International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622
© Gynaecology Journal
www.gynaecologyjournal.com
2021; 5(5): 152-156
Received: 16-07-2021
Accepted: 18-08-2021

Dr. Rekha Yadav
Post Graduate 3rd Year,
M.S Department of Obstetrics and Gynaecology, Teerthanker Mahaveer Medical College, Moradabad, Uttar Pradesh, India

Dr. Kanchan Rani
Professor, Department of Obstetrics and Gynaecology, Teerthanker Mahaveer Medical College, Moradabad, Uttar Pradesh, India

Dr. Rehana Najam
Professor and Head of Department, Department of Obstetrics and Gynaecology, Teerthanker Mahaveer Medical College, Moradabad, Uttar Pradesh, India

Corresponding Author:
Dr. Rekha Yadav
Post Graduate 3rd Year,
M.S Department of Obstetrics and Gynaecology, Teerthanker Mahaveer Medical College, Moradabad, Uttar Pradesh, India

Maternal and fetal outcomes in pregnancies complicated with intrahepatic cholestasis of pregnancy

Dr. Rekha Yadav, Dr. Kanchan Rani and Dr. Rehana Najam

DOI: https://doi.org/10.33545/gynae.2021.v5.i5c.1033

Abstract
Background: Intrahepatic cholestasis of pregnancy (ICP) is the most common liver disease seen in pregnancy. By definition, ICP is apprehended to pregnancy and the post delivery period and is characterised following debarring of all other causes of cholestasis. Intrahepatic cholestasis of pregnancy affects 0·1–2% of pregnant women.
Materials and Method: It is a retrospective study done at Teerthanker Mahaveer medical and research center, department of obstetrics and gynaecology including 128 females with intrahepatic cholestasis of pregnancy over a period of 2 years.
Results: The mean age of the study population was 26.09±4.90 years and mean Gestational Age of the study population was 37.15±3.09 weeks. The clinical symptom of Jaundice was reported among 24.22% and Generalised Pruritus in second and third trimester was seen in all the patients. ALP was elevated in 44.44%, SGOT in 79.26%, SGPT in 73.33%, Total Serum bilirubin in 76.30%, Hypoglycemia in 11.11% and HbSAg was positive in 2.22% women. The perinatal outcome showed that Meconium was found in 37.04%, Apgar score at 1 minute (< 7) in 12.59%, Apgar score at 5 minutes (< 7) in 8.89%, Hyperbilirubinemia in 2.96% and NICU admission in 42.96% infants. Maternal complications and co-morbidities Pre-eclampsia is seen in 21.88%, hypoglycemia 10.16%, Hbsag in 3.13%, deranged coagulation profile 7.03% and post partum haemorrhage 14.06%.
Interpretation: ICP is a comparatively frequent cause of hepatic deterioration in pregnancy. There are adverse pregnancy outcomes associated with intrahepatic cholestasis of pregnancy.

Keywords: fetal outcomes, pregnancies complicated, intrahepatic cholestasis, pregnancy

Introduction

Intrahepatic cholestasis of pregnancy (ICP) is the most frequent liver disorder seen in pregnancy. It is ordinarily a reversible cholestatic disease seen commonly in the later half of pregnancy and is identified by pruritus predominantly of the palms and soles, increased levels of serum aminotransferases and/or increased serum bile acid levels (>or=10micromol/L) with spontaneous alleviation of laboratory derangements and symptoms immediately after parturition but not after one month post- parturition [1, 2].

As per definition, ICP is apprehended to pregnancy and the post delivery period and is characterised following debarring all other causes of cholestasis. Usually incorporating with maternal symptoms, ICP can be associated with adverse neonatal outcomes, seen as meconium stained liquor amnii, premature labour and stillborn; hence, prompt identification and management are important [3].

It has been seen that 0·1–2% of pregnant females are affected by Intra hepatic cholestasis of pregnancy; [4, 6]. It is diagnosed in females with generalised pruritus in second and third trimester and with elevated serum bile acids, and complications can be seen as meconium stained liquor amnii, premature labour, and stillborn [7].

As per a large Swedish cohort study stated that pregnant females in which the serum bile acid concentration was of 40 μmol/L or more. These pregnancies were more predilected to be complicated by premature labour, meconium-stained liquor amnii, and birth asphyxia [8].

Another study on UK cohort stated that pregnancy outcome in females with intrahepatic cholestasis of pregnancy having serum bile acids of 40 μmol/L or more backed these findings and also displayed relation with intrauterine fetal demise (adjusted odds ratio = 3.05] when correlated with statistics from 2205 women with singleton pregnancies with no complications in the UK [3].

The correlation of increased maternal serum bile acids concentrations with intrauterine fetal demise is consistently seen in retrospective studies of females with intrahepatic cholestasis of pregnancy in the USA8 and Scandinavian countries [9]. The 2007 stillborn workshop [10] stated that intrahepatic cholestasis of pregnancy as a medical disorder with elevated maternal serum bile acid concentration and that can lead to intrauterine fetal demise in pregnancies [1, 8, 11].

Most patients with ICP do not develop clinical jaundice. The liver function predominantly shows features of cholestasis. The most characteristic laboratory abnormality is high serum bile acid levels (≥10 µmol/L) which may be elevated up to 100- fold. Severe obstetric cholestasis is defined by levels >40 µmol/L. Other findings are conjugated hyperbilirubinemia, increase in serum ALP, gamma glutamyl transferase (GGT) and serum aminotransferases are normal or only minimally elevated. The synthetic function of the liver and the liver architecture remains unaltered. ICP progresses until the time of delivery. Pruritus disappears within 24-48 hours postpartum, but biochemical and histological abnormalities may take weeks to months to resolve. ICP may recur in subsequent pregnancies in 60-70%, although not necessarily as severe as the first episode [3].

Materials and method

It is a retrospective study done at Teerthanker Mahaveer medical and research center, Moradabad, department of obstetrics and gynaecology. The study was conducted over a period of 24 months (Jan 2018– Jan 2020) from which included 128 patients diagnosed as ICP.

Inclusion criteria

Patients were admitted with diagnosis of IHCP and their clinical and biochemical charaterstics were noted from the record files of the patients.

Maternal and fetal outcomes were noted in terms of: gestational age at delivery and onset of labour, mode of onset of labour and delivery (vaginal or LSCS), complications such as ante partum haemorrhage, Disseminated Intravascular Cougulopathy, postpartum haemorrhage, premature birth, intrauterine demise, still born, fetal birth weight and Apgar score taken at birth and at 5 min, fetal distress and neonatal ICU admissions.

The biochemical ranges were studied about upper limit of serum aspartate aminotransferase (AST), total bilirubin levels (TB), serum alkaline phosphatase (ALP), serum alanine aminotransferase (ALT), serum bile acids levels.

Maternal co-morbidities were noticed in patients like pre-eclampsia, hypoglycemia, Hbsag, deranged coagulation profile, Post – partum Haemorrhage.

Statistical analysis

The specifics were introduced into the Microsoft excel. The statistical analysis was done by software SPSS version 26.0. The Numerical variables (Quantitative) were taken in the form of mean and standard deviation and the Categorical variables (Qualitative) were taken in the form of frequency and percentage (%).

The chi-square test was used for corelating the frequency whereas the student t-test was used for corelating the mean values between the 2 groups whereas. The p-value of less than 0.05, was taken to be significant.

Results

The mean age in the study population seen as 26.09±4.90 years. The Gestational mean Age seen in the study population was 37.15±3.09 weeks. Most of the women had delivery at term (84.38%) followed by pre-term (11.72%) and post-term (3.91%). The distribution onset of the symptom onset showed that majority of the women had symptom onset at 36 weeks (68.75%) followed by 28-32 weeks (21.09%), > 36 weeks (5.47%) and < 28 weeks (4.69%).

Vaginal delivery was done for 26.56% and LSCS for 73.44% women. The clinical symptoms of generalized Pruritus (in second and third trimester) and Jaundice was reported among 24.22% of women. ALP was elevated in 44.53%, SGOT in 79.69%, SGPT in 73.44%, Total Serum bilirubin in 76.56%.

Maternal complications and co- morbidities Pre-eclampsia is seen in 21.88%, hypoglycemia 10.16%, Hbsag in 3.13%, deranged coagulation profile 7.03% and post-partum haemorrhage 14.06%,

The perinatal outcome showed that Meconium was found in 37.50%, Apgar score at 1 minute (< 7) in 12.50%, Apgar score at 5 minutes (< 7) in 8.59%, Hyperbilirubinemia in 3.13% and NICU admission in 42.97% infants.

Discussion

ICP is a pregnancy specific liver disorder seen in the later half of the pregnancy and is associated with increased numbers of adverse neonatal outcomes. Though, maternal consequences of ICP are benign; however, clear association is seen amongst ICP and higher prevalence of fetal distress, pretmature delivery, and sudden intrauterine demise. Most common symptom was pruritus and most of the patients developed pruritus between 32weeks to 36 weeks period of gestation [12].

In this study, most of the women had delivery at term which contrasted with the study by *Senocak et al*, [13] most of the women delivered at ≤37 weeks' gestation. The preterm delivery (≤36 weeks' gestation) and spontaneous preterm delivery rates were high. The incidence of foetuses with SGA was low; however, the number of foetuses with low birth weight was more, resembling the high preterm delivery rate. A high rate of preeclampsia was noted.

In Intra hepatic cholestasis of pregnancy generalised pruritus is the first clinical symptom. Pruritus can be mild and bearable for some females, but can also be very grave and incapacitating. It may also lead to incapacitating the patient's sense of well-being by insomnia, mental sufferings and even increased suicidal tendencies.

Pruritus is more grave in later half of the day, more seen in the palms of the hands and soles of the feet, and is not seen with any particular dermatologic lesions. It most commonly seen after thirty weeks of period of gestation, but rarely can be seen as early as six to ten weeks period of gestation [14, 16].

Moderately elevated levels of conjugated bilirubin occurs is 10-15% patients presents as mild jaundice [14, 17]. Jaundice can sometimes be the initial symptom but usually develops one to four weeks after the onset of pruritus [18, 19]. Subclinical steatorrhea is usually seen in patients with poor fat absorption which van in turn cause vitamin K deficiency leading to prolongation of PT (prothrombin time) and post-partum haemorrhage.

Women with history of intrahepatic cholestasis of pregnancy, even in fist degree relatives are seen to have higher chances of developing gall stones and cholecystitis in the ratio 3:7 [22].

Increased levels of serum bile acids and serum aminotransferase levels are seen as most common biochemical derangements [23]. Serum total bile acids levels may be elevated by ten to hundred times more than the average and if womens fasting serum bile acid levels are more than 40 µmol/L it most commonly leads to

fetal complications [24, 27]. In intrahepatic cholestatsis of pregnancy, cholic acid levels are more increased than chenodeoxcholic acid [28, 30].

A Section of healthy pregnant females with no symptoms but with serum bile acids levels more than 11 µM in second and third trimester gestation and liver enzymes in normal range has lately been characterised as asymptomatic hypercholanemia in pregnancy (AHP) [31, 32].

Aminotransferases levels are also increases two –ten-fold more than the average in twenty–sixty percent of females with pruritus, and can exceed to 1000 U/L in rare circumstances [14, 33]. Serum aminotransferases help in better follow up of the patients once we start treatment with urssodeoxycholic acid rather with fasting serum bile acid levels (total) in patients which firstly are elevated secondary to elevated levels in serum urodeoxycholic acid (UDCA) levels. Serum levels of GGT can be normal or moderately increased in fifty percent of the patients, around four times the above the normal values [14, 15].

Due to increased in levels of placenta isoenzyme, increased levels of serum alkaline phosphatase can be difficult to recognize [34]. With the symptoms, increased serum bile acid levels are considered in the diagnosis of ICP in a majority of studies. The levels of ALT and AST also increase in a majority of women with ICP, and the increment may precede an elevation in serum bile acids level by one to two weeks.

In current study, majority of the women had their symptom onset during the 32-36 weeks of gestation which was in line with the research work by *Senocak et al*, [13] the onset of symptoms occurred in the third trimester in 90% of the women presenting after 30 weeks of gestation, which is similar to that reported in other studies [3, 35].

In our study, vaginal delivery was done for 26.67% and LSCS for 73.33% deliveries which was similar to the study by Rizvi and Raina, LSCS was done in 69% cases [36]. Higher caesarean section rates were due to meconium staining of liquor amnii, previous LSCS and fetal distress. Meconium staining of liquor occurred in 57.8% of cases (versus 26.2%) which was statistically significant. In a study by *Brouwers L et al*, meconium staining of liquor occurred in 47.6% [37].

According to the statistics that the incidence of hyaline membrane disease leading to respiratory depression in neonates of mothers diagnosed with intrahepatic cholestasis of pregnancy is double than that in neonates of normal population [38, 39]. Respiratory depression in neonate can also be due to pre-term delivery, but based on study of fluid taken from bronchoalveolar lavage of newborn of mothers with intrahepatic cholestasis of pregnancy it demonstrates that respiratory depression is specifically associated with ICP [39].

It has been postulated that increased levels of serum bile acids can lead to depletion of surfactant in the alveoli of lungs of fetus [38, 39].

The chances of fetal affection in ICP is more than that of normal population. Though in our study there were no cases of intra uterine fetal demise, but the overall fetal affection rate is still alarming. Lately management of intra hepatic cholestasis of pregnancy is induction of labor at 36–38 weeks period of gestational age, mostly used for patients with serum bile acids <40 µmol/L [1].

A study conducted by Glantz *et al*. stated that patients with serum bile acids values >40 µmol/L had higher fetal risk of premature delivery, birth asphyxia, meconium staining of liquor amnii, and greenish appearance of placenta and membranes, and patients with serum bile acids ranging from 10–39 µmol/L had decreased risk to no risk compared to patients with generalised pruritus but normal serum bile acids, and depending on these discovery the second set of patients could be treated with expectant management, and thus can decrease the expenditure of health care [42].

In this study, no clinical or biochemical predictors association with increased fetal affection were significant enough. This can be due to contrast in basic practice, where we essentially terminate pregnancy in females diagnosed ICP at ~37 weeks gestational age, where as in the Glantz *et al*. [42].

Patients with liver or biliary disease may have higher chances for fetal and neonatal affection.

The mean period of gestation seen with history of intrahepatic cholestasis of pregnancy was 37 weeks (ranging between36–39), and the mean period of gestation in patients that had no history of intrahepatic cholestasis of pregnancy in last pregnancies was also noticed as 37 weeks (ranging between 33-40). The percentage of deliveries with a period of gestation more than 37 weeks was seen as 35% and women with a history of intrahepatic cholestasis of pregnancy and 26% in those without a history of intrahepatic cholestasis [1].

Interpretation

ICP is a comparatively frequent cause of hepatic deterioration in pregnancy. Maternal morbidity is increased in terms of increased LSCS rates and discomfort due to pruritus. Maternal cholestasis is transient with postnatal resolution. ICP is associated with adverse perinatal outcome. There is higher risk of meconium staining of liquor amnii, birth asphyxia, premature delivery and sudden intrauterine demise at term as evidenced in this study.

Table 1: Mean age and Gestational Age of the study population

	Number	Percentage
Age (Mean±SD)	26.09±4.90	
Gestational Age (Mean±SD)	37.15±3.09	

Table 2: Distribution of study patients as per gestational age at delivery

Gestational age at delivery	Number	Percentage
Pre-term	15	11.72%
Term	108	84.38%
Post-term	5	3.91%

Table 3: Gestational age at the onset of symptoms

Gestational age (weeks)	Number	Percentage
< 28	6	4.69%
28-32	27	21.09%
32-36	88	68.75%
> 36	7	5.47%

Table 4: Distribution of study patients as per mode of parturition

Mode of parturition	Number	Percentage
Vaginal	34	26.56%
LSCS	94	73.44%

Table 5: Maternal complications Pruritus was seen all the patients diagnosed as Intra hepatic cholestasis of pregnancy.

Maternal outcomes		Number	Percentage
Clinical	Jaundice	31	24.22
Biochemical	ALP	57	44.53%
	SGOT	102	79.69%
	SGPT	94	73.44%
	Total Serum bilirubin	98	76.56%

Table 6: Maternal complications and associated co- morbidities

	Number	Percentage
Pre-eclampsia	28	21.88%
HBsAG	4	3.13%
Hypoglycaemia	13	10.16%
Deranged coagulation profile	9	7.03%
Post – partum haemorrhage	18	14.06%

Table 7: Perinatal outcome

Perinatal outcomes	Number	Percentage
Meconium	48	37.50%
Apgar score at 1 minute (< 7)	16	12.50%
Apgar score at 5 minutes (< 7)	11	8.59%
Hyperbilirubinemia	4	3.13%
NICU admission	55	42.97%
NICU stay (days) (Mean±SD)	12.13±3.98	

References

1. Rook M, Vargas J, Caughey A, Bacchetti P, Rosenthal P, Bull L. Fetal outcomes in pregnancies complicated by intrahepatic cholestasis of pregnancy in a Northern California cohort. PLoS One. 2012;7(3):e28343.
2. Arrese M, Reyes H. Intrahepatic cholestasis of pregnancy: a past and present riddle. Ann Hepatol 2006;5:202-5.
3. Geenes V, Chappell LC, Seed PT, Steer PJ, Knight M, Williamson C. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: a prospective population-based case-control study. Hepatol 2014;59:1482-91.
4. Lin J, Gu W, Hou Y. Diagnosis and prognosis of early-onset intrahepatic cholestasis of pregnancy: a prospective study. J Matern Fetal Neonatal Med 2017.
5. Allen AM, Kim WR, Larson JJ, *et al*. The epidemiology of liver diseases unique to pregnancy in a US community: a population-based study. Clin Gastroenterol Hepatol 2016;14:287-94.
6. Marathe JA, Lim WH, Metz MP, Scheil W, Dekker GA, Hague WM. A retrospective cohort review of intrahepatic cholestasis of pregnancy in a South Australian population. Eur J Obstet Gynecol Reprod Biol 2017;218:33-8.
7. Williamson C, Geenes V. Intrahepatic cholestasis of pregnancy. Obstet Gynecol 2014;124:120–33.
8. Glantz A, Marschall HU, Mattsson LÅ. Intrahepatic cholestasis of pregnancy: relationships between bile acid levels and fetal complication rates. Hepatology 2004;40:467-74.
9. Laatikainen T, Ikonen E. Serum bile acids in cholestasis of pregnancy. Obstet Gynecol 1977;50:313-18.
10. Reddy UM, Goldenberg R, Silver R, *et al*. Stillbirth classification-developing an international consensus for research. Obstet Gynecol 2009;114:901-14.
11. Herrera CA, Manuck TA, Stoddard GJ, *et al*. Perinatal outcomes associated with intrahepatic cholestasis of pregnancy. J Matern Fetal Neonatal Med 2018;31:1913-20.
12. Hassan N, Khurshid R, Muzamil M, Parveen S. Cholestasis of pregnancy: effects on maternal and fetal outcome. Int J Reprod Contracept Obstet Gynecol 2020;9:3202-7.
13. Cimilli Senocak GN, Topdagi Yılmaz EP. Maternal and Fetal Outcomes in Pregnancies Complicated by Intrahepatic Cholestasis. Eurasian J Med 2019;51(3):270-2.
14. Bacq Y, Sapey T, Brechot MC, Pierre F, Fignon A, Dubois F. Intrahepatic cholestasis of pregnancy: a French prospective study. Hepatology 1997;26:358-364.
15. Fagan EA. Intrahepatic cholestasis of pregnancy. Clin Liver Dis 1999;3:603-32.
16. Brites D, Rodrigues CM, Cardoso MC, Graca LM. Unusual case of severe cholestasis of pregnancy with early onset, improved by ursodeoxycholic acid administration. Eur J Obstet Gynecol Reprod Biol 1998;76:165-8.
17. Serrano MA, Brites D, Larena MG, Monte MJ, Bravo MP, Oliveira N, *et al*. Beneficial effect of ursodeoxycholic acid on alterations induced by cholestasis of pregnancy in bile acid transport across the human placenta. J Hepatol 1998;28:829-39.
18. Knox TA, Olans LB: Liver disease in pregnancy. N Engl J Med 1996;335:569-76.
19. Nichols AA. Cholestasis of pregnancy: a review of the evidence. J Perinat Neonatal Nurs 2005;19:217-25.
20. Mullally BA, Hansen WF: Intrahepatic cholestasis of pregnancy: review of the literature. Obstet Gynecol Surv 2002;57:47-52.
21. Reyes H, Radrigan ME, Gonzalez MC, Latorre R, Ribalta J, Segovia N, *et al*. Steatorrhea in patients with intrahepatic cholestasis of pregnancy. Gastroenterology 1987;93:584-90.
22. Ropponen A, Sund R, Riikonen S, Ylikorkala O, Aittomaki K. Intrahepatic cholestasis of pregnancy as an indicator of liver and biliary diseases: a population-based study. Hepatology 2006;43:723-8.
23. Poupon R. Intrahepatic cholestasis of pregnancy: from bedside to bench to bedside. Liver Int 2005;25:467-8.
24. Heikkinen J, Maentausta O, Ylostalo P, Janne O. Changes in serum bile acid concentrations during normal pregnancy, in patients with intrahepatic cholestasis of pregnancy and in pregnant women with itching. Br J Obstet Gynaecol 1981;88:240-5.
25. Brites D, Rodrigues CM, van Zeller H, Brito A, Silva R. Relevance of serum bile acid profile in the diagnosis of intrahepatic cholestasis of pregnancy in an high incidence area: Portugal. Eur J Obstet Gynecol Reprod Biol 1998;80:31-8.
26. Brites D. Intrahepatic cholestasis of pregnancy: changes in maternal-fetal bile acid balance and improvement by ursodeoxycholic acid. Ann Hepatol 2002;1:20-8.
27. Glantz A, Marschall HU, Mattsson LA. Intrahepatic cholestasis of pregnancy: Relationships between bile acid levels and fetal complication rates. Hepatology 2004;40:467-74.
28. Brites D, Rodrigues CM, Oliveira N, Cardoso M, Graca LM. Correction of maternal serum bile acid profile during ursodeoxycholic acid therapy in cholestasis of pregnancy. J Hepatol 1998;28:91-8.
29. Heikkinen J. Serum bile acids in the early diagnosis of intrahepatic cholestasis of pregnancy. Obstet Gynecol 1983;61:581-7.
30. Bacq Y. Intrahepatic cholestasis of pregnancy. In UpToDate Edited by: Rose and BD. Waltham, MA 2006.
31. Pascual MJ, Serrano MA, El Mir MY, Macias RI, Jimenez F, Marin JJ. Relationship between asymptomatic hypercholanaemia of pregnancy and progesterone metabolism. Clin Sci (Lond) 2002;102:587-593.
32. Castano G, Lucangioli S, Sookoian S, Mesquida M, Lemberg A, Di Scala M, Franchi P, Carducci C, Tripodi V: Bile acid profiles by capillary electrophoresis in intrahepatic cholestasis of pregnancy. Clin Sci (Lond) 2006;110:459-465.
33. Lunzer M, Barnes P, Byth K, O'Halloran M. Serum bile acid concentrations during pregnancy and their relationship to obstetric cholestasis. Gastroenterology 1986;91:825-829.

34. Palmer DG, Eads J. Intrahepatic cholestasis of pregnancy: a critical review. J Perinat Neonatal Nurs 2000;14:39-51.
35. Kenyon AP, Piercy CN, Girling J, Williamson C, Tribe RM, Shennan AH. Obstetric cholestasis, outcome with active management: a series of 70 cases. BJOG. 2002;109:282-8.
36. Rizvi SM, Raina R. Fetomaternal outcome in jaundice complicating pregnancy. J Soc Obstet Gynaecol Pak 2018;8(3):176-9.
37. Brouwers L, Koster MP, Page-Christiaens GC, Kemperman H, Boon J, Evers IM, *et al*. Intrahepatic cholestasis of pregnancy: maternal and fetal outcomes associated with elevated bile acid levels. Am J Obstet Gynecol 2015;212(1):100.e1-7.
38. Zecca E, De Luca D, Marras M, Caruso A, Bernardini T, *et al*. Intrahepatic Cholestasis of Pregnancy and Neonatal respiratory Distress Syndrome. Pediatrics. 2006;5:1669–72.
39. Zecca E, DeLuca D. Bile acid induced lung injury in newborn infants: a bronchoalveolar lavage fluid study. Pediatrics 2008;121(1):146-9.
40. Kaneko T, Sato T, Katsuya H, Miyauchi Y. Surfactant therapy for pulmonary edema due to intratracheally injected bile acid. Crit Care Med 1990;18:77–83.
41. Hills BA, Chen Y, Masters IB, Hills YC. Raised bile acid concentrations in SIDS lungs at necropsy. Arch Dis Child 1997;77:120-3.
42. Glantz A, Marschall HU, Mattsson LA. Intrahepatic Cholestasis of Pregnancy: Relationships between Bile Acid Levels and Fetal Complication Rates. Hepatology 2004;40(2):467-74.