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Original Research Article

Maternal and perinatal outcome in pregnancy complicated by obstetric cholestasis: study from a tertiary care centre in North India

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ABSTRACT

Background: Intrahepatic cholestasis of pregnancy (IHCP) is the most common pregnancy related liver disorder. It typically presents with troublesome itching and can lead to complications for both mother and foetus. Present study was carried out to study the incidence of Obstetric Cholestasis and its fetomaternal outcome in a tertiary care hospital.

Methods: It was a prospective epidemiological study during a period of one year (May 2020 to April 2021) over 120 pregnant ladies suffering from pruritus and detected as having Obstetric Cholestasis. They were followed up and maternal as well as perinatal outcome recorded. Appropriate statistical analysis done as applicable.

Results: The incidence of Obstetric Cholestasis in our hospital was 9.3%. Majority of cases delivered at term (78.3%). 41.6% patients delivered vaginally, 43.3% had emergency caesarean section, and 2.5% patients had instrumental delivery. Maternal morbidities are due to sleep disturbance (60%), coagulation abnormality (13.3%), increase chance of operative delivery (55.8%) and postpartum haemorrhage (12.5%). Neonatal complications include meconium aspiration (46.6%), NICU admission (36.6%), prematurity (5%) and perinatal mortality (3.3%).

Conclusions: Cholestasis of pregnancy causes maternal pruritus with impaired liver function tests. Maternal morbidity is increased in terms of increased caesarean section rates and discomfort due to pruritus. A timely intervention at 37-38 weeks will reduce the adverse perinatal outcome.

Keywords: Intrahepatic cholestasis of pregnancy, Pruritus

INTRODUCTION

Obstetric cholestasis (OC) or Intrahepatic cholestasis of pregnancy (ICP) is a cholestatic disorder characterized by unexplained pruritus during pregnancy with elevated serum bile acids ($>10 \mu\text{mol/L}$) and/or transaminases in late second and third trimester of pregnancy, in absence of other liver disease, and spontaneous resolution of signs and symptoms within two to three weeks after delivery.^{1,2}

Obstetric cholestasis has been observed in almost all ethnic groups, but there is relevant geographical variation in its incidence. The incidence of OC among Indian women has been reported to be about 1%.^{3,4} Cholestasis of pregnancy is caused by an impairment of bile secretion in the liver.

As the bile backs up in the liver, the level of bile acids increases in the bloodstream. The bile acids are deposited in the maternal tissues like skin, causing intense pruritus (Heather Brannon, 2004). Obstetric cholestasis clinically manifests in the 2nd or 3rd trimester of pregnancy with generalized pruritus but without any skin rash (McDonald, 2002).

Pruritus begins in the palms and soles, with progression to the arms and legs, eventually, reaching the trunk and face. Pruritus is most severe at night. Jaundice is relatively uncommon, complicating only the most severe and prolonged cases (Milkiewicz et al., 2002). The condition worsens as pregnancy proceeds and there is spontaneous relief of symptoms and signs within two to three weeks

after delivery. Intrahepatic cholestasis of pregnancy can have devastating consequences for the foetus with perinatal mortality reaching up to 11% to 20% in untreated cases.⁵ Adverse foetal outcomes associated with the conditions include preterm labour, preterm pre labour rupture of membranes, foetal distress, abnormal CTG, meconium staining, spontaneous intrauterine death.^{6,7}

Ursodeoxycholic acid (UDCA) is considered to be a safe treatment option in the later part of pregnancy.^{8,9} The condition typically resolves within 48 hours of women giving birth with biochemical markers predominantly becoming normal within 2-4 weeks postnatally.¹⁰

Present study is aimed to detect the incidence of OC in our hospital and follow up those pregnancies to evaluate maternal and perinatal outcome.

METHODS

Our prospective epidemiological study was performed in the department of obstetrics and gynaecology in Government medical college Kathua in the union territory of Jammu and Kashmir over one year (May 2020 to April 2021). The study group included 120 patients which were enrolled from the outpatient department as well as from the patients admitted in the labour room with the history of intra hepatic cholestasis.

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 5 mg/dl.

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. History taking, clinical examination and laboratory investigations were carried out to diagnose obstetric cholestasis. LFT was repeated every 2-4 weeks interval as required. All patients included in the study were given ursodeoxycholic acid 300-1200 mg/day in divided doses for the rest of the antenatal period. The data were collected in preformed proforma and written and informed consent was taken.

Maternal outcome was noted in terms of gestational age at delivery, mode of delivery and complications which includes sleep disturbance due to severe pruritus, deranged coagulation profile (increase PT), preterm labour, operative delivery and postpartum haemorrhage. Foetal outcome was studied in reference to prematurity, abnormal CTG, meconium stained liquor, NICU admission rate and perinatal death. Symptomatic relief of pruritus and liver function test was determined in all women two weeks after

the delivery. The data obtained was entered in MS excel sheet and tabulated.

RESULTS

During the study period out of the 1280 antenatal registered women, 120 were diagnosed as having cholestasis of pregnancy giving an incidence of 9.3%. 76 (63.3%) were primigravida and 44 (36.6%) were multigravidas. Majority of the patients were in the age group of 26-30 years (48.3%) (Table 1). 78.6% patients delivered at term. 5% had preterm delivery (Table 2).

Table 1: Demographic analysis.

Variables	No. of cases	%
Age		
<20 years	8	6.6
21-25 years	38	31.6
26-30 years	58	48.3
>30 years	16	13.3
Parity		
Primipara	76	63.3
Multipara	44	36.6

Table 2: Distribution of patients according to gestational age at delivery.

Gestational age	No. of cases	%
<37 weeks	6	5
37-40 weeks	94	78.6
>40 weeks	20	16.6

Table 3: Distribution of patients according to liver function tests.

Variables	No. of cases	%	
Serum bilirubin (mg/dl)	0.2-0.6	58	48.3
	0.6-1.0	40	33.3
	1.0-1.4	16	13.3
	>1.4	6	5
SGOT (IU/L)	0-100	46	38.3
	100-200	52	43.3
	200-300	15	12.5
	>300	7	5.8
SGPT (IU/L)	0-100	54	45
	100-200	44	36.6
	200-300	17	14.16
	>300	5	4.16
Serum alkaline phosphatase	0-200	18	15
	200-400	48	40
	400-600	42	35
	>600	12	10

Jaundice was noticed in 18.3%. Maximum 43.3% patients had SGOT in the range of 100-200. Maximum 45% patients had SGPT in the range of 0-100 (Table 3).

Table 4: Distribution of patients according to mode of delivery.

Mode of delivery	No. of cases	%
Elective CS	15	12.5
Emergency CS	52	43.3
Forceps	3	2.5
Vaginal delivery	50	41.6

In the study group, 87.5% (105/120) women went into labour either spontaneously or after induction. 43.3% had emergency caesarean section and 41.6% patients delivered vaginally. 2.5% of the patients had instrumental delivery. Elective caesarean section rate was 12.5% (Table 4).

Table 5: Distribution of maternal outcome.

Variables	No. of cases	%
Sleep disturbance	72	60
Deranged coagulation profile	16	13.3
Preterm labour	6	5
Operative delivery	67	55.8
Postpartum haemorrhage	15	12.5

Among 120 patients included in the present study 60% had sleep disturbance due to pruritis. Deranged coagulation profile was seen in 16 (13.3%) patients. 55.8% of the patients underwent operative delivery. Preterm labour was present in 5% patients. Incidence of postpartum haemorrhage was 12.5% (Table 5). Preterm labour was present in 5% patients. Incidence of postpartum haemorrhage was 12.5% (Table 5).

Table 6: Distribution of foetal outcome.

Variables	No. of cases	%
Abnormal CTG	24	20
Meconium stained liquor	56	46.6
NICU admission	44	36.6
Perinatal death	4	3.3
Preterm birth	6	5

Table 7: Postpartum resolution after 6 weeks of delivery.

Postpartum resolution	No. of cases	%
Normal LFTs	118	98.3
Persisting raised LFTs	2	1.6

During labor an abnormal CTG was noted in 20% of the cases, while meconium staining of liquor was seen in 46.6% of the cases. NICU admission was seen in 36.6% newborns of which perinatal death was present in 3.3% cases. 5% patients had preterm birth (Table 6). In present study, in most of the cases normal LFT (98.3%) was found after 6 weeks of delivery and symptomatically pruritus

relieved. So the disease resolved within 6 weeks of delivery. (Table-7).

DISCUSSION

The study was conducted to determine maternal outcome in patients with cholestasis of pregnancy. 120 patients were studied. Incidence of obstetric cholestasis was 9.3% in the present study comparable to the study of Kaur et al (16.75%).¹¹

Majority of the patients were in the age group of 26-30 years (48.3%). Brouwers et al also performed similar study on subjects with intrahepatic cholestasis.¹² In a prospective population-based study by Geenes et al to assess outcome in severe IHCP, mean age was 29.6 (\pm 6.3) years. Both the studies were in accordance to present study with mean age also similar to population of present study. In a study by Shoballi et al with similar objectives also the age of IHCP subjects was found to be 29.18 \pm 3.54 and those of the controls was 29.86 \pm 4.37 years.¹³ Out of 120 patients, 78.3% delivered at term, 5% patients had preterm delivery. Our results were consistent with Rasheed et al.¹⁴

In present study various parameters of liver damage including total bilirubin, direct bilirubin, aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase were found to be significantly elevated. Jaundice was present in 22 (18.3%). SGOT in maximum number of patients 52 (43.3%) were in the range of 100-200, SGPT in maximum patients 54 (45%) were in the range of 0-100. ALP was in the range of 400-600 in 35% of the patients (Table 3). Although serum bile acids are considered to be very sensitive indicator of obstetric cholestasis, but as bile acid assessment was not available locally, we could not determine the levels in our patients. The above results are consistent with Rasheed et al, they found liver functions deranged in 73.3% and 22% had elevated bilirubin. In a study by Brouwers et al, bilirubin and all liver enzymes including AST, ALT, ALP, GGT, and LDH were found to be elevated. Surprisingly these parameters were highest in subjects with moderate severity of IHCP.¹²

In the present study 41.6% delivered vaginally. Caesarean section was done in 67 (55.8%) patients (Table 4). Out of 67 caesarean sections, 15 were elective because of obstetric indications like malpresentations, previous LSCS, CPD etc and 52 were emergency LSCS. Most of the emergency LSCS were done at \geq 38 weeks GA and hence, were due to foetal distress. Foetal distress was more common after 38 weeks of gestation. Instrumental delivery rate was 2.5%. The above result is consistent Ray Alokanda et al, they found LSCS rate to be 31.2%, however, and instrumental delivery rate was 25% which was higher than in our study.¹⁵ This study shows 60% of the patients had sleep disturbance, due to severe pruritus at night. Generalized pruritus more affecting to palm and sole were the cardinal features without skin rash and clinical jaundice. In this study, we treated our patients with topical

emollients like calamine lotion and oral Ursodeoxycholic Acid (300-1200) in divided doses.

In the present study 13.3% of the patients had deranged coagulation profile with increased PT or APTT level. Postpartum haemorrhage accounted for 12.5% in the present study. Dang et al (29.78%) and Ray et al (25%) reported significant increased incidence of PPH, as a result of malabsorption of vitamin K, due to steatorrhoea of cholestasis, leading to coagulation problem.^{16,17} Kenyon AP et al found a high incidence of PPH in OC patients who did not receive vitamin K compared to those who did (45% vs 12%).¹⁸

Abnormal CTG was found in 20% of the cases in present study. 56 patients had meconium stained liquor during delivery (46.6%) which was significantly higher. Alsulyman et al also found that risk of meconium passage was higher in the cholestasis group (44.3% cases vs. 7.6% of control).¹⁹ It has been suggested that both foetal distress and increased gut motility by bile acids is the cause of raised incidence of meconium stained liquor.

Perinatal death was found in 6 (5%) cases in the study. This includes one intrauterine foetal death and 5 neonatal deaths. Alsulyman et al also found 2 of 79 patients having intrauterine foetal death in Obstetric Cholestasis group at 36 to 37 weeks of gestation.¹⁹ In 36.6% of the cases NICU admission were required in this study. According to Heinonen et al intrahepatic cholestasis increases the need for intensive neonatal care in general population.²⁰

In present study, in most of the cases (98.3%) normal LFT was found after 6 weeks of delivery and symptomatically pruritus relieved. According to Rasheed et al postnatal resolution of pruritus and liver function test occurred within 5-14 days with a mean of 8 day \pm 2.52.²¹

CONCLUSION

Cholestasis of pregnancy is a relatively common cause of hepatic impairment in pregnancy. It has a complex etiology with genetic, hormonal and environmental components. Maximum patients are delivered at 37 to 38 weeks, due to active maternal and foetal surveillance and early intervention to prevent sudden foetal death at late gestation. Maternal morbidity is increased in terms of increased LSCS rates. Neonatal morbidities are mainly due to foetal distress, prematurity, low birth weight and meconium staining of amniotic fluid. Foetal outcomes are improved with a variety of strategies of active management, although the most effective intervention has not currently been established. Ursodeoxycholic acid treatment is associated with marked improvement of symptoms and biochemical abnormalities. Almost all patients have postnatal resolution within 6 weeks of delivery.

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