IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 2 Ser.8 (February. 2020), PP 28-32
www.iosrjournals.org

A Study of Obstetric Cholestasis in Goa Medical College.

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Objective(s): *To study the epidemiology and outcome of pregnancy complicated by obstetric cholestasis (OC) in Goa Medical College.*
Methods(s): *Prospective case series of 50 women with OC at Goa Medical College, a tertiary government teaching hospitalfrom August 2018 to September 2019. Statistical analysis was performed using SPSS 22. A p value <0.05 was considered statistically significant using z test.*
Results: *The incidence of OC was 1.53%. The most common symptom was generalized pruritus which appeared after 28 weeks in 88%of cases. A higher incidence of meconium staining in amniotic fluid at delivery (20% vs 8%, p<0.01) and preterm premature rupture of membranes (10% vs 1%, p<0.01) was noted with a significant increase in preterm delivery rate (26% vs 9%,p<0.01). The rate of caesarean section was88%. There was no statistically significant difference found in the cardiotocography tracings, 1-5 minute Apgar score <7, intrauterine growth restriction(IUGR), neonatal intensive care admission or perinatal mortality. There was one case of postpartum hemorrhage.*
Conclusion: *The incidence of OC is not very high in this population. Perinatal outcome is good in actively managed women, perhaps due to a high level of vigilance and also a high intervention rate.*
Key words: *obstetric cholestasis, perinatal mortality.*

Date of Submission: 30-01-2020 Date of Acceptance: 15-02-2020

I. Introduction

Obstetric cholestasis (OC), also known as intrahepatic cholestasis of pregnancy is a hepatic disease unique to pregnancy which presents with intense generalized pruritus without any skin rash[1].It is a condition caused by maternal liver dysfunction during pregnancy and blood tests reveal increased levels of one or more of the liver enzymes[2].The pathophysiology of intrahepatic cholestasis is not yet certain [3]. Other common causes of itching and abnormal liver function tests (LFTs) should be excluded before making a diagnosis of obstetric cholestasis [1,2]. Postnatal resolution of pruritus and abnormal LFTs should be confirmed to establish the diagnosis[2].

The recognition of the entity of OC lies in the significance of its association with adverse pregnancy outcome. The potential risks are intrauterine foetal death, prematurity (usually iatrogenic), foetal distress and postpartum haemorrhage (PPH)[3-6]. It is also associated with significant maternal morbidity due to persistent itching and consequent sleep deprivation[2].

Our study was aimed at determining the incidence of OC in our hospital, studying the course of pregnancy and evaluating the pregnancy outcome in these women.

II. Method

This prospective case series study was conducted in the Department of Obstetrics and Gynaecology, Goa Medical College. The medical records of all women with OC who delivered between August 2018 and September 2019 were reviewed.Two women were chosen as control for each case, the woman delivering before and after the OC case. From the case records the patient profile, complaints, associated medical and obstetric complications were noted. The records of investigations, treatment and the pregnancy outcome were studied.

The diagnosis of OC was made on the basis of the symptom of persistent generalized pruritus, biochemical evidence of altered LFTs and the remission of both following delivery. Pregnancy specific ranges of LFTs were used. For the transaminases, gamma glutamyl transferase (GGT) and bilirubin in pregnancy, the upper limit of normal value is 20% lower than that in the non pregnant state. Alkaline phosphate (ALP) is raised normally in pregnancy and is considered abnormally high if there is at least a three fold increase over the non-pregnant normal value (upper limit of normal range). Other causes of altered LFTs were excluded by hepatitis serology, hepatobiliary sonography and liver autoimmune screen (for primary biliary cirrhosis) wherever indicated.

The monitoring of women with OC included regular prenatal visits with LFTs every 7 days till 32 weeks with admission at 32 weeks. Further foetal surveillance was done with daily maternal recording of fetal movements, regular sonography including amniotic fluid index every 7 days and twice weekly nonstress test

(NST) beginning at 32 weeks of gestation. The controls had regular prenatal visits and NST as needed for obstetric indications.

We noted the occurrence of complications of pregnancy including preterm premature rupture of membranes (PPROM), (defined as the occurrence of spontaneous rupture of membranes before the onset of labor in pregnancies <37 weeks of gestation) and preterm delivery (defined as delivery at <37 completed weeks of gestation). We also noted the mode of delivery, the cardiotocographic findings during fetal surveillance, the presence of meconium during delivery, Apgar score at 1 and 5 minutes, intrauterine growth restriction (IUGR) (defined as birth weight <10th percentile for gestational age), need for neonatal intensive care (NICU) admission and perinatal mortality.

Statistical analysis was performed using the z test when appropriate. A p value <0.05 was considered statistically significant.

III. Results

During the study period 3256deliveries were performed in our institution. Of these women, 50 (1.53%) were diagnosed with OC. The mean age of these women was 26 years (19-33 years). Thirty one were primiparous and of the 19 who were parous women nine (47.3%) had a previous history of cholestasis. Women in the study group and the control group were similar in age and parity (Table1).

The most common symptom seen in these women was generalized pruritus worsening at night, which was seen in 88% of all the women with cholestasis. The palms and the soles were worst affected by the pruritus in 28/50 (56%) women. Five women complained of high coloured urine (10%).

In 47 (94%) women the gestational age at diagnosis of OC was after 28 weeks with the maximum number being diagnosed between 28.1 to 32 weeks. In only 2/50 (4%) women the symptom started before 24 weeks (Fig 1).

Using pregnancy specific ranges for the LFTs it was found that the most frequent abnormality encountered in OC was elevated transaminases, SGOT raised in 84 %, SGPT raised in 88%, and GGT raised in 42 %). The value of SGOT and SGPT in our study ranged from 37-648IU/Land 24-606IU/L respectively. The value of ALP in these women varied from 66 to 878IU/L. Mild hyperbilirubinemia was present in 24% of the women and the highest bilirubin level noted was 2.8mg% (Table 2).

Treatment consisted of topical emollients and oral antihistaminics to all the subjects for symptomatic relief of pruritus with which 10/50 women (20%) had partial relief; 40/50 (80%) women were given ursodeoxycholic acid (UDCA) in a dose of 600-1800 mg/day. All the women reported partial or complete relief of pruritus and there was biochemical improvement in 42/50 (84%) women. 19/50 (38%) women were prescribed parental vitamin K.

The incidence of PPROM was significantly higher in the study group compared to the control group (10% vs 1%, p<0.05). The mean gestational age at delivery in the OC group ranged between 32-39 weeks with most of the women delivering at 37 weeks (Table 5). The incidence of preterm delivery was higher in the study group (26% vs 9%) (p< 0.01). It is important to mention that many of the preterm deliveries were planned elective deliveries. The caesarean section (CS) rate was higher in the study group (88% vs 55%. p< 0.01).The higher CS rate was mainly due to a higher rate of elective CS (62% vs 48 %). There was one case of PPH.In the OC groupthere wasa higher incidence of meconium staining of amniotic fluid (20% vs 8%).There were no significant differences in the incidence of abnormal cardiotocography,Apgar score at 1 minute and 5 minutes, incidence of IUGR or NICU admissions.No significant difference was noted in the perinatal mortality rates between the two groups. A single stillbirth and no neonatal deaths were observed in the OC group while in the control group there was one stillbirth, and one neonatal death.

Table 1: Age and parity

Maternal characteristics	Cholestasis of pregnancy N=50	Control N=100
Mean age	26 years (19 to 33)	27.8 (18 to 34)
Primiparous (%)	31	64
Multiparous (%)	19	36

Table 2: Liver function tests in obstetric cholestasis

LFT	Results (range)	Normal value (non pregnant upper limit)	Normal value (pregnancy upper limit)	Raised in (%)
SGOT (iu/L)	31-648	40	30	84
SGPT (iu/L)	24-606	40	32	88
GGT (iu/L)	10-989	50	41	42
ALP (iu/L)	66-878	130	41	18
SB (mg %)	0.3-2.8	0.8	0.8	24
Bile acids	0-10	10	8	88

Table 3: Complications of pregnancy

Complications	Obstetric cholestasis (n=50) (%)	Control (n=100) (%)	p value
PPROM	5 (10%)	1 (1%)	<0.01
Preterm delivery	13 (26%)	9 (9%)	<0.01
Total caesarean	44 (88%)	55 (55%)	<0.01
Elective caesarean	31 (62%)	48 (48%)	-
PPH	1 (2%)	0	-

Table 4: Gestational age at diagnosis of Obstetric Cholestasis

Gestational age	Number
<24 weeks	2
24.1 to 28 weeks	1
28.1 to 32 weeks	28
32.1 to 36 weeks	13
>36.1	6

Table 5: Gestational age at delivery in Obstetric Cholestasis

Gestational age	Number of women
32	2
33	0
34	2
35	3
36	8
37	24
38	9
39	2

Table 6: Perinatal outcome

	Cholestasis (n=50) (%)	Control (n=100) (%)	p value
Meconium staining of amniotic fluid	10 (20%)	8	<0.01
Abnormal CTG	3 (6%)	10	>0.05
Apgar <7 at 5 minute	4 (8%)	5	>0.05
IUGR	7 (14%)	9	>0.05
Neonatal ICU admission	9 (18%)	9	>0.05

Table 7: Perinatal Mortality

	Cholestasis (n=50)	Control (n=100)
Stillbirths	1	1
Neonatal deaths	0	1
Perinatal deaths	1	2

IV. Discussion

Obstetric cholestasis is influenced by genetic and environmental factors and the incidence varies between populations[3]. It is most common in Chile where 2.4% of all pregnancies are affected with 5% prevalence in women of Araucanian-Indian origin[2]. The incidence of OC among Indian women has been reported as about 1%[4,7]. We found an incidence of 1.53% in our study. However it is prudent to mention that our hospital is a tertiary referral government hospital and the incidence of high risk pregnancy is higher. Hence the incidence of OC is expected to be higher than that in the community.

The mean age was 26 years (range 19-33yrs in our study although some authors have reported that women of relatively advanced age (>35 yrs) are at increased risk of developing OC. There was no significant difference between the two groups in maternal age or parity. OC tends to recur in subsequent pregnancies in upto 60-70% of the women[3]. In the present study the recurrence rate was 47.3% among multiparous women.

In 94% of women, OC was diagnosed in the third trimester which is similar to that seen in other studies[4,7]. Generalized pruritus was the cardinal symptom in all and was most pronounced in the palms and soles in 88%of the women. It has been reported that severe pruritus of the soles of the feet may be a pointer to OC[4]. We found no case of clinical jaundice, however it has been reported in upto 10% of women[5].

Abnormalities in one or more of the transaminases, GGT, bilirubin and/or bile salts are consistent with a diagnosis of OC. The most commonly elevated LFTs have been reported as transaminases and total serum bile acids and typically the transaminases range from just normal to several hundreds[2]. In our study the

transaminases were raised in 84-88%of the women and the maximum value encountered in our study was twenty times the normal value in pregnancy. Various studies have reported that elevated levels of GGT and bilirubin have been noted in upto 50% and 22-56% patients respectively but clinical jaundice is rare[(1)].In our study we found raised levels of GGT in 42% patients and hyperbilirubinemia in 24% women. There was no case of jaundice. Bile acids were raised in 88% of cases, and formed a very significant marker for obstetric cholestasis.

Topical emollients like calamine lotion and oral antihistaminics like chlorpheniramine are safe in pregnancy and for some women may provide temporary relief of pruritus[2]. In our study 20% of the women reported relief and were able to sleep better. Several studies demonstrate that in addition to providing safe and effective relief of pruritus and improving LFTs, UDCA may improve the prenatal outcome[9,10] by preventing the accumulation of biliary constituents of maternal origin in the fetus, which may contribute to the risk of fetal distress and even stillbirth. In our study UDCA was prescribed in 80% of the women and there was partial or complete relief of pruritus in all with biochemical improvement in 94% women. Kenyon et al[4] found a high incidence of PPH in women with OC who did not receive vitamin K compared to those who did (45% vs 12%), but we found only one case of PPH, though only 42 % of the women on our study received vitamin K.

The disease has been related to a high incidence of perinatal complications including an increase in perinatal mortality rate (35/1000), a high incidence of meconium stained amniotic fluid (upto 45%), preterm labor (upto 44%), and fetal distress (upto 22%)[5,6]. Our study shows a significant increase in the incidence of PPROM, preterm delivery and caesarean section rate and meconium staining of amniotic fluid in the OC group. It has been suggested that both fetal distress and increased stimulation of colonic motility by bile acids is the cause of increased incidence of meconium staining on OC[6]. Unlike other studies we did not find a significant increase in fetal distress, NICU admissions or perinatal mortality. No association with IUGR has been reported[4,5,11] and in this study also we found no significant increase in growth restriction.

As the pathophysiological basis of the fetal risks in OC is not clear, conventional fetal surveillance is not always helpful in determining the risk of fetal compromise[11]. Increased perinatal mortality rate (1.3-3.5%) and increased stillbirth rate ranging from 2.5-11% has been reported[5]. Intrauterine fetal demise appears to be an acute anoxic event and the high concentrations of fetal bile acids may contribute to this acute event. The risk of fetal death increases near term and most deaths occur after 37-38 weeks. To avoid the risk many hospitals adopt a policy of active management with antenatal surveillance and early elective delivery at 37-38 weeks[1]. In our studyactive management including intensive fetal surveillance with delivery between 37-38 completed weeks of gestation was used.

The only stillbirth in the OC group in our study was an unbooked woman who came in at 39 weeks gestation with the complaint of loss of fetal movements and ultrasonography on admission confirmed fetal demise. The mother did not have other complications of pregnancy and the fetus was grossly normal with appropriate weight for gestational age. All the stillbirths in the control group were in unbooked women who presented with intrauterine fetal death. The neonatal death was due to extreme prematurity and IUGR.

Apart from the significant morbidity due to the intense pruritus, OC does not seem to have serious health consequences for the mother. There is an increased risk of delivery by caesarean section (25.9-36%)[5] though it is not clear whether the high rates are due to active management or because of complications as a result of the disease or both. PPH has been observed in 2-25% patients in some studies[4,7].In our study the CS rate of 88% was high and could be attributed to the more active rate of planned intervention at term.

V. Conclusion

The incidence of OC is not very high in our hospital, a tertiary care hospital unit. Larger studies are needed to assess the correct incidence in the general population. Cholestasis of pregnancy has an adverse effect on the fetal outcome and hence early diagnosis with careful clinical examination and biochemical testing, specially bile acid estimation is essential. Affected women should be offered treatment with UDCA. This provides symptomatic relief, improvement of liver function and may contribute to improvement in the perinatal outcome. The obstetric intervention rate is high in our study as we adopted a policy of active management with close antenatal surveillance and elective delivery at 37 completed weeks to improve the perinatal outcome.

Limitations of our Study

The incidence of OC in our hospital may not be relective of the incidence in the general population as ours is a tertiary referral centre. Also we did not use steroids in the management of OC in our study, and this management option could be studied.

References

[1]. Kenyon AP, Girling JC, Obstetric cholestasis. In, Studd J. (Editor), Progress in Obstetrics and Gynaecology Edin- burgh: Churchill

Livingstone, 2005;37-56.
[2]. Royal College of Obstetricians and Gynecologists. Obstetric cholestasis. RCOG Guideline No.43, 2006.
[3]. Reyes H. The spectrum of liver and gastrointestinal disease seen in cholestasis of pregnancy. GastroenterolClin North Am1992;21:905-21.
[4]. Kenyon AP, Piercy CN, Girling J et al. Obstetric cholestasis, outcome with active management: a series of 70 cases. BJOG 2002;109:282-8.
[5]. Rioseco AJ, Ivankovic MB, Manzur A et al. Intrahepatic cholestasis of pregnancy: a retrospective case-control study of perinatal outcome. Am J ObstetGynecol1994;170:890-5.
[6]. Fisk NM, Storey GN. Fetal outcome in obstetric cholestasis. Br J ObstetGynaecol1988;95:1137-43.
[7]. Ray A, Tata RJ, Balsara R et al. Cholestasis of pregnancy. J ObstetGynecol India 2005;55:247-50.
[8]. Heinonen S, Kirkinen P. Pregnancy outcome with intra- hepatic cholestasis. ObstetGynecol1999;94:189-93.
[9]. Zapata R, Sandoval L, Palma J et al. Ursodeoxycholic acid in the treatment of intrahepatic cholestasis of pregnancy. A 12 year experience. Liver Int2005;25:548-54.
[10]. Rodrigues CM, Marin JJ, Brites D. Bile acid patterns in meconium are influenced by cholestasis of pregnancy and not altered by ursodeoxycholic acid treatment. Gut 1999;45:446-52.
[11]. Alsulyman OM, Ouzounian JG, Ames-Castro M et al. Intrahepatic cholestasis of pregnancy: perinatal outcome associated with expectant management. Am J ObstetGynecol1996;175:957-60

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