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ORIGINAL RESEARCH

Perinatal outcomes among pregnant women with intrahepatic cholestasis: A comparative prospective study from North India

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Abstract

Background: Postpartum haemorrhage, dyslipidemia, preterm labour, and surgical interference are all higher risks for women with intrahepatic cholestasis of pregnancy (IHCP). Increased incidences of fetal distress (abnormal cardiotocography [CTG], meconium staining), rupture of membrane (preterm and prelabour) and intrauterine death (spontaneous), have been observed in pregnant women with IHCP. So, the present study was conducted with an aim to assess the maternal and fetal outcome among pregnant women with IHCP (intrahepatic cholestatic of pregnancy).

Methods: The present prospective study was conducted among singleton pregnant women (18 or more years, gestational age > 28 weeks) with complaints of pruritis (in palm and sole) in the outpatient (OPD) and labor room of the department of Obstetrics and Gynecology in tertiary care teaching hospital of North India for 12 months (June 2021 to May 2022) after obtaining the ethical approval from the institutional ethical committee. A preformed questionnaire was used for data collection to document sociodemographic, laboratory investigations, maternal outcome, and fetal outcome. The collected data was entered in the Microsoft (MS) Excel Spreadsheet and also, analysis of data carried out using MS Excel Spreadsheet.

Results: In our study, the prevalence of IHCP was among enrolled subjects was 5.15% (41/795).The chi-square analysis showed that the mode of delivery as caesarean section was higher among subjects with IHCP (58.5%) when compared to the subjects without IHCP (35.4%) and this association was statistically significant (p=0.0027). The chi-square analysis showed that the prevalence of low birth weight (IHCP: 46.3% vs without IHCP: 34.4%), meconium-stained liquor (IHCP: 41.5% vs without IHCP: 8.5%) and NICU stay (IHCP: 17.1% vs without IHCP: 4.0%) was significantly higher among subjects with IHCP as compared to without IHCP ($p<0.05$).

Conclusion: One of the frequent causes of hepatic impairment in pregnancy is intrahepatic cholestasis. ICP is linked to poor foetal outcomes include low birth weight, early birth, and abnormal CTG results.

Keywords: Perinatal outcome, intrahepatic cholestasis, pregnancy, bile acid, low birth weight

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Introduction

The several organs impacted by the physiological and hormonal changes that take place during pregnancy include the liver. Pregnancy may have no impact on or may worsen hepatic abnormalities that were identified prior to pregnancy. The morbidity and death rates of the mother and foetus may be significantly impacted by liver diseases such intrahepatic cholestasis of pregnancy (IHCP), toxaemias, and HELLP syndrome (haemolysis, elevated liver enzymes, low platelet count) [1,2].

The cholestatic syndrome known as intrahepatic cholestasis of pregnancy (IHCP) is marked by pruritus that starts in the second or third trimester of pregnancy, raised bile acid and serum aminotransferases levels, and a subsequent improvement of symptoms and signs within 2 to 3 weeks of postpartum period. Involving the palms, soles, trunk and extremities, but sparing the mucous membranes, pruritus is a distinguishing trait that can occur with or without jaundice in IHCP.IHCP accounts for 20% of cases of jaundice during pregnancy, placing it second only to viral hepatitis. In contrast to viral hepatitis, patients with obstructive jaundice experience pale stools and dark urine in addition to their jaundice, but they are otherwise felt well [3,4].

Apparently stated incidence rates of IHCP may varies based on race and geography.The countries with the highest incidence rates of IHCP include Chile (12–20%), Bolivia (9%), and Sweden (2–3%) [5,6]. According to studies, around 1percent of Indian women are estimated to have IHCP. IHCP's precise aetiology is unknown, but genetic, hormonal, and exogenous variables probably have an impact [6].

Significant maternal morbidities are correlated with IHCP. Postpartum haemorrhage, dyslipidemia, preterm labour, and surgical interference are all higher risks for women with IHCP. Increased incidences of fetal distress (abnormal cardiotocography [CTG], meconium staining), rupture of membrane (preterm and prelabour) and intrauterine death (spontaneous), have been observed in pregnant women with IHCP [7,8]. So, the present study was conducted with an aim to assess the maternal and fetal outcome among pregnant women with IHCP (intrahepatic cholestatic of pregnancy).

Materials and methods

The present prospective study was conducted among singleton pregnant women (18 or more years, gestational age > 28 weeks) with complaints of pruritis (in palm and sole) in the outpatient (OPD) and labor room of the department of Obstetrics and Gynecology in tertiary care teaching hospital of North India for 12 months (June 2021 to May 2022) after obtaining the ethical approval from the institutional ethical committee. The criteria to define patient with intrahepatic cholestasis (IHCP) was based clinically evident unexplained pruritus especially in palms, soleswithout skin lesion with increased intensity at night and abnormal liver function test (LFT) i.e., abnormal transaminase enzyme level of greaterthan twice the normal valueand bile acid levels. The informed written consent was obtained from the pregnant mothers prior to the enrollment into the study. The subjects with pregnancy induced hypertension (PIH), HELLP and other causes of cholestasis (viral hepatitis, gall stones, etc) were excluded.

Data collection

A preformed questionnaire was used for data collection to document sociodemographic (age, parity, smoking history), laboratory investigations (total bilirubin, serum glutamic oxaloacetic transaminase [SGOT], serum glutamic pyruvic transaminase [SGPT], alkaline phosphatase [ALP], and serum bile acid [SBA]), maternal outcome (insomnia due to severe pruritis, caesarean delivery/normal delivery, pre-rupture of membrane [PROM], and postpartum hemorrhage [PPH]), and fetal outcome(preterm/term, meconium stained liqour, abnormal

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cardiotocography, neonatal intensive care unit [NICU] stay, low birth weight, small for gestational age [SGA], and alive/intrauterine death). An obstetric examination was done.Routine antenatal investigations with liver functiontests and serum bile acid tests (fasting) were collected.

The pregnant women with IHCP were subsequently treated with tablet ursodeoxycholic acid (UDCA) 10-15 mg/kg/day in divideddoses according to the level of serum bile acid. Liver enzymes were tested weekly/biweekly till delivery. The pregnant women with IHCP were clinically monitored and followed up in high-risk antenatal clinics weekly. Fetalsurveillance was done bymodified biophysical profile (non-stress test [NST] and amniotic fluid index [AFI]) and obstetric ultrasonography.

Extreme elevation of LFT results combined with abnormal fetal heart rate (FHR) or decreased AFI necessitated hospitalization for induction of delivery process. Otherwise, labor was induced routinely at 38–40 weeks' gestation. Subsequently, they werefollowed till 14 days post-delivery

Statistical analysis

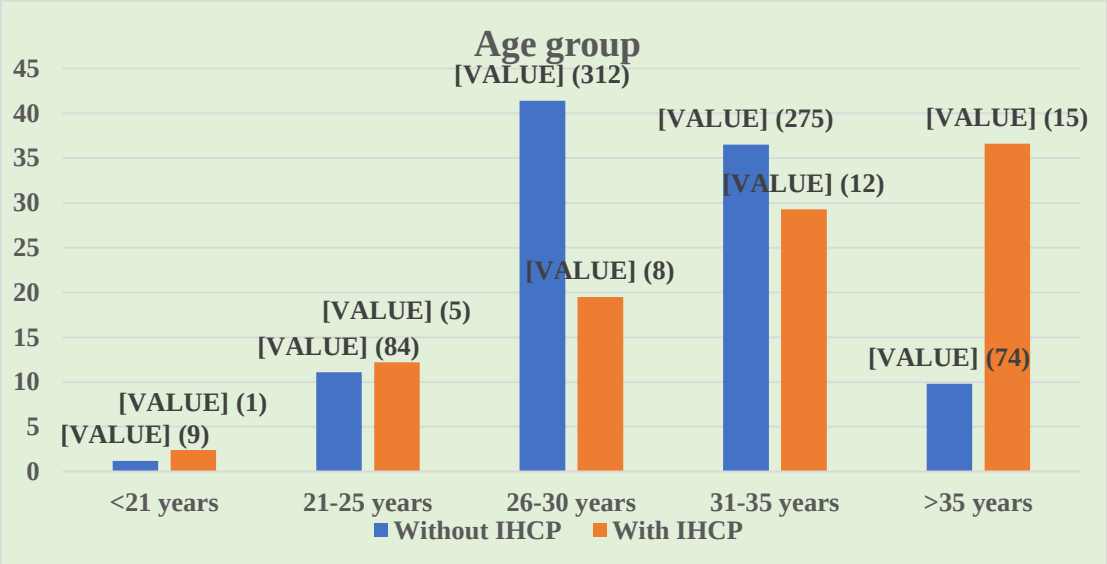
The collected data was entered in the Microsoft (MS) Excel Spreadsheet and also, analysis of data carried out using MS Excel Spreadsheet. The qualitative variables were expressed as number and percentages and quantitative variables were expressed in mean and SD. Chi square test was used to find association between IHCP and maternal/fetal outcome, and independent T test was used to find the association between IHCP and laboratory parmeters, and a p value of <0.05 was considered as statistically significant.

Results

In our study, a total of 839 singleton pregnant women (18 or more years, gestational age > 28 weeks) with complaints of pruritis (in palm and sole) attended either outpatient (OPD) or admitted in labor room between June 2021 to December 2021, but 44 subjects were lost to follow up and their maternal and fetal outcome was unknown, so they were not included in the data analysis and data analysis was done among only 795 subjects.

Among 795 subjects, 41 subjects were diagnosed with IHCP and 754 subjects were without IHCP. A specific pattern was observed in our study, that the prevalence of the IHCP increased with the increase in the age of subjects and around among one third of subjects with IHCP (36.6%) were having age of >35 years, and this pattern was statistically significant ($\chi 2=30.590$, df=4, $p<0.0001$) (Figure 1).

Figure 1: Age wise distribution of pregnant women with IHCP and without IHCP.



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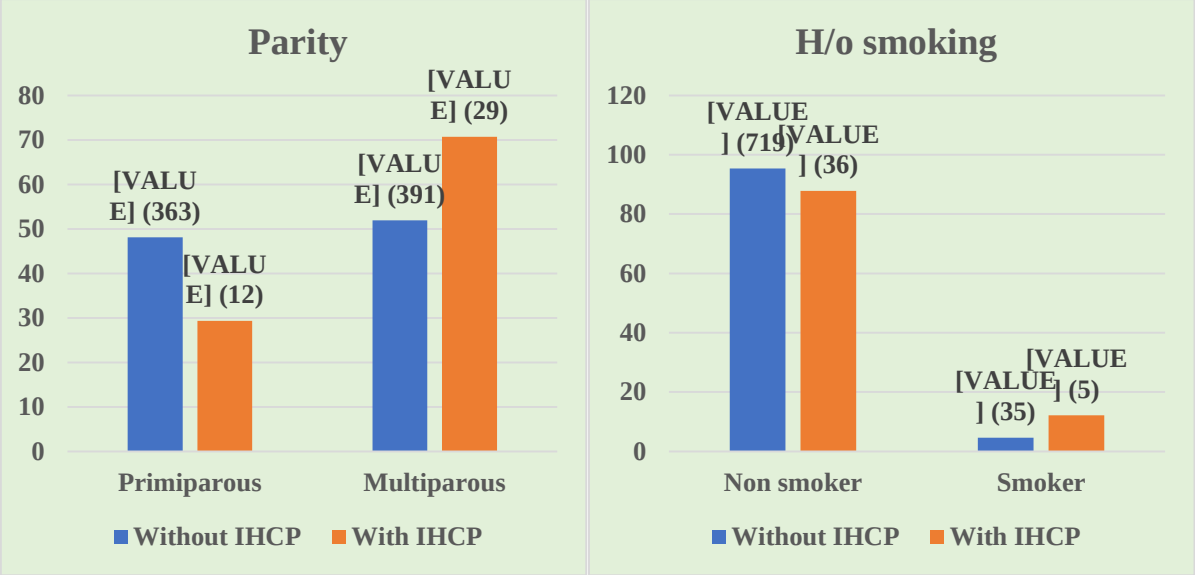
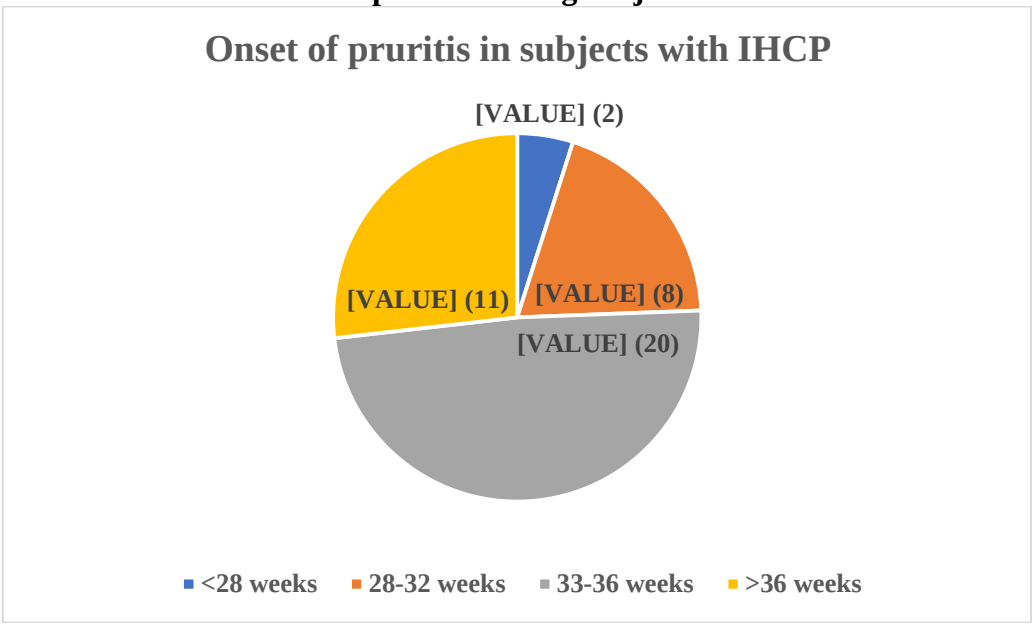
In our study the prevalence of IHCP was significantly higher ($\chi 2=5.559$, df=1, p=0.018) among multiparous subjects (70.7%) compared with the primiparous subjects (29.3%). Also, there statistically significant difference ($\chi 2=4.642$, df=1, p=0.031) among subjects with history of smoking for occurrence of IHCP (12.2%) and no IHCP (4.6%) (Figure 2).

Figure 2: Baseline comparison of pregnant women with IHCP and without IHCP.



It was observed in our study that onset of pruritis among subjects with IHCP increased with the increase gestational age (< 28 weeks: 4.9%, 28-32 weeks: 19.5% and 33-36 weeks: 48.8%) and started reducing on the subjects with age >36 weeks of gestational age (26.8%) (Figure 3).

Figure 3: Distribution of onset of pruritis among subjects with IHCP.



The laboratory parameters (total bilirubin, SGOT, SGPT, ALP, SBA) were significantly (p<0.05) raised among subjects with IHCP as compared to the subjects without IHCP. The mean total bilirubin levels among subjects with IHCP and without IHCP were 0.81±0.73 mg/dL and 0.55±0.42 mg/dL respectively. The mean SGOT levels among subjects with IHCP and without IHCP were 107.3±94.3 IU/L and 32.4±10.3 IU/L respectively.The mean ALP levels among subjects with IHCP and without IHCP were 234.8±124.2 IU/Land 138.3±78.5 IU/L respectively (Table 1).

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Table 1: Laboratory parameters among pregnant women with IHCP and without IHCP.

Lab parameters	With IHCP (n=41)	Without IHCP(n=754)	Test of significance
Total Bilirubin (mg/dL)	0.81±0.73	0.55±0.42	T=3.677, df=793, p=0.0003
SGOT (IU/L)	107.3±94.3	32.4±10.3	T=19.929, df=793, p<0.0001
SGPT (IU/L)	121.4±98.7	25.8±11.2	T=24.127, df=793, p<0.0001
ALP(IU/L)	234.8±124.2	138.3±78.5	T=7.391, df=793, p<0.0001
SBA(mg/dL)	16.81±14.32	6.23±5.34	T=10.785, df=793, p<0.0001

The chi-square analysis showed that the mode of delivery as caesarean section was higher among subjects with IHCP (58.5%) when compared to the subjects without IHCP (35.4%) and this association was statistically significant (p=0.0027). Also, insomnia due to severe pruritis was higher among subjects with IHCP (61.0%) when compared to the subjects without IHCP (23.9%) and this association was statistically significant (p<0.0001).In our study the occurrence of PPH was higher among subjects with IHCP (19.5%) when compared to the subjects without IHCP (9.4%) and this association was statistically significant (p<0.035).Althoughthe occurrence of PROM was higher among subjects with IHCP (17.1%) when compared to the subjects without IHCP (10.1%) and but this association was statistically non-significant (p>0.05) (Table 2).

Table 2: Maternal outcome among pregnant women with IHCP and without IHCP.

Maternal outcome	With IHCP (n=41)	Without IHCP (n=754)	Test of significance
Mode of delivery			
Caesarean section	24 (58.5)	267 (35.4)	χ^2=8.961, df=1, p=0.0027
Vaginal	17 (41.5)	487 (64.6)	
Insomnia due to severe pruritis			
Yes	25 (61.0)	180 (23.9)	χ^2=27.972, df=1, p<0.0001
No	16 (39.0)	574 (76.1)	
Pre-rupture of membrane (PROM)			
Yes	7 (17.1)	76 (10.1)	χ^2=2.034, df=1, p=0.153
No	34 (82.9)	678 (89.9)	
Postpartum hemorrhage (PPH)			
Yes	8 (19.5)	71 (9.4)	χ^2=4.412, df=1, p=0.035
No	33 (80.5)	683 (90.6)	

In our study the CTG was abnormal higher among 17.1% of subjects with IHCP as compared to subjects without IHCP (6.0%). The rate of preterm birth was higher among subjects with IHCP (41.5%) as compared to subjects without IHCP (29.0%). The proportion of infants with SGA was higher in subjects with IHCP (34.1%) as compared to subjects without IHCP (14.3%). The chi-square analysis showed that the prevalence of low birth weight (IHCP: 46.3% vs without IHCP: 34.4%), meconium-stained liquor (IHCP: 41.5% vs without IHCP: 8.5%) and NICU stay (IHCP: 17.1% vs without IHCP: 4.0%) was significantly higher among subjects with IHCP as compared to without IHCP (p<0.05) (Table 3).

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Table 3: Fetal outcome among pregnant women with IHCP and without IHCP.

Fetal outcome	With IHCP (n=41)	Without ICHP (n=754)	Test of significance
Cardiotocography (CTG)			
Abnormal	4 (17.1)	45 (6.0)	$\chi2$=0.964, df=1, p=0.326
Normal	37 (82.9)	709 (94.0)	
Birth			
Preterm	17 (41.5)	219 (29.0)	$\chi2$=2.872, df=1, p=0.090
Term	24 (58.5)	535 (71.0)	
Meconium-stained liquor			
Yes	17 (41.5)	64 (8.5)	$\chi2$=46.208, df=1, p<0.0001
No	24 (58.5)	690 (91.5)	
Birth weight			
Low	19 (46.3)	259 (34.4)	$\chi2$=4.412, df=1, p=0.035
Normal	22 (53.7)	495 (65.6)	
Small for Gestational Age (SGA)			
Yes	14 (34.1)	108 (14.3)	$\chi2$=2.458, df=1, p=0.116
No	27 (65.9)	646 (85.7)	
Neonatal Intensive Care Unit (NICU) stay			
Yes	7 (17.1)	30 (4.0)	$\chi2$=15.025, df=1, p<0.0001
No	34 (82.9)	724 (96.0)	

Discussion

In our study, the prevalence of IHCP was among enrolled subjects was 5.15% (41/795), which was quite higher than the study by Ray et al., where the reported prevalence was less than 1 percent [9].

A specific pattern was observed in our study, that the prevalence of the IHCP increased with the increase in the age of subjects and around among one third of subjects with IHCP (36.6%) were having age of >35 years, and this pattern was statistically significant ($\chi2$=30.590, df=4, p<0.0001). A similar pattern was noted in the studies by Heinonen et al., and Gardiner et al., [10,11].

In our study the prevalence of IHCP was significantly higher ($\chi2$=5.559, df=1, p=0.018) among multiparous subjects (70.7%) compared with the primiparous subjects (29.3%). Also, there was statistically significant difference ($\chi2$=4.642, df=1, p=0.031) among subjects with history of smoking for occurrence of IHCP (12.2%) and no IHCP (4.6%). In contrast to present study, no association of IHCP was observed with parity or smoking statusin the study by Medda et al., [12].

It was observed in our study that onset of pruritis among subjects with IHCP increased with the increase gestational age (< 28 weeks: 4.9%, 28-32 weeks: 19.5% and 33-36 weeks: 48.8%) and started reducing on the subjects with age >36 weeks of gestational age (26.8%). A similar pattern was observed in the study done by Geenes et al., and Estiú et al., [13,14].

In our study, the laboratory parameters (total bilirubin, SGOT, SGPT, ALP, SBA) were significantly (p<0.05) raised among subjects with IHCP as compared to the subjects without IHCP. The mean total bilirubin levels among subjects with IHCP and without IHCP were 0.81±0.73 mg/dL and 0.55±0.42 mg/dL respectively. Similar pattern of raised bile acids among pregnant women with IHCP was observed in the study by Guntupalli et al., [15].

The chi-square analysis showed that the mode of delivery as caesarean section was higher among subjects with IHCP (58.5%) when compared to the subjects without IHCP (35.4%)

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and this association was statistically significant (p=0.0027) and was similar to the studies by Kant et al., and Herrara et al., [16,17].

In our study the CTG was abnormal higher among 17.1% of subjects with IHCP as compared to subjects without IHCP (6.0%). The rate of preterm birth was higher among subjects with IHCP (41.5%) as compared to subjects without IHCP (29.0%). The proportion of infants with SGA was higher in subjects with IHCP (34.1%) as compared to subjects without IHCP (14.3%). The chi-square analysis showed that the prevalence of low birth weight (IHCP: 46.3% vs without IHCP: 34.4%), meconium-stained liquor (IHCP: 41.5% vs without IHCP: 8.5%) and NICU stay (IHCP: 17.1% vs without IHCP: 4.0%) was significantly higher among subjects with IHCP as compared to without IHCP ($p<0.05$). Similarly in studies the by Heinonen et al., and Medda et al., showed higher incidences of LBW and meconium-stained liquor among pregnant women with IHCP [10,12]. In the study by Kenyon et al., Rioseco et al., Williamson et al., and Kawatika et al., have shown that rate of NICU admission for newborn was higher among subjects with IHCP as compared born to mothers without IHCP [18,19,20,21].

Conclusion

One of the frequent causes of hepatic impairment in pregnancy is intrahepatic cholestasis. ICP is linked to poor foetal outcomes include low birth weight, early birth, and abnormal CTG results. ICP is linked to several maternal outcomes, including PPH, dyslipidemia, and insomnia. The prognosis for maternal outcomes is good, but timely and efficient intervention can enhance foetal outcomes.

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