RESEARCH ARTICLE

Perinatal Outcomes among Women with Cholestasis of Pregnancy

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Abstract

Introduction: Intrahepatic cholestasis of pregnancy (ICP), also described as obstetric cholestasis is the second most common cause of icterus in pregnancy. Although not fully understood, proposed theories indicate it could be due to decreased bile flow through the liver and its poor excretion, leading to increased levels of colic and chenodeoxycholic acid. It is known to be associated with adverse maternal and fetal outcomes.

Materials and methods: The data were collected by retrospective record review for the past 2 years and the information collected included obstetrical outcomes and complications in mothers with ICP admitted in a tertiary care hospital.

Results: Among the 64 pregnant women admitted with ICP, 56.2% of women were booked pregnancies and 47 (73.4%) were in the age groups of 21–30 years. Most women presented with ICP at gestational ages of >37 weeks 51 (79.9%), with the onset of symptom around 33–36 weeks of gestation 21 (32.8%). Common complications encountered were severe preeclampsia and gestational diabetes mellitus 6 (9.3%). Among neonates, meconium-stained liquor (MSL) and low appearance pulse rate grimace activity respiration (APGAR) at 1 minute were common complications. Mothers with ICP were induced with PGE2 (dinoprostone) and 54.7% delivered vaginally. Pregnancies induced with PGE2 and PGE1 (misoprostol) had a higher chance of undergoing lower segment cesarean section (LSCS) 19 (29.6%).

Conclusion: Mothers with ICP should be screened antenatally for preeclampsia. The delivery team should be prepared to manage meconium aspiration in the newborn, although most patients deliver vaginally.

Key message: Newer modalities of treatment with better pregnancy outcomes in mothers with ICP.

Keywords: Cholestasis, Lower segment cesarean section, Preeclampsia, Pregnancy, Ursodeoxycholic acid.

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Introduction

Intrahepatic cholestasis of pregnancy (ICP), which has also been described as obstetric cholestasis or hepatosis gestational, is a common liver disorder among pregnant women and it is the second most common cause of icterus in pregnancy after viral hepatitis.[1] It manifests in the second or third trimester, with itching being the most common presenting complaint.[1–3] The other manifestations of the disease are fatigue, anorexia, weight loss, steatorrhea, dark urine, insomnia, etc.[2,3] It is usually detected based on clinical signs and symptoms.[3] Certain specific biochemical markers detect the presence of ICP, like bile salts, liver biopsy, etc., which are generally not a part of the routine tests in most of the developing countries including India. Hence, it is usually a diagnosis by exclusion of various hepatic diseases associated with cholestasis.[3]

Intrahepatic cholestasis of pregnancy is known to have a genetic predisposition and its high prevalence has been reported from Chile-Bolivia (6–27%) and Sweden (1–1.5%).[2,4] Studies have shown significant differences in the myocardial tissue velocities of both mitral and tricuspid valves in fetuses of mothers with ICP with increased bile salts >40 mmol/L.[4] Intrahepatic cholestasis of pregnancy is associated with an increased risk of preterm deliveries (19–60%), fetal distress (22–41%), and even intrauterine deaths (0.75–1.6%).[2,5]

Although the underlying cause is not fully understood, it has been attributed to decreased bile flow through the liver and/or its poor excretion, increased levels of cholic and chenodeoxycholic acid, and is associated with adverse maternal and fetal outcomes, which are reversed with the delivery of the placenta, as seen by the disappearance of signs and symptoms.[6]

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More recently mutated genes responsible for ICP have been described in familial cases.[3] Two such mutated genes are MDR3 and ABCB4.[7,8] Secondary effects of cholestasis as observed in animal studies, show estradiol 17 β-D-glucuronide to be cholestatic.[9] In addition, substantial amounts of sulfated progesterone metabolites in the urine of pregnant women are additionally conjugated with *N*-acetyl glucosamine and the formation of such metabolites is selective for β-hydroxy bile acids, such as, ursodeoxycholic acid (UDCA) which are a front-line treatment for ICP.[9] In the recent past, the debate has been that in addition to bile acids other biochemical parameters have to be tested. Commonly used biochemical markers like alanine aminotransferases (ALT) and aspartate aminotransferase (AST) which are also commonly raised in ICP could benefit in early diagnosis of ICP.[7]

Hence, accurate and rapid diagnosis and quality treatment help prevent adverse perinatal outcomes.[10] Various therapies have been administered, for ICP like antihistamines, cholestyramine resin, UDCA, etc.[10] Based on high rates of neonatal and maternal complications, induction at 36 to 37 weeks of gestation after documented fetal lung maturity has been the definitive treatment for ICP.[10]

The objective of this study was to assess the changes in routine biochemical parameters apart from liver function tests (LFT) and outcomes of pregnancy among women presenting with ICP in a tertiary health care hospital, South Indian.

Materials and Methods

The data were collected by review of the record for the past 2 years (January 1, 2018, to April 30, 2020) of a tertiary care hospital. Records of all pregnant women diagnosed with ICP either by the presence of clinical signs and/or symptoms, altered biochemical markers, or a diagnosis by exclusion were included. The other causes of cholestasis (viral hepatitis, gall stones, etc.) were excluded based on the criteria set by Ambros-Rudolph et al. and Kawakita et al.[10,11] Ethical approval was obtained from the Institutional Ethics Committee before the start of the study (IEC Ref No.221/2020).

The following information regarding maternal and fetal was collected.

Maternal Variables

Number of antenatal visits, assessment of fetal growth, development of any new symptoms like jaundice, itching (including of palms and soles), decreased fetal movements, pain abdomen, bleeding or leaking per vagina, etc., were noted. Blood parameters like complete hemogram, AST and ALT levels, and renal function tests of the mother at admission were documented. Pregnancy outcomes like the need for induction of labor, mode of delivery (vaginal or cesarean) was recorded. Complications like severe preeclampsia, postpartum hemorrhage (PPH), a dose of UDCA, and use of other newer medications, need for admission into intensive care unit (ICU), etc., were documented. Monitoring of blood loss during vaginal delivery or lower segment cesarean section (LSCS) and quantifying the blood loss at the time of delivery as described by Baucom et al. was studied.[12] Treatment of patients during the antenatal, intrapartum, and postnatal period was also studied.

Fetal Variables

Neonatal outcomes like complications at birth, preterm births, appearance pulse rate grimace activity respiration (APGAR) scores, need for neonatal intensive care unit (NICU) admission, and birth weight were reviewed.

Analysis

Data were analyzed using SPSS version 16 after it was manually entered in Microsoft Excel. Interquartile ranges were deduced for variables, such as, gestational age, gestational age of diagnosis, etc., for analysis of pregnancy outcomes in ICP. The Pearson's Chi-square, Fisher's exact was used as the test for significance, and a value <0.05 was considered significant.

Results

Demographic Details

Among the 64 pregnant women diagnosed and admitted with ICP, 36 (56.2%) were booked pregnancies. Forty-seven (73.4%) patients were in the age group between 21 and 30 years and 44 (68.7%) were primigravida. Sixteen (25%) of them had a significant prior history of at least one abortion ($p < 0.001^b$) and one had a history of intrauterine fetal demise in her previous pregnancy. Although 15 (23.4%) patients presented with the first onset of symptoms of ICP <28 weeks of gestation, 11 (17.1%) between 29 and 32 weeks, and 21 (32.8%) patients between 33 and 36 weeks of gestation, most 51 (79.6%) delivered after 37 weeks of gestation and 50 (78.1%) delivered babies of birth weight ranging from 2.5 to 3.5 kg (Table 1).

Generalized itching was found to be the most common presenting complaint 23 (35.9%) followed by decreased fetal movement in 10 (15.6%), pain abdomen in 9 (14.0%), and increased blood pressure in 4 (6.3%) women. Eighteen (28.2%) women were admitted for safe confinement.

Obstetric Complications

Gestational diabetes (GDM) 6 (9.3%), preeclampsia 6 (9.3%), and hypertension 1 (1.5%, $p < 0.001^b$) were significant complications of mothers with ICP seen especially at 29–32 weeks of gestation and 10 had hypothyroidism complicating pregnancy.

Mode of Delivery (Vaginal Delivery)

Labor was induced for all study subjects, 32 (50%) with PGE2, 2 (3.1%) with PGE1, and with PGE1 and PGE2 in 30 (46.9%). Intrahepatic cholestasis of pregnancy was the common indication for induction in 35 (54.7%) patients. Vaginal delivery was achieved in 35 (54.7%) patients, full-term vaginal delivery (FTVD) in 32 (50%) and preterm vaginal delivery (PTVD) in 3 (4.7%) patients, respectively ($p < 0.001^b$). Lower segment cesarean section was performed in 29 (45.3%) mothers and fetal distress 15 (23.4%) was the most common indication followed by cephalo-pelvic disproportion (CPD) 6 (9.2%) and 9 (14%) had meconium of varying grades as shown in Table 2.

Clinical manifestations of symptoms of ICP in pregnancy were noticed commonly between 33 and 36 weeks of gestation 12 (18.7%) and all these were delivered *via* FTVD ($p = 0.016^b$). Patients with coexisting hypothyroidism and ICP had a higher chance of preterm delivery 2 (3.1%, $p = 0.44^b$).

Mode of Delivery (LSCS)

In addition to other indications of LSCS (Table 3), CPD 5 (7.8%, $p = 0.013$), non reactive non stress test (NRNST) 4 (6.2%, $p = 0.044^b$) previous LSCS 2 (3.1%, $p = 0.021^b$), nonprogress of labor 1 (1.5%, $p = 0.006^b$), grade III meconium stained liquor (MSL) 4 (6.2%, $p = 0.044^b$) were other common indications for emergency LSCS in women with ICP. One patient who had undergone an elective LSCS had grade I MSL as an intraoperative finding 1 (1.5%, $p < 0.001^b$). A common intraoperative finding during an emergency LSCS was grade III MSL 5 (7.8%, $p = 0.013^b$).

Postpartum hemorrhage was seen in one woman who was <20 years of age (1.5%, $p = 0.032^b$) with ICP and she had a blood loss of >1,000 mL ($p = 0.004^b$) after the emergency LSCS 1 (1.5%).

Treatment Modalities

In our study, 33 (51.5%) and 14 (21.8%) women were treated with UDCA and levocetirizine, respectively (Table 4). The first line of treatment in pregnancies with symptoms of ICP manifesting at earlier gestations of <32 weeks 19 (29.6%, $p = 0.012^a$), and 33 to 36 weeks of gestation 8 (12.5%, $p = 0.113^b$) was UDCA. Other medications like antihistamines, e.g., levocetirizine 13, (20.3%) were used commonly after 37 weeks of gestation, especially in patients with a history of previous pregnancy complicated by ICP 2 (3.1%, $p = 0.007^b$) (Table 5).

Table 1: Frequency of study population

Variable		*Frequency (total N = 64)*	*Percentage*
Booked		36	56.2
Unbooked		28	43.8
Age (years)	<20	4	6.2
	21–30	47	73.4
	>31	13	20.3
Obstetric score	Primigravida	44	68.7
	Multigravida	18	28.1
	Grand multigravida	2	3.1
Number of abortions in the past	One	16	25.0
	Two	1	1.5
	Three	1	1.5
Number of intrauterine fetal deaths in the past		1	1.5
Gestational age at onset of the first symptom (weeks)	<28	15	23.4
	29–32	11	17.1
	33–36	21	32.8
	>37	17	26.5
Gestational age at the time of delivery	29–32	3	4.6
	33–36	10	15.6
	>37	51	79.6
Indication for cesarean section	Cephalopelvic disproportion	6	9.2
	Fetal distress	4	6.2
	NRNST	4	6.2
	Grade III MSL	4	6.2
	Grade II MSL	3	4.6
	Previous SLCS	3	4.6
Gender of the baby	Boy	40	62.5
	Girl	24	37.5
Birth weight (kg)	<2.5	9	14.0
	2.5–3.5	50	78.1
	>3.5	5	7.9

Table 2: Association between induction of labor and mode of delivery

Variables	*Total N = 64*	*PGE1 (misoprostol)*	*PGE2 (dinoprostone)*	*PGE1 + PGE2*	*p value*
FTVD	32 (50.0)	2 (3.1)	19 (29.7)	11 (17.2)	$p < 0.001$[a]*
PTVD	3 (4.7)	0 (0)	3 (4.7)	0 (0)	
LSCS	29 (45.3)	0 (0)	10 (15.7)	19 (29.6)	

*Statistically significant at $\alpha = 5\%$
FTVD, full-term vaginal delivery; PTVD, preterm vaginal delivery; LSCS, lower segment cesarean section
[a]Fisher's exact

Neonatal Outcomes

The majority of the babies born had a good APGAR score >8 at 1 minute 42 (65.6%) and APGAR >8 at 5 minutes 59 (92.2%) of life. Babies born beyond 37 weeks of gestation 36 (56.2%, $p < 0.001$[b]) had a good APGAR score of >8 at 1 minute when compared to those born between 28 and 32 weeks of gestation 2 (3.1%), who had APGAR score <5 at 1 minute of life. APGAR scores at 5 minutes increased to 8 in >90% of the babies probably due to good resuscitative measures since this is a tertiary care hospital.

Forty-three (84.3%) pregnancies with ICP beyond 37 weeks of gestation delivered babies with a normal birth weight of between 2.5 and 3.5 kg, three women (4.6%, $p < 0.001$[b]) had low birth weight babies <2.5 kg at 28 to 32 weeks of gestation.

Boy babies were commonly found to have CPD as an indication for LSCS 6 (9.3%, $p = 0.046$[b]) and had GDM as a complication of pregnancy 6 (9.3%, $p = 0.046$[b]).

Placental weight was found to be higher (500–1,000 g) in 43 (67.1%) of term pregnancies and 7 (10.9%) pregnancies at 33–36 weeks of gestation ($p = 0.008$[b]) (Table 6).

Biochemical Parameters

Total white blood cells (WBCs) count was significantly found to be >13,600/µL in those women whose first symptom of ICP was between 33 and 36 weeks of gestation 5 (7.8%, $p = 0.036$[b]). Moderate anemia 7–8.9 g% (WHO classification) was seen in those women <20 years of age 2 (3.1%) in comparison to those who had

Table 3: Association between indication for lower segment cesarean section in intrahepatic cholestasis of pregnancy and weeks of termination of pregnancy

	Variable	*Weeks of gestation*	*N = 64 (%)*	*p value*
Indication for LSCS	Failed induction	33–36 weeks	2 (3.1)	$p = 0.44^{b*}$
	Non-progress of labor	29–32 weeks	1 (1.5)	$p < 0.001^{b*}$
	Severe preeclampsia	29–32 weeks	2 (3.1)	$p < 0.001^{b*}$
	Chronic hypertension	29–32 weeks	1 (1.5)	$p < 0.001^{b*}$
	HELLP syndrome	29–32 weeks	1 (1.5)	$p < 0.001^{b*}$

*Statistically significant at $\alpha = 5\%$
[a]Chi-square
[b]Fisher's exact

Table 4: Treatment modalities

Variable	*Frequency (total N = 64)*	*Percent*
UDCA	33	51.5
Levocetirizine	14	21.8
Calamine lotion	7	10.9
UDCA + levocetirizine	7	10.9
UDCA + calamine lotion	3	4.6

Table 5: Association between gestational age and APGAR at 1 and 5 minutes

Variables	*Total (N = 64)*		*APGAR at 1 minute*		*p value*
Gestational age		<5	6–7	>8	$p < 0.001^{b*}$
28–32 weeks	3 (4.68)	2 (3.12)	1 (1.56)	0 (0)	
33–36 weeks	10 (15.62)	0 (0)	4 (6.25)	6 (9.37)	
>37 weeks	51 (79.68)	1 (1.56)	14 (21.87)	36 (56.25)	
Variables	*Total (N = 64)*	*APGAR at 5 minutes*			*p value*
Gestational age		<5	6–7	>8	$p < 0.001^{b*}$
28–32 weeks	3 (4.68)	0 (0)	2 (3.12)	1 (1.56)	
33–36 weeks	10 (15.6)	0 (0)	0 (0)	10 (15.62)	
>37 weeks	51 (79.68)	1 (1.56)	2 (3.12)	48 (75.00)	

*Statistically significant at $\alpha = 5\%$
[a]Chi-square
[b]Fisher's exact

a hemoglobin of ≥11 g% 36 (56.2%, $p = 0.002$) >20 years of age. Blood urea was >41 mg/dL in one patient (1.5%) >30 years of age in comparison to women of other age groups with normal urea levels ($p = 0.036^{b}$). Women >30 years with ICP in pregnancy were found to have FBS of >96 mg/dL 3 (4.6%, $p = 0.038^{b}$). Although 53 (82.8%) of women with ICP did not report being diagnosed with ICP in previous pregnancies, they were found to have a total bilirubin value of 0.2–1.2 mg/dL. One patient had bilirubin of >1.3 mg/dL and had a history of ICP in the previous pregnancy ($p < 0.001^{b}$). Grand multigravida women with ICP had thyroid stimulating hormone (TSH) values ≥4.95 mIU/L, 1 (50%, $p = 0.026^{b}$).

Discussion

As there is a need for a more comprehensive established guideline to evaluate ICP and there is a constant need for an emphasis on the treatment modalities and outcome of the disease, our study showed that early diagnosis and termination of pregnancy at an appropriate gestational age ensured better fetal outcome which is similar to other study findings.[1,11]

A study by Geenes et al. showed 80% of women with ICP presented after 30 weeks of gestation.[13,14] Estiú et al. had observed the majority of cases to be detected between 32 and 37 weeks of gestation, although 18.8% were diagnosed at later gestational ages.[15] Similarly, the cases diagnosed with ICP in our study were detected between 33 and 36 weeks of gestation with 26.6% being diagnosed after 37 weeks of gestation.[15] This common time of clinical presentation of cholestasis should anticipate vigilant screening of all mothers for ICP between 30 and 34 weeks of gestation.

The itching was a pronounced symptom in 35.9% of the pregnancies with ICP in our study. Similar findings were seen by Stulic et al. and Pusl and Beuers, with a higher predilection to involve palms and soles.[16,17] Icterus was a clinical sign affecting 10–15% of pregnancies with ICP as stated by Geenes et al.[14] In contrast, none of our study patients had icterus as a clinical manifestation of ICP, possibly due to varied clinical manifestation of the two compared populations.

Estiu et al. stated that preeclampsia was known to complicate 1.2% of pregnancies with severe ICP.[15] Another study by Ovadia et al. showed a higher prevalence of preeclampsia in women with ICP in comparison to those without the disease.[18] Our study showed 9.2% of women to have preeclampsia and GDM, inferring the

Table 6: Investigation for intrahepatic cholestasis of pregnancy

Variable		*Frequency (total N = 64)*	*Percent*
Hemoglobin	9–10.9 g/dL	12	18.7
	7–8.9 g/dL	5	7.8
	≥11 g/dL	47	73.5
Total count	4.5–13.5/µL	24	37.5
	≥13.6/µL	5	7.8
	Not done	35	54.7
Platelet count	<50,000 lakhs	1	1.5
	50,000–1 lakhs	2	3.2
	1–1.5 lakhs	7	10.9
	>1.5 lakhs	29	45.3
	Not done	25	39.1
Thyroid-stimulating hormone	0.35–4.94 µIU/mL	53	82.8
	≥4.95 µIU/mL	3	4.6
	Not done	8	12.6
Fasting blood sugar	<95 mg/dL	41	64.0
	>96 mg/dL	4	6.3
	Not done	19	29.7
Blood urea	≤14 mg/dL	11	17.1
	15–40 mg/dL	10	15.7
	≥41 mg/dL	1	1.5
	Not done	42	65.7
Serum creatinine	≤0.56 mg/dL	9	14.1
	0.57–1.11 mg/dL	18	28.1
	Not done	37	57.8
Uric acid	2.6–6 mg/dL	10	15.6
	3 mg/dL	8	12.6
	Not done	46	71.8
Total protein	≤6.3 g/dL	25	39.0
	6.4–8.3 g/dL	30	46.8
	Not done	9	14.2
Albumin	≤3.4 g/dL	52	81.3
	3.5–5.2 g/dL	12	18.7
Total bilirubin	≤0.1 mg/dL	1	1.5
	0.2–1.2 mg/dL	53	82.8
	≥1.3 mg/dL	1	1.5
	Not done	10	15.7
Direct bilirubin	0.0–0.5 mg/dL	49	75.5
	≥0.51 mg/dL	4	6.2
	Not done	11	17.3
AST	5–34 U/L	37	57.8
	≥35 U/L	22	34.3
	Not done	5	7.9
ALT	Up to 55 U/L	40	62.5
	≥56 U/L	19	29.6
	Not done	5	7.9
GGT	≤8 U/L	6	9.3
	9–36 U/L	33	51.5
	≥37 U/L	13	20.3
	Not done	12	18.9
LDH	≤124 U/L	1	1.5
	125–220 U/L	5	7.8
	≥221 U/L	15	23.4
	Not done	43	67.3
Amniotic fluid index	<10 cm	8	12.5
	11–20 cm	46	71.8
	>21 cm	2	3.1
	Not done	8	12.6

association of ICP and the development of preeclampsia or GDM. Pusl and Beuers showed gestational hypertension to be seen in 2.2% of pregnancies with mild ICP and 1.2% with severe ICP.[17] Our study noticed 1.5% of patients with gestational hypertension had ICP, showing that both diseases can coexist with ICP.

HELLP syndrome was associated with 1.5% of the pregnancies complicated by ICP and similar such associations were seen with a study by Jebbink et al.[19] Anemia was seen in 46.15% of participants with severe ICP in a study by Yang et al., which was not similar to those with ICP who presented with moderate anemia (7.81%) in our study.[20]

Most studies state that pregnancies complicated with ICP delivered before 37 weeks of gestation.[18,21] Contrasting to these results, our study showed most women delivered beyond 37 weeks of gestation 51 (73.6%), because of early admission and antepartum fetal surveillance.

Normal vaginal delivery and emergency cesarean section were seen in 7.69 and 57.69% of pregnancies with ICP, respectively, as seen by Yang et al.[20] Our study showed 54.6% of the pregnancies with ICP had normal vaginal delivery compared to those who underwent LSCS. Similar findings to our study were seen by Chappell et al. and Arthuis et al.[22,23] This study shows that ICP is not an indication for LSCS and most women can undergo a safe vaginal delivery.

Mohan et al. reported that induction of labor resulted in high cesarean section rates, but in our study, 54.6% of patients who were induced with E2 and/or E1 had a normal vaginal delivery.[24]

In this study, 31 (48.4%) women had FTVD contrary to a study by Geenes and Williamson who showed that preterm deliveries were significantly associated with ICP.[13] Another study by Kong et al. stated 21% of ICP occurred as premature deliveries.[25] The vigilant antepartum fetal surveillance could be a major contribution to achieving full-term deliveries in our population.

Abnormal LFT was noticed in 65.38% of pregnancies with severe ICP in a Chinese study, whereas 71.6% of our patients had abnormal LFT.[20]

Literature reports that postpartum hemorrhage is 2.33 times more common in pregnancies complicated by ICP as compared to pregnancies not complicated by ICP.[24] Another study in France showed 20.7% of pregnant women with ICP had PPH. Our study shows one woman (1.5%) to have PPH, contrary to the above studies ($p = 0.032^{b}$).[23]

Pregnancies complicated by ICP had 2.6 times the chance of MSL as per the study by Caroline et al.[18] MSL was observed in 16% of ICP cases in the UK by Geenes et al.[26] Our study results had a similar correlation, leading to the need for further studies to look into the association of ICP and its effect on the neonatal parasympathetic system.

Low APGAR scores <7 at 5 minutes were seen in 2.9% of pregnancies with ICP compared to the control group in a study done in France.[22] Arthuis et al. showed no difference in APGAR scores between the study group or the placebo group in a study done in UK.[23] APGAR score >8 at 1 minute was seen in 56.2% of pregnancies >37 weeks of gestation, and 75% at 5 minutes, possibly due to strict and timely neonatal resuscitation protocols. At gestations between 28 and 32 weeks, 3.12% had Apgar scores of <5 at 1-minute gestation, which improved to 4.6% having APGAR score >6 at 5 minutes.

Birth weight of neonates of mothers with ICP was low for gestational age as analyzed by Li et al.[27] Chappell et al. differed from this by showing babies born to mothers on UDCA had normal birth weights ranging from 2,775 to 3,390 g.[22] Our study showed 78.1% of neonates having normal birth weight (>2,500 g), indicating that ICP does not affect the overall growth of the fetus. Similar findings were seen by Ovadia et al.[18]

Stillbirths and perinatal deaths within 7 days of delivery are adverse neonatal outcomes of ICP.[18,21] No pregnancy complicated by ICP resulted in stillbirth in our study population, although one patient had a history of an IUD, probably due to genetic background or action of UDCA in the South Indian population. The reason for a less number of stillbirths and perinatal deaths could be due to strict government protocols of early registration, frequent antenatal visit and early diagnosis, and appropriate management. Our study shows that timely induction and effective management of ICP had better fetal and maternal outcomes at our institution.

Ursodeoxycholic acid showed improvement of itching in five trials as seen in the Cochrane review.[28] Other similar benefits were seen in a UK study.[13] An Argentinean study showed 83.3% of women with severe ICP to receive UDCA as a line of treatment.[13,15] Our study shows 81.8% of women between 29 and 32 weeks of gestation and 66.7% of women <28 weeks of gestation received UDCA as a form of treatment for ICP. Most women had a better obstetrical outcome due to the early administration of therapy in the antenatal period.

Various modalities of treatment in addition to UDCA have been suggested, such as, dexamethasone, antihistamines, Vitamin K, and rifampicin (although no published studies have reported its use for liver disease in pregnancy).[17,29,30] Some clinical studies have treated ICP with 8 to 10 mg/kg body weight, while others have started with a daily dose of 1,000 mg of UDCA, increased in increments of 500 mg/day every 14 days to a maximum of 2,000 mg/day.[17,21] Geenes et al. stated the use of UDCA with a starting dose of 50 mg/day.[26] Our study participants received UDCA from a starting dose of 300 mg twice daily to titrated doses of 300–150—300 mg, not exceeding 1–2 g/day. Our study showed 21.8% to be on levocetirizine and 10.9% on calamine lotion. Estiu et al. showed 1.2% of severe ICP patients to be on levocetirizine, showing the need for a symptomatic approach to the treatment of ICP in conjunction with UDCA.[15]

Conclusion

Intrahepatic cholestasis of pregnancy poses risks to the mother and fetus. Mothers with ICP should be screened antenatally and have careful antepartum fetal surveillance as the chances of severe preeclampsia and GDM are high in such pregnancies. Although a review of literature states that pregnant women with ICP have high rates of cesarean section, our study shows women to have a normal vaginal delivery after induction with E2 and/or E1. This shows that LSCS need not be the gold standard as a mode of delivery for mothers with ICP. Fetal complications like MSL should be anticipated and predict the outcomes of pregnancy when complicated by ICP. Two-thirds of the babies born to mothers with ICP had APGAR scores >8 at 1 and 5 minutes of life, due to timely and efficient neonatal resuscitation. Ursodeoxycholic acid continues to remain the gold standard for the treatment of ICP. Close monitoring in the antenatal period with regular LFT and fetal surveillance increases the chance of a good outcome of the pregnancy complicated with ICP.

Limitations

Postintervention analysis could not be performed.

Importance

One among the first few papers where the outcomes of pregnancy in women with ICP has been studied in detail and observed various treatment options in an Indian setting.

Scope for the Future

Maternal and Child Health Mission should accentuate the need for consideration of a separate scheme for ICP, with incentives to relieve the burden of illness on mothers and their families.

Pros of the study	*Cons of the study*
One of the protocol-based studies on cholestasis of pregnancy.	It could have been a prospective study.
This study shows the basis for new schemes and guidelines such as early termination for better pregnancy outcome in ICP.	Genetic analysis could also have been considered to differentiate it from other hepatic disorders in pregnancy like AFLP, etc.

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