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Original Article

Cholestasis of pregnancy

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Abstract

Objectives : To study the nature and outcome of pregnancy in Obstetric Cholestasis. *Methods :* This study included 892 women admitted during the period April 2003-March 2005. Eighty three women were diagnosed as having obstetric cholestasis. The protocol for antenatal checkup and induction of labor was as per obstetric indications. All the patients were given ursodeoxycholic acid. *Results:* Incidence was 9.3% (83/892). Symptoms appeared after 30 weeks in 85% (71/83). Multipara were 16% (13/83) and primipara were 84% (70/83). Cesarean section rate was 66% (55/83). Intrapartum abnormal cardiotocography was noted in 7.2% (6/83) and thick meconium was in 9.6% (8/83). Women delivering after 38 weeks had a higher incidence of thick meconium, 12.9% (8/62) and abnormal CTG was 9.6% (6/62). There was no patient with meconium and abnormal CTG before 38 weeks. There was no neonatal nursery admission and no perinatal mortality. The difference regarding thick meconium was statistically not significant by Fisher's exact test (P=0.19) although the number of cases with meconium after 38 weeks were more. *Conclusions :* Obstetric cholestasis is associated with increased perinatal mortality and morbidity if delivered after 38 weeks. An attempt to deliver prior to 38 weeks may improve the perinatal outcome.

Key words: intrahepatic cholestasis of pregnancy (IHCP), pruritus.

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 the associated maternal and perinatal mortality. The incidence of intrahepatic cholestasis of pregnancy (IHCP) has been difficult to estimate as a result of likely underreporting or failure to recognize mild cases. The prevalence, presentation and severity of the condition vary worldwide. A low incidence of 0.2% in Europe and a high incidence of 4-14% in Chile has been reported. The disease course is also known to be more severe in Chile than in other parts of the world[1]. Hence it may not be possible to extrapolate the outcome across different populations. We therefore undertook this study to determine the nature and outcome of obstetric cholestasis amongst women attending our antenatal clinic.

The cause of IHCP has not been definitively shown. Hormonal and genetic factors clearly play a role, but the pathophysiologic mechanism is unclear. Women in whom intrahepatic cholestasis has developed because of oral contraceptive or estrogen ingestion are also more likely to develop IHCP. Challenging the women with a history of IHCP with estrogens may precipitate pruritus and jaundice.

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The spectrum of clinical illness varies from pruritus gravidarum, defined as diffuse itching to severe, cholestasis with jaundice [1]. The onset of IHCP is most common in the third trimester, although it has been reported as early as in the second and rarely, in the first trimester[1]. In almost all affected women, the presenting symptom is pruritus, which can involve any part of the body, including the palms and the soles [2,3]. It tends to be particularly severe at night and may account for emotional distress, resulting in insomnia, anorexia, and malaise. Pruritus resolves within two days of delivery but rarely extends beyond two weeks postpartum [1].

The symptoms can be severe and incapacitating to the mother, however the clinical course is usually benign. In the fetus, a high frequency of preterm labor and delivery and still birth of unknown etiology has been reported. In our study it was found that ursodeoxycholic acid was effective in altering the bile acid composition which had a bearing on pruritus [2].

Methods

From April 2003 – March 2005 women with obstetric cholestasis (n=83) were recruited for study from amongst 892 booked antenatal women attending our antenatal clinic.

The diagnosis of obstetric cholestasis was based upon the clinical symptom of persistent pruritus without a skin rash associated with the biochemical evidence of mild to moderate cholestasis in the absence of any other liver disease, which resolved postnatally. Abnormal liver function was defined as at least 2-4 fold increase in transaminases not exceeding 250 IU/ml with or without mild increase in serum bilirubin not exceeding 5mg/dl. Alkaline phosphatase which is a good marker of cholestasis in nonpregnant state is not of much help because of its pregnancy associated increase coming from placenta.

Women with positive serology for Hepatitis A, B or C, previous history or sonographic evidence of gall bladder disease, PIH and those in whom liver function did not normalize within two weeks of delivery were excluded from this study. Once identified, the women were asked regarding nature and severity of pruritus.

All women were offered palliation initially with topical emollients with or without chlorpheniramine. Ursodeoxycholic acid was given to all the pregnant females complaining of pruritus. In all the women LFT were repeated every two weeks. Antenatal care protocol with respect to interval between clinical examination, USG, CTG and induction of labor was decided on the merit of obstetric indication.

Obstetric 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, need for nursery admission in the new born and maternal postpartum complications. Symptomatic relief of pruritus and liver function test was determined in all women two weeks after the delivery.

Results

During the study period out of the 892 antenatal registered women, 83 were diagnosed as having cholestasis of pregnancy giving an incidence of 9.3%. 70 (84.3%) were primigravidas, 13 (15.6%) were multigravidas. The cardinal symptom of obstetric cholestasis was pruritus which appeared after 30 weeks in 85% of the women (71/83). When asked to list all parts where pruritus was perceived, 80% (66/83) reported it to be all over. When asked about the single site where pruritus was most severe 20% (16/83) women reported it to be on palms and soles.

Biochemical Results:

Most of the patients had serum bilirubin less than 2mg% (74%) (8).

Alkaline phosphatase levels were less than 1000 kA units

SGOT levels were less than 400 IU

SGPT levels were less than 600 IU

All the women under the study were given ursodeoxycholic acid. All of them had good symptomatic relief and 48% (40/83) of the women reported complete relief. There was also biochemical improvement with reduction in serum bilirubin and transaminase level in 72.2% (60/83) of the women. In the study group, 78% (65/83) women went into labor either spontaneously or after induction. Elective cesarean section rate was 22% (18/83).

Among the women, 80% (56/65) went into labor spontaneously. In the spontaneous group 72% (40/56) delivered vaginally and cesarean section rate was 28% (16/56).

13.8% (9/65) of the women underwent induction of labor, all of them beyond 38 completed weeks. The method of induction depended on the cervical score, AFI and CTG pattern prior to induction. The cesarean section rate in this group was 33% (3/9) as compared to 28.5% (16/56) in the spontaneous onset group.

During labor an abnormal CTG was noted in 9.2% (6/65) of the cases, while meconium staining of liquor was 9.6% (8/83) of the cases. The overall cesarean section rate in our study was 44.5% (37/83); emergency cesarean section rate was 29% (19/65). Birth weights were appropriate for gestational age in all infants. A/S was 10/10 in all the newborns. There was no neonatal nursery admission and perinatal mortality. The difference regarding thick meconium was found to be statistically not significant by Fisher's exact test (P=0.19), although the number of cases with meconium after 38 weeks were more. No case of PPH in the mother occurred and hence no added maternal morbidity and mortality.

Table 1. Total no. of Patients – 83.

Results of Investigations		
Investigations	**Number**	**Percentage**
S. Bilirubin (mg/dl)		
0.2 – 0.6 mg/dl	37	44.5
0.6 – 1.0 mg/dl	25	30.1
1.0 – 1.4 mg/dl	18	21.6
1.4 – 1.8 mg/dl	3	3.6
SGOT IU/L		
0 – 100	52	62.6
100 – 200	17	20.4
200 – 300	9	10.8
300 – 400	5	6.02
SGPT (IU/L)		
0 – 100	42	50.6
100 – 200	21	25.3
200 – 300	9	10.8
300 – 400	7	8.4
400 – 500	3	3.6
500 – 600	1	.01
S. alkaline phosphatase (IU)		
0 – 200	12	14.4
200 – 400	39	46.9
400 – 600	23	27.7
600 – 800	7	8.4
800 – 100	2	2.4

Discussion

This study describes the nature and outcome of obstetric cholestasis. The incidence was 9.3% which is comparable to the study of Devinder Kaur (16.75%)[3]. IHCP is a recurrent condition and in multigravidas there was history of pruritus in previous pregnancy in 50% of the patients[4]. In our series 85% of the women presented after 30 weeks of pregnancy which is comparable to the study of Ray et al. (84.3%)[4]. UDCA 300mg BD was used in all the cases of pruritus. It was very effective in reducing pruritus as well as improving the biochemical parameters [2,5]. The altered biochemical parameters reduced the fetomaternal transfer. The increase in bile acids is toxic to the fetus[6]. In 20% of the patients pruritus was most severe on the soles which was comparable with the study of Ray et al [4]. In fact this may be suggestive of obstetric cholestasis. There was no effect on the prothrombin time. The Biochemical results in our study were comparable to study of Ray et al [4].

On further analysis of the data we found that the period of gestation at the time of delivery affected intrapartum events and perinatal outcome. Women delivering after 38 weeks had a higher incidence of thick meconium 12.9% (8/62) as compared to the study of Ray et al (45%)[4]. Abnormal CTG was 9.6% (6/62) as compared to 35% in Ray et al series. In our series this difference was not statistically significant in the patients delivering before 38 weeks and after 38 weeks. IHCP occurs mainly in the final months of pregnancy with pruritus as the cardinal symptom and has a high recurrence in the future pregnancies. It is associated with increased maternal morbidity and perinatal morbidity and mortality. Risk to the fetus increases as pregnancy advances and particularly after 38 weeks regardless of serum bilirubin and hepatic enzyme levels. Continuous monitoring of fetus with USG and CTG may not prevent sudden fetal distress and IUFD. Induction of labor between 37 and 38 weeks may improve perinatal outcome. All our patients were on UDCA 300mg BD and it was quite effective in lowering the incidence of pruritus, severity of pruritus and improving fetal outcome.

Dexamethasone has also shown promise as a potential therapy for IHCP through suppression of fetoplacental estrogen production. Dexamethasone therapy may lead to amelioration of the symptoms. S-adenosyl-L methionine therapy showed promise in early studies for symptomatic and laboratory improvement in IHCP[1]. There was no premature delivery in our series as

compared to that of Choudhri et al[7] in which prematurity complicates 60% of the pregnancies with cholestasis (compared with normal 8%).

Conclusions

Obstetric cholestasis is associated with increased perinatal mortality and morbidity if delivered after 38 weeks. An attempt to deliver prior to 38 weeks may improve the perinatal outcome. Pruritus with or without jaundice is a hallmark feature of IHCP.

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