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Original Research Article

Feto-maternal Outcome in intrahepatic cholestasis of pregnancy

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Abstract: The aim of the study is to find out the incidence & maternal and fetal outcome in intrahepatic cholestasis of pregnancy. This prospective study was conducted during the period of June, 2015 to May 2016 in Gauhati Medical College and Hospital. Out of 417 cases diagnosed as intrahepatic cholestasis of pregnancy, 100 cases were selected at random for inclusion in our study. Diagnosis of intrahepatic cholestasis was based on clinical and laboratory parameters and disappearance of symptoms after delivery. All the patients were given ursodeoxycholic acid. All cases were followed up to the delivery to find out feto-maternal outcome. Incidence of intrahepatic cholestasis was found to be 2.59%. Most of the cases were diagnosed in third trimester. Pruritus was the chief complaint which was relieved with ursodeoxycholic acid and 100% recovery was observed after delivery. Serum bile acids and Liver enzymes were raised in all cases. Adverse fetal outcomes were mainly associated with raised maternal serum bile acids level. No significant adverse maternal outcome was observed except increased rate of instrumental delivery including LSCS. Intrahepatic cholestasis of pregnancy is found to be associated with adverse perinatal outcome, incidence of which correlates with raised serum bile acids level. Serum bile acids level should be checked in clinically suspected cases for deciding optimal timing of delivery to avoid adverse fetal outcome.
Keywords: Intrahepatic Cholestasis, Bile acid, Perinatal Outcome, Pruritus, Meconium stained liquor

INTRODUCTION

Intrahepatic cholestasis of pregnancy (ICP) also known as Obstetric Cholestasis (OC) is defined as generalised pruritus including palms and soles late in pregnancy that resolve following delivery and may recur in future pregnancy [1,2]. For the diagnosis of ICP other causes of pruritus should be excluded [3, 4]. It is usually associated with elevated serum bile acid levels and/or elevated serum aminotransferases level with reversal of laboratory abnormalities promptly after delivery but no later than one month postpartum [5,6]. The use of ursodeoxycholic acid (UDCA) provides symptomatic relief of pruritus [7, 8]. The incidence of ICP varies widely from 0.1-24% based on geographical location and ethnicity [5, 9]. Incidence of ICP has been reported 1% in Indian women [10]. Use of oral contraceptive pills for contraception can cause pruritus in patients having history of cholestasis in pregnancy [11]. ICP is relatively benign to women but it is reported to have important fetal implications. ICP is linked with the higher risk of preterm delivery, meconium stained liquor, fetal distress and intrauterine fetal death [12, 13]. Optimal timing of delivery to prevent adverse fetal outcome is still debated [14, 15]. Diagnosis of ICP is important for management of current pregnancy, subsequent pregnancy and to avoid the use of OCPs as contraception.

This study was conducted to find out the incidence of ICP among our population and feto-maternal outcome in pregnancies affected by intrahepatic cholestasis.

MATERIAL AND METHODS

Out of the 417 cases diagnosed as intrahepatic cholestasis in 1 year of study period, 100 cases were selected at random for inclusion in our study. The diagnosis of intrahepatic cholestasis of pregnancy was based upon history, scratch marks, elevated levels of serum bile acids and liver enzymes in the absence of any other liver disease and postpartum relief of symptoms. To rule out other causes of pruritus, dermatology consultation was taken and trans-abdominal USG to rule out liver and gall bladder

pathology and blood test for hepatitis B surface antigen and hepatitis C antibody was done. For pruritus, Ursodeoxycholic acid (UDCA) was administered in dose of 600 mg/daily as it has antipruritic effect.

The pregnancy course in our cases was carefully monitored upto 38 weeks gestation or spontaneous onset of labour. Labour was induced in patients who were not in spontaneous labour by 38 weeks of gestation. Maternal evaluation included observation for development of jaundice, any change in urine or stool colour, or bleeding tendency. Fetal surveillance was done with daily fetal movements count, clinical fetal heart rate monitoring and ultrasonography (when indicated). Cases were analysed for gestational age at diagnosis, gestational age at delivery, onset of labour, mode of delivery, birth weight, presence of meconium stained liquor, fetal distress, meconium aspiration, respiratory distress, PPH, APGAR score at 1 and 5 minutes, sepsis, pneumonia, need for neonatal intensive care (NICU) admission and perinatal mortality. Time required for postnatal resolution of symptoms was noted.

The data were presented as mean ± 1SD or percentages. Logistic regression analysis was done to find the possible correlation between maternal serum biochemical assays and adverse fetal outcomes (preterm delivery, meconium stained liquor and NICU admission). P value <0.05 was considered to be statistically significant.

RESULTS

Among the 16,044 pregnant women in our hospital, 417 women were diagnosed with intrahepatic cholestasis of pregnancy. So the incidence was found to be 2.59%. Patients in the study group were in age range of 18 to 36 years and mean age was 25.98±4.17 (mean±SD) years. 62% patients were nullipara and 38% were multipara. 63.15% of multipara had past history suggestive of ICP. 16% patients gave family history of ICP. Gestational age at the time of diagnosis of ICP varied in range of 27 weeks to 39 weeks. Maximum cases (22%) were diagnosed at 34 weeks. The mean gestational age at the time of diagnosis was 33.32 ± 2.81 (mean ± SD) weeks. Main symptom of ICP was pruritus (100% cases) which involved palms & soles (47% cases) and caused disturbed sleep (65% cases) and scratch marks (82% cases). 16% of cases also complained of dark colour urine. Among 23% patients who had used oral contraceptive pills (OCPs) as contraceptive method, 39.13% patients gave history of pruritus with the use of OCPs. Serum bile acids and Liver enzymes were raised in all cases (100%) while s. bilirubin was slightly raised in 94% of cases. Range, mean values and standard deviation from mean value of liver enzymes, serum bilirubin and serum bile acids are shown in Table no. 1.

Table 1: Laboratory values of patients with ICP

Investigation	Normal values in pregnancy	Range	Mean	Standard Deviation
Serum Bile Acid [µmol/L]	<10	12-52.4	26.81	±9.85
AST (SGOT) [U/L]	17-59	68-331	109.38	±43.09
ALT (SGPT) [U/L]	21-72	76-308	112.18	±37.60
Serum Total Bilirubin [mg/dl]	0.2-1.3	0.2-1.5	0.632	±0.298
ALKP [U/L]	38-126	143-906	349.2	±177.52

UDCA was prescribed in 82% of cases. Among them, 89.02% cases had relief from symptoms. Gestational age at delivery of patients ranged from 30 weeks to 40 weeks. Mean estimated gestational age at delivery was 37 weeks ±1.78 SD. There were 23 preterm deliveries and 77 term deliveries in our study. Out of the 100 cases of ICP, 62 cases went into spontaneous labour, 26 patients received induction of labour and rest 12 cases had elective LSCS. There were 63 vaginal deliveries and LSCS was done in 37% cases [12% elective and 25% emergency LSCS]. Among 63% vaginal delivery, 52% cases had spontaneous delivery and 11% cases had instrumental delivery. Incidence of spontaneous delivery was 64.5% in patients in whom labour was spontaneous in onset while it was 46.15% in induced labour group. Instrumental delivery rates in both groups were 8.06% and 23.06% respectively. Incidence of emergency LSCS is 30.76% in patients in whom labour was induced which is higher than in the patients (27.41%) in whom labour was spontaneous in onset. Most common indication of LSCS was meconium stained liquor (40.54%). Other indications were CPD, fetal bradycardia, prolonged labour, breech presentation, bad obstetric history, 1st twin breech in twin pregnancy & post caesarean pregnancy.

Mean birth weight was 2.625 kg. 77% patients had birth weight 2.5kg or more than that while 23% patients had birth weight less than 2.5kg. Mean one minute and five minutes APGAR scores were 8.5 (S.D. ±1) and 8.9 (S.D. ±1). There were no 5 minute APGAR scores less than 7. There were 2 cases of IUFD in our study. Both presented with complaint of loss of fetal movement at 39 weeks for the first time. On delivery of

both IUFD patients, liquor was thickly meconium stained. There was no congenital anomaly, birth weights were 2.8kg & 2.6kg, placenta was normal except stained with meconium, no retro placental clots were seen. Fetal outcome which we found were 23% preterm delivery, 29% patients had meconium stained liquor, 2% IUFD and 21% NICU admissions. APGAR score was normal in all cases of meconium stained liquor. Indications of NICU admissions were meconium aspiration in 4 cases (19.04%), prematurity and low birth weight in 6 cases (28.57%), early onset sepsis in 7 cases (33.33%) and hyperbillirubinaemia in 4 cases (19.04%).

Table 2: Fetal outcome in patients with ICP

Fetal outcome	No. of cases
Preterm delivery	23
Meconium stained liquor	29
IUFD/still born	02
NICU admission	21

There was no significant maternal complication seen except that 6 patients had PPH which was managed conservatively. Maternal outcomes showed that 11 patients had instrumental delivery and 37 patients had LSCS.

Table 3: Maternal outcomes in patients with ICP

Maternal outcome	No. of cases	Percentage
Induction of labour	26	26%
Instrumental delivery	11	11%
LSCS	37	37%
PPH	6	6%

Fetal outcome were not correlated with serum bilirubin and Liver transaminases (AST and ALT) level. Serum bile acids level showed no significant correlation with preterm labour but showed significant correlation with meconium staining of liquor and NICU admissions. Fetal complications were observed in all cases having serum bile acid level >40 µmol/l. The two-sided P value is for this relation was 0.0007, considered extremely significant.

Table 4: Correlation of serum bile acids with fetal outcome

Fetal outcome	Correlation coefficient	P value	Significance
Preterm labour	0.05	0.060	Not significant
Meconium stained liquor	0.25	0.028	Significant
NICU admission	0.25	0.0285	Significant

DISCUSSION

In our hospital incidence of ICP is found to be 2.59%. Results of our study is comparable to the study done by Nalini sharma *et al.;* (2.4%) [16]. Incidence, Mean age, parity, recurrence rate and gestational age at diagnosis were comparable to other studies shown in Table no. 5.

Table 5: Comparison among different studies

Patient characteristic	Lt Col G Singh *et al.*; [17]	M Padmaja *et al.*; [18]	Dang Arbinder *et al.*; [19]	Gupta Amita *et al.*; [20]	Nalini sharma *et al.;* [16]	Present study
Incidence	1.8%	8.2%	0.79%	9.3%	2.4%	2.59%
Mean age (years)	25.8	28.7	26.5	-	-	25.9
Parity	48(P0) & 52(≥P2)	68.8(P0) & 31.1(≥P2)	72.3(P0) & 27.6(≥P2)	-	-	62(P0) & 38(≥P2)
Recurrence rate	-	64.3%	-	50%	-	61.3%
Gestational age at diagnosis	-	32weeks	31weeks	30 weeks	30 weeks	34weeks

P0- nullipara, ≥P2- multipara

Main symptom was pruritus mainly affecting palms and soles, 16% cases had dark colour urine with no case of clinical jaundice which is comparable to that reported by M Padmaja *et al.;* [18] where 11.1% cases had dark colour urine with no case of clinical jaundice. UDCA showed effectiveness in improvement of symptoms in 89.02% cases which is similar to that reported by Lt Col G Singh *et al.;* [17] in 88.89% and Gupta Amita *et al.;* [20] in 100% cases. In our study, serum bile acids & liver enzymes were raised in all cases (100%) while S. bilirubin was slightly raised in 94% of cases. Lt Col G Singh *et al.;* [17], M Padmaja *et al.;* [18], and Hani A *et al.;* [21] also found that fasting bile acids, Liver enzyme and total bilirubin level were high in ICP group.

Mean estimated gestational age at delivery was 37 weeks comparable to that reported by M Padmaja *et al.;* [18] and Hani A *et al.;* [21] which were 37 weeks and 36.6 weeks respectively. There were 23% preterm deliveries and 77% term deliveries. Various others studies [17-19] have reported high incidence of preterm delivery in pregnancies affected by ICP (shown in Table no. 6). Mean birth weight was 2.6±0.4 kg which is appropriate for gestational age. It is similar to that reported by Lt Col G Singh *et al.;* [17] and Dang Arbinder *et al.;* [19] which were 2.792±0.566 kg & 2.92±0.4 kg. It indicates that birth weight is not affected by ICP. Rate of instrumental delivery including LSCS is higher in pregnancies affected by ICP due to increased incidence of meconium staining of liquor and induction of labour. However, in spite of high incidence of meconium staining, APGAR score is nearly normal in all studies [18, 20]. It shows that meconium staining of amniotic fluid seen in ICP is not due to fetal distress; instead it is because of bile acids as bile acids are suggested to increase colonic motility and meconium passage [22]. Apart from preterm delivery and meconium staining of amniotic fluid, there are risks of IUFD/still born and increased chances of NICU admission as reported by different authors (Table no.6)

Table 6: Fetal outcome in different studies

Study	Preterm delivery	Meconium stained liquor	IUFD/ stillborn	NICU admission
Lt Col G Singh *et al.;* [17]	14.81%	18.52%	0%	0%
M Padmaja *et al.;* [18]	24.4%	17.8%	01%	15.6%
Dang Arbinder *et al.;* [19]	19.14%	40.4%	0%	4.25%
Gupta Amita *et al.;* [20]	0%	9.6%	0%	0%
Present study	23%	29%	02%	21%

There are no significant adverse maternal outcome was reported in intrahepatic cholestasis of pregnancies except increased incidence of instrumental delivery including LSCS which was also seen in other studies (17-20).

Table 7: Maternal outcome in different studies

Study	Instrumental delivery	LSCS	PPH
Lt Col G Singh *et al.;* [17]	7.41%	29.63%	0%
M Padmaja *et al.;* [18]	0%	93.3%	0%
Gupta Amita *et al.;* [20]	0%	44.5%	0%
Hani A *et al.;* [21]	0%	19.7%	4%
Present study	11%	37%	6%

Glantz A *et al.;* [23] reported increased adverse fetal outcome if serum bile acid was >40 µmol/l. In our study also, we found that patients having s. bile acid level >40 µmol/l seem to have more fetal complications (p value 0.0007). Hani A *et al.;* [21] reported that significant positive correlation was seen between maternal fasting bile acids level and Meconium staining of amniotic fluid (P value <0.001) which was found in our study also (P value 0.02) .

CONCLUSION

Intrahepatic cholestasis of pregnancy is found to be associated with adverse perinatal outcomes (meconium staining of amniotic fluid and NICU admission), incidence of which correlates with raised serum bile acids level. Serum bile acids level should be checked in clinically suspected cases for deciding optimal timing of delivery to avoid adverse fetal outcome.

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