

ORIGINAL RESEARCH

Preterm labour and fetomaternal outcome in cholestasis of pregnancy in elderly women

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ABSTRACT

Background: Intrahepatic cholestasis of pregnancy (ICP) is the most common liver disease seen in pregnancy. Intrahepatic cholestasis of pregnancy (IHCP) is characterized by pruritus of the hand and sole with abnormal liver function test and bile acid metabolism. IHCP occurs in the second and third trimesters of pregnancy and usually resolves after delivery. ICP has been found to be associated with increased risk of preterm delivery, meconium staining of amniotic fluid, fetal bradycardia, fetal distress and fetal demise.

Material and methods: The present prospective observational study was conducted in the Postgraduate Department of Obstetrics and Gynaecology, SKIMS Srinagar Jammu and Kashmir over a period of 18 months and total of 150 patients were enrolled in study. After taking history and examination, baseline investigations were done. Patients diagnosed with cholestasis of pregnancy were followed till delivery and post delivery and preterm births and foeto maternal outcome was assessed.

Results: The maternal and foetal outcomes in 150 consecutive women with ICP during the study period were assessed. Majority of women, i.e. 98(65.3%) were multigravida. Period of gestation at diagnosis was 28-36+6 weeks in 85(56.6%) of patients and ≥ 37 weeks in 65(43.3%) of patients. 48(32%) patients had spontaneous onset of labour and in 102(68%) patients labour was induced. 86(57.4%) of patients belong to age group of 35-40 years and 64(42.6%) patients belong to age group of 41-45 years. Patients with cholestasis of pregnancy had fetal tachycardia in 46(30.6%) of fetuses, fetal bradycardia in 36(24%) of fetuses, poor variability in 9(6%) of fetuses, decelerations in 39(26%) of fetuses and arrhythmia in 20(13.3%) of fetuses.

Conclusion: Intrahepatic cholestasis of pregnancy is associated with adverse foeto-maternal and the adverse outcome is more common in elderly patients. Itching over whole body was the predominant presenting complaints of cholestasis of pregnancy. Cholestasis in elderly patients was associated with higher rates of LSCS, preterm births, non reassuring fetal heart pattern and higher rates of NICU admissions. By proper antenatal assessment and timely intervention the outcome can be improved to the large extent.

Keywords: Pruritis, cholestasis, LSCS, preterm birth

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INTRODUCTION

Intrahepatic cholestasis of pregnancy (ICP) is the most common liver disease seen in pregnancy. The incidence of ICP has been found to be variable, with 0.1–1.5% of the population of Central and Western Europe and North America, and 1.5–4% in Chile and Bolivia¹. There is minimal data on the incidence of ICP in the United States, with recent reports stating an incidence of 0.3%, and a recent study on a Latina population in Southern California that determined the overall prevalence in their population to be 5.6%, 10 to 100 times higher than previously reported for the U.S. population²⁻⁴. It is possible that the low incidence and prevalence rates in the United States may be due

to underdiagnosis. The pathogenesis of ICP, although not well defined, is thought to be multifactorial, including an environmental, genetic and hormonal basis for disease⁵. ICP is relatively benign to women, but it has been reported to have important fetal implications. ICP has been found to be associated with increased risk of preterm delivery, meconium staining of amniotic fluid, fetal bradycardia, fetal distress and fetal demise^{2,5,6}. Intrahepatic cholestasis of pregnancy (IHCP) is characterized by pruritus of the hand and sole with abnormal liver function test and bile acid metabolism. IHCP occurs in the second and third trimesters of pregnancy and usually resolves after delivery. A diagnosis of ICP is made when

serum bile acid or amino transferase levels increases with pruritus. Serum aminotransferases more than two times of normal level and elevated alkaline phosphatase (ALP) levels are seen in IHCP but it is not specific for cholestasis. Total bilirubin concentrations rarely exceed 5 mg/dl³. The hepatic functions during pregnancy are affected by increased serum estrogen and progesterone levels. Physical findings such as palmer erythema, spider angioma which may suggest liver disease may be found normally during pregnancy.² Pruritus of cholestasis is different from other diseases characterised by high transaminase levels, such as acute fatty liver of pregnancy and haemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome or severe preeclampsia. The absence of primary skin lesions together with itching helps distinguish pruritus of cholestasis from pruritic dermatoses specific to pregnancy and skin conditions not related to pregnancy. An infectious etiology is excluded through serological tests⁷.

AIMS AND OBJECTIVES

To determine fetomaternal outcome in elderly patients with cholestasis of pregnancy. To determine preterm births in cholestasis of pregnancy.

MATERIAL AND METHODS

The present prospective observational study was conducted in the Postgraduate Department of Obstetrics and Gynaecology, SKIMS Srinagar Jammu and Kashmir over a period of 18 months and total of 150 patients were enrolled in study. Patients were enrolled after getting the proper informed consent in local language. The diagnostic criteria used for IHCP were clinically evident unexplained pruritus especially in palms, soles without skin lesion with increased intensity at night and abnormal transaminase enzyme level of greater than twice the normal value and with serum bile acids more than 10 micromole/L. Women included are patients with cholestasis of pregnancy, singleton, cephalic, >35years and > 28 weeks of gestation. Exclusion criteria are Dermatological conditions leading to pruritis, Viral hepatitis, HELLP syndrome, Acute fatty liver of pregnancy and Obstructive jaundice. After taking informed consent all patients who attended our opd and labour room were subjected to detailed history regarding age, parity, obstetric history, drug history, family history

of diabetes, hypertension or IHCP, general physical examination and obstetric examination. Routine antenatal investigations with liver function tests and serum bile acid tests (fasting) were. The patients were treated with tablet ursodeoxycholic acid (UDCA) 10-15 mg/kg/day in two to three divided doses followed by weekly/biweekly with liver function test till delivery. Fetal surveillance was done by non-stress test, modified biophysical profile and ultrasonography as per the hospital protocol. The patients who did not have spontaneous preterm birth were admitted by 36 to 37+6 weeks of gestation and were delivered by the suitable method. Subsequently, they were followed till 14 days post-delivery. The fetal-maternal outcome in the form of POG at the termination of pregnancy, onset of labor, mode of delivery, outcome of pregnancy, post-partum complication, APGAR score at birth and at 5 mins after delivery, birth weight, neonatal intensive care unit (NICU) admissions and other fetal and neonatal morbidity were recorded.

STATISTICAL METHOD

The data obtained was saved in Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS 23.0). The data was represented in graphs. Student's 't' test was used to assess the p value and a p value < 0.05 was considered as statistically significant.

RESULTS

The maternal and foetal outcomes in 150 consecutive women with ICP during the study period were assessed. Majority of women, i.e. 98(65.3%) were multigravida. Period of gestation at diagnosis was 28-36+6 weeks in 85(56.6%) of patients and ≥ 37 weeks in 65(43.3%) of patients. 48(32%) patients had spontaneous onset of labour and in 102(68%) patients labour was induced. A total of 150 patients enrolled in the study were in the age group of 35-45 years with majority, i.e. 86(57.4%) of patients belong to age group of 35-40 years and 64(42.6%) patients belong to age group of 41-45 years. This is explained by the fact that with increasing age the chances of conception decreases and the findings of our study are consistent with the study c

Table1:Age of study patients		
Age(years)	Number	Percentage
35-40	86	57.4
41-45	64	42.6
Total	150	100

Table 1: shows 86(57.4%) of patients belong to age group of 35-40 years and 64(42.6%) patients belong to age group of 41-45 years.

Table2:Nonreassuring fetal heart pattern		
Fetal heart pattern	Number	Percentage
Tachycardia	46	30.6
Bradycardia	36	24
Poor variability	9	6
Deceleration	39	26
Arrhythmai	20	13.3

Table 2 shows that patients with cholestasis of pregnancy had fetal tachycardia in 46(30.6%) of fetuses,fetal bradycardia in 36(24%) of fetuses,poor variability in 9(6%) of fetuses, decelerations in 39(26%) of fetuses and arrhythmia in 20(13.3%) of fetuses.

Table3:Period of gestation at delivery		
Period of gestation	Number	Percentage
<36 weeks	20	13.4
36-37+6 weeks	58	38.6
>=38 weeks	72	48
Total	150	100

Table3showsthatmajorityofpatientsi.e.72(48%)havinggestationalageof \geq 38weeks at the time of delivery

Table4:Mode of delivery		
Modeofdelivery	Number	Percentage
NVD	62	41.3
LSCS	88	58.7
Total	150	100

Table4 shows majorityofwomeni.e. 88 (58.7%) deliveredbylower segment

Table5:Meconium in liquor		
Meconium in liquor	Number	Percentage
yes	58	38.6
no	92	61.3
Total	150	100

asereansectionwhileas62(41.3%)patientsdeliveredbynornalvaginaldelivery.

Table 5 shows meconium stained liquor was present in 58 (38.6%) of babies and liquor was clear in 92 (61.3%) of babies.

Table6:Outcome of pregnancy		
Outcome	Number	Percentage
Live	141	94
Intrauterine fetal death	7	4.6
Stillbirth	2	1.4

Table 6: shows live births occurred in 141(94%) of patients with cholestasis of pregnancy,stillbirth in 2(1.4%)and IUD in 7(4.6%) of patients.

Table7:1minuteapgarscoreofstudyneonates		
Apgarscore	Number	Percentage
<7	78	55.3
≥7	63	44.7
Total	141	100

Table7: showsApgarscoreat1minutewas<7in78 (55.3%)neonatesand≥7in63(44.7%)neonates.

Table8:5minuteApgarscoreofstudyneonates		
Apgarscore	Number	Percentage
<7	44	31.3
≥7	97	68.7
Total	141	100

Table8: showsApgarscoreat5minutewas<7in44(31.3%)neonatesand≥7in97(68.7%)neonates.

Table9:Baby weight		
Baby weight(kg)	Number	Percentage
<1.5	19	12.6

1.5-2.5	33	22
Total	150	100

Table 9 :shows that baby weight of ≥ 2.5 kg was seen in 98(65.4%) of babies. Baby weight of 1.5-2.5kg was seen in 33(22%) of babies and baby weight of < 1.5 kg was seen in 19(12.6%) of babies. A total of 150 patients enrolled in the study were in the age group of 35-45 years with majority i.e 86(57.4%) of patients belong to age group of 35-40 years and 64(42.6%) patients belong to age group of 41-45 years. This is explained

Table 10: Neonatal outcome		
Outcome	Number	Percentage
Hospitalized	18	12.7
Not hospitalised	123	87.2
Total	141	100

Table 10: shows majority i.e 123(87.2%) of babies does not required hospitalisation and 18(12.7%) were hospitalized.

DISCUSSION

A total of 150 patients enrolled in the study were in the age group of 35-45 years with majority i.e 86(57.4%) of patients belong to age group of 35-40 years and 64(42.6%) patients belong to age group of 41-45 years. This is explained by the fact that with increasing age the chances of conception decreases and the findings of our study are consistent with the study conducted by Shukla et al⁹ In the present study majority of women i.e 98(65.3%) were multigravida and the findings are inconsistent with the study conducted by Pillarisetty and Sharma¹⁰. Period of gestation at diagnosis was 28-36+6 weeks in 85(56.6%) of patients and ≥ 37 weeks in 65(43.3%) of patients. 48(32%) patients had spontaneous onset of labour and in 102(68%) patients labour was induced. In the present study, 52% (n=78) of pregnant women had a preterm delivery as opposed to a national preterm birth rate of 8-12%⁹. This is explained by the fact that elderly pregnancies especially elderly primigravidas are precious pregnancies so both patient and obstetrician have low threshold for any problem that arises during course of pregnancy. Majority of women i.e 88 (58.7%) delivered by lower segment caesarean section while 62(41.3%) patients delivered by normal vaginal delivery. About 86.6% of patients had nonreassuring fetal heart rate pattern; to provide standard antenatal care and to prevent adverse perinatal outcomes the decision of emergency LSCS was taken which was also advocated by Puljic et al¹⁴. Meconium stained liquor was present in 58 (38.6%) of babies and liquor was clear in 92 (61.3%) of babies. Live births occurred in 141(94%) of patients with cholestasis of pregnancy, stillbirth in 2(1.4%) and IUD in 7(4.6%) of patients. In IHCP, the risk of stillbirth varies from 0.4% to 7%^{3,15}. It implies that pregnant with

cholestasis warrant strict fetomaternal surveillance to prevent adverse perinatal outcomes. Apgar score at 1 minute was < 7 in 78 (55.3%) neonates and ≥ 7 in 63(44.7%) neonates. Apgar score at 5 minutes was < 7 in 44(31.3%) neonates and ≥ 7 in 97(68.7%) neonates. Baby weight of ≥ 2.5 kg was seen in 98(65.4%) of babies. Baby weight of 1.5-2.5kg was seen in 33(22%) of babies and baby weight of < 1.5 kg was seen in 19(12.6%) of babies. So low birth weight babies are more common in pregnancies with cholestasis because premature deliveries are common in them. Majority i.e 123(87.2%) of babies does not required hospitalisation and 18(12.7%) were hospitalized.

CONCLUSION

Intrahepatic cholestasis of pregnancy is associated with adverse fetomaternal and the adverse outcome is more common in elderly patients. Itching over whole body was the predominant presenting complaints of cholestasis of pregnancy. Cholestasis in elderly patients was associated with higher rates of LSCS, preterm births, nonreassuring fetal heart pattern and higher rates of NICU admissions. By proper antenatal assessment and timely intervention the outcome can be improved to the large extent.

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REFERENCES

- Arrese M and Reyes H. Intrahepatic cholestasis of pregnancy: a past and present riddle. *Ann Hepatol* 2006; 5: 202-205.

2. Kondrackiene J, Beuers U, Zalinkevicius R, Tauschel HD, Gintautas V, et al. Predictors of premature delivery in patients with intrahepatic cholestasis of pregnancy. *World J Gastroenterology* 2007; 13(46): 6226–30.
3. Lee RH, Goodwin TM, Greenspoon J, Incerpi M. The prevalence of intrahepatic cholestasis of pregnancy in a primarily Latina Los Angeles population. *Journal of Perinatology* 2006; 26: 527–2.
4. Laifer SA, Stiller RJ, Siddiqui DS, Dunston-Boone G, Whetham JC. Ursodeoxycholic acid for the treatment of intrahepatic cholestasis of pregnancy. *J Matern Fetal Med* 2001; 10(2): 131–5.
5. Kondrackiene J and Kupcinskis L. Intrahepatic cholestasis of pregnancy current achievements and unsolved problems. *World J Gastroenterology* 2006; 14(38): 5781–8.
6. Pusl T and Beuers U. Intrahepatic cholestasis of pregnancy. *Orphaned Journal of Rare Diseases* 2007; 2: 26.
7. Glantz A, Marschall HU, Mattsson LA: Intrahepatic cholestasis of pregnancy: relationships between bile acid levels and fetal complication rates. *Hepatology*. 2004, 40:467-474. 10.1002/hep.20336
8. Kamalajayaram V, Devi RA A study of maternal morbidity and mortality in jaundice J *Obstet Gynecol India* 1988;38:439-41.
9. Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. *World J Gastroenterol* 2009; 15: 2049-66.
10. Shukla A, Saxena P, Yadav A: Evaluation of serum glutathione-S transferase-alpha as a biomarker of intrahepatic cholestasis of pregnancy. *J Assoc Physicians India*. 2018, 66:42-44.
11. Pillarisetty LS, Sharma A: *Pregnancy Intrahepatic Cholestasis*. StatPearls Publishing, Treasure Island (FL);2022.
12. Puljic A, Kim E, Page J, Esakoff T, Shaffer B, La Coursiere DY, Caughey AB: The risk of infant and fetal death by each additional week of expectant management in intrahepatic cholestasis of pregnancy by gestational age. *Am J Obstet Gynecol*. 2015, 212:667.E1-667.E5. 10.1016/j.ajog.2015.02.012
13. Posh S, Ajaz S, Jeelani B, Khurshid R: Impact of obstetric cholestasis on fetal outcome - An observational study. *J Sci Soc*. 2020, 47:28-32.
14. Puljic A, Kim E, Page J, Esakoff T, Shaffer B, LaCoursiere DY, Caughey AB: The risk of infant and fetal death by each additional week of expectant management in intrahepatic cholestasis of pregnancy by gestational age. *Am J Obstet Gynecol*. 2015, 212:667.E1-667.E5. 10.1016/j.ajog.2015.02.012.
15. Posh S, Ajaz S, Jeelani B, Khurshid R: Impact of obstetric cholestasis on fetal outcome - An observational study. *J Sci Soc*. 2020, 47:28-32.