MATERNAL AND NEONATAL OUTCOME IN OBSTETRIC CHOLESTASIS: A COMPARISON OF EARLY VERSUS LATE TERM DELIVERY

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ABSTRACT

Objective: To evaluate maternal and neonatal outcome in Obstetric Cholestasis (OC) in early versus late term delivery.

Study Design: Retrospective cohort study.

Place and Duration of Study: Aga khan hospital for women (AKHW) Karimabad, Karachi, from 1st Jan, 2011 to 31st Oct, 2012.

Patient and Methods: This was a retrospective cohort study. All patients of OC with singleton pregnancy, admitted for labor induction between Jan 2011 to Oct 2012 were included in the study. At or after 37 week of gestation, patient is offered labor induction. Patients were divided in two groups as in early term delivery (Group A) and late term delivery (Group B). Early term delivery is taken from 37+o to 37+6 and late term delivery at or after 38 weeks of gestation. The demographic, laboratory and clinical data of these patients were collected from their medical record. Maternal and neonatal outcome were analyzed using SPSS version 19.

Results: The study found that in obstetric cholestasis patients admitted for labor induction, the risk of caesarean delivery was higher in group A (before 38 weeks) as compared to group B (after 38 weeks). There was no difference in postpartum hemorrhage and drop in hemoglobin between two groups. Obstetric cholestasis was not associated with adverse perinatal outcome such as intrauterine death (IUD), low Apgar Scores, respiratory distress and neonatal intensive care admission in both the groups. However more cases of neonatal jaundice were observed in babies born after 38 weeks.

Conclusion: OC patients who deliver after 38 weeks of gestation have a higher chance of vaginal delivery without increasing the risk of IUD.

Keywords: Caesarean section, Labor induction, Obstetric cholestasis, Pregnancy outcome.

INTRODUCTION

Obstetric Cholestasis (OC) is a liver disease of pregnancy characterized by deranged liver function and raised bile acids in the absence of other liver diseases. Serum transaminases are raised two to tenfold depending upon the severity of the disease. It may rise before or after serum bile acid. Bilirubin is normal in majority of the cases. Alkaline Phosphatase level may rise in OC but has limited diagnostic value because of production of large amount of placental isoform[1].

The most common presenting symptom is pruritus without rash, more marked on palm and soles. It usually presents in third trimester and progressively become severe as pregnancy advances. The symptoms and biochemical markers usually become normal within two weeks of delivery[2].

It is multi factorial in etiology[3] and its prevalence also varies with geographical and ethnicity differences. It affects about 1.2 to 1.5% of women of Indian Asian or Pakistani Asian origin[4,5].

OC is associated with adverse fetal outcome which includes preterm birth, meconium stained liquor, fetal distress and intra uterine death. In recent studies[5-7] there is considerable debate on the extent of the fetal risks. Most of these studies are small and therefore it is not possible to quantify the frequency of the complication. Correlation of maternal serum biochemistry with fetal outcome has been tried in many studies[8]. Higher rates of fetal complication have been reported if serum bile acids are above 40 micromole per liter[8] or if women had jaundice along with pruritus. This suggest that fetal risk is directly associated with severity of the

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disease and mild cases of OC has no increased fetal risk[1].

Although relation of bile acid level with severity of disease and its outcome have been studied but in this part of world serum transaminases levels are done to establish the diagnosis and extent of disease.

OC is treated with anti histamines, topical emollients and Ursodeoxycholic acid (UDCA) to reduce the symptoms of itching and biochemical abnormalities. Vitamin K added in therapy decreases the risk of post partum and intra ventricular hemorrhage of newborn.

Irrespective of OC severity, elective delivery at 37 to 38 weeks of gestation is widely practiced to prevent the increased risk of still birth at later gestation. However there have been few report of gestational weeks at which the intra uterine death occurs. Whether it is early delivery or drug treatment that prevents adverse fetal outcome is still a debate[6]. To date there is no study to compare maternal and neonatal outcome in early and late term delivery. On the contrary, potential risk of perinatal and maternal complication as a result of labor induction at early delivery raises concerns against its potential benefits.

Perinatal complication as a result of elective early term delivery includes birth asphyxia, iatrogenic prematurity, respiratory morbidity, hospital admission and long standing illnesses[11,12] where as maternal complication include increased cesarean section and its consequences, instrumental delivery, post partum hemorrhage and febrile morbidity. Therefore the aim of study was to evaluate maternal and neonatal outcome in early versus late term delivery so that we will be able to recommend that delivery at late term is associated with higher chances of vaginal delivery without increasing maternal and neonatal morbidity.

PATIENTS AND METHODS

This was a retrospective cohort study conducted in Aga Khan Hospital Karimabad, a secondary unit of Aga Khan University Hospital Pakistan.

All patients of OC with singleton pregnancy, admitted for labor induction between Jan 2011 to Oct 2012 were included in the study. Patients with other indications for labor induction were excluded. During these 22 months, 5805 patients delivered in AKHW-Karimabad. In 1334 (23%) patient, labor was induced out of which 54 patients (0.93%) had induction due to OC. More than half of the patients 36 (67%) were induced at more than 38 weeks of gestation.

Obstetric cholestasis was diagnosed on the basis of generalized itching without rash in second or third trimester of pregnancy, raised SGOT and SGPT and negative for Hepatitis B and C in antenatal screening.

Currently there is no hospital protocol for management of OC. Therefore some variation is seen in this regard among obstetrician practices. Mostly after establishing the diagnosis, antenatal women are treated with Ursodeoxycholic acid (UDCA) 500 to 1500mg per day in divided doses, antihistamine and topical emollient. Fetal well being is monitored by cardiotocography (CTG), biophysical profile (BPP), Doppler ultrasonography and growth scan, weekly or biweekly depending upon the gestation. Serum transaminases are repeated weekly or biweekly. At or after 37 week of gestation, patient is offered labor induction. Early term delivery is taken from 37+o to 37+6 and late term delivery at or after 38 weeks of gestation. Labor induction and management protocol was followed after patient's hospitalization. Maternal and neonatal outcome is documented in medical records.

Data Analysis

The demographic, laboratory and clinical data of these patients were collected from their medical record and entered on pre designed performa. Maternal and neonatal outcome were analyzed utilizing SPSS version 19. Frequencies and means and standard deviations were determined for categorical and continuous variables respectively. Women were categorized into two groups. Group A –in whom induction of labor was done before 38 weeks and Group B – in whom labor was induced at or after 38 weeks of gestation.

Comparison of two groups was done by applying Fisher's Exact and Student's t-test.

RESULTS

During 22 months of study duration, 5805 patients delivered in 22 months in AKHW-Karimabad. In 1334 (23%) patient, labor was induced out of which 54 patients (0.93%) had induction due to OC. More than half of the patients 36 (67%) were induced at more than 38 weeks of gestation.

Among 54 OC patients, 48 (89%) were between 20 to 30 years of age, 31 (57%) were nullipara.

There were 13 (29%) vaginally delivered patients who were induced before 38 weeks of gestation and32 (71%) in group induced after 38 weeks. However difference was not significant among both groups (p-value 0.14). Cases of meconium stained liquor were almost equally distributed in both groups (p-value 0.14)

Babies born after 38 weeks of gestation were of more weight 3.06 versus 3.04 Kg but there was no statistical difference (p-value 0.85). Neonatal jaundice was seen in 6 babies of group B as compared to only one neonate with jaundice in group A but association was not significant (p-value 0.4). Neonatal outcome was equally good in both groups. Women who delivered at < 38 weeks or at > 38 weeks has no intrauterine death, RDS or meconium aspiration syndrome and none of the babies needed NICU care. Neonate's APGAR score was good (> 7) in both groups.

DISCUSSION

Obstetric cholestasis is the most common liver disorder in pregnancy. Its reported incidence in Pakistani Asian population is 1.2 to 1.5%. We cannot calculate the true incidence of OC as we have taken only those patients of OC who were delivered electively by induction of labor.

OC is associated with increased risk of prematurity, fetal distress, and stillbirth[10] depending upon disease severity. Recent studies have shown a relationship of raised serum bile acids of 40 micromol or more per liter with fetal distress and intrauterine fetal death[11].

In most laboratories in Karachi, serum bile acid test is not available. Therefore serum transaminases SGOT and SGPT test is performed in OC patients. Studies on the relationship of raised serum transaminases level and severity of disease and fetal outcome are also nominal. In our study raised level of serum transaminases was not associated with poor fetal outcome. Meconium stained liquor was seen in 16% of cases while 15% has been reported in other studies[11,14,15]. This passage of meconium is not associated with intra uterine growth restriction. 5 out of 6 patients with meconium had initial transaminases level of100 mg/dl or more. But none of the newborns develop respiratory distress syndrome.

The reason of good perinatal outcome in our study could be related to its management or milder form of the disease as majority of the cases had serum transaminases level below 100mg/dl.

Table-1: Baseline characteristics of pregnant women with obstetric cholestasis.

Variables		Frequency (%) n=54
Gestational age at delivery	<38 weeks ≥38 weeks	18(33) 36(67)
Age of patient	<20 years 20-30 years > 30 Years	1(2) 48(89) 5(9)
Parity	< 1 ≥1	31(57) 23(43)
History of obstetric cholestasis	Yes No	9(17) 45(83)
Family history of obstetric cholestasis	Yes No	6(11) 48(89)
SGPT	<100 U/L >100 U/L	24(44) 30(56)
Mode of delivery	Vaginal delivery Caesarean Section	45(83) 9(17)

Labor is induced whenever continuation of pregnancy exposes mother or fetus to increased risk of adverse outcome. And its intent is to deliver vaginally. One of the factors associated with failed labor induction is unfavorable cervix[15]. Success rate increases with good Bishop Score (>5). As gestation advances at term, cervical changes occur and Bishop Score improves. Conducting labor induction at 37 weeks of gestation for elective delivery exposes patient to more risk of Caesarean section like increased risk of infection, need for blood transfusion, prolonged labor delivery interval and increase need of analgesia as compared to labor induction at 38 weeks or more.

Table-2: Comparison of maternal and neonatal outcome between pregnant women with obstetric cholestasis induced at < 38 weeks and ≥ 38 weeks of gestation.

Variable		Gestational Age		*p*-values
		<38 n (%) 18(33.3)	≥38 n (%) 36(66.7)	
Mode of delivery	Vaginal delivery	13 (29)	32 (71)	0.14
	Caesarean Section	5 (56)	4 (44)	
Postpartum complications	Yes	1 (50)	1 (50)	1.00
	No	17 (33)	35 (67)	
Meconium stained liquor	No	13 (29)	32 (71)	.14
	Yes	5 (56)	4 (44)	
Hospital stay	Short stay	16 (31)	35 (69)	0.25
	Long stay	2 (67)	1 (33)	
Drop in Hb	≤ 2 grams	17 (32)	36 (68)	0.33
	> 2 grams	1 (100)	0 (0)	
Neonatal jaundice	Yes	1 (14)	6 (86)	0.4
	No	17(36)	30(64)	
Weight of baby (kg)*	Mean ± SD	3.04 ± 0.51	3.06 ± 0.36	0.85

Since there is uncertainty of the magnitude of fetal risk in OC patient[6], exposing these patients to increase morbidity due to early term labor induction needs to be weighed against its benefit. In mild cases of OC, studies have not shown an increase in stillbirth, but practice of elective delivery at 37 to 38 weeks of gestation in such cases, increase the risk of complication of pregnancy outcome and its cost. In our study Caesarean Section rate was high (56%) in group A than in Group B (44%). Four out of five caesarean in group A and three out of four in group B were due to non progress in labour. One ceasarean in group A was due to intrapartum haemorrhage and one in group B was due to presumed fetal distress. There was no difference in the two groups regarding post partum hemorrhage or drop in hemoglobin. There was no perinatal mortality and none of the babies needed NICU care. Neonatal jaundice was seen in six neonates in group B who received phototherapy in level II nursery.

This study has limitations. It is retrospective and the size is small. Not all patient of OC in 18 month of study could be included because their medical record number was not available.

We recommend that a larger prospective study be conducted in Pakistan context to understand the magnitude of this disease, relation of serum transaminases with the severity of the disease and decide the gestation for labor induction in OC to outweigh the benefit in terms of maternal and neonatal outcome.

CONCLUSION

OC patients who deliver after 38 weeks of gestation have a higher chance of vaginal delivery without increasing the risk of stillbirth. With close monitoring of OC patients

pregnancy can be followed till -38+6 completed weeks and then induced in order to reduce induction delivery interval and caesarean section.

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CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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