ISSN: 2091-2331 (PRINT) 2091-234X (ONLINE)

Journal of Nobel Medical College
Available Online: www.nepjol.info, www.nobelmedicalcollege.com.np
Volume 5, Number 1, Issue 8, January-July 2016, 20-25

Original Article

Feto-Maternal outcomes in Intrahepatic Cholestasis in Pregnancy in a Tertiary Care Centre in Eastern Nepal

Sita Pokhrel (Ghimire), Ashima Ghimire, Gauri Shankar Jha, Manisha Chhetry and Mahanand Kumar
Department of Obstetrics and Gynecology, Nobel Medical College Teaching Hospital, Biratnagar
Received: 28th April, 2016; Revised after peer review: 3rd June, 2016; Accepted: 25th June, 2016

Abstract

Background

Intrahepatic cholestasis of pregnancy has poor feto-maternal outcomes. To date there has been sparse publications regarding impact of intrahepatic cholestasis in feto-maternal outcomes in our setting. Therefore, we aimed to study the feto-maternal outcome in patients with intrahepatic cholestasis of pregnancy.

Material and Methods

A hospital based prospective cross-sectional study carried out in department of Obstetrics and Gynecology of Nobel Medical College, Biratnagar, Nepal from 1st January 2014 to 30th December 2015 in women who presented with pruritus in third trimester of pregnancy and having deranged liver function tests. All the cases were followed from admission to discharge. Socio-demographic, clinico-laboratory profile and feto-maternal outcomes were recorded in a preformed structured proforma. Descriptive statistics was used to present the data.

Results

Among 6,780 women admitted for delivery, 80 had cholestasis of pregnancy with incidence of 1.15%. 83% were of 18-35 years and 65% were primigravida. Most distressing symptom was generalized pruritus (75.0 %). The cesarean delivery rate was 46.25% and labor induction rate was (47.5%). Fetal complications were seen in majority of cases that included meconium aspiration syndrome 26 (32.5%), intrapartum fetal distress 21 (26.25%) and requirement of: intensive care 38 (48.75%). There were 7 perinatal and 3 neonatal deaths.

Conclusion

Intrahepatic cholestasis of pregnancy seems fairly common among pregnant women. It may be responsible for a large number of perinatal and neonatal deaths especially after 36 weeks of gestation. A large prospective study is needed to address the problems in time.

Key Words: *Feto-maternal outcome, Intrahepatic cholestasis in pregnancy, pruritus*

Introduction

Intrahepatic Cholestasis in pregnancy (ICP) is defined as pruritus with onset in pregnancy which is associated with abnormal liver function test in the absence of other diseases which resolves following delivery. It typically occurs during third trimester of pregnancy and seldom occurs before 25 weeks period of gestation [1]. Its incidence varies in different countries and is very low in Europe (0.1 to 1.5%) whereas in Chile it is very high (14%) [2].

Correspondence Address:** ***Dr.Sita Pokhrel (Ghimire), Assistant Professor, | E-mail: sitap661@gmail.com

It is 1.2-1.5% in India and Pakistan [3]. Maternal consequences in ICP occurs due to increase in plasma protein concentration leading to alteration in carbohydrate metabolism and renal and intestinal function [4]. Steatorrhoea leading to deficiency in vitamin K dependent clotting factors and subsequent Post partum haemorrhage (PPH) has been reported [5]. In women of ICP, there is chance of 1.5 fold increase in cesarean delivery and 8 fold increase in duration of hospital stay for more than 10 days, 3 fold increase in induction of labor [6]. Adverse perinatal outcome is a major concern in intrahepatic cholestasis in pregnancy(ICP). The potential risks are fetal distress, intrauterine fetal death (IUFD), iatrogenic preterm delivery, meconium stained liquor, low birth weight and still birth [7 ,8]. Most distressing pruritus leads to sleep deprivation in pregnant women [9]. To the best of my knowledge, till this date,there are hardly any studies regarding this obstetric problem in our country. When data are extrapolated from different south Asian studies to our country, it is high likely that, ICP is common in our setting with poor fetomaternal outcomes. With this hypothesis, we aimed to study the fetomaternal outcomes in ICP in our setting.

Material and Methods

It was a Cross-sectional study design carried out in department of Obstetrics and Gynecology of Nobel Medical College, Biratnagar, Nepal from 1st January 2014 to 30th December 2015. Ethical clearance from institutional ethical review board (IERB) was obtained before conducting the study. Informed verbal and written consent was taken from the women before enrollment in the study. Any women with pruritus in 3rd trimester pregnancy underwent liver function test. Patients with history of itching and deranged liver function tests for which there was no explanation other than pregnancy were included in our study. Every case was evaluated in detail, demographic, clinical and laboratory parameters were recorded in well-structured proforma. Cases were followed from admission to discharge.

All the maternal and fetal outcomes were noted. Information related to admitted newborn was obtained from neonatal intensive care unit(NICU). The collected data were entered in Microsoft Excel 2007 worksheet and statistically analyzed using the SPSS software version 11.5. Descriptive statistical data were presented as Mean, Standard Deviation, and percentage and proportions, and interquartile range, and the information were illustrated in graphical and tabular formats.

Results

During the one-year period, 6,780 women came for delivery and 87 had pruritus in third trimester. Liver Function test were abnormal in nearly 98% of the cases. Among them seven women were lost to follow up. The incidence of ICP was found to be 1.15%

Table 1: Demographic characteristic of patients

Characters		Number (n = 80)	Percent
	< 18 years	8	10
	18-35 yrs	67	83.7
Age	> 35 yrs	5	6.25
Gravidity	Primigravida	52	65
	Multigravida	24	30
	Grand multigravida	4	5
		Total 80	

Sixty-seven (83.7%) of the cases were in the age group of 18-35 years. Fifty-two (65%) were primigravidas and 24 (30%) were multigravida. All women were presented with complain of whole body itching more in palm and sole however 60(75%) women were having severe ithching leading to disturbed sleep. While

analyzing past obstetric history, out of 80 women 11(13.7%) had history of previous pregnancy loss. Out of them ,4 (5%) had history of early pregnancy loss whereas remaining 4(5%) had history of intrauterine fetal death and 3 gave history of fresh still birth. Among 7 women of late pregnancy loss, only 3 (3.75%) women gave history of itching in palm and sole but none of them sought medical advice for this complain.

All 4(5%) cases of IUFD had reached hospital with history of not perceiving fetal movement for more than 24 hours. The 3 (3.75%) cases of fresh stillbirth had reached hospital in previous pregnancy with history of per vaginal leaking but not associated with pain at 38- 39 weeks period of gestation. While analysing gestational age at onset of pruritus, 38 (47.5%) women had onset at 32 -36 weeks period of gestation whereas 22 (27.5%) had onset at 28-32 weeks period of gestation. 11(13.75%) women had onset of pruritus at 24-28 weeks period of gestation and 9 (11.25%)women had after 36 weeks period of gestation. None of the women gave history of pruritus before 24 weeks period of gestation.

Table 2 : Liver Function Tests

Parameters	Value	Percentage of women
Alanine - aminotransferase(ALT)	38-650 IU/L	97.8
Aspartate - aminotransferase(AST)	40-640 IU/L	97.8
Alkaline phosphatase	70-1890 IU/L	45.5
Total Billirubin	1.0 - 3.8 mg%	11

Among 5 cases of Intrauterine fetal deaths, 3 were admitted with complain of whole body itching since 10 to 15 days and not being able to perceive fetal movement at 37-38 weeks' period of gestation. While remaining 2 admitted with labor pain and on further asking gave history of itching particularly in palm and sole. All 5 cases were unbooked.

Table 3 : Gestational age at delivery

Weeks of Gestation	Number (n = 80)	Percent
< 34 weeks	9	11.2
34-36 weeks	24	30
37-40 weeks	41	51.25
> 40 weeks	6	7.5

Table 4 : Complications of pregnancy

Complications	Number n = 80	Percent
PPROM	5	6.25
Preterm delivery	15	18.7
PROM	8	10
Elective caesarean section	8	10
Emergency caesarean section	29	36.25
Postpartum Haemorrhage	9	11.25

Table 5 : Neonatal outcome

Outcome	Number n = 80	Percent
APGAR score < 7 at 5 minutes	11	13.75
Birth weight in grams < 2500 grams	18	22.5
Intrapartum fetal distress	21	26.25
Meconium stained liquor	26	32.5
`Spontaneous preterm delivery	8	10
Intrauterine fetal death	5	6.25
Fresh still birth	2	2.5

Out of 80 neonates, 38(48.75%) neonates were admitted in NICU. The causes of neonatal admission was preterm for supportive care 6(7.5%), presumed sepsis in 7(8.75%), neonatal sepsis 5(6.25%), meconium aspiration syndrome in 13(16.25%) and birth asphyxia 8,(10%) .

There were 2 (2.5%) cases of fresh stillbirth; both the cases had undergone induction for obstetric cholestasis with

postdated pregnancy. Out of 38 cases of NICU admission, 1 case went home against medical advice on second day of delivery, 3 cases had neonatal death and remaining 34 cases were discharged after treatment. Among 3 cases of Neonatal death, 2 were admitted for meconium aspiration syndrome and remaining one for presumed sepsis.

Discussion

This prospective study describes the fetomaternal outcome of obstetric cholestasis in referral center of Eastern Nepal. During the study period, there were 6,908 women admitted for deliveries. The incidence of obstetric cholestasis was 1.15% which is comparable to the previous study done by Sultana and her colleagues [3]. In our study 38(47.5%) of women were induced which is almost similar to study done by Turunen et al [6]. Eight (10%) women were induced at 34-36 weeks period of gestation for increasing level of liver enzymes despite medical treatment with ursodeoxycholic acid. However, 17(21.25%) women were induced at 37-38 weeks period of gestation for persistent pruritus though liver parameters were improving. Six women (7.5%) went induction postdated as they were lost in follow up and were admitted after crossing 40 weeks period of gestation only and rest 7(8.75%) women were induced at 38-40 weeks period of gestation. Out of 25 cases (31.25%) of early induction i.e. before 37 weeks,11 women (13.75%) underwent cesarean delivery for failed induction. In our study, out of 80 women, 46.25% underwent cesarean section, out of which 10% were elective cesarean section and 36.25% emergency cesarean section. It is comparatively higher than previous study [6] (14.8%), the reason maybe we had gone for early induction in 31.25%, so increased rate of cesarean for failed induction 11(44%). In our study 11.25% women had postpartum hemorrhage whereas Wang et al (2010) found it to be 1.4% [10]. The reason for high incidence of PPH in our study is attributed to high incidence of anemia in our area, poor antenatal visits and low socioeconomic status and only 72% of women had injecton vitamin k before delivery.

While analyzing Neonatal outcomes the incidence of low APGAR score <7 in 5 minutes was in 13.75% which is almost similar to previous study done by Alokananda et al in 2005 (18.5%) [2]. However, it is very high (4.4%) when compared with next study done in India [11]. The reason maybe we have 87% unbooked obstetric cholestasis cases and their higher rate of cesarean section (93.3%). The disease has been related to a high incidence of perinatal complications leading to 45 % meconium stained liquor, 44% preterm delivery and higher incidence of fetal distress (upto22%) [12,13].

It is suggested that both intrapartum fetal distress and increase incidence of meconium stained liquor is due to the stimulation of colonic motility by bile acids on Obstetric Cholestasis [13]. Like other study [14] (33.3%) we have also observed higher incidence of meconium stained liquor in 32.5%. But Padmaja M et al had not shown significant incidence of meconium stained liquor,which is attributed to proper antenatal visit leading to on time intervention of Obstetric Cholestasis [11].

In our study we observed that 15(18.75%) were preterm (iatrogenic 7 and spontaneous 8) which is almost similar to study done by Roncaglia N et al showing incidence of 19.5% [15]. Our study had similar finding 6.25% to previous study by Sultana et al 6.67% in relation to intra uterine fetal death [3]. But it is high when compared to study done by Aloknanda [2] where incidence of IUFD was found to be only 3.1% which is attributed to our poor number of booked cases and all 5 cases

had intrauterine fetal death before being admitted in hospital. We found only two (2.5%)case of fresh stillbirth like in study done by Turunen et al [6] (1.2%) where as another study done in India [11] had shown very low i.e only 0.02% which is attributed to booking status, good antepartum care and higher incidence of cesarean section. In a study conducted by Zecca E and colleagues, IUFD was found to be in 6% patients which is similar to our study (6.25%) [16].

We had 38(47.55%) NICU admissions which are comparatively higher then study done by Deveer et al where the incidence was only 27% [17] which is due to higher number of intrapartum fetal distress and higher percentage of meconium stained liquor (32.5%) in our study. Another study by Sebiha et al had also found almost similar to our finding where incidence of meconium stained liquor to be 25-45%, pretem labor 44% and IUFD upto 5% [18]. Obstetric cholestasis is associated with premature delivery both spontaneous and iatrogenic and increase incidence of IUFD and the perinatal mortality from Obstetric Cholestasis is 10.6\1000 live birth [19]. Intrauterine fetal death is usually sudden and seems to be due to Acute anoxia [20].

Conclusion

Intrahepatic cholestasis of pregnancy seems fairly common among pregnant women in our setting. It was found to be responsible for a large number of perinatal and neonatal deaths especially after 36 weeks of gestation. A large prospective study is needed to find the clinic-epidemiological pattern of this obstetric problem. In the mean time, it is important to realise that by increasing awareness among the health personnel caring for the pregnant women that pruritus of pregnancy is a high risk condition and close fetal monitoring and timely intervention will decrease perinatal mortality significantly.

References

1. Madazil R ,Yuksel MA,Oncul M,Tuten A,Guralp O, Aydin B, Pregnancy Outcomes and prognostic factors in patients with intrahepatic cholestasis of pregnancy, J Obstet Gynaecol. 10 (2014) 1-4.
2. Alokananda R,Tata Rashne J,Roshan B ,Sangeeta S.Cholestasis of pregnancy, J Obstet Gynaecol India. 55:3 (2005) 247-50.
3. Sultana R,Sarwar I,Fawad A,Noor S,Bashir R, Neonatal outcome in obstetric cholestasis patients at Ayub Teaching Hospital abbottabab, J Ayub Med Coll Abbottabad 21:4 (2009) 76-8.
4. Ranta T, Unnerus HA, Rossi J, Seppala M, Elevated plasma prolactin concentration in cholestasis of pregnancy, Am J ObstetGynecol. 134(1979) 1-3.
5. Germain AM, Carvajal JA,Glasinovic JC ,Kato C S, Williamson C.Intrahepatic cholestasis of pregnancy :an intriguing pregnancy-specific disorder, J Soc Gynecolinvestig. 9:1 (2002) 1-4.
6. Turunen K, Sumanen M, Haukilahti RL, Kirkinen P, Mattila K, Good pregnancy outcome despite intrahepatic cholestasis, Scand J Prim Health Care. 28:2 (2010) 102-7.
7. Reyes H, The spectrum of liver and gastrointestinal disease seen in cholestasis of pregnancy, Gastroenterol Clin North Am. 21(1992) 905-21.
8. Kenyon AP, Piercy CN, Girling J et al, Obstetric cholestasis, outcome with active management: a series of 70 cases, BJOG 109 (2002) 282-8.
9. Royal College of Obstetricians and Gynecologists, Obstetric cholestasis, RCOG Guideline No.43, 2006.
10. Wang XD,Peng B, Yao Q ,Zhang L,Ai Y,Xing AY et al, Perinatal outcomes of intrahepatic cholestasis of pregnancy : analysis of 1210 cases, Zhonghua Yi Xue ZaZhi. 86:7 (2006) 446-9.
11. Padmaja M, Bhaskar P, Gupta JK, Ramamurthy S, Chaudhri M, A study of obstetric cholestasis, J Obstet Gynecol India. 60:3 (2010) 225-31.
12. Rioseco AJ, Ivankovic MB, Manzur A, Intrahepatic cholestasis of pregnancy: a retrospective case-control study of perinatal outcome, Am J Obstet Gynecol. 170 (1994) 890-5.
13. Fisk NM, Storey GN, Fetal outcome in Obstetric Cholestasis, Br J Obstet Gynaecol. 95 (1988) 1137-43.
14. Mei-Ting LAM, Tsz-Kin LO, Wai-Lam LAU, Sidney TAM,Wing –Cheong LEUNG ,Cohort Study of Suspected Obstetric Cholestasis – What have We Learned?, Hong Kong J GynaecolObstet Midwifery. 14:1 (2014) 51-6.
15. Roncaglia N, Trio D, Roffi L, Ciaria I, Tampieri A, Scian A et al. Intrahepatic Cholestasis in

pregnancy :incidence, clinical course, complications, Ann OstetGinecol Med Perinat . 112:3 (1991) 146-51.
16. Zecca E, De Luca D, Marras M, Caruso A, Bernardini T, Romangnoli C, Intrahepatic Cholestasis of pregnancy and neonatal respiratory distress syndrome, Paediatrics. 117:5 (2006) 1669-72.
17. Deveer R, Engin-Ustun Y ,Celen S, Eryilmaz OG,Tonguc E, Mollamahmutoglu L et al, Two – year experience of obstetric cholestasis : outcome and management, Clin Exp Obstet Gynecol. 38:3 (2011) 256-9.
18. Sebiha D, Yasinc C, Orhan VO, Sule Y, Review of a challenging clinical issue: Intrahepatic Cholestasis in pregnancy, World J Gastroenterol. 21:23 (2015) 7134-41.
19. Gonzalez CG, Reyes H, Arrese M, Figueroa D, Lorca B, Andersen M et al., Intrahepatic cholestasis of pregnancy in twin pregnancies, J Hepatol. 9 (1989) 84-90.
20. Zimmeqman P,Koshiken J, Vaalamo P, Ranta T, Doppler Umbilical artery velocimetry in pregnancies complicated by Intrahepatic Cholestasis, J Perinat Med. 19 (1991) 351-5.