ORIGINAL RESEARCH PAPER

Gynaecology

KEY WORDS: Obstetric cholestasis, meconium staining and LSCS

OBSTETRIC CHOLESTASIS IN A TERITIARY HOSPITAL

Dr.S.V.R.Thenmozhi Assistant Professor of Obstetrics & Gynaecology, KMC Hospital.

Dr.S.Sreeranjani Assistant Professor of Obstetrics & Gynaecology, KMC Hospital.

Dr.S.Geethanjali Consultant, Dept.of Obstetrics & Gynaecology, Mehta Hospital.

S.Padmanaban Research Scientist B(Non Medical), NIRRH Field unit, KMC Hospital.

ABSTRACT

BACKGROUND:
Obstetric cholestasis is a liver disease unique to pregnancy. Once assumed to be benign condition, its significance has been highlighted only recently due to associated maternal & perinatal morbidity & mortality.So, careful history taking and simple biochemical tests will be helpful in early diagnosis and appropriate intervention in these patients. This will lead to significant reduction in maternal and perinatal morbidity and mortality.

AIM OF THE STUDY
To determine the incidence of obstetric cholestasis, study the course of pregnancy and evaluate pregnancy outcome in women with obstetric cholestasis.

MATERIALS AND METHODS
The antenatal women in late second trimester and third trimester (24 – 40 weeks of gestational age) attending antenatal clinic, Kilpauk Medical College Hospital, Chennai, with complaints of pruritus and who satisfy exclusion criteria are included in the study. The period of study was between july 2010 and August 2012, for a period of 2 years.

Results:
75 antenatal patients out of 1000 screened, who fulfilled the inclusion criteria were included in the study and followed up till 2 weeks after delivery.
The incidence of meconium staining of liquor in patients with obstetric cholestasis was 49.33%.
- The incidence of low birth weight in patients with cholestasis was 17.3%.
- 50.67% of obstetric patients were delivered by LSCS and 49.33% were delivered by labour natural.

INTRODUCTION:
Obstetric cholestasis is a liver disease unique to pregnancy. Once assumed to be benign condition, its significance has been highlighted only recently due to associated maternal & perinatal morbidity & mortality.

Its incidence varies with the population. The incidence of obstetric cholestasis has been difficult to estimate as a result of likely under reporting or failure to recognize mild cases. So, careful history taking and simple biochemical tests will be helpful in early diagnosis and appropriate intervention in these patients. This will lead to significant reduction in maternal and perinatal morbidity and mortality.

As obstetric cholestasis rarely presents with jaundice, and with non specific symptoms such as pruritis and disturbed sleep, it is difficult to diagnose.

AIM OF THE STUDY
To determine the incidence of obstetric cholestasis, study the course of pregnancy and evaluate pregnancy outcome in women with obstetric cholestasis.

Pregnancy outcome is evaluated in terms of term/preterm/post term delivery, Mode of delivery, Meconium staining of liquor, Birth weight of baby, NICU admissions, Fetal growth restriction.

The efficacy of UDCA in controlling pruritis is also evaluated.

PATHOGENESIS
Cholestasis (failure of bile formation) represents an exaggerated response of the liver to the normal increase in endogenous estrogens during pregnancy. Leslie and colleagues(2000) reported that plasma estrogen levels are decreased in affected women. Bile acids are incompletely cleared by the liver and accumulate in plasma.

There is role for mutations in the genes that control hepatocellular transport systems. One of such genes is Multidrug resistance 3 (MDR3) gene found with progressive familial intrahepatic cholestasis. This genetic predisposition shows autosomal dominance.

The elevation in maternal levels of bile acids impairs the normal feto-maternal transfer and excess bile acids with abnormal profiles accumulates which are toxic to the fetus.

The drugs which decrease the canalicular membrane transport of bile acids aggravate this disorder. There are few case reports of cholestatic jaundice in pregnant women taking azathioprine after renal transplantation. The end effect is that, bile acids are incompletely cleared and they accumulate in plasma. Even before bile acid levels increase, associated dyslipidemia is evident.

Hyperbilirubinemia is due to accumulation of conjugated pigment, but the total level never exceeds 4to5 mg%. Liver biopsy shows mild cholestasis with bile plugs in hepatocytes and canaliculi of centrilobular regions, but without inflammation or necrosis. The changes disappear after delivery. Similar changes are seen in women using Oral contraceptive pills and cyclically during menstruation.

MATERIALS AND METHODS

SELECTION OF CASES:

INCLUSION CRITERIA:

The antenatal women in late second trimester and third trimester (24 – 40 weeks of gestational age) attending antenatal clinic, Kilpauk Medical College Hospital, Chennai, with complaints of pruritus and who satisfy exclusion criteria are included in the study.

The period of study is between july 2010 and August 2012, for a period of 2 years.

EXCLUSION CRITERIA

1. Positive serology for hepatitis A,B,C.
2. Previous history of gall bladder disease.
3. Sonographic evidence of gall bladder disease.
4. Hypertension complicating pregnancy.
5. Liver function did not normalize within two weeks after delivery.
6. Autoimmune diseases like primary biliary cirrhosis, autoim mune chronic active hepatitis.

METHODOLOGY

- An interview was conducted using a questionnaire.
- Around 75 patients satisfying above criteria were chosen.
- LFT including Serum bilirubin, SGOT, SGPT, SAP, GGT was done. Patients were followed up with LFT and it was repeated at an interval of 2 weeks.
- LFT is repeated at 2 weeks after delivery.
- All patients were given Urso Deoxy Cholic Acid (UDCA) 8mg/kg/day in two divided doses.
- Time taken for onset of relief of pruritis was observed.
- Review of obstetric notes was done for Gestational age, Meconium staining of liquor, Mode of delivery, APGAR score, NICU admission, Birth weight.

SAMPLE SIZE

The sample size was calculated using the formula,

n = Z2* P (1-P)/d2

Z – Constant (1.96)

P – Prevalence (0.05)

d - Desired precision (0.05)

By using this formula, n comes to 72 and the sample size for my study is 75.

Results & Analysis:

1000 patients were screened and 75 were diagnosed as having obstetric cholestasis, the incidence being 7.5%.

Mean serum bilirubin level in patients with obstetric cholestasis is 0.74mg/dl.

Highest serum bilirubin value – 0.9 mg/dl.

Lowest serum bilirubin value – 0.6mg/dl.
Table:1

ASSOCIATION BETWEEN SERUM BILIRUBIN AND MECONIUM

STAINING OF LIQUOR

Meconium staining			Std. Deviation	Std. Error Mean	
of liquor		N	Mean		
Serum	Yes	36	.74	.080	.013
bilirubin					
Mean	No	37	.74	.073	.012

P = 0.809 not significant.

OBSTETRIC CHOLESTASIS AND SGOT

Mean SGOT level in patients with obstetric cholestasis – 60.5 IU/L.

Highest SGOT value – 146 IU/L.
Lowest SGOT value – 22IU/L.

Table:2 ASSOCIATION BETWEEN SGOT LEVELS AND MECONIUM STAINING OF LIQUOR

Meconium staining				Std. Deviatio	Std. Error Mean
of liquor		N	Mean		
	1	37	65.65	32.466	5.337
SGOT mean					
	0	38	55.42	18.686	3.031

P = 0.098 not significant.

OBSTETRIC CHOLESTASIS AND SGPT

Mean SGPT level in patients with obstetric cholestasis – 57.8 IU/L.
Highest SGPT value – 124 IU/L.

Lowest SGPT value – 42 IU/L.

Table:3 ASSOCIATION BETWEEN SGPT LEVELS AND MECONIUM STAINING OF LIQUOR

Meconium staining					
of liquor	N	Mean	Std. Deviation	Std. Errod Mean	
	1	37	62.54	22.665	3.726
SGPT mean					
	0	38	53.00	13.164	2.136

P = 0.028 significant.

OBSTETRIC CHOLESTASIS AND SGPT

Mean SGPT level in patients with obstetric cholestasis – 57.8 IU/L.
Highest SGPT value – 124 IU/L.

Lowest SGPT value – 42 IU/L.

Table:3 ASSOCIATION BETWEEN SGPT LEVELS AND MECONIUM STAINING OF LIQUOR

Meconium staining					
of liquor	N	Mean	Std. Deviation	Std. Errod Mean	
	1	37	62.54	22.665	3.726
SGPT mean					
	0	38	53.00	13.164	2.136

P = 0.028 significant.

OBSTETRIC CHOLESTASIS AND GGT

GGT is raised only in 33.33% of patients with obstetric cholestasis.
Mean GGT level in patients with obstetric cholestasis is 36.4 IU/L.
Highest GGT value – 66 IU/L.

Table:4 ASSOCIATION BETWEEN GGT LEVELS AND MECONIUM STAINING OF LIQUOR

Meconium staining				Std. Deviation	Std. Error Mean
of liquor		N	Mean		
	1	37	37.22	17.003	2.795
GGT mean					
	0	38	35.58	14.899	2.417

P = 0.658 not significant.

OBSTETRIC CHOLESTASIS AND SAP

Mean SAP level in patients with obstetric cholestasis – 448.6 IU/L.
Highest SAP value – 786 IU/L.

Lowest SAP value – 380 IU/L.

Meconium staining					
of liquor	N	Mean	Std. Deviation	Std. Error Mean	
	Yes	37	469.35	75.535	12.418
SAP mean					
	No	38	427.82	70.455	11.429

P = 0.016 significant.

ASSOCIATION BETWEEN MECONIUM STAINING OF LIQUOR

AND MODE OF DELIVERY

Out of 37 babies with meconium staining of liquor, 24 (64.9%) were delivered by labour naturals and 13(35.1%) were delivered by LSCS.

		Meconium Staining of Liquor			
			NO	YES	TOTAL
		Count	13	24	37
Mode of	LN	% within meconium			
		staining of liquor	34.2	64.9	49.3
Delivery		% of Total	17.3	32.0	49.3
		Count	25	13	38
	LSCS	% within meconium			
		staining of liquor	65.8	35.1	50.7
		% of Total	33.3	17.3	50.7
		Count	38	37	75
	Total	% within Meconium			
		staining of liqour	100.0	100.0	100.0
		% of Total	50.7	49.3	100.0

Chi square = 7.048

P value = 0.08 significant

SUMMARY

75 antenatal patients out of 1000 screened, who fulfilled the inclusion criteriawere included in the study and followed up till 2 weeks after delivery.

- 75 patients out of 1000 screened were found to be having obstetric Cholestasis (7.5%).
- Mean age of patients with obstetric Cholestasis was 23.5 yrs.
- Mean birth weight of babies of mothers with obstetric cholestasis was 2.6kg.
- The incidence of meconium staining of liquor in patients with obstetric cholestasis was 49.33%.
- The incidence of low birth weight in patients with cholestasis was 17.3%.
- 50.67% of obstetric patients were delivered by LSCS and 49.33% were delivered by labour natural.
- Out of 75 patients with obstetric cholestasis, 50 (66.67%) were primigravida.
- Babies of 55 patients with obstetric cholestasis (73.33%) were admitted in NICU.
- Meconium staining of liquor contributed to 67.27% of NICU admissions.
- The mean gestational age at diagnosis of obstetric cholestasis was 32weeks
- All the patients with obstetric cholestasis were given UDCA and all of them were completely relieved of their symptoms. 23 patients (30.6%) had onset of relief in 2 weeks and 52 patients (69.33%) had onset of relief in a week.
- Mean serum bilirubin level in obstetric cholestasis was 0.74mg/dl.
- Highest serum bilirubin value – 0.9mg/dl.
- Lowest serum bilirubin value – 0.6mg/dl.
- There is no significant correlation between serum bilirubin levels and meconium staining of liquor.
- Mean SGOT levels in patients with obstetric cholestasis is 60.5 IU/L.
- Highest SGOT value – 146 IU/L.
- Lowest SGOT value – 22 IU/L.
- There is no significant correlation between SGOT levels and meconium staining of liquor.
- Mean SGPT levels in patients with obstetric cholestasis is 57.5 IU/L.
- Highest SGPT value – 124 IU/L.
- Lowest SGPT value – 42 IU/L.
- There exists significant correlation between SGPT levels and meconium staining of liquor.
- Mean SAP levels in patients with obstetric cholestasis is 448.6 IU/L.
- Highest SAP value – 786 IU/L.
- Lowest SAP value – 380 IU/L.
- GGT is raised only in 33.33% of patients with obstetric cholestasis.
- Mean GGT levels in patients with obstetric cholestasis is 36.4 IU/L.
- Highest GGT value – 66 IU/L.
- Lowest GGT value – 18 IU/L.
- There is no significant correlation between GGT levels and meconium staining of liquor
- There exists a significant correlation between SAP levels and meconium staining of liquor.

CONCLUSION

- The incidence of obstetric cholestasis in antenatal OP population of Kilpauk Medical College, a tertiary care center is 7.5%.
- Obstetric cholestasis is more common in primigravida than in multigravida.
- There is a significant association between obstetric cholestasis and meconium staining of liquor and NICU admissions.
- Obstetric cholestasis is more common in the age group of 21 – 24 years.
- The mean gestational age at diagnosis of obstetric cholestasis is 32 wks.
- There exists a significant correlation between SGPT levels, SAP levels and meconium staining of liquor.
- GGT and SGOT levels do not have significant association with meconium staining of liquor.
- Serum bilirubin levels were normal in all cases of obstetric cholestasis.
- UDCA provided symptomatic relief in all the patients with obstetric cholestasis.
-
- The incidence of preterm deliveries in obstetric cholestasis is 8%.
- There were no cases of prolonged pregnancy and intrauterine growth retardation in patients with obstetric cholestasis.
- The mean birth weight of babies with obstetric cholestasis is 2.6kg.
- Mode of delivery does not have significant correlation with obstetric cholestasis.

REFERENCES

1. Greentop guidelines 43 Obstetric Cholestasis.
2. R.poupon, Liver International 2005-Wiley online library.
3. Moses S. Pruritus. Am Fam Physician. 2003;68(6):1135–42. [PubMed]
4. Ambros-Rudolph CM. Dermatoses of pregnancy—clues to diagnosis, fetal risk and therapy. Ann Dermatol. 2011;23(3):265–75. Epub 2011 Aug 6. [PMC free article][PubMed]
5. Ambros-Rudolph CM, Müllegger RR, Vaughan-Jones SA, Kerl H, Black MM. The specific dermatoses of pregnancy revisited and reclassified: results of a retrospective two-center study on 505 pregnant patients. J Am Acad Dermatol. 2006;54(3):395–404.[PubMed]
6. Lammert F, Marschall HU, Glantz A, Matern S. Intrahepatic cholestasis of pregnancy: molecular pathogenesis, diagnosis and management. J Hepatol. 2000;33(6):1012–21.[PubMed]
7. Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. World J Gastroenterol. 2009;15(17):2049–66. [PMC free article] [PubMed]
8. Davies MH, da Silva RCMA, Jones SR, Weaver JB, Elias E. Fetal mortality associated with cholestasis of pregnancy and the potential benefit of therapy with ursodeoxycholic acid. Gut. 1995;37(4):580–4. [PMC free article] [PubMed]
9. Palma J, Reyes H, Ribalta J, Hernández I, Sandoval L, Almuna R, et al. Ursodeoxycholic acid in the treatment of cholestasis of pregnancy: a randomized, double-blind study controlled with placebo. J Hepatol. 1997;27(6):1022–8. [PubMed]
10. Roncaglia N, Arreghini A, Locatelli A, Bellini P, Andreotti C, Ghidini A. Obstetric cholestasis: outcome with active management. Eur J Obstet Gynecol Reprod Biol. 2002;100(2):167–70. [PubMed]