

STUDY TO SHOW THE EFFECT OF INTRAHEPATIC CHOLESTASIS OF PREGNANCY ON PERINATAL OUTCOME IN UNCOMPLICATED PREGNANCY

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ABSTRACT

OBJECTIVE

To study the effect of Intrahepatic Cholestasis of Pregnancy on perinatal outcome with medical management and timely intervention in the form of induction of labour or Caesarean Section and its comparison with Control group.

METHODS

This prospective study was conducted on pregnant women attending the Antenatal Clinic of Outpatient and Indoor Department of Obstetrics and Gynaecology of Maharaja Agrasen Hospital, Punjabi Bagh, New Delhi from August 2009 till July 2011; 50 Pregnant patients who developed pruritus during 2nd and 3rd trimester of pregnancy with or without jaundice and were having elevated total bile acids > 10 umol/L with or without deranged liver function tests were taken as cases and 50 Pregnant patients without ICP were taken as control.

RESULTS

In our study, intrahepatic cholestasis was associated with:

1. Increased incidence of intrapartum thick meconium staining of amniotic fluid (30% in Cases and 10% in Control).
2. The rate of induced delivery in the form of emergency caesarean section or induced labour was also high (34% in Cases and 14% in Control).
3. Increased incidence of low birth weight (<2500 gms) and low mean birth weight, i.e. 21.5% in Cases and 6% in Control group with active intervention at 37 weeks.

CONCLUSION

From the above study we concluded that ICP is associated with increased rate of preterm delivery, caesarean sections, low birth weight babies and still birth.

KEYWORDS

ICP, Meconium Staining, Preterm.

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INTRODUCTION

Pregnancy is a nature's precious gift, which has to be nurtured during its entire nine months of duration to achieve good maternal and foetal outcome. There are several complications, which may impair a favourable pregnancy outcome. During this physiological event some women develop liver disorders during their second or third trimester of pregnancy that may endanger the mother, her baby or both. Approximately, 3-5% of pregnant women have deranged liver function tests with or without jaundice.

Causes of Jaundice or Deranged Liver Function Tests Specific to Pregnancy Include

- Pre-eclampsia associated with HELLP syndrome (Haemolysis, Elevated Liver Enzymes and Low Platelet Count).

- Acute fatty liver of pregnancy.
- Hyperemesis gravidarum.
- Intrahepatic Cholestasis of Pregnancy (ICP), also known as cholestasis of pregnancy, recurrent jaundice of pregnancy or pruritus gravidarum.

Intrahepatic Cholestasis of Pregnancy is an uncommon cholestatic liver disorder characterized by pruritus with onset in the 2nd or 3rd trimester of pregnancy with or without increase in serum bilirubin, serum aminotransferases, alkaline phosphatases and elevated total bile acid level more than 10 micromoles/litre.^{1,2} The diagnosis is based on history, clinical examination and laboratory findings, but in general ICP is a diagnosis of exclusion. Once the diagnosis of ICP is made, treatment should be initiated immediately.

In contrast to favourable prognosis for the mother, ICP poses significant risk for the foetus. The rate of malformation and abortion is not increased in ICP. There is increased risk of spontaneous preterm labour in ICP.^{3,4} The incidence of meconium staining of amniotic fluid in normal term pregnancy is approximately 15% and is considered to be a sign of foetal distress.⁵ In ICP incidence of meconium staining of amniotic fluid has been reported to be 16-58%. ICP have reported a perinatal mortality of 10-15%.

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This has been reduced to 3.5% or less in more recent studies employing policies of active management. Many pharmacological agents have been used in the treatment of Intrahepatic Cholestasis of Pregnancy (ICP).⁶ These include phenobarbital, hydroxyzine, glutathione precursor such as S-adenosyl methionine (SAME), cholestyramine and dexamethasone. UDCA is the drug of choice for the treatment of ICP.^{7,8}

UDCA at a daily dose ranging from 600-2000 mg was effective at reducing pruritus, decreasing the total serum bile acid levels, ALT values and bilirubin levels. The purpose of this work is to study the effect of intrahepatic cholestasis of pregnancy on perinatal outcome in uncomplicated pregnancy.

MATERIAL AND METHODS

This is a prospective clinical study conducted on 100 patients in Maharaja Agrasen Hospital, Punjabi Bagh, Delhi who attended outpatient and indoor Department of Obstetrics and Gynaecology.

Inclusion Criteria

1. 50 Pregnant patients who developed pruritus during 2nd and 3rd trimester of pregnancy with or without jaundice and were having elevated total bile acids >10 umol/L with or without deranged liver function tests were taken as cases.
2. 50 Pregnant patients without ICP were taken as control.

Exclusion Criteria

1. Signs of dermatological disease on clinical examination.
2. Itching due to allergic disorders.
3. Presence of other active liver disease.
4. HELLP syndrome, acute fatty liver of pregnancy.

Detailed medical history (Especially regarding onset of pruritus, site of pruritus, diurnal variation and development of jaundice), obstetrics history with clinical examination was recorded at every visit. The maternal data collected included maternal age, gestational age at the time of delivery, parity, history of ICP in previous pregnancies, history of biliary or any liver disease and mode of delivery. The biochemical investigations done were serum total bile acids, serum bilirubin, serum aminotransferases, serum alkaline phosphatases. Serum laboratory tests were done at the onset of signs and symptoms of ICP.

Patients were given palliation initially with topical emollients, antihistaminics and Ursodeoxycholic Acid (UDCA) during antenatal and postnatal period up to 2 weeks. Patients were monitored after 32 weeks weekly by NST. Pregnancy complicated by ICP were managed actively at 37 weeks of gestation or when the patient presented first after 37 weeks or earlier if required in patients developing other obstetrics complication. Incidence of meconium stained liquor at the time of delivery, preterm delivery i.e. <37 weeks, APGAR score at 5 mins. <7, low birth weight i.e. <2500 gms, neonatal admission to nursery and perinatal death were noted. The incidence of these perinatal outcome parameters in Control group were also noted.

In our study, levels were measured by enzymatic spectrophotometric method. In this method, the enzyme 3- α - hydroxysteroid dehydrogenase converts bile acids to 3 keto-steroids and Thio-NADH.

In the presence of excess NADH, enzyme cycling occurs efficiently and rate of formation of Thio-NADH is determined by measuring specific change of absorbance at 405 nm.

In our study serum bile acids were measured by kit available from Diazyme Laboratories in name of Total Bile Acids Assay Kit. Statistical analysis was conducted with the Statistical Package for the Social Sciences (SPSS) version 12.0.

Means, standard deviations and ranges were calculated for descriptive purposes. A P value <0.05 was considered significant.

RESULTS

The mean age of patients in Study group was 28.04 \pm 3.68 and in Control group was 27.64 \pm 3.70. The difference in the age of two groups was statistically not significant. In Study group, 34 (68%) were primigravida and in Control group 33 (66%). The mean gestational age in ICP group was 30 \pm 4.7 weeks. The mean age of Control group was 31.2 \pm 3.3 weeks. Only one twin pregnancy in Study group, but none in control one. In Study group 22% have non-reassuring CTG, while only 10% in Control group. The two-sided P value is 0.1651, considered not significant; 28% and 10% preterm deliveries in Study and Control group respectively.

Meconium staining was present in 30% and in 10% in Study and Control group. Induction was done in 34% cases in Study group and 14% cases in Control group. Caesarean section was done in 40% and 20% cases in study and Control group respectively. Most common indication for caesarean section was non-reassuring CTG during intrapartum period. Low birth weight babies were 21.5% and 6% in Study and Control group. Apgar score <7 in 19.26% cases and 8% cases in Study and Control group respectively; 38% of neonates in Study group and 24% in Control group got admitted to NICU. There was 2 perinatal deaths in Study group as compared to nil in Control group.

	Spontaneous Preterm Delivery	Induced Preterm Delivery
Study Group	10	04
Control Group	03	02

Table 1: Comparison of Spontaneous versus Induced Preterm Delivery in Study and Control Group

	Meconium Stained Amniotic Fluid	Normal Amniotic Fluid	
Study Group	15	35	15/50 (30%)
Control Group	05	45	05/50 (10%)

Table 2: Comparison of Meconium Stained Amniotic Fluid in Study and Control Group

	Induced Labour	Spontaneous Labour	
Study Group	17	33	17/50(34%)
Control Group	07	43	07/50(14%)

Table 3: Comparison of Induced Labour in Study and Control Group

	Caesarean Section	Normal Delivery	
Study Group	20	30	20/50(40%)
Control Group	10	40	10/50(20%)

Table 4: Comparison of Caesarean Section Done in Study and Control Group

	Birth Weight < 2.500 kg	Birth Weight > 2.500 kg	
Study Group	11	40	11/51(21.5%)
Control Group	03	47	03/50(06%)

Table 5: Comparison of Low Birth Weight (< 2.500 kg) in Study and Control Group

	Apgar Score < 7	Apgar Score > or=7	
Study Group	11	40	11/51 (19.26%)
Control Group	04	46	04/50 (08%)

Table 6: Comparison of Apgar Score at 5 mins. in Study and Control Group

	Neonate Admitted to Nursery	Neonate Discharged	
Study Group	20	31	20/51(38%)
Control Group	12	38	12/50(24%)

Table 7: Comparison of Neonate Admitted to Nursery in Study and Control Group

	Perinatal Death	Neonate Discharged	
Study Group	02	49	02/51(04%)
Control Group	00	50	

Table 8: Comparison of Perinatal Death in Study and Control Group

DISCUSSION

ICP is considered to be a pathology exclusive of gestation associated with adverse perinatal outcome.⁹ The period of gestation of presentation of ICP is mostly during 3rd trimester of pregnancy in 80% of patients, which is comparable with mean period of gestation in previous studies done by Anna P et al and Bacq Y et al.

Most common presenting symptom was itching. Clinical jaundice was rare as presenting symptoms in our study, which was comparable with studies by Palma J et al and Bacq Y et al. In our study, mean level of ALT and number of patients with raised ALT are lower than previous study.

ICP carries a risk of spontaneous preterm delivery.¹⁰ In our study, 20% (10/50) had spontaneous preterm delivery which is three-fold as compared to Control group 06% (03/50) (As shown in Table 1).

In our study, 30% of patients in Study group had intrapartum meconium staining of amniotic fluid as compared to 10% in Control group, which is statistically significant (Table 2).

We in our study also found a statistically significant difference in the ratio of induced to spontaneous labour in Study group as compared to Control group (Table 3).

In our study, the incidence of caesarean section is 40% in Study group as compared to 20% in Control group and found this difference to be statistically significant (Table 4). Kenyon

AP et al and Ray Alokanda et al found an incidence of 36% and 31.2% respectively for caesarean section.

In our study, the incidence of low birth weight (<2500 gms) is 20% in Study group as compared to 6% in Control group (Table 5). The mean birth weight in Study group is 2.720 ± .468 gms and Control group is 2.914 ± .361 gms and the difference between the two is statistically significant (P value .0221). Heinonen S et al and Reid R et al found lower mean birth weight in ICP group.

Foetal distress is indicated by parameter like low Apgar score (<7 at 5 mins.) and neonatal admission to nursery after birth. In our study, we also found difference in the incidence of Apgar score <7 at 5 mins. in ICP group (19.26%) as compared to non-ICP group (8%), but this difference was not statistically significant (Table 6). All the 11 neonates with Apgar score <7 were having thick intrapartum meconium stained liquor and were kept in nursery (Table 7).

There was 2 perinatal deaths in Study group as compared to nil in Control group. Both foetuses died in ICU due to a possible lethal idiopathic respiratory distress syndrome with prematurity (Table 8).

CONCLUSION

From the above study we concluded that ICP is associated with increased rate of preterm delivery, both spontaneous and induced, increased incidence of meconium staining, caesarean sections, low birth weight babies and still birth.

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