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ORIGINAL RESEARCH

Intrahepatic cholestasis of pregnancy prevalence and feto maternal outcome

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ABSTRACT

Background: Cholestasis is defined as impairment of bile flow due to intrahepatic or extrahepatic causes, leading to retention of hepatotoxic compounds; specifically bile acids. The present study was conducted to evaluate the feto-maternal outcome in patients with intrahepatic cholestasis of pregnancy.

Materials & Methods: It included 190 subjects in the study. Group A consisted of 95 women who presented with pruritis in their second & third trimester of pregnancy with associated abnormal liver function in the absence of other liver and skin disease. 95 women with uncomplicated pregnancy and no history of pruritis& with normal liver function test were taken as Group B/control.

Results: out of 95 participants total induction were 45 (47.36%) in group A and 13 (13.68%) in group B. Out of 45 (47.36%) total induction, 30 (31.57%) had vaginal delivery and 15 (15.78%) had LSCS in group A. Similarly, out of 13 (13.68%) total induction, 11 (11.57%) had vaginal delivery and 2 (2.10%) had LSCS in group B. ICP was significantly associated with induction of labour. There is higher incidence of caesarean section in induced patients. There is significant correlation in group A and group B in terms of fetal complications ($p<0.001$). 1 (1.05%) participants of APGAR score <7 at 5 minutes of age in group A and group B each. The risk of adverse fetal outcomes increases with increasing levels of maternal serum bile acid. 24 (25.26 %) babies of group A and 7 (7.36 %) babies of group B were admitted in NICU.

Conclusion: Higher rates of gestational diabetes and pre-eclampsia are new findings, and need to be considered in management of ICP pregnancies. Caesarean section as mode of delivery found significantly associated with ICP. Maternal outcomes have good prognosis but foetal outcomes can be improved by timely and effective interventions.

Key words: Caesarean section, Cholestasis, feto maternal

Introduction

Obstetric cholestasis is a liver disease unique to pregnancy. Once assumed to be a benign condition, its significance has been highlighted only recently due to associated maternal & perinatal morbidity & mortality.[1]Cholestasis is defined as impairment of bile flow due to intrahepatic or extrahepatic causes, leading to retention of hepatotoxic compounds; specifically bile acids. Extrahepatic cholestasis is caused by obstruction of the bile duct, in particular by gallstones or pancreatic tumors whereas intrahepatic cholestasis indicates functional impairment of bile secretion.[2]

Intrahepatic cholestasis of pregnancy is the most common pregnancy-specific liver disease, with a global incidence of between 0·2% and 2.0%. Intrahepatic cholestasis of pregnancy is characterized by otherwise unexplained symptoms like pruritis, typically starting in the late second or third trimester of pregnancy, increased serum bile acid concentration or transaminase concentration, or both, and spontaneous relief of symptoms and normalization of biochemical abnormalities postpartum. Intrahepatic cholestasis of pregnancy is associated with various adverse pregnancy outcomes,

including fetal distress, meconium- stained amniotic fluid, spontaneous and iatrogenic preterm birth, neonatal unit admission, and stillbirth.[3]

The risk of non-lethal adverse pregnancy outcomes in intrahepatic cholestasis of pregnancy increases with serum bile acid concentrations of 40 μmol/L or more and risk of stillbirth increases with serum bile acid concentrations of 100 μmol/L or more The etiology of obstetric Cholestasis is multifactorial and genetic, Environmental and hormonal factors have important roles6. ICP poses a significant risk for the fetus in terms of perinatal morbidity-mortality, preterm delivery, fetal distress, and meconium staining. The rates of fetal malformations and abortions are not shown to be increased, and fetal birth weight for gestational age appears to be adequate in ICP.[4]

ICP is thought to be the result of insufficient capacity of liver to metabolize high amounts of placenta-derived sex steroids during pregnancy.[5] The familial occurrence of ICP in some cases suggests hereditary susceptibility and the increasing understanding of the genetic background of cholestatic diseases in general has aroused interest in the search for genes and mutations predisposing to ICP. Moreover, the increased rate of cholelithiasis in these women may imply that ICP is not specific to pregnancy.[6]The present study was conducted to evaluate the feto-maternal outcome in patients with intrahepatic cholestasis of pregnancy.

Materials & Methods

The present Prospective comparative observational study was conducted in the Department of Obstetrics and Gynaecology, Dr. Ram ManoharLohia Institute of Medical Sciences, Lucknow

It included 190 subjects in the study. Group A consisted of 95 women who presented with pruritis in their second & third trimester of pregnancy with associated abnormal liver function in the absence of other liver and skin disease. 95 women with uncomplicated pregnancy and no history of pruritis& with normal liver function test were taken as Group B/control.

A standard interview based questionnaire used to obtain data on demography, clinical and family history. LFT repeated every two weeks in group A. Group B has regular antenatal visits and all ante-natal investigations were done as and when required. Ante-natal care protocol with respect to interval between clinical examination, USG, CTG and induction of labor was decided on the merit of obstetric indication. NST was done on basis of Obstetrics indications. Obstetrics notes were reviewed to determine the maternal and fetal outcome with respect to intrapartum events such as abnormal CTG pattern or meconium staining, the mode of delivery, Apgar score and maternal postpartum complications. Symptomatic relief of pruritis and liver function test was determined in all women one week after the delivery.

Blood sample collection and biochemical analysis. 5 ml venous Blood samples drawn from all the subjects following a fast of 12 hours and blood sample was withdrawn for measurement of fasting serum total bile acids, alanine transaminase (ALT), aspartate transaminase (AST) and serum bilirubin. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I Patientsdistribution accordingtoage

Agegroups	GroupA	GroupB
18to20years	4(4.21%)	6(6.31%)
21to25years	23(24.21%)	21(22.10%)
26to30years	54(56.84%)	59(62.10%)
31to35years	14(17.73%)	9(9.40%)
Total	95	95

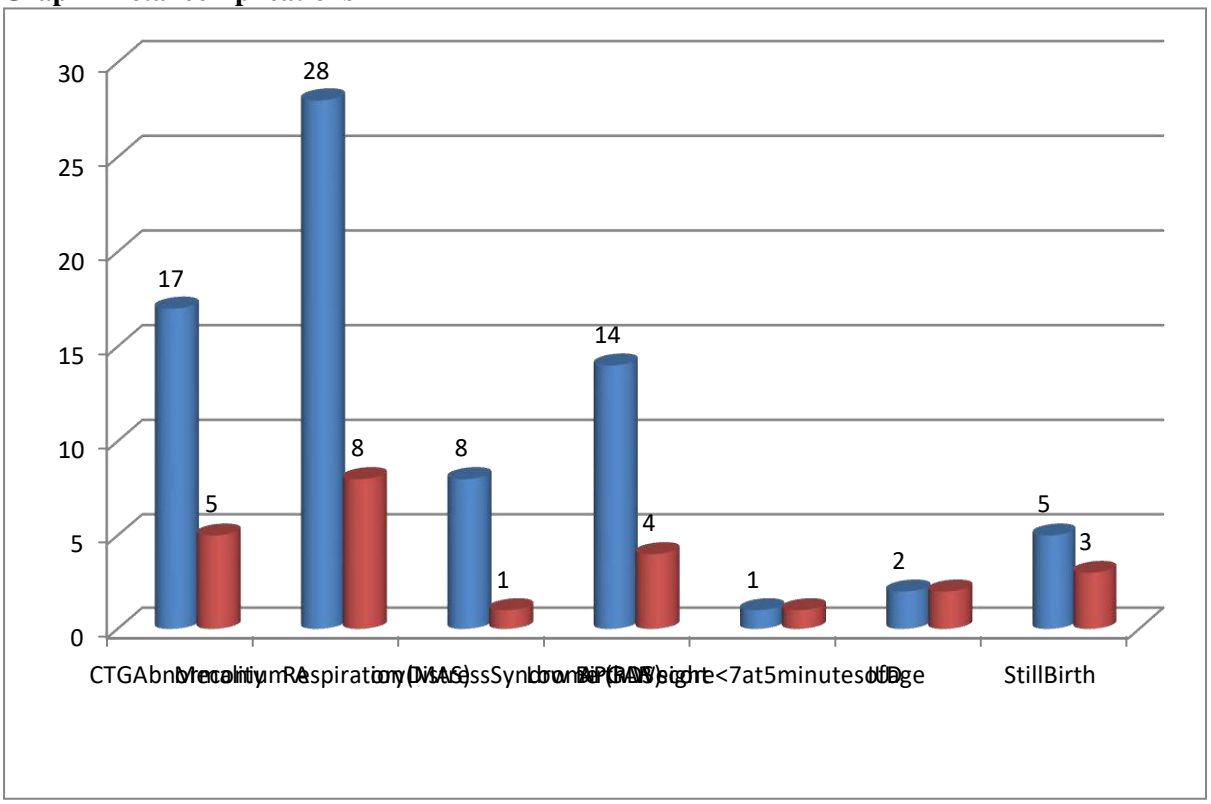
Table Ithat that 4 (4.21%) participants of group A and 6 (6.31%) participants of group B were in 18 to 20 years age group, 23 (24.21%) participants of group A and 21 (22.10%) participants of group B were found in 21 to 25 years of age group. 54 (56.84%) participants of group A and 59 (62.10%) participants of group B were found in 26 to 30 years age group. 14 (17.73 %) participants of group A and 9 (9.40 %) participants of group B were 31 to 35 years age group. The difference was significant (P< 0.05).

Table II Distribution ofpatientsaccording toinductionoflabour andmodeofdeliveryinbothgroups

	GroupA	GroupB	pvalue
VaginalDelivery	30(31.57%)	11(11.57%)	0.002
LSCS	15(15.78%)	2(2.10%)	0.001
TotalInduction	45(47.36%)	13(13.68%)	<0.001

Table II shows that out of 95 participants total induction were 45 (47.36%) in group A and 13 (13.68%) in group B. Out of 45 (47.36%) Total induction, 30 (31.57%) had vaginal delivery and 15 (15.78%) had LSCS in group A. Similarly, out of 13 (13.68%) total induction, 11 (11.57%) had vaginal delivery and 2 (2.10%) had LSCS in group B. ICP was significantly associated with induction of labour. There is higher incidence of caesarean section in induced patients.

Graph I Fetal complications



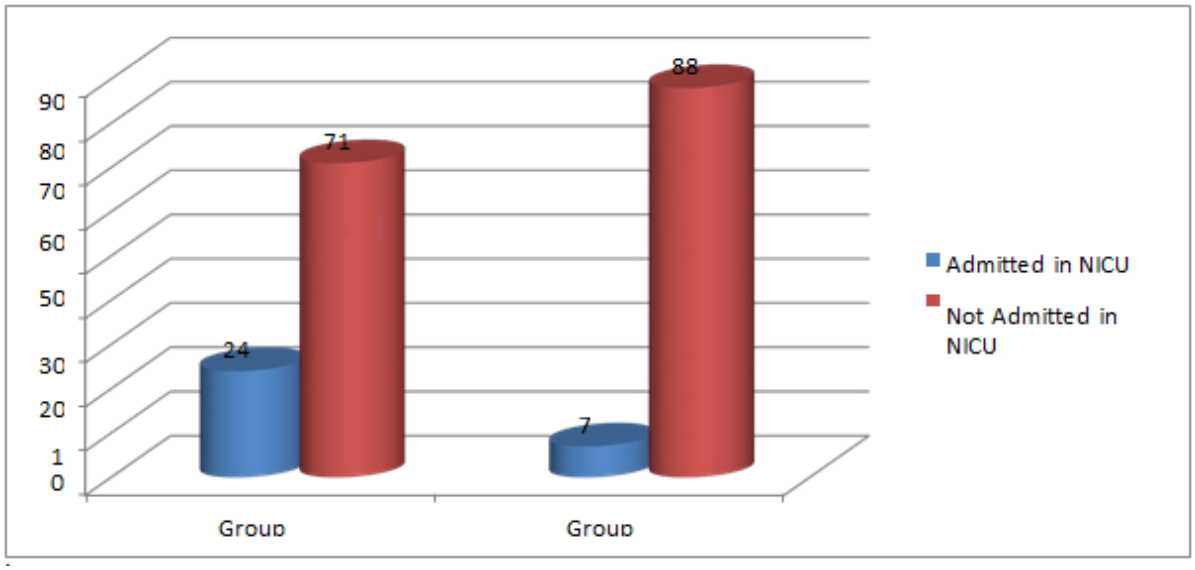
Graph I shows that there is significant correlation in group A and group B in terms of fetal complications (p<0.001). 1 (1.05%) participants of APGAR score <7 at 5 minutes of age in group A and group B each.

Table III Association between serum bile acid & adverse foetal outcome inintrahepaticcholestasisofpregnancy

AdversefetalOutcome	Complication		Pvalue
	Present	Absent	
Group A(Mean±SD)	34.65±10.3(n=58)	22.61±7.63(n=37)	0.003

Table III shows that risk of adverse fetal outcomes increases with increasing levels of maternal serum bile acid.

Graph II ICP and NICU admission



Graph II showed that 24 (25.26 %) babies of group A and 7 (7.36 %) babies of group B were admitted in NICU.

Table IV: Distribution of patients according to pregnancy outcome in terms of mode of delivery

Mode of delivery		Group A	Group B
LSCS	Elective	25 (45.6 %)	11 (33.3 %)
	Emergency	30 (54.4 %	22 (66.7 %)
	Total	55 (57.9%)	33 (34.73%)
Vaginal Delivery	Total	40 (42.1%)	62 (65.6%)

Table V: Distribution of patients according to maternal complications

Risk factor	Group A	Group B
Insomnia	58 (61.05 %)	24 (25.26 %)
Gestational DM	3 (3.15 %)	1 (1.05 %)
Pre-eclampsia	9 (9.47 %)	5 (5.26 %)
Placental Complication (APH)	2 (2.10 %)	1 (1.05 %)
PPH	18 (18.4%)	9 (9.4 %)
No Complication	5 (5.26%)	55 (57.89%)
Total	95 (100 %)	95 (100 %)

Table VI: Patients distribution on basis of foetal complication

Foetal Complication	Group A	Group B	p value
CTG Abnormality	17 (17.89 %)	5 (5.26)	<0.001
Meconium Aspiration (MAS)	28 (29.47 %)	8 (8.42 %)	<0.001
Respiratory Distress Syndrome (RDS)	8 (8.42 %)	1 (1.05 %)	0.001
Low Birth Weight	14 (15.78 %)	4 (5.26 %)	<0.001
APGAR score <7 at 5 minutes of age	1 (1.05%)	1 (1.05%)	0.366
IUD	2 (2.10%)	2 (2.10 %)	1.32
Still Birth	5 (5.26 %)	3 (3.15 %)	0.95
Total	75 (78.9%)	24 (25.26%)	<0.001

Table VII: ICP and NICU admission NICU admission status

NICU admission status	Mean±SD	
	Group A	Group B
Admitted in NICU	24 (25.26 %)	7 (7.36 %)
Not Admitted in NICU	71 (74.73 %)	88 (92.63 %)

Table VIII: Association between S bile acid level and feto-maternal outcomes

Parameter	Group A	
	r value	p value
Serum bile acid with NICU admission		
Below 10 µmol/L	0.302	0.012
Equal to or above 10 µmol/L	0.412	<0.001
Serum bile acid with Mode of Delivery		
Below 10 µmol/L	0.559	0.041
Equal to or above 10 µmol/L	0.297	0.001

Discussion

This Prospective Comparative Observational study was conducted in the Department of Obstetrics and Gynaecology, Dr. Ram ManoharLohia Institute of Medical Sciences, Lucknow from April 2020 to April 2021 with the aims to evaluate the fetomaternal outcome in patients with Intrahepatic Cholestasis of Pregnancy. This prospective comparative observational study was carried out on 190 patients.

Total 2475 pregnant women were registered during study period. As per diagnostic criteria for ICP for present study 108 patients were found to be suffering from ICP. Thus overall prevalence for ICP is 4.3 % for present study. We found an incidence of 4.3% in our study, however it is prudent to mentioned that our hospital is a tertiary referral centre and incidence of high risk pregnancy is higher. Hence the incidence of ICP is expected to be higher than that in the community.

In our study 4 (4.21%) participants of group A and 6 (6.31%) participants of group B were in 18 to 20 years age group, 23 (24.21%) participants of group A and 21 (22.10%) participants of group B were found in 21 to 25 years of age group. 54 (56.84%) participants of group A and 59 (62.10%) participants of group B were found in 26 to 30 years age group. 14 (17.73 %) participants of group A and 9 (9.40 %) participants of group B were 31 to 35 years age group. Obstetrics Cholestasis is more common in age group from 26 to 30 years. Similar results were reported by Heikkinen J et al.[7]

In our study out of 95 participants of group A, 31 (32.63%) participants were primigravida and 64 (67.36%) participants were multi gravida. Similarly from 95 participants of group B, 29 (30.52%) participants were primigravida and 66 (69.47%) participants were multigravida. In the present study, a majority of pregnant women with intrahepatic cholestasis of pregnancy were multipara. Significant association (p=0.035) has been found between parity and intrahepatic cholestasis of pregnancy in our study. Kondrackieneet al[8] had similar results.

We observed in our study that out of 95 participants of group A, 34 (35.78%) participants were of 28 to 32 weeks of gestational age, 54 (56.84%) participants were of 32 to 36 weeks of gestational age and 7 (7.36%) participants were above 36 weeks of gestational age. In group B, 20 (21.05 %) participants were between 28 to 32 weeks, 69 (72.63 %) participants were between 32 to 36 weeks and 6 (6.31%) participants were found to be above 36 weeks. Puslet al[9] found mean gestational age of delivery as 37 weeks.

In the present study, group A out of 55 LSCS deliveries, 25 (45.6%) were elective LSCS and 30 (54.4%) were emergency LSCS where as in Group B 11 (33.3%) were elective and 22 (66.7%) participants had emergency LSCS delivery. In group A 40 participants had vaginal delivery. Similarly 62 participantsin group B had vaginal delivery. Maximum number of patients has emergency LSCS in group A due to meconium and CTG abnormality. Caesarean section as mode of delivery found significantly associated (p=0.0033) with ICP in study done by Lammertet al.[10]

Out of 95 participants of group A, 75 (78.9%) participants had foetal complications with IUD in 2 (2.10%) participants, Respiratory Distress Syndrome (RDS) in 8 (8.42%), Low Birth weight in 15 (15.78%), Still birth in 5 (5.26%). ICP of pregnancy poses little risk to mother but there is a significant risk to fetus such as preterm delivery, foetal bradycardia, meconium staining and IUD. Beuerset al[11] found increased incidence of fetal asphyxia in patients with IHCP. The higher incidence of preterm delivery was because of induction of labour before 37 weeks of pregnancy due to worsening of pruritis. Pouponet al[12] found 14% incidence of preterm labour. In our study increase incidence of pre-term delivery was because of increase incidence of CTG abnormality, meconium and induction of labour due to worsening of pruritis in patients with ICP.

In our study 16 (16.84%) babies were below 2.5 kg and 79 (83.15%) babies were above 2.5 kg in group A, where 4 (4.21%) babies were below 2.5 kg and 91 (95.79%) babies were above 2.5 kg in group B. It is consistent with the studies by Bacqet al.[13] In this study, 24 (25.26 %) babies of group A and 7 (7.36 %) babies of group B were admitted in NICU. NICU reported 14% admission. Fagan et al[14]reported 27% NICU admissions.We observed that there is highly significant positive correlation between serum bile acid and NICU admission and mode of delivery (p<0.001).

Conclusion

Authors found that highly significant positive correlation between serum bile acid and NICU admission and mode of delivery. Obstetric cholestasis is more common in multigravida than in primigravida. Intrahepatic Cholestasis is more common in the age group of 26-30 years. ICP is associated with adverse foetal outcomes like low birth weight, pre mature infants, abnormal CTG and

meconium aspiration syndrome. ICP is associated with maternal outcomes like insomnia, PPH. Higher rates of gestational diabetes and pre-eclampsia are new findings, and need to be considered in management of ICP pregnancies. Caesarean section as mode of delivery found significantly associated with ICP. Maternal outcomes have good prognosis but foetal outcomes can be improved by timely and effective interventions.

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