Maternal and Fetal Outcome in Intrahepatic Cholestasis of Pregnancy at Tertiary Care Institute of Kashmir Valley in North India

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ABSTRACT

Introduction: Intra Hepatic cholestasis of pregnancy (IHCP) is one of the specific disorders of pregnancy presenting with severe pruritus without any primary skin lesion with raised liver enzymes and bile acids. Maternal complication associated with IHCP include increased risks of post-partum haemorrhage, operative delivery, dyslipidaemia and deranged coagulation profile, preterm prelabour rupture of membrane while adverse perinatal outcomes like spontaneous preterm birth, meconium staining of the amniotic fluid and stillbirth can also be seen. So, the present study is designed with an aim to offer a novel look into the trends of fetomaternal outcome among cases of IHCP as well as to find the incidence of IHCP among study population.

Material and Methods: Case control study conducted over a period of 12 months where patients with diagnosis of IHCP were recruited in the case group while apparently healthy pregnant women with singleton pregnancy were included in the control group. Diagnosis of IHCP was made with complaints of pruritus and deranged liver enzymes (serum transaminases), alanine transaminase (ALT/ > 40 IU/L)/ aspartate transaminase (AST > 35 IU/L), or serum bile acids >14 µmol/L. All confirmed cases of IHCP were advised to take ursodeoxycholic acid (UDCA) 10–15 mg/kg/day.

Results: The incidence of IHCP in our study population was 3.73%. 70% had pruritus all over the body followed by extremities in 16% Elevated ALT levels were detected in 53% while 61% had raised AST levels. Bile acids levels were >14 µmol/l in 86% of patients. Induction of labour was done in 62% cases compared to 22% patients in control group. There was a significant difference found in rate of total caesarean section 50% versus 36% in the case and control groups, respectively. Preterm delivery rate was also higher among IHCP patients at 24 % cases. Present study also showed an increased cases of IHCP complicated by Meconium-stained liquor 28% with approximately 38% associated with preterm birth. There was statistically significant difference noted in neonatal jaundice cases between two groups. In 68% of cases, pruritus got relieved within 1 week and persisted for >1 week in 18% of cases.

Conclusion: Pruritus all over the body rather may be the first complaints of IHCP while increased bile acids are the definitive diagnostic test which could have an adjuvant diagnostic use raised liver enzymes. Early termination of pregnancy is advised in whom liver enzymes/bile acids and symptoms gets resolved with UDCA whereas earlier induction can be advocated in cases with intense itching and persistently raised liver enzymes/bile acids for favourable fetal outcome.

Keywords: Maternal and Fetal Outcome, Intrahepatic Cholestasis, Pregnancy

INTRODUCTION

Pregnancy is a unique physiological phenomenon resulting in almost all systemic systems undergoing adaptations and changes during its course with hepatobiliary system being no exception. One such disorder specific to pregnancy is Intra Hepatic cholestasis of pregnancy (IHCP). IHCP is found globally with protean incidence affecting 0.2-2% of pregnant women worldwide with highest incidence of 4% found in indigenous women from Latin America. [1,2] Contributing factors such as advanced age, multiple pregnancy, family history, and history of cholestasis in previous pregnancy have shown increased prevalence in these patients [3,4] Clinically, it presents with severe pruritus throughout the body predominantly over palms and soles without any primary skin lesion with raised liver enzymes and bile acids. Maternal complication associated with IHCP are increased risks of post-partum haemorrhage, operative delivery, dyslipidaemia and deranged coagulation profile, preterm prelabour rupture of membrane.[5] IHCP is associated with increased risk of adverse perinatal outcomes like spontaneous preterm birth, meconium staining of the amniotic fluid and stillbirth.[6] Due to lack of any specific antenatal fetal monitoring tests to predict sudden intrauterine fetal deaths among such cases, termination of pregnancy is recommended near 36–37 weeks of gestation to avoid perinatal mortality.[7,8,9] There is marked variation in incidence and fetomaternal complications of such cases among pregnant women in literature. So, the present study is designed with an aim to offer a novel look into the trends of fetomaternal outcome among cases of IHCP as well as to find the incidence of IHCP among study population.

MATERIAL AND METHODS

This was a case control study conducted over a period of 12 months from July 2021 to June 2022 in the department of obstetrics and gynaecology GMC Srinagar after approval

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from institutional ethical committee and obtaining Informed consent from patients. Patients with diagnosis of IHCP were recruited in the case group (n = 50) whereas apparently healthy pregnant women with singleton pregnancy were included in the control group (n = 50). All patients underwent testing for complete hemogram, liver function test, aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum bile acids, urine routine, and microscopy test. Difference in the levels of liver enzymes in the 1st and 3rd week of testing was also noticed. Viral markers and ultrasonography of hepatobiliary system and pancreas were also done in all patients to exclude any other pathology. Dermatology consultation was also taken wherever required. Diagnosis of IHCP was made in pregnant women with complaints of pruritus and deranged liver enzymes (serum transaminases), alanine transaminase (ALT/ > 40 IU/L)/ aspartate transaminase (AST > 35 IU/L), or serum bile acids >14 µmol/L. All confirmed cases of IHCP were advised to take ursodeoxycholic acid (UDCA) 10–15 mg/kg/day, with a maximum dose of 300 mg 8 hourly by oral route. Fetal surveillance was done in confirmed cases with biweekly biophysical profile till delivery. All women in the case group received three doses of 10 mg Vitamin K by intramuscular route. An elective termination of pregnancy was done at 37–38 weeks of gestation in all except those induced or had spontaneous labour before this gestation. Incidence of meconium-stained liquor, preterm delivery, mode of delivery, and any complication during labor and delivery were also noted. Fetal outcome such as Apgar score, need of intensive care, and neonatal jaundice in both the groups was also observed. All women were followed up till 6–8 weeks postpartum with liver function test.

Parameter		Number	Percentage
Age (Years)	21-26	11	22
	27-34	31	62
	35-39	8	16
Parity	0	26	52
	1	12	24
	2	8	16
	3	6	12
Gravida	1	22	44
	2	13	26
	3	7	14
	4	5	10
	5	3	6
Pruritus	All over the body	35	70
	Extremities	8	16
	Abdominal and Trunk	5	10

Table-1: Baseline distribution of Cases (n=50)

STATISTICAL ANALYSIS

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Student's independent t-test or Mann-Whitney U-test, whichever feasible, was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A P-value of less than 0.05 was considered statistically significant.

RESULTS

The mean age among cases group of the study population was 29.7 ± 4.73 and range of patient age was 21 to 39 years. IHCP was found more in primigravida 44%. On the bases of parity of cases, IHCP was found more among nullipara i.e 52 % (Table 1) Age and parity of patients between both the groups (cases and controls) had no statistical difference. History of recurrent cholestasis has been found in 25% of multiparous women. The incidence of IHCP in our study population was 3.73%. Dermatologist examined all cases and out of 50 cases, 70% had pruritus all over the body followed by extremities in

Obstetrical outcome	Case (n=50)	Control (n=50)	P-value
Preterm birth	12 (24%)	08 (16%)	0.317
Birth weight (kg)	2.71±1.24	2.62±1.37	0.731
Intrauterine fetal death	02 (04%)	01 (02%)	1.000
Induced labour	31 (62%)	11 (22%)	<0.001*
Mode of delivery			
Vaginal delivery	24 (48%)	32 (64%)	0.118
Forceps delivery	01 (02%)	00 (00%)	
Elective caesarean	16 (32%)	07 (14%)	
Emergency caesarean	09 (18%)	11 (22%)	
Meconium-stained liquor	14 (28%)	05(10%)	0.021*
Fetal distress	8 (16%)	03(06%)	0.201
Perinatal outcome			
Respiratory distress	1 (2%)	1 (2%)	1.000
Jaundice	1 (2%)	4 (8%)	0.359
NICU admission	3 (6%)	2 (4%)	0.646

*Statistically Significant Difference (P-value<0.05)

Table-2: Comparisons of Materno-obstetric outcome between both the groups

16% and itching abdominal pruritis was seen in only in 10% cases. Elevated ALT levels were detected in 54% while 62% had raised AST levels. bile acids levels were >14 µmol/l in 86% of patients. Induction of labour was done in 62% cases compared to 22% patients in control group. There was a significant difference found in rate of total caesarean section 50% versus 36% in the case and control groups, respectively. Preterm delivery rate was also higher among IHCP patients at 24 % cases. Present study also showed an increased cases of IHCP complicated by Meconium-stained liquor 28% with approximately 38% associated with preterm birth. There was no significant difference found in birth weight, sex preponderance, and need of neonatal intensive care between both the groups. There was statistically significant difference noted in neonatal jaundice cases between two groups. (Table 2) There was no significant difference found in rate of postpartum haemorrhage with 6% and 4% in cases and control, respectively. In 68% of cases, pruritus got relieved within 1 week and persisted for >1 week in 18% of cases.

DISCUSSION

Our study had prevalence of 3.73% of IHCP in the population similar to Arora S et al [10] who had a prevalence of 4.08% in their similar study. Our centre being a tertiary care centre might explain the prevalence on a higher side due to referrals from all peripheral areas. The age of the study population in the current study was in the range of 21-39 years with a mean age at presentation as 29.7 ± 4.73 years similar to a similar study by Morton et al [11] who had a mean age of 29 years in their study. In our study the gestational age had a range of 33–39 weeks with a mean gestational age of 35 ± 2.64 weeks similar to Mitra B et al [12] who had a mean gestational age of 37 weeks and 2 days, Studies in the past have showed IHCP to be more common among multigravida lady especially with advanced maternal age.[2,6] However in our study IHCP was more common in nullipara and primigravida similar to studies by Mitra et a l[12] and Kant A et al[13]. History of cholestasis in previous pregnancy was 26% in the present study whereas it was reported in the range of 14.9 to 44 % in other studies.[10,11,14] Pruritis over extremities are more often seen in cases IHCP, however in the present study 70 % of the cases described pruritus predominantly over whole body rather than over extremities similar to study by Arora S et al [10] who had body itching in 65% of the cases. %. In the current study elevated ALT levels were detected in 54% while 62% had raised AST levels whereas bile acids levels were increased in 86% of patients. The findings are similar to the finding by Arora S et al [10] who in their study had raised ALT as 57% and 58% had raised AST levels while 89% of patients has increased bile salt levels. On the other hand, Morton et al [11] in their study had elevated liver enzymes in 52% cases. Improvement of itching and deranged liver function UDCA was seen in the present study as seen in other studies like Arora S et al [10] and Kong et al.[15] unlike Morton et al [11] where increase in liver function test was seen even with UDCA treatment which might be due to inclusion of various medical disorders leading to raised liver enzymes or bile acids. Preterm delivery rate was higher among IHCP patients (24%) similar to study by Dang A et al[16] reported 19.14% of preterm delivery in IHCP patients. Present study also showed overall 28% delivery complicated by MSL. Asulum A et al[17] reported that IHCP was associated with 44.3% rate of MSL in their study. They further explained the probable cause of such high MSL was mainly due to fetal distress and bile acid induced increase in gut motility of foetus. Induction of labour was done in 62% cases compared to 22% patients in control group in the present study. There was also a significant difference found in rate of total caesarean section 50% versus 36% in the case and control groups, respectively however emergency caesarean section difference among both groups was not statistically significant. High incidence of fetal distress in the case group can be explained by induced labour associated adverse events as well as Meconium stained Liquor as there was no significant difference seen in neonatal respiratory distress syndrome in both the groups which may also be attributed to timely termination of pregnancy and immediate decision of caesarean section in the current study as is seen in the study by Puljic et al[8] Also favourable fetal outcome in terms of decreased in fetal distress and neonatal respiratory distress syndrome, NICU admission can be attributed to use of UDCA treatment. [15] There were more cases of jaundice in the control group as compared to cases ($P < 0.033$) in the present study which could be explained by UDCA being a treatment modality in neonatal jaundice.

CONCLUSION

Pruritus all over the body rather may be the first complaints of IHCP while increased bile acids are the definitive diagnostic test which could have an adjuvant diagnostic use raised liver enzymes. Early termination of pregnancy at 37–38 weeks is advised in whom liver enzymes/bile acids and symptoms gets resolved with UDCA whereas earlier induction can be advocated in cases with intense itching and persistently raised liver enzymes/bile acids for favourable fetal outcome.

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