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Original Research Article

A PROSPECTIVE STUDY ON PERINATAL OUTCOME OF OBSTETRIC CHOLESTASIS IN A TERTIARY CARE CENTRE

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Abstract

Background: The present study was done to evaluate the perinatal outcomes, maternal outcomes and fetal outcomes, of intrahepatic cholestasis in an Indian population. **Materials and Methods:** This was a prospective observational study, carried out to analyse the impact of intrahepatic cholestasis of pregnancy on the maternal and fetal outcome. The study was conducted in Department of Obstetrics and Gynaecology, Madhubani Medical College, Madhubani, Bihar. from October 2022 to September 2023. The study was approved by Institutional Ethics Committee. Written informed consent was obtained from patient before enrolling them into the study. Total 550 pregnant women were screened during the study period. Patients with ICP were identified in maternity care units after eliciting history about itching. The data was entered in the excel sheet. The data was analyzed using descriptive statistics. **Result:** Total 550 pregnant women were screened during the study period. As per the diagnostic criteria defined criteria for intrahepatic cholestasis of pregnancy (ICP) for the present study, 31 pregnant women have been found to be suffering from ICP. This give the overall prevalence of 5.63% of HG for the present study. **Conclusion:** Intrahepatic cholestasis of pregnancy is one of the common causes of hepatic impairment in pregnancy. Maternal outcomes have good prognosis but fetal outcomes can be improved by timely and effective intervention.

INTRODUCTION

The liver is one of the many organs affected by the physiological and hormonal changes that occur during pregnancy.[1] Hepatic disorders diagnosed before pregnancy may be unaffected or exacerbated by the pregnant state.[2] Liver disorders like intrahepatic cholestasis of pregnancy (ICP), toxaemias, HELLP syndrome may have a profound impact on the morbidity and mortality rates of the mother and fetus.[3] Although an equivocal diagnosis is often difficult to make, it should be attempted in a timely manner so that optimal treatment can be determined.3 Intrahepatic cholestasis of pregnancy (ICP) is a cholestatic syndrome characterized by Pruritus with onset in the second or third trimester of pregnancy, Elevated serum aminotransferases and bile acid levels, Spontaneous relief of signs and symptoms within two to three weeks after delivery.[4] The syndrome of ICP, the most frequent of liver disorders specific to pregnancy, was recognized by Ahlfeld in 1883 as maternal pruritus and jaundice in the last trimester of pregnancy disappearing after delivery.[5] The most comprehensive studies of modern era initially were performed in Scandinavian women in 1950s by Svanborg and Thorling.[6-8]

Reported incidence rates may vary with geographic location and race.8 Highest incidence rates of 12-20% are in Chile and rest include 9% in Bolivia, 2%-3% in Sweden 0.2%-0.8% in Australia, 0.2% in France, 0.13% in china and 0.1% in Canada.[9-11] The incidence of ICP among Indian women has been reported to be around 1%.[12,13] The exact cause of ICP is not known but genetic, hormonal and exogenous factors do play a role.[14]

Pruritus with or without jaundice, is a hall mark feature and involves palms, soles, extremities and trunk but spares mucous membranes.[8,10,11] Pruritus persists with fluctuating severity till delivery and disappears after parturition.[10,11]

ICP is second only to viral hepatitis as a cause of jaundice during pregnancy and accounts for 20% of cases.[15] Whenever jaundice occurs, it generally follows onset of pruritus by 2-4 weeks and usually resolves by 1 4 weeks post- partum.[16] Typical features of obstructive jaundice, including pale stools

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and dark urine, accompany jaundice, but the patients feel generally well in contrast to viral hepatitis.[17,18]
ICP is associated with significant maternal morbidities. Women with ICP have an increased risk for postpartum haemorrhage, dyslipidaemia, preterm labour and operative interference.[19,20] Fetus in ICP has been associated with an increased incidence of preterm labour, preterm prelabour rupture of membrane, fetal distress, abnormal CTG, meconium staining, spontaneous intrauterine death.[19-22]
The present study was done to evaluate the perinatal outcomes, maternal outcomes and fetal outcomes, of intrahepatic cholestasis in an Indian population.

MATERIALS AND METHODS

This was a prospective observational study, carried out to analyse the impact of intrahepatic cholestasis of pregnancy on the maternal and fetal outcome. The study was conducted in Department of Obstetrics and Gynaecology, Madhubani Medical College, Madhubani, Bihar. from October 2022 to September 2023. The study was approved by Institutional Ethics Committee. Written informed consent was obtained from patient before enrolling them into the study. Total 550 pregnant women were screened during the study period. Patients with ICP were identified in maternity care units after eliciting history about itching. The diagnosis was based on Clinical examinations, generalized pruritus in the absence of any dermatologic condition, Laboratory results, cholestatic pattern: serum aspartate and alanine transferase exceeding 40 U/L; that returned to normal after delivery, No signs of viral hepatitis, negative results in assays for hepatitis B surface antigen and anti-hepatitis A and C antibodies, Normal ultrasonography of the liver and biliary tract.
To eliminate confounding factors for the present study, pregnancies with pregnancy induced hypertension and other liver diseases in pregnancy were excluded.
The pregnant women with ICP, underwent careful weekly outpatient clinical monitoring. During the visit, the patients were advised Nonstress Test (NST), amniotic fluid (AF) volume assessment using the four-quadrant amniotic fluid index (AFI) and liver function tests (LFT). 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.
Patients' demographic data and pregnancy outcome measures were recorded in case record form. For the present study, following maternal outcomes were studied: insomnia due to severe pruritus; dyslipidemia; abnormal coagulation profile (increase PT); mode of delivery; preterm pre-labour rupture of membrane (PROM); and postpartum hemorrhage.
Abnormal cardiotocography (CTG); Birth weight (low birth weight <2.5kg); small for gestational age (SGA: the bottom tenth percentile for weight according to week of gestation and gender); pre-term delivery (birth before 37 weeks of gestation); meconium stained liquor were assigned as fetal outcomes.
The data was entered in the excel sheet. The data was analyzed using descriptive statistics. The test variables were compared using Chi-square test for qualitative variables and Student's test for quantitative variables. The p-value < 0.05 was considered statistically significant for difference and association between variables.

RESULTS

Total 550 pregnant women were screened during the study period. As per the diagnostic criteria defined criteria for intrahepatic cholestasis of pregnancy (ICP) for the present study, 31 pregnant women have been found to be suffering from ICP. This give the overall prevalence of 5.63% of HG for the present study.
[Table 1] shows the distribution of patients according to age. Out of 550 patients 31 pregnant women have been found to be suffering from ICP (5.63%). In the category of patients without ICP 6 patients were less than 20 years (1.15%), 58 patients were in between 20-24 years (11.17%), 215 patients were in between 25-29 years (41.42%), 189 patients were in between 30-34 years (36.41%) and 51 patients were more than 35 years (9.82%). In the category of patients with ICP 0 patients were less than 20 years, 4 patients were in between 20-24 years (12.90%), 7 patients were in between 25-29 years (22.58%), 9 patients were in between 30-34 years (29.03) and 11 patients were more than 35 years (35.48%).
According to [Table 1], the most frequently affected age-group with ICP were belong to age > 35 years (11,35.48%), followed by age groups of 30-34 years (9, 29.03%) and 25-29 years (7, 22.58%).
[Table 2] shows the distribution of patients according to socio-economic factors. In the category of patients without ICP, 225 patients were from lower class (43.35%), 199 patients were from lower middle class (38.34%), 68 patients were from upper middle class and 27 patients were from higher class (13.10%). In the category of patients with ICP ,11 patients were from lower class (35.48%), 9 patients were from lower middle class (29.03%), 7 patients were from upper middle class (22.58%) and 4 patients were from higher class (12.90%).
Out of 69 patients 27 patients were from lower class (39.13%), 21 were from lower middle class (30.43%),14 patients were from upper middle class (20.28%) and 7 patients were from higher class (10.14%). Maximum number of patients with abnormal uterine bleeding presented in lower middle class whereas least patients presented in higher class.
[Table 3] shows the distribution of patients according to parity. In the category of patients without ICP 259 patients were of primipara (49.90%) and 260 patients were of multipara (50.09%). In the category of patients with ICP 9 patients were of primipara

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(29.03%) and 22 patients were of multipara (70.97%). A majority of pregnant women with intrahepatic cholestasis of pregnancy was of multipara.

[Table 4] shows the distribution of patients according to smoking habit. In the category of patients without ICP 495 patients did not smoke (95.38%) and 24 patients used to smoke (4.62%). In the category of patients with ICP 27 patients did not smoke (87.10%) and 4 patients used to smoke (12.90%). There were no association found between smoking habit with development of intrahepatic cholestasis of pregnancy.

[Table 5] shows the distribution of patients according to fetal outcomes of pregnancy. Development of intrahepatic cholestasis of pregnancy was highly significantly associated with small for gestational age (SGA, p-value: 0.0003); abnormal cardiotocography (CTG, p-value: 0.0002); and meconium-stained liquor (p-value: 0.0001). There were no association found between pre-term delivery and low birth weight with ICP.

[Table 6] shows the distribution of patients according to mode of delivery. In the category of patients without ICP proportion of mothers who delivered vaginally was 335 (64.55%) and CS rate was 184 (35.45%). In the category of patients with ICP proportion of mothers who delivered vaginally was 18 (58.06%) and CS rate was 13 (41.94%).

Table 1: Distribution of patients maternal according to age.

Age	No. of patients without ICP	Percentage	No. of patients with ICP	Percentage
<20 years	6	1.15%	0	0%
20-24 years	58	11.17%	4	12.90%
25-29 years	215	41.42%	7	22.58%
30-34 years	189	36.41%	9	29.03%
>35 years	51	9.82%	11	35.48%
Total	519	100%	31	100%

Table 2: Distribution of patients according to socio-economic factors.

Socio-economic factors	No. of patients without ICP	Percentage	No. of patients with ICP	Percentage
Lower class	225	43.35%	11	35.48%
Lower middle class	199	38.34%	9	29.03%
Upper Middle class	68	13.10%	7	22.58%
Higher class	27	5.2%	4	12.90%
Total	519	100%	31	100%

Table 3: Distribution of patients according to parity.

Parity	No. of patients without ICP	Percentage	No. of patients with ICP	Percentage	P value
Primipara	259	49.90%	9	29.03%	0.0428
Multipara	260	50.09%	22	70.97%	
Total	519	100%	31	100%	

Table 4: Distribution of patients according to smoking habits.

Smoking habits	No. of patients without ICP	Percentage	No. of patients with ICP	Percentage	P value
Non-smoker	495	95.38%	27	87.10%	0.0832
Smokers	24	4.62%	4	12.90%	
Total	519	100%	31	100%	

Table 5: Distribution of patients according to fetal outcomes of pregnancy.

Fetal outcomes	No. of patients without ICP	Percentage	No. of patients with ICP	Percentage	P value
Low births weight	188	36.22%	9	29.03%	0.8128
SGA	84	16.18%	7	22.58%	0.0003
Pre-term	161	31.02%	8	25.80%	0.0602
Abnormal CTG	41	7.89%	3	9.67%	0.0002
Meconium-stained liquor	45	8.67%	4	1.29%	0.0001
Total	519	100%	31	100%	-

Table 6: Distribution of patients according to mode of delivery.

Mode of delivery	No. of patients without ICP	Percentage	No. of patients with ICP	Percentage	P value
CS	184	35.45%	18	58.06%	0.0033
Vaginal	335	64.55%	13	41.94%	
Total	519	100%	31	100%	

Table 7: Distribution of patients according to maternal outcomes.

Maternal outcomes	No. of patients without ICP	Percentage	No. of patients with ICP	Percentage	P value
Insomnia	198	38.15%	11	35.48%	0.0045
Dyslipidemia	162	31.21%	7	22.58%	0.0011
ACP	74	14.25%	8	25.8%	0.2388
PRM	44	8.47%	1	3.22%	0.1252
PH	41	7.89%	2	6.45%	0.0122

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Total	519	100%	31	100%	-

ICP: Intrahepatic cholestasis of pregnancy; * p-value < 0.05: significant difference; ** p-value < 0.001: significant difference, MOD: Mode of delivery; CS: Caesarean section; ACP: Abnormal coagulation profile; PRM: Pre-labour rupture of membrane; PH: Postpartum hemorrhage.

DISCUSSION

In the present study, total 550 pregnant women were screened, and 31 pregnant women have been found to be suffering from ICP with prevalence of 5.64% and this give the overall prevalence of 5.63% of HG for the present study. The different study reported different incidence rates according to their geographic location and race.[8]

According to [Table 1], the most frequently affected age-group with ICP were belong to age > 35 years (11,35.48%), followed by age groups of 30-34 years (9, 29.03%) and 25-29 years (7, 22.58%). The reported incidence of ICP are-Chile: 12-20%; Bolivia: 9%; Sweden: 2%-3%; 35 years significantly (p-value: 0.0099) associated with development of intrahepatic cholestasis of pregnancy. Around two-third of the pregnant women with ICP were of more than 30 years. In a study done by Heinonen S et al., pregnant women with relatively advanced age (>35 years) were at increasing risk of developing ICP.[23] The average maternal age of pregnant women with ICP has been found more than 30 years in an Australian study.24 There are many risk factors has been found for ICP which include advanced maternal age (≥35 years); history of hepatitis C; cholelithiasis; cholecystectomy; previous history of ICP; family history of ICP; and multiple gestation pregnancy.[25-27]

In the present study, a majority of pregnant women with intrahepatic cholestasis of pregnancy was of multipara. Table 3 shows the distribution of patients according to parity. In the category of patients without ICP 259 patients were of primipara (49.90%) and 260 patients were of multipara (50.09%). In the category of patients with ICP 9 patients were of primipara (29.03%) and 22 patients were of multipara (70.97%). The significant association (p-value: 0.0428) has been found between parity and intrahepatic cholestasis of pregnancy. There was no significant difference in incidence according to parity (primigravida 9.7% and multigravida 10.0%) in a study done by Medda, et al.[28]

There were no association found between smoking habit with development of intrahepatic cholestasis of pregnancy. Table 4 shows the distribution of patients according to smoking habit. In the category of patients without ICP 495 patients did not smoke (95.38%) and 24 patients used to smoke (4.62%). In the category of patients with ICP 27 patients did not smoke (87.10%) and 4 patients used to smoke (12.90%).

Development of intrahepatic cholestasis of pregnancy was highly significantly associated with small for gestational age (SGA, p-value: 0.0003); abnormal cardiotocography (CTG, p-value: 0.0002); and meconium-stained liquor (p-value: 0.0001) in the present study. A similar study done by Medda, et al., including 100 patients with ICP, had shown following fetal outcomes: fetal distress (23%); abnormal CTG (17.0%), meconium-stained liquor (41.0%), preterm birth (22.0%) excluding IUFD; low birth weight babies (32.0%); neonates required admission to NICU (27.0%).[28]

There are other studies in which lower mean birth weight has been noted, although this does not appear to be due to intrauterine growth restriction.[23,29,30] Several studies have shown that there is no increase in the number of small for gestational age infants born to women with ICP.[31,32]

Abnormalities in CTG, both ante- and intrapartum, have been reported in association with ICP.[30,33] In normal term pregnancies, the incidence of meconium staining of amniotic fluid (MSAF), a sign of fetal distress, is approximately 15%. In case pregnancies complicated by ICP, the incidence of MSAF has been reported to increase up to 58%.[30,34]

CONCLUSION

Intrahepatic cholestasis of pregnancy is one of the common causes of hepatic impairment in pregnancy. ICP is associated with adverse fetal outcomes like, low birth weight babies; premature infants; abnormalities in CTG. ICP is also associated with maternal outcomes like, insomnia, dyslipidemia, PPH. Maternal outcomes have good prognosis but fetal outcomes can be improved by timely and effective intervention.

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