Obstetric Outcome During an Era of Active Management for Obstetrics Cholestasis

Nalini Sharma¹ · S. Panda¹ · Ahanthem Santa Singh¹

Received: 31 January 2015 / Accepted: 13 August 2015 / Published online: 8 September 2015
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About the Author

Dr. Nalini Sharma is working as an Assistant Professor of Obstetrics and Gynaecology in North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS), Shillong, Meghalaya. She is having 13 years of post PG experience. She has many national and international publications. She has keen interest in laparoscopic surgeries, high-risk pregnancy, and social obstetrics.

Abstract

Objective To study the incidence, maternal, and perinatal outcomes in intrahepatic cholestasis of pregnancy with active management.

Materials and Methods This observational study included 48 cases diagnosed as intrahepatic cholestasis of pregnancy. Medical treatment and active management (fetal

surveillance and termination of pregnancy at 37–38 weeks) were offered to all. Maternal and perinatal outcomes are studied.

Results Incidence of ICP was 2.4 %. More than 86 % of patients presented with generalized pruritus mostly after 30 weeks. Incidences of Intrapartum abnormal cardiotocography (12.5 %) and thick meconium (8.33 %) were high. Cesarean section rate was high (41.66 %). Most common indications were CDMR, fetal distress, and non-progress of labor. Incidence of preterm labor, IUGR, Apgar score (<7), and neonatal admission rate were not high. There was one stillbirth at 36 weeks of gestation. Serum transaminase levels tended to be higher in patients with poor perinatal outcomes, such as stillbirth, fetal distress, and meconium-stained amniotic fluid.

Conclusion Serum transaminase levels tended to be higher in patients with poor perinatal outcome. Perinatal outcome is good with active management, at the cost of higher LSCS rate. Further randomized controlled trial of early versus spontaneous delivery may be justified.

Nalini Sharma is an Assistant Professor; S. Panda is an Associate Professor and Ahanthem Santa Singh is a Professor and Head at the Department of Obstetrics and Gynaecology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya.

✉ Nalini Sharma
nalinisharma100@rediffmail.com

¹ Department of Obstetrics and Gynaecology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS), Mawdiangdiang, Shillong, Meghalaya 793018, India

Keywords Intrahepatic cholestasis of pregnancy · Perinatal outcome · Active management · Obstetrics cholestasis

Introduction

Obstetric cholestasis (OC) is the most common pregnancy-related liver disorder. It is a cholestatic disorder characterized by pruritus, elevated serum aminotransferase and bile acid levels with onset in the second or third trimester of pregnancy, and spontaneous relief of sign and symptoms within 2 or 3 weeks after delivery [1–3]. The incidence of ICP varies widely with geographical location and ethnicity [4]. In South Asian population, it varies from 0.8 to 1.4 %. The low incidence of intrahepatic cholestasis may indicate an underestimation of the problem due to unawareness among clinicians about this entity and growing awareness of the condition will probably increase the number of cases of intrahepatic cholestasis. The etiology of ICP is elusive, although current investigations suggest a combination of hormonal, genetic, and inflammatory factors that impair bile secretory function, which increases maternal serum bile acid and elevates the production of liver enzymes [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 [5, 6]. Routine tests for fetal monitoring such as cardiotocography and umbilical artery Doppler cannot predict fetal outcome. Stillbirth in obstetric cholestasis has been reported throughout the gestation. As the majority of intrauterine death in singleton pregnancies complicated by ICP occurs after 37 weeks of gestation, delivery has been recommended on or after 37–38 weeks of gestation [7]. As gestation advances, the risk of delivery (prematurity, respiratory distress, failed induction) versus the uncertain fetal risk of continuing the pregnancy (stillbirth) may justify offering women induction of labor after 37 weeks of gestation [8]. Clinical trials are required to identify the most suitable monitoring modalities that can specifically predict poor perinatal outcome. This study aimed at finding the incidence, obstetrical, and perinatal outcomes in intrahepatic cholestasis of pregnancy. We undertook this study to determine the nature and outcome of obstetric cholestasis when actively managed.

Materials and Methods

This observational study included all the cases of intrahepatic cholestasis of pregnancy, diagnosed and managed in the past 1 year in the Department of Obstetrics & Gynaecology. Diagnosis of cholestasis of pregnancy was made by excluding other liver and dermatological

disorders. Subject's personal, family, medical, and drug histories were taken in detail pertaining to the case. Diagnosis of OC was made on the basis of symptoms of persistent pruritus (generalized/localized), biochemical evidence of altered LFT, and remission of both following delivery. The upper end of the normal range in pregnancy was assumed to be 80 % of the level quoted in non-pregnant women. Severity of pruritus was noted by using subjective scale (0–4). After diagnosis with ICP, subjects were treated by ursodeoxycholic acid (UDCA) 20 mg/kg/day in divided doses. Subjects had regular weekly antenatal checkup. LFT was done weekly. Fetal surveillance was done by daily maternal recording of fetal movements, CTG, modified BPP, or Doppler USG twice a week after 32 weeks of gestation. Any complications during pregnancy such as PPRM and preterm labor were noted. Women with 37 weeks of gestation were offered active management, i.e., termination of pregnancy either by induction or by elective LSCS (if indicated). The CTG finding during fetal surveillance and the presence of meconium-stained amniotic fluid were noted. Mode of delivery, Apgar score at 1 and 5 min, and the need for NICU admission or any perinatal mortality were noted. Maternal complications such as postpartum hemorrhage were noted. LFT was repeated every 2 weeks after postpartum.

Results

A total of 1996 women were delivered during the study period, and 48 women were diagnosed with intrahepatic cholestasis of pregnancy, giving an incidence of 2.4 % in our institute.

Table 1 shows the clinical characteristics of patients regarding age, gravidity, and gestational age at presentation. Table 2 shows biochemical characteristics of patients. 30 (62.5 %) women were primigravida. 9 out of 18 multiparous women had history of ICP. 18 % of the women had family history of ICP. We noticed seasonal variation, which was more during rainy season. Cardinal symptom was pruritus which was generalized in 86 % of patients. 60 % of the women graded their severity of symptoms as 4, and palm and soles were the worst affected areas in 40 % of women. All women reported partial or complete relief of pruritus, and there was an improvement in the biochemical parameters, i.e., reduction in serum transaminase and bilirubin levels with UDCA. Four women were delivered before 37 weeks. Of the four, two had preterm labor, one had PPRM, and in one, LSCS was done due to abnormal CTG finding. Most of them went into labor either spontaneously or after induction. LSCS rate (41.66 %) was high in these women. 11 cases underwent elective LSCS (Tables 3, 4, 5).

Table 1 Patients characteristics

	Min–max	Mean $\pm$ SD
Age (years)	19–38	26.33 $\pm$ 4.05
Gravidity	1–6	1.97 $\pm$ 1.17
Onset time of pruritus gestational age (week)	28–37	33.5 $\pm$ 2.61

Table 2 Biochemical characteristics of patients

	Min–max	Mean $\pm$ SD
SGOT	35–600	176.12 $\pm$ 109.5
SGPT	38–540	188.562 $\pm$ 116.78
Serum bilirubin	1.2–4.2	1.7 $\pm$ 1.26

Discussion

The incidence of ICP in Indian women has been reported to be about 1 % [9, 10]. In our study, its incidence was high, which was 2.4 %. The mean age was 26.3 years, although some studies reported relatively higher mean age [11]. In our study, 18 % of women have family history and recurrence was noted in 50 % of women. 96 % of women presented after 30 completed weeks of pregnancy similar to other study [9]. Generalized pruritus was the most common symptom. Palms and soles were more severely affected areas. It has been reported that severe pruritus of palm and soles may be particular suggestive of this condition. The main biochemical alterations are elevation of serum bile acid and transaminase levels. In the present study, transaminases were raised in >94 % women in the range of 35–600 mIU. Two women with generalized pruritus initially presented with normal transaminase levels. On repeat liver function test after 1 week, transaminases were found elevated. It has been reported that itching may be present either before or after abnormal liver function test is detected and this may reflect the heterogeneous nature of the condition [10]. Serum bilirubin was elevated in 40 % of cases comparable to other studies [12], but there was only one case of clinical jaundice. ICP has been associated with increased risk of preterm delivery (up to 19–60 %), meconium staining of amniotic fluid (up to 27 % cases), fetal bradycardia (up to 14 %), fetal distress (22–41 %), and fetal loss (0.4–4.1 %) [5, 6] particularly when serum bile acid level goes beyond 40 mmol/l [11, 13].

In the present study, incidences of premature delivery and meconium-stained liquor were relatively less, 6.22 and 8.33 %, respectively. There was no significant association of IUGR and neonatal ICU admission. More than 95 % of babies

had Apgar score more than 7, and there was no neonatal mortality. Unfortunately, there was one stillbirth (2.08 %) at 36 weeks of gestation. Woman having intrauterine fetal death had normal AFI, CTG tracing, and Doppler 12 h prior to detection of fetal death. No other pregnancy complication was seen in the mother. Fetus was grossly normal. This woman was unbooked, presented 2 days before fetal death. Cause of IUFD may be due to acute anoxic event due to direct cardiotoxic effect of bile acid or vasoconstriction of placental vessel [4, 7]. In the present study, we could not measure the level of bile acid, but in this woman, transaminase levels were 20 times (500–600 U/L) more than normal. There are data relating to prediction of fetal death and liver enzyme concentration which showed more fetal distress with high alanine aminotransferase level. It has been reported that higher bile acid level (>40 mmol/l) is associated with higher rate of preterm delivery [11, 13], fetal death, passage of meconium [13], and abnormal cardiotocography [6, 13]. All women with OC were prescribed UDCA 20 mg/kg/day. In the present study, apart from reducing pruritus as well as improving biochemical parameters, various perinatal complications such as preterm labor, fetal distress, meconium staining of liquor, and PPH were relatively less. It may be due to early pharmacological intervention in the form of UDCA in all cases. Although the mechanism of action is not fully understood, it has been postulated that UDCA works by displacing hydrophobic endogenous bile salts from the bile acid pool, protecting hepatocytes from their toxic effects, and enhancing bile acid clearance across the placenta from fetus [8]. LSCS rate (41.66 %) was higher in pregnancy with ICP and comparable to other studies [5]. Higher rate of LSCS may be due to active management or complication of the disease. The percentage of normal vaginal delivery was higher in women where labor started spontaneously. Most common indications for LSCS were cesarean section on maternal request (CDMR), fetal distress, and non-progress of labor. In the present study, women did not receive vitamin K. In all women, coagulation profile was within normal limit, and no woman had postpartum hemorrhage. It was quite different from other studies in which the incidence of postpartum hemorrhage was quite high in those women who did not receive vitamin K [9, 11]. Weakness of the study lies in the fact that it measures the incidence of OC at a tertiary care institute and not from a general population. Study should be carried out at multiple centers so we can have large number of patients to find out the possible reductions in perinatal mortality in the active management group.

Another limitation was the absence of an unaffected control group. For further research it is advisable that we can grade ICP into mild, moderate and severe variety on the basis of levels of serum transaminase and can choose conservative management in less severe cases. It provides another area of study.

Table 3 Pregnancy outcome

Preterm labor	2 (4.16 %)
PPROM	1 (2.08 %)
Thick meconium-stained liquor	4 (8.33 %)
Fetal distress	6 (12.5 %)
LSCS	20 (41.66 %)
Apgar < 7	2 (4.16 %)
Neonatal nursery admission	5 (10.41 %)
IUFD	1 (2.08 %)
NND	Nil
PPH	Nil

Table 4 Mode of delivery

Normal delivery	24 (50 %)
Instrumental delivery	4 (8.33 %)
Elective LSCS	11
Emergency LSCS	09

Table 5 Indications of LSCS

Elective LSCS	11
CDMR	6
Previous LSCS	3
Twin pregnancy	1
Breech	1
Emergency LSCS	9
NPOL	4
Failed induction	2
Fetal distress	3

Conclusion

In the present study, serum abnormality in LFT (serum transaminases) tended to be higher in women with poor perinatal outcome. LSCS rate is higher with active management. Further randomized controlled trial of early versus spontaneous delivery may be justified.

Compliance with Ethical Standards

Conflict of Interest Nalini Sharma, Subrat Panda, and Ahanthem Santa Singh declared that they have no conflict of interest.

Ethical Approval Institutional ethical Committee clearance was obtained for study.

Informed Consent Informed consent was obtained from all patients for being included in study.

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