Original Research Article

Study to Determine the Incidence and Pregnancy Outcomes in Women With Obstetric Cholestasis in a Tertiary Care Centre

Indrani Dutta[1*], Atima Bharti[2]

[1]Senior Resident, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India
[2]Associate Professor, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India

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Abstract

Background: Obstetric cholestasis is the most common liver disorder during pregnancy which normally presents in the second half of pregnancy. The present study has made an effort to determine the incidence and pregnancy outcomes in women with obstetric Cholestasis. **Aims and Objectives:** To determine the incidence and analyse pregnancy outcome in women with obstetric cholestasis. **Methodology:** Cross Sectional Prospective Study. **Results:** The incidence of obstetric cholestasis hence was found to be 2%.Most of the patients belonged to age group 20-24 years. (52.86%), of gestational age 32-36 weeks at diagnosis (67.14%), of >36 weeks gestational age at delivery (64.29%), mostly primigravida (64.29%) and non smoker (92.86%).47.14% Patients had vaginal delivery of which 12.5% was spontaneous, 16.25% was induced, and 12.5% was instrumental.52.86% patients delivered by lower segment caesarean section of which 12.5% was elective, 6.25% was due to failed induction, and 15% was due to meconium stained liquor and foetal distress. 54.29% patients got relief from pruritus in 1 week of administration of UDCA. Regarding complications, about 15.71% landed in postpartum hemorrhage, 11.42% had altered coagulation profile, 35.71% had preterm labour, 24.29% had altered lipid profile and 17.14% had insomnia. 21.4% of babies had low birth weight, 35.71% were preterm, 30% small for gestational age, 15.71% had abnormal CTG, 48.57% had meconium stained liquor,11.42% had respiratory distress, 21.4% needed NICU admission and 1.43% had intrauterine death. **Conclusion:** Considering the adverse effects on foetus, pregnant women should be judiciously followed through the antenatal period till delivery. Decision regarding early induction should be taken considering risk of prematurity, low birth weight and NICU admission.

Keywords: cholestasis, meconium, low birth weight, prematurity, pruritus.

Introduction

Obstetric cholestasis is the most common liver disorder during pregnancy which normally presents in the second half of pregnancy.It tends to recur in subsequent pregnancies and is associated with significantly high adverse maternal and foetal outcome. Since there is under reporting of mild cases, judicious history taking and biochemical tests help in early diagnosis and management. Most cases present with non specific symptoms like pruritus and disturbed sleep, but associated with intrauterine death, premature labour, meconium stained liquor and postpartum hemorrhage[1-4]. Higher incidence of obstetric cholestasis have been reported in Scandinavia and Chile(2%-4%)[5-6]. Several studies have also used varying definition for the pathology observed and differing inclusion and exclusion criteria[7-11]. The present study has made an effort to determine the incidence and pregnancy outcomes in women with obstetric Cholestasis at Rajendra Institute of Medical Sciences, Ranchi which caters to the health services of Jharkhand.

Aims and Objectives

1. To determine the incidence of obstetric cholestasis.
2. To analyse pregnancy outcome in women with obstetric cholestasis.

Methodology

Study Type

Cross sectional prospective study

*Correspondence
Dr. Indrani Dutta
Senior Resident, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India

Place of study

Out patients dept and labor ward (Dept Of Obstertics and Gynecology, RIMS, Ranchi)

Duration of study

January 2019 To December 2019.

Inclusion Criteria

The antenatal women in late second trimester and third trimester (24 – 40 weeks of gestational age) with complaints of pruritus and who satisfy exclusion criteria were included in the study.

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. Autoimmune diseases like primary biliary cirrhosis, autoimmune chronic active hepatitis.
6. Liver or gall bladder malignancies
7. Medications altering liver function tests

Sample Size

Sample size was calculated for continuous outcome and means by the statistical formula as follow;

$n = \{z2\ p\ (1-p)\}/d2$

z = Z is standard normal variate at level of significance (i.e. 1.96 for 95% confidence level)

p= Expected prevalence or proportion = 5% = 0.05
d= Precision = 0.05 (Type 1 error)
Therefore, n = {z2 p (1-p)}/d2 = {(1.96)2 (0.05) (1 – 0.05)}/ (0.05)2 = 72 ≈ 70
An interview was conducted using a questionnaire.
Around 70 patients satisfying above criteria were chosen. Liver function tests including Serum bilirubin, SGOT, SGPT, SAP, GGT, bile acids, PT-INR Lipid profile was done. Patients were followed up with LFT and it was repeated at an interval of 2 weeks. LFT was 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 pruritus was observed.The frequency of Obstetric cholestasis in the hospital, the period of gestation at which it appeared, and the relationship of obstetric cholestasis with maternal Age and Parity were studied. Maternal Outcomes were studied with reference to mode of delivery - vaginal delivery, forceps application, elective and emergency caesarean section, Postpartum Haemorrhage. Foetal Outcome were studied in reference to Foetal Distress, Meconium Stained Liquor, Preterm Birth (delivery before 37 weeks of gestation), Low Birth Weight.Women were followed at 6 weeks of post-partum period for resolution of symptoms as well as for normal or altered LFT.

Results

1. Incidence of obstetric cholestasis

During the course of study period (January 2019- December 2019) about 3500 patients were screened, 70 patients were found to have obstetric cholestasis. The incidence hence was found to be 2%.

2. Background Characteristics

Parameters	N(Number)	Percentage
Maternal Age		
<20years	3	4.29%
20-24years	37	52.86%
25-29years	15	21.43%
30-34years	10	14.29%
>35years	5	7.14%
Gestational Age At Diagnosis		
<28 Weeks	3	4.29%
28-32weeks	10	14.29%
32-36weeks	47	67.14%
>36weeks	10	14.29%
Gestational Age At Delivery		
<28 Weeks	5	7.14%
28-32weeks	10	14.29%
32-36 Weeks	10	14.29%
>36 Weeks	45	64.29%
Parity		
Primigravida	45	64.29%
Multigravida	25	35.71%
Smoking Habit		
Smoker	5	7.14%
Non Smoker	65	92.86%

Most of the patients belonged to age group 20-24 years. (52.86%), of gestational age 32-36 weeks at diagnosis (67.14%), of>36 weeks gestational age at delivery (64.29%), mostly primigravida(64.29%) and non smoker(92.86%).

3. Maternal Outcomes

Parameters	Number	Percentage
Mode Of Delivery		
Vaginal Spontaneous	10	12.5% (Total 47.14%)
Induced	13	16.25%
Instrumental	10	12.5%
Lscs Elective	10	12.5% (Total 52.86%)
Failed Induction	5	6.25%
Msl And Fetal Distress	12	15%
Relief With Ucda		
1 Week	38	54.29%
>1 Week	32	45.715%
Postpartum Hemorrhage	11	15.71%
Altered Coagulation	8	11.42%
Prom	25	35.71%
Altered Lipid Profile	17	24.29%
Insomnia	12	17.14%

47.14% Patients had vaginal delivery of which 12.5% was spontaneous, 16.25% was induced, and 12.5% was instrumental.52.86% patients delivered by lower segment caesarean section of which 12.5% was elective, 6.25% was due to failed induction, and 15% was due to meconium stained liquor and fetal distress.
54.29% patients got relief from pruritus in 1 week of administration of UDCA. Regarding complications, about 15.71% landed in postpartum hemorrhage, 11.42% had altered coagulation profile,35.71% had preterm labour, 24.29% had altered lipid profile and 17.14% had insomnia.

4. Maternal Biochemical Profile in Association With Meconium Stained Liquor.

Meconium Stained Liquor	N	Mean	Upper Limit Normal In Pregnancy	Results Range

SERUM (Mg/Dl)	YES	34	0.74	0.8	0.6-0.9
Bilirubin	No	36	0.74		
Sgot (Iu/L)	Yes	34	65.65	30	22-146
No		36	55.42		
Sgpt (Iu/L)	Yes	34	62.54	32	42-124
No		36	53.00		
Ggt (Iu/L)	Yes	34	37.22	42.9	18-66
No		36	35.58		
Sap (Iu/L)	Yes	34	469.35	418	380-786
No		36	427.82		

Mean serum bilirubin level in patients with obstetric cholestasis is 0.74 mg/dl. Highest serum bilirubin value – 0.9 mg/dl. Lowest serum bilirubin value – 0.6 mg/dl.
Mean SGOT level in patients with obstetric cholestasis – 60.5 IU/L. Highest SGOT value – 146 IU/L. Lowest SGOT value – 22 IU/L
Mean SGPT level in patients with obstetric cholestasis – 57.8 IU/L. Highest SGPT value – 124 IU/L. Lowest SGPT value – 42 IU/L.
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
Mean SAP level in patients with obstetric cholestasis – 448.6 IU/L. Highest SAP value – 786 IU/L. Lowest SAP value – 380 IU/L

5. Fetal Outcomes

Parameters	Number	Percentage
Low Birth Weight	15	21.4%
Preterm	25	35.71%
SGA	21	30%
Abnormal CTG	11	15.71%
Meconium Stained Liquor	34	48.571%
Respiratory Distress	8	11.42%
Nicu Admission	15	21.4%
Intrauterine Death	1	1.43%%

21.4% of babies had low birth weight, 35.71% were preterm, 30% small for gestational age, 15.71% had abnormal CTG, 48.57% had meconium stained liquor, 11.42% had respiratory distress, 21.4% needed NICU admission and 1.43% had intrauterine death.

Discussion

Obstetric Cholestasis is a irreversible condition which presents in second to third trimester. It is characterised by pruritus affecting palms and soles, elevated liver enzymes specially bile acids. It usually resolves after delivery[12].
Incidence of obstetric cholestasis in this study was found to be 3% when compared with studies of Padmaja et al[13] and Geenes V[14] et alwho found incidence of 8.2% and 6.5% respectively. Our results were consistent with studies of Hafeez et al[15], Sohail et al[16], Furrer et al[17], and Rook et al[18] who found incidences to be 3.1%, 2.8%, 2.3%,1.9%. The variation may be attributed to ethnicity, dietary habits, environmental factors or sample size calculation.
Most of the patients in this study belonged to age group 20-24 years (52.86%) and of gestational age 32-36 weeks (67.14%). Clinicians often recommend management ranging from surveillance to iatrogenic delivery to prevent the risk of intrauterine death between 36-40 weeks, though evidence is scarce[19]. Studies by authors Rook et al (37 W)[18], Medda et al (37.28W)[20], Alakananda et al[21](37+1.7W) which was not consistent with my study. This can again be attributed to the extensive monitoring in my study in assessing for the clinical history and biochemical monitoring. This may be again be due to ethnicity and dietary factor variations of different study populations.
In the current study 47.14% patients had vaginal delivery of which 12.5% was spontaneous, 16.25% was induced, and 12.5% was instrumental. Total number of vaginal deliveries was almost comparable to studies by by Mahajan et al[22] (50.67%), Hak et al[23] (50.67%) and Ghimire et al[24] (51.25%) .Vaginal delivery both spontaneous and induced was 28.75% and 12.5% instrumental. Our result was consistent with Sultana et al who found a total of 46.37% had vaginal delivery and 13.33% instrumental delivery.
52.86% patients delivered by lower segment caesarean section of which 12.5% was elective, 6.25% was due to failed induction, and 15% was due to meconium stained liquor and fetal distress. The total number of caesarean section was comparable to observations by Sultana et al[25] and Ghirmire et al[24].
In present study, MSL and fetal distress was noticed in 15% of cases which was not consistent with findings of Sultana et al[25] (20%) Singla et al(26)((32.5%), Ghimire et al (32.5%) and Medda et al[20] (42%) who found higher incidence of MSL and Sharma et al[23]((8.33%) who found lower incidence of MSL. This variability in my study was due to regular antenatal check up of the study population and early intervention in form of UDCA. All of the sample size were booked cases. Our findings on fetal distress were not consistent with Medda et al[20] (23%), Ghimire et al (26.25%)[24] and Singla et al (17.5%)[26] since strict monitoring of fetal heart rate was done and necessary interventions like starting of intravenous drip , left lateral position and continuous support during labor and encouraging the presence of birth attendant were present. Sultana et al[25] found higher incidence of MSL i.e. 33.3% may be because they studied unbooked cases. In obstetric cholestasis, bile acid increases colonic motility stimulation leading to passage of meconium and foetal distress which further leads to hypoxia and passage of meconium.
PROM was found in 25 (35.71%) cases. No clear reason for occurrence of Prom in obstetric cholestasis could be found. This could be attributed to could be to altered biochemical changes and added anxiety of parturient mothers. The finding were not consistent with Singla et al (20%)[26]. Ghimire et al (10%)[24] and Medda et al (10%)[20] who found lower incidences of PROM.. This can again be attributed to the ethnicity, anxiety level variations and food habits which lead to varied levels of altered liver enzymes.
In Obstetric Cholestasis, pruritus is specifically confined to palm and sole and mainly at night. This pruritus leads to sleep disturbances in patients with OC. In my study most subjects complained of generalised pruritus which prevented them from getting adequate sleep. Insomnia in present study was 17.14% % which was not comparable to studies done by authors as Medda et al (60%)[20] and Alakananda et al (65%)[21]. Patients in my study did not complain of skin rash nor presented with clinical jaundice. 54.29% patients got relief from pruritus in 1 week of administration of UDCA, rest patients took more than 1 week for relief of symptoms. The reason may be attributed to early administration of UDCA in this study.

In present study, alteration in coagulation profile was 11.42 % which was not comparable to that of Medda et al (19%)[20]. Patients presented with raised PT INR in present study. Patients with deranged coagulation were given Vitamin K injection on five consecutive days. The rate of PPH in present study was 15.71% which was not comparable to those observed by Medda et al (10%)[20] and Ghimire et al (11.25%)[24] or Dodampahala et al[27] (29.6%) .Our results were comparable with Mahajan et al[22] who observed 16% rates of PPH. We administered Vit K and UDCA to patients with deranged coagulation and transfused FFP in patients with raised serum bilirubin.Some amount of PPH is expected in patients with Obstetric Cholestasis which cannot be prevented altogether.PPH that occurred in our patients was mild and managed medically.

Abnormalities in transaminase, GGT, bilirubin and or bile salts are consistent with diagnosis of obstetric cholestasis. The most commonly elevated LFTS are transaminase and bile acids[12].Various studies have reported elevated levels of GGT and serum bilirubin upto 50% and 22-56%, but clinical jaundice is less[28]. In our study GGT was raised in 33% of patients. Since bile salt estimation was not available at our centre at the time of study, we could not estimate bile salt levels in our study. There was no correlation between serum bilirubin, SGOT, GGT levels with meconium stained liquor, but some amount of correlation between SGPT and SAP with meconium stained liquor. No supporting studies could be found regarding this finding.

40% of babies had low birth weight, 35.71% were preterm, 30% small for gestational age, 15.71% had abnormal CTG, 48.57% had meconium stained liquor, 11.42% had respiratory distress, 30% needed NICU admission and 4.2% had intrauterine death.

Few researchers found correlation of Serum bile acids with foetal complication but that was not elucidated in present study because of non-availability of serum bile acid testing. Percentage of preterm birth in present study was found to be 35.71% with 45 cases delivered at >36 weeks,10 cases at 32-36 weeks, 10 cases at 28-32weeks and 5 cases at<28 weeks. The findings does not correlate with studies of Padmaja et al (24.4%)[13], Sohail et al (25.8%)[16], Alakananda et al (23%)[21] and others. Preterm birth was mostly due to PROM in my study.

In the current study 15.71% had abnormal CTG, 48.57% had meconium stained liquor,11.42% had respiratory distress. Obstetric Cholestasis has been related with high incidences of perinatal mortality(35/1000), meconium stained liquor(45%),preterm labour(44%) and fetal distress(22%)[29-30].

LBW seen in 21.4% of cases in present study which was again not comparable to other study of Sohail et al(17.1%)[16] or Medda et al(32%)[20], but comparable with Singla et al (21.5%) and Alakananda et al(23%)[21]. Medda et al(32%)[20]found higher LBWs rate which may be due to elective early induction in study by Medda et al. LBW in the current study was mostly due to preterm delivery.

In present study, the rate of NICU admission was 21.4% of cases which was comparable with other study of Alakananda et al(21%)[21]. Geenes et al[31] found less NICU admission which may be due to good antenatal surveillance and better environmental and socio-demographic factor. NICU admission in the current study was mostly due to preterm birth, low birth weight, respiratory distress and few with meconium aspiration syndrome.

Percentage of IUFD in present study was 1.43% which was somewhat comparable with other studies like those of Alakananda et al (2%)[21], Medda et al (2%)[20]. In the current study there was only one case of IUFD occurred in booked case who admitted for induction for obstetric cholestasis with PIH who landed in antepartum eclampsia. She needed to be taken for emergency LSCS due foetal bradycardia, but baby could not be revived. Exact pathophysiology about fetalrisks in obstetric cholestasis cannot be understood hence fetal surveillance is always not helpful to prevent fetal distress[32]. Some studies report about 2.5-11% of still birth[29].

Conclusion

Obstetric cholestasis causes benign maternal complications like pruritus, insomnia, increases chances of operative delivery. Foetal complications are are quite significant like low birth weight, meconium aspiration and NICU admission. Hence considering the adverse effects on foetus, pregnant women should be judiciously followed through the antenatal period till delivery. Decision regarding early induction should be taken considering risk of prematurity, low birth weight and NICU admission.

Limitations

Since this study was taken in tertiary hospital which deals with high risk pregnancy cases bit more, results cannot be extrapolated to general population. Only UDCA was used in present study and no other drugs were studied. We could do only biochemical tests which were available at our centre.

References

1. Fisk NM, Storey GNB. Fetal outcome in obstetric cholestasis. Br J Obst Gynaecol 1988;95:1137–43.
2. Laatikainen T, Ikonen E. Fetal prognosis in obstetric hepatosis. Ann ChirGynecFenniae 1975;64:155–64
3. Rioseco AJ, Ivankovic MB, Manzur A, et al. Intrahepatic cholestasis of pregnancy – a retrospective case-control study of perinatal outcome. Am J ObstetGynecol 1994;170:890–5
4. CESDI Consortium. Study of Antepartum Term Stillbirths. Maternal and Child Health Research Consortium. Confidential Enquiry into Stillbirths and Deaths in Infancy. 5th Annual Report, 1995, pp 41–50
5. 5.Abedin P, Weaver JB, Eggington E. Intrahepatic cholestasis of pregnancy: prevalence and ethnic distribution. Ethnicity Health 1999;4:35–7
6. . Reyes H. Intrahepatic cholestasis. A puzzling disorder of pregnancy. J Gastroenterol Hepatol 1997;12:211–6
7. Roger D, Vaillant L, Fignon A, et al. Specific pruritic diseases of pregnancy – a prospective study of 3192 pregnant women. Arch Dermatol 1994;130:734–9
8. Shanmugam S, Thappa DM, Habeebullah S. Pruritus gravidarum: a clinical and laboratory study. J Dermatol 1998;25:582–6
9. Ylostalo P, Ylikorkala O. Itching during pregnancy. Ann ChirGynecFenniae 1975;64:123–7
10. Glantz A, Marschall HW, Mattsson LA. Intrahepatic cholestasis of pregnancy: relationships between bile acid levels and fetal complication rates. Hepatology 2004;40:467–74
11. Gabzdyl EM, Schlaeger JM. Intrahepatic cholestasis of pregnancy: a critical clinical review. J Perinat Neonatal Nurs 2015;29(1):41-50.
12. Royal College of Obstetricians and Gynaecologists. Obstetric cholestasis. Green-Top Guideline No 43. 2011
13. Padmaja M, Pal B, Gupta JK, et al. A study of obstetric cholestasis. J ObstetGynaecol India 2010;60(3):225-31.
14. Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. World Journal of Gastroenterology 2009;15(17):2049-66.
15. Hafeez M, Ansari A, Parveen S, et al. Frequency of intrahepatic cholestasis of pregnancy in Punjab Pakistan: a single centre study. J Pakistan Med Assoc 2016;66(2):203-6.
16. Sohail S, Dar LR, Munawar S. Perinatal outcome in pregnancy complicated by obstetric cholestasis. PJMHS 2016;10(1):262
17. Furrer R, Winter K, Schäffer L, et al. Postpartum blood loss in women treated for intrahepatic cholestasis of pregnancy. ObstetGynecol 2016;128(5):1048-52
18. Rook M, Vargas J, Caughey A, et al. Foetal outcomes in pregnancies complicated by intrahepatic cholestasis of pregnancy in a Northern California cohort. PLoS One
19. Henderson CE Shah RR Gottimukkala , S Ferreira , KK Hamaoui ,Mercado .Primum non nocere: how active management became modus operandi for intrahepatic cholestasis of pregnancy .Am J Obstet Gynecol.2014 ; 211:189-196.

20. Medda S, Sengupta S, Palo U. A study of the outcome of pregnancy complicated by obstetric cholestasis. Int J Reprod Contracept Obstet&Gynecol 2018;7(3):996- 1001.
21. Alakananda, Bhattacharrya A, Kavita. Foeto-maternal outcome in intrahepatic cholestasis of pregnancy. Sch J App Med Sci 2016;4(10D):3837-41
22. Mahajan N, Afzal A, Lone MI. Outcome of pregnancy complicated by obstetric cholestasis: a prospective study. Int J Sci Stud 2017;5(3):271-4.
23. Hak J, Sharma N. Maternal and perinatal outcome in patients with cholestasis of pregnancy. J K Science 2015;17(4):168-71.
24. Ghimire SP, Ghimire A, Jha GS, et al. Foeto-Maternal outcomes in intrahepatic cholestasis in pregnancy in a tertiary care centre in Eastern Nepal. Journal of Nobel Medical College 2016;5(1):20-5.
25. Sultana R, Sarwar I, Fawad A, et al. Neonatal outcome in obstetric cholestasis patients at Ayub Teaching Hospital Abbottabad. J Ayub Med Coll Abbottabad 2009;21(4):76- 8
26. Singla S, Aggarwal P, Mittal A. Study to show the effect of intrahepatic cholestasis of pregnancy on perinatal outcome in uncomplicated pregnancy. J Evolution Med Dent Sci 2016;5(69):4964-6.
27. Dodampahala SH, Pieris H, Chandrasena LG, et al. Presence of obstetric cholestasis in mothers presenting with pruritus in pregnancy: in a low resource South Asian setting. Adv Reprod Sci 2016;4(2):37-45.
28. Kenyon AP, Girling JC, Obstetric Cholestasis. In Studd J(Editor), Progress in Obstetrics and Gynecology, Edinburg: Churchill Livingstone,2005:37-56.
29. Rioseco AJ, Ivankovic MB, Manzur A et al, Intrahepatic Cholestasis of Pregnancy: a retrospective case control study of perinatal outcome. Am JObstetGynecol 1994; 170:890-4.
30. Fish NM, Storey GN, Fetal Outcome in Obstetric Cholestasis. Br J ObstetGynaecol 1988; 95,1137-43.
31. Geenes V, Chappell LC, Seed PT, et al. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: a prospective populationbased case-control study. Hepatology 2014;59(4):1482- 9
32. Alsulyman OM, Ames Castro M et al: Intrahepatic Cholestasis of Pregnancy: Perinatal outcome with expectant management. Am J ObstetGynaecol 1996, 175 :957-60.

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