patients was done and haematological profile was obtained. Regular follow-up and check-up of all patients was done throughout the pregnancy extending upto a time period to 3 weeks postpartum. Complications, if any, were recorded separately. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software.

Results

In the present study, a total 25 pregnant women with confirmed diagnosis of IHCP and 25 healthy pregnant women (taken as control) were enrolled. 12 subjects of IHCP group and 10 subjects of control group belonged to the age group of 25 to 30 years. 4 subjects of IHCP group and 5 subjects of control group belonged to the age group of 31 to 35 years. Among the patients of IHCP group, pruritus onset occurred in between 33 to 36 weeks of gestation in 12 subjects, while it occurred at more than 36 weeks of gestation in 7 subjects.

In the present study, mean bilirubin levels among the subjects of IHCP group and control group were found to be 0.78 mg/dL and 0.51 mg/dL respectively. Mean SGOT levels among the subjects of IHCP group and control group were found to be 223.5 IU/L and 38.3 IU/L respectively. Mean SGPT levels among the subjects of IHCP group and control group were found to be 201.8 IU/L and 36.7 IU/L respectively. Mean serum bilirubin, SGOT and SGPT levels of the subjects of the IHCP group were found to be significantly higher in comparison to the subjects of the control group.

In the present study, pre-term deliveries were found to be present in 5 subjects of the IHCP group, while they were present in 2 subjects of the control group. Fetal distress was found to be present in 6 subjects of the IHCP group in comparison to the 3 subjects of the control group. Adherent placenta was found to be present in 1 subject of the contour group. While comparing the intra-partum complications in between the two study groups, non-significant results were obtained.

In the present study, NICU stay was found to be present in 4 neonates of the IHCP group while it was present in 1 neonate of the control group. Mean birth weight was found to be 3.45 Kg in the IHCP group while it was found to be 3.19 Kg in the control group. Morbidity was absent in both the study groups.

Discussion

Intrahepatic cholestasis of pregnancy (ICP) is the most common liver disease in pregnancy characterized by pruritus, elevated total serum bile acids, and elevated liver enzymes. ICP is associated with increased risk of preterm birth (19-60%), meconium passage <37 weeks (17.9%), intrapartum nonreassuring fetal heart tracing (22-41%), respiratory distress syndrome (RDS) (29%), and stillbirth (0.75-7%). Based on high rates of stillbirth and neonatal morbidity, early delivery is often advocated to reduce the risk of term stillbirth.[7–9] Hence; the present study was planned for assessing the maternal and perinatal outcome in cholestasis of pregnancy.

In the present study, a total 25 pregnant women with confirmed diagnosis of IHCP and 25 healthy pregnant women (taken as control) were enrolled. 12 subjects of IHCP group and 10 subjects of control group belonged to the age group of 25 to 30 years. 4 subjects of IHCP group and 5 subjects of control group belonged to the age group of 31 to 35 years. Among the patients of IHCP group, pruritus onset occurred in between 33 to 36 weeks of gestation in 12 subjects, while it occurred at more than 36 weeks of gestation in 7 subjects.

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Table 1: Age-wise distribution andage of onset of pruritus

Parameter		IHCP group	Control group
Age group (years)	Less than 25	5	7
	25 to 30	12	10
	31 to 35	4	5
	More than 35	4	3
Onset of pruritus	Less than 28 weeks of gestation	1	N.A
	28 to 32 weeks of gestation	5	
	33 to 36 weeks of gestation	12	
	More than 36 weeks of gestation	7	

Table 2: Comparison of laboratoryinvestigations

Parameter	IHCP group	Control group	p- value
Mean Bilirubin (mg/dL)	0.78	0.51	0.00 (Significant)
Mean SGOT (IU/L)	223.5	38.3	0.00 (Significant)
Mean SGPT (IU/L)	201.8	36.7	0.01 (Significant)

SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamicpyruvic transaminase

Table 3: Intra-partum complications

Complications	IHCP group (n)	Control group (n)	p- value
Pre-term delivery	5	2	0.13
Abruption	1	0	
Fetal distress	6	3	
Adherent placenta	0	1	
Others	1	0	

Table 4: Neonatal outcome

Complications	IHCP group (n)	Control group (n)	p- value
Preterm	5	2	0.85
NICU stay	4	1	0.32
Meconium	5	2	0.12
Mean birth weight (Kg)	3.45	3.19	0.00
Morbidity	0	0	-

NICU: Neonatal intensive care unit

of the IHCP group in comparison to the 3 subjects of the control group. Adherent placenta was found to be present in 1 subject of the contour group. While comparing the intra-partum complications in between the two study groups, non-significant results were obtained. Herrera CA et al examined perinatal outcomes associated with cholestasis of pregnancy according to bile acid level and antenatal testing practice. Women were stratified by bile acid level: no cholestasis (<10 μmol/L), mild (10-39 μmol/L), moderate (40-99 μmol/L), and severe ($\geq$100 μmol/L). The primary outcome was composite neonatal morbidity (hypoxic ischemic encephalopathy, severe intraventricular hemorrhage, bronchopulmonary dysplasia, necrotizing enterocolitis, or death). 785 women were included; 487 had cholestasis (347 mild, 108 moderate, 32 severe) and 298 did not. After controlling for gestational age (GA), severe cholestasis was associated with the composite neonatal outcome (aRR 5.6, 95% CI 1.3-23.5) and meconium-stained fluid (aRR 4.82, 95%CI 1.6-14.2). Bile acid levels were not correlated with the frequency of testing (p = .50). Women who underwent twice weekly testing were delivered earlier (p = .016) than women tested less frequently, but the difference in GA was $\leq$4 d. Abnormal testing prompting delivery was

uncommon. Among women with cholestasis, there were three stillbirths. One of these women was undergoing antenatal testing, which was normal 1 d prior to the fetal demise. Severe cholestasis is associated with neonatal morbidity which antenatal testing may not predict.[11]

In the present study, NICU stay was found to be present in 4 neonates of the IHCP group while it was present in 1 neonate of the control group. Mean birth weight was found to be 3.45 Kg in the IHCP group while it was found to be 3.19 Kg in the control group. Morbidity was absent in both the study groups. Kawakita T et al determined predictors of adverse neonatal outcomes in women with intrahepatic cholestasis of pregnancy (ICP).Obstetric and neonatal complications were evaluated according to total bile acid (TBA) level. Predictors including TBA level, hepatic transaminase level, gestational age at diagnosis, underlying liver disease, and use of ursodeoxycholic acid were evaluated. Of 233 women with ICP, 152 women had TBA levels 10-39.9 μmol/L, 55 had TBA 40-99.9 μmol/L, and 26 had TBA $\geq$100 μmol/L. There was no difference in maternal age, ethnicity, or prepregnancy body mass index according to TBA level. Increasing TBA level was associated with higher hepatic transaminase and total bilirubin level ($P < .05$). TBA levels $\geq$100 μmol/L were associated with increased risk of stillbirth ($P < .01$). Increasing TBA level was also associated with earlier gestational age at diagnosis ($P < .01$) and ursodeoxycholic acid use ($P = .02$). After adjusting for confounders, no predictors were associated with composite neonatal morbidity. TBA 40-99.9 μmol/L and TBA $\geq$100 μmol/L were associated with increased risk of meconium-stained amniotic fluid (adjusted odds ratio, 3.55; 95% confidence interval, 1.45-8.68 and adjusted odds ratio, 4.55; 95% confidence interval, 1.47-14.08, respectively). In women with ICP, TBA level $\geq$100 μmol/L was associated with increased risk of stillbirth.[12]

Conclusion

From the above results, the authors concluded that pregnant women with IHCP are at a higher risk for having pre-term delivery. Although, no significant difference was observed in terms of complications, still these subjects are slightly higher risk of adverse events. Hence; further studies with larger sample size are recommended.

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