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Fetomaternal Outcome In Intrahepatic Cholestasis Of Pregnancy At Sms Medical College,Jaipur Rajasthan

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Abstract

Background: ICP is a multigenic disease, mutations of genes encoding several proteins involved in the hepatobiliary transport have been associated with ICP.

Methods: Hospital based comparative analysis in pregnant women was conducted at Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur

Results: 8.00% women had PROM, 16.00% women had preterm delivery in ICP group. 22.00% neonates were admitted to NICU in group. 44.00% baby's birth weight was more than 2.5 kg in cases group. Intrauterine death was seen in 2% in ICP group.

Conclusion: Cholestasis of pregnancy has an adverse effect on the fetal outcome and hence early diagnosis with careful clinical examination and biochemical testing is essential.

Keywords: Cholestasis, Prom, Nicu.

Introduction

Intrahepatic cholestasis of pregnancy (ICP) is a liver disease unique to pregnancy. It is characterised by pruritus associated with elevated serum bile acid and/or aminotransferase level with spontaneously relief of sign & symptom with in 2-3 week of delivery .[1]

The aetiology and pathogenesis of obstetric cholestasis is multifactorial and yet not fully elucidated. Pathogenesis is related to increased sex hormone synthesis, environmental factors and genetic predisposition. Bile acid when applied to skin elicits itch.10 Lysophosphatidic Acid (LPA), a potent pruritogen produced from lysophosphatidylcholine by the action of autotoxin enzyme. Autotoxin activity is found to be elevated in serum of patients of obstetric cholestasis.[2]

ICP is a multigenic disease, mutations of genes encoding several proteins involved in the hepatobiliary transport have been associated with ICP. Heterozygous mutations in gene ABCB4 (adenosine triphosphate-binding cassette ,subfamily B, member 4), which encodes the hepatic phospholipid transporter MDR3 (multidrug resistance 3), have been found in patients with ICP. Mutations in genes ATP8B1, ABCB11, or NRH1HA encoding familial intrahepatic cholestasis 1 protein (FIC1), the bile salt export pump, or farnesoid X receptor (a regulator of bile acid synthesis and transport in the hepatocyte), respectively, have less frequently been found in patients with ICP.[1]

According to several studies, although the maternal course is usually benign, there is an increased risk of spontaneous preterm delivery, fetal compromise, meconium stained amniotic fluid, and intrauterine fetal demise. (preterm delivery in 19-60%, intrapartum fetal distress in 22-41% and intrauterine fetal death in 0.75-1.6%). [3]

Routine tests for fetal monitoring such as cardiotocography (CTG) and umbilical artery colour Doppler cannot predict fetal outcome. As the majority of intrauterine death occurs after 37 weeks of gestation, delivery has been recommended on or after 37-38 weeks of gestation.[4]

CTG is normal for up to 2 days before fetal demise. bile acids may cause fetal cardiac arrest after entering cardiomyocytes in abnormal amounts. Using fetal myocyte cultures, they showed expression of several genes that may play a role in bile transport.[5]

The purpose of the present study is increased the awareness and early identification of mother with obstetric cholestasis, their active management will help reducing the fetal morbidity and mortality, as well as maternal morbidity.

Material and Methods

Type of Study: Prospective study

Study Design: Hospital based comparative analysis in pregnant women.

Place of Study: Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur

Duration of Study: April 2017 onwards for a period of one year or till desired sample size was reached for data collection and 2 month for statistical analysis.

Institutional review board and ethical committee clearance was taken.

Inclusion Criteria

For case group:- (group A)

Singleton pregnancy in the age group of 20-30 year, after 28 weeks of gestation.

With history of pruritus without a rash.

Altered liver function tests (serum bilirubin:- 3-5 mg/dl, SGOT& SGPT:-Upper limit of normal value is 20% lower than that in non pregnant state, ALP:-Increase 2 to 3 fold in pregnancy).

Remissions of both following delivery.

Women giving informed & written consent.

For control group:- (group B)

Singleton pregnancy in the age group of 20-30 year, after 28 weeks of gestation.

Without history of pruritus and rash.

Normal liver function tests.

Women giving informed & written consent.

Exclusion Criteria

Excluding liver diseases (hepatitis A , B , C or E , autoimmune hepatitis).

Dermatological conditions (eczema, scabies, pruritus eruption of pregnancy).

Urinary tract infection.

Sample Size : is calculated at 80% study power and alpha error of 0.05 expecting meconium stained amniotic fluid in 17.1% case of obstetric cholestasis group and 1.1% controlled group as per result of reference study (M Padmaja, Pal Bhaskar, Gupta Jayanta Kumar, Ramamurthy Seetha, Chaudhuri Mahasweta. A study of obstetric cholestasis. J Obstet Gynecol India vol.60, No. 3 : May-June 2010 pg. 225-331.)[8]

50 Patients in each group were required as sample size following above assumption which was increased to 55 patients in each group as final sample size for present study expecting 10% dropout / attrition.

Data collection

A detail history, physical & obstetrical examination was done.

Gestational age was determined by asking the women the date of last menstrual period, if reliable or from earliest ultrasonography.

Detail history of pruritus specifically regarding the site & severity according to prefixed score was taken.

Routine investigations– complete blood count, fasting blood sugar, ABORh, VDRL, HIV, HBsAg. urine complete microscopy, serum electrolytes, coagulation profile ,USG whole abdomen.

Liver function tests was done weekly.

Liver function tests was repeated after 2 week postpartum.

Statistical Analysis

Continuous variables was summarized as mean and standard deviation while nominal/ categorical variables as proportions(%).

Unpaired 't' test was used for comparison of continuous variables where as chi-square test/fisher exact test for nominal/categorical variables.

P value <0.05 was taken as significant.

Medcalc 16.4 version software was used for all statistical calculations.

Observations

The socio-demographic variable difference in both groups was stastically Insignificant and both groups were Comparable.

Table-1 Distribution Of Cases Based On Mode Of Delivery

Mode of delivery		Group-A (n=50)		Group-B (n=50)		Total	
		No	%	No	No	%	No
Vaginal	Spontaneous	6	12.00	17	34.00	23	23.00
	Induction	36	72.00	27	54.00	63	63.00
LSCS	Elective	7	14.00	2	4.00	9	9.00
	Emergency	12	24.00	8	16.00	20	20.00

12% women of group A and 34% women of group B had spontaneous vaginal delivery. Induction of labour was done 72% women in group A and 54% women in group B out of which 18% women had emergency LSCS in group A and group B it was 6%. Remaining 6% of women in group A and 10% of women in group B taken for emergency LSCS straight away. Elective LSCS was done 14% in group A and 4% in group B.

Table-2 Distribution of Cases Based On Indication Of LSCS

Indication of LSCS		Group-A(n=19)		Group-B(n=11)	
		No	%	No	%
Elective	Previous LSCS	3	6.00	1	2.00
	CPD	3	6.00	0	0.00
	BOH	1	2.00	1	2.00
	Breech	0	0.00	1	2.00
Emergency	Fetal distress	7	14.00	6	12.00
	MSL	5	10.00	2	4.00

Previous caesarean was most common indication for elective caesarean section in both groups which was 6%. 14% of women in a group A and 12% of women group B had fetal distress for which emergency LSCS was done. 10% of women in group A and 4 %of women in group B had meconium stained liquor for which emergency CS was done,

24% cases of group A have abnormal CTG, out of which 22% cases had emergency LSCS (Indication of 10 % was meconium stained liquor and 12% was fetal distress) and 2% had normal delivery.

Table-3 Distribution of Cases Based On Maternal Outcome

Maternal outcome	Group-A(n=50)		Group-B(n=50)		p-value
	No	%	No	%	

PROM	4	8.00	1	2.00	0.359
Preterm delivery	8	16.00	4	8.00	0.356
PPH	0	0.00	1	2.00	0.99

In our study 8.00% women had PROM, 16.00% women had preterm delivery in group A whereas 2.00% women had PROM, 8.00% women had preterm delivery in group B.

None of all women had PPH in group A , 2% of women had PPH in the group B. The p-value was 0.99 which was stastically insignificant.

Table-4 Distribution of Cases Based On Nicu Admissions

NICU admission	Group-A(n=50)		Group-B(n=50)		Total	
	No	%	No	No	%	No
Present	11	22.00	2	4.00	13	13.00
Absent	39	78.00	48	96.00	87	87.00
Total	50	100.00	50	100.00	100	100.00
p-value			0.017			

In present study 22.00% neonates were admitted to NICU in group A and 4.00 % neonates were admitted in NICU in group B. The differences between both groups were found stastically significant(p-value=0.017)

Table-5 Distribution Of Cases Based On Birth Weight

Birth weight (KG)	Group-A(n=50)		Group-B(n=50)		Total	
	No	%	No	%	%	No
<1.5	3	6.00	2	4.00	5	5.00
1.5-2.5	25	50.00	24	48.00	49	49.00
>2.5	22	44.00	24	48.00	46	46.00
Total	50	100.00	50	100.00	96	96.00
Mean	2.39±0.39		2.53±0.43		2.49±0.68	
p-value			0.858			

In present study 44.00% baby's birth weight was more than 2.5 kg in cases group and 48.00% in control group. The birth weight differences in both group was found stastically insignificant.

Table-6 Distribution of Cases Based On Perinatal Complication

Perinatal complication	Group-A(n=50)		Group-B(n=50)		p-value
	No	%	No	%	
MSL	12	24.00	3	6.00	0.02
IUGR	2	4.00	1	2.00	0.99
RDS	4	8.00	1	2.00	0.359

In our study meconium stained liquor was present in 24% and 6% in group A and B respectively.Intrauterine growth retardation was seen in 4% in group A,whereas it is 2% in group B. RDS was present in 8% and 2% in group A and B respectively.

Table-7 Distribution of Cases Based On Perinatal Mortality

Perinatal mortality	Group-A(n=50)		Group-B(n=50)		p-value
	No	%	No	%	
IUD	1	2.00	1	2.00	0.99
Still birth	1	2.00	2	4.00	0.97
Neonatal death	1	2.00	2	4.00	0.97

In our study Intrauterine death was seen in 2% in group A and B. Stillbirth and Nenonatal death were 2% and 4% in group A and B respectively. The p-value was .97 ,which was stastically insignificant.

Discussion

Table 1- 12% women of group A and 34% women of group B had spontaneous vaginal delivery. Induction of labour was done 72% women in group A and 54% women in group B out of which 18% women had emergency LSCS in group A and group B it was 6%. Remaining 6% of women in group A and 10% of women in group B taken for emergency LSCS straight away. Elective LSCS was done 14% in group A and 4% in group B.

In a study done by Ray Alokananda (2005)[6] et al found that 66.6% women of the study group delivered vaginally

and 33.3% had caesarean section. Garg Renu (2017)[7] et al reported in their study that 64% women of the study group delivered vaginally and 36% had caesarean section.

In a study done by Dr.Alakananda (2016) [8] et al found that 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 women 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.

Table 2- Previous caesarean was most common indication for elective caesarean section in both groups which was 6%. 14% of women in a group A and 12% of women group B had fetal distress for which emergency LSCS was done. 10% of women in group A and 4 %of women in group B had meconium stained liquor for which emergency CS was done, 24% cases of group A have abnormal CTG, out of which 22% cases had emergency LSCS (Indication of 10 % was meconium stained liquor and 12% was fetal distress) and 2% had normal delivery.

In a study done by Ray Alokananda (2005)[6] et al found that the most common indications were post-dated pregnancy and worsening symptoms. Garg Renu (2017)[7] et al reported in their study that most common indication of caesarean section in both the groups was previous caesarean section.

M.Padmaja (2010)[9] et al reported in their study that it is important to mention that many of the preterm deliveries were planned elective deliveries. The Cesarean section rate was higher in the study group (93.3% vs 76.6%), but even this did not attain statistical significance ($p<0.05$) The higher CS rate was mainly due to a higher elective CS (76.2% vs 65.2%).

In a study conducted by Dr. Alakananda (2016)[8] et al that 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 and post dated pregnancy.

Table 3- In our study 8.00% women had PROM, 16.00% women had preterm delivery in group A whereas 2.00% women had PROM, 8.00% women had preterm delivery in group B. None of all women had PPH in group A , 2% of women had PPH in the group B. The p-value was 0.99 which was stastically insignificant.

In a study done by Ray Alokananda (2005)[6] et al found that PPH occurred in 25%.of these ,one had received vitamin K 24 hours prior to induction of labour. M.Padmaja (2010)[8] et al reported in their study that 8.9% was PPROM, 24.4% was preterm delivery.there was no case of PPH in either group.

In a study conducted by Dr. Alakananda (2016) [8] et al that There was no significant maternal complication seen except that 6 patients had PPH which was managed conservatively.

Garg Renu (2017)[7] et al reported in their study that no significant difference was seen in the occurrence of PPH between the study and control group (6% vs 4%).

Table 4:- In present study 22.00% neonates were admitted to NICU in group A and 4.00 % neonates were admitted in NICU in group B. The differences between both groups were found stastically significant(p-value=0.017)

In a study done by Ray Alokananda (2005)[6] et al that the overall perinatal mortality rate (PMR) and nursery

admission rate in the study group were much higher than those for all booked women during the same period (PMR 64.5 vs 14.5 per 1000 live births and nursery admissions 40.6% vs 13.05% respectively). In a study conducted by M.Padmaja (2010) [8] et al that NICU admission was 15.6%. Garg Renu (2017)[7] et al reported in their study that higher rate of NICU admissions was 20%. Indications being respiratory distress syndrome (5 neonates), meconium aspiration syndrome (4 neonates),and transient tachypnoea of newborn (1 neonate). In a study conducted by Dr. Alakananda (2016) [48] et al that NICU admissions was 21 %.

Table 5- In present study 44.00% baby's birth weight was more than 2.5 kg in cases group and 48.00% in control group. The birth weight differences in both group was found stastically insignificant.

In a study conducted by Dr. Alakananda (2016)[8] et al that 28.57% was premature and low birth weight .

Table 6- In our study meconium stained liquor was present in 24% and 6% in group A and B respectively.Intrauterine growth retardation was seen in 4% in group A,whereas it is 2% in group B. RDS was present in 8% and 2% in group A and B respectively.

In a study conducted by M.Padmaja (2010)[9] et al that higher incidence of MSL was 17.7% in study group and 1.1% control group ($p<0.05$).

Garg Renu (2017)[7] et al reported in their study that higher incidence of MSL was 24% in study group and 8% control group. Sita pokhrel (2017)[46] et al reported in their study that 32.5% was MSL In a study conducted by Dang Arbinder (2010)[10] et al 40.4% was meconium stained liquor.

In a study conducted by Dr. Alakananda (2016)[8] et al that women delivering after 38 weeks had a higher incidence of MSL 45% in study group and 11.1 % control group. Gupta Amita (2009)[40] et al reported in their study that 9.6% was meconium stained liquor.

Table 7- In our study Intrauterine death was seen in 2% in group A and B. Stillbirth and Nenonatal death were 2% and 4% in group A and B respectively. The p-value was .97 ,which was stastically insignificant.

In a study conducted by M.Padmaja (2010)[9] et al that still birth rate (per 1000 total birth) was 22.2% and perinatal mortality rate 22.7% . IUFD was 1%. In a study conducted by Dr. Alakananda (2016)[8] et al that IUFD was 2%. Garg Renu (2017)[33] et al reported in their study that IUFD was 2% .

In a study done by Ray Alokananda (2005)[6] et al that IUFD was 5% , neonatal mortality rate was 5%, perinatal mortality rate was 105/1000 live birth.

Conclusion

Cholestasis of pregnancy has an adverse effect on the fetal outcome and hence early diagnosis with careful clinical examination and biochemical testing is essential.

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