ORIGINAL ARTICLE

MATERNAL AND PERINATAL OUTCOMES IN OBSTETRIC CHOLESTASIS – DATA OF A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To find out the maternal and perinatal outcome of intrahepatic cholestasis of pregnancy.

Material and Methods: The study was conducted in the Gynae and Obstetric department of Khyber Teaching Hospital Peshawar, Pakistan. This was a retrospective data review extending over two years period (from March 2018 to March 2020). Antenatal patients having clinical and investigative findings suggestive of intrahepatic cholestasis were enrolled in the study. With a sample size of 82, patients having cholestasis due to other pathologies were excluded. Outcome measures were mean age, mean parity, and mean gestational age at diagnosis and at delivery. Type of labor, whether induced or spontaneous, mode of delivery, and indications of cesarean delivery were observed. Maternal and perinatal complications encountered like post-partum hemorrhage, preterm labor, intrauterine growth restriction, meconium aspiration, nursery, and neonatal intensive care unit admissions were noted.

Results: Mean age was 29.6±4.64, mean parity 2.8±1.68, while the mean period of gestation at diagnosis 33.46±2.67, and the mean period of gestation (POG) at delivery 37.6±2.56. Patients who delivered vaginaly were 59 (71.91%) and via cesarean delivery were 23 (28.09%). Out of 23 patients who had cesarean delivery main indications were fetal distress in 11 patients, meconium-stained liquor (MSL) found in 16(19.51%) patients, preterm labor in 3(3.65%), and preterm premature rupture of membranes (PPROM) in 3 (3.65%). Primary postpartum hemorrhage (PPH) was observed in 4(4.87%). Babies born with Apgar score less than 7 were 12(14.65%) and those admitted in nursery and NICU were 14(17%).

Conclusion: Intrahepatic cholestasis of pregnancy has a significant association with perinatal morbidity and mortality. The study found MSL in 16(19.51%) cases and fetal distress encountered in 13(15.85%) cases. 14(16.27%) newborns got admitted to nurseries and NICU. Close monitoring in the antenatal period and induction of labour at 37- 38 weeks improve the perinatal outcomes.

Keywords: Obstetric Cholestasis, Intrahepatic Cholestasis of Pregnancy, Liver Function Test.

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INTRODUCTION

Intrahepatic cholestasis of pregnancy (ICP) is a complication in 0.2-2% of pregnancies. It leads to pruritus, increased serum bile acids (BA), liver transaminases, and bilirubin[1]. Pathogenesis is unclear but hormonal changes, and the multi-drug resistance (MDR) 3 mutation gene may influence it. With a good maternal prognosis after delivery, symptoms and abnormal liver function tests are reversible. Pregnancy complications include fetal distress, spontaneous and iatrogenic preterm birth, and still birth[2,3].

None of the antenatal fetal monitoring modalities cardiotocography (CTG), ultrasound, and doppler scans are reliable in predicting or preventing fetal death in obstetric cholestasis (OC). Placental insufficiency, intrauterine growth restriction (IUGR), and oligohydramnios are not features of the disease. Similar poor outcomes cannot be predicted by biochemical results and delivery decisions shouldn't be based on lab results alone[4,5].

According to Royal College of Gynecologists (RCOG) guidelines no sufficient data exists to practice early (at 37 weeks period of gestation) induction of labour with the objective to reduce the incidence of stillbirths. Many advocate deliveries at 38 weeks of gestation except in cases of severely deranged liver biochemical parameters where early delivery is advised [6,7].

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MATERIALS AND METHODS

The study was conducted in Gynae and Obstetric department, Khyber Teaching Hospital Peshawar, Pakistan from March 2018 to March 2020. It is a retrospective observational hospital-based study. The sample size was 82. All admitted women diagnosed with OC who were de-

livered at the hospital were included in the study. Patients were identified from the medical record maintained at the department. Data was collected on a structured proforma where all the necessary patient data including the clinical details such as age parity, symptoms like itching, rash, the color of urine and stool, and appetite collected from patients' files and registers. Recorded family history of intrahepatic cholestasis and drug history especially use of oral contraceptive pills. Detailed general physical examination (GPE) and systemic examination of patients were also noted. Investigations were full blood count (FBC), urine routine examination (R/E), liver function tests, viral serology hepatitis B, C, D, and E, abdominal ultrasound, obstetrical scan, and doppler scan also carried out.

OC was diagnosed if the patient had persistent pruritis and abnormal liver function tests in absence of other liver diseases. Cases with other causes of pruritis during pregnancy like hepatitis and liver involvement due to pre-eclampsia were excluded. Other liver diseases like hepatitis, biliary cirrhosis, symptomatic cholelithiasis, Wilsons disease, Acute Fatty Liver of Pregnancy (AFP) and coagulopathies, and liver tumors were also excluded. Outcomes measured were mean age, mean parity, mean POG, labour - whether spontaneous or induced, mode of delivery - vaginal or operative, maternal complications like PPH and fetal complications like preterm labour, IUGR, meconium aspiration syndrome (MAS), and NICU admissions were also noted. Intrauterine deaths and neonatal deaths were also noted. All data were collected and analyzed using descriptive statistics focusing on frequency, mean, and percentages.

RESULTS

The study included 82 antenatal patients with obstetric cholestasis. The mean gestational age at diagnosis was 33.46 ± 2.67 weeks and the mean gestational age of the patient at delivery was 37.6 ± 2.64 weeks. The mean age of the patient was 29.6 ± 4.64 and the mean parity was 2.8 ± 1.68.

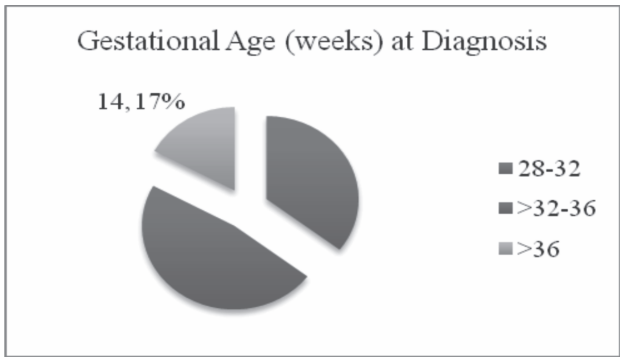

Fig 1: Percentage distribution of gestational age at diagnosis of Obstetric Cholestasis

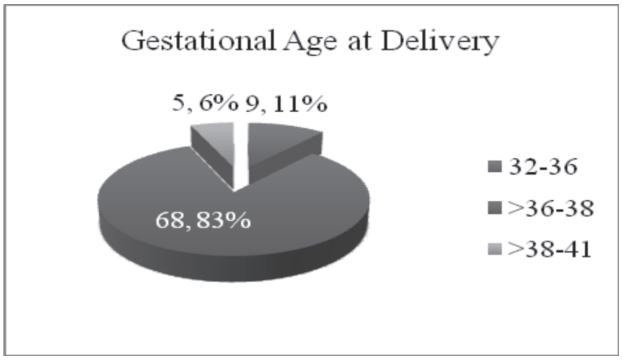

Fig 2: Percentage distribution of gestational age at delivery

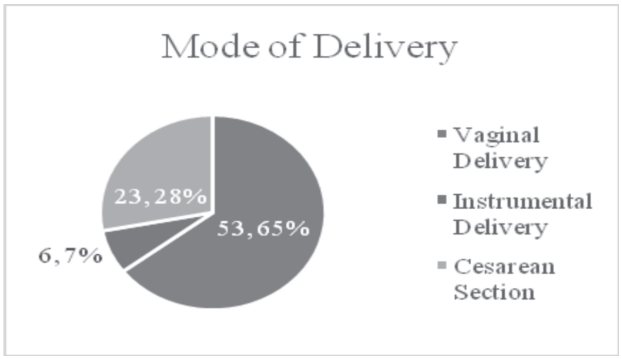

Fig 3: Percentage distribution of Mode of Delivery

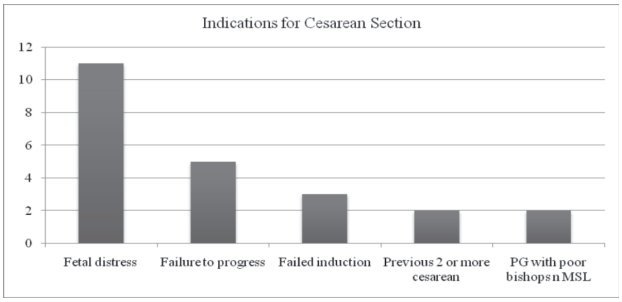

Fig 4: Indication of Cesarean Section (N = 23)

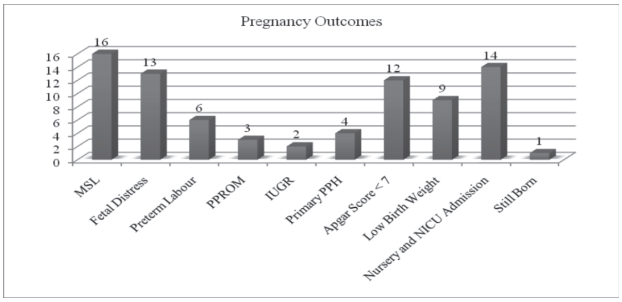

Fig 4: Outcome of Obstetric Cholestasis of Pregnancy (N=82)

Table 1: Risk Factors of Obstetric Cholestasis

Risk Factor	Cases	Percentage
History of Pruritis in previous pregnancy	17	20.70
Family history	6	7.31
Previous use of oral contraceptive Pills	5	6.09
Multiple pregnancy	4	4.87
History of gall stones	2	2.43
Co-existent diabetes	4	4.87
Associated mild hypertension	7	8.5
Diabetes and hypertension both	1	1.22

DISCUSSION

Genetic and environmental factors are related to the causation of obstetric cholestasis which has varied incidence in different parts of the world. Various studies reported the incidence of obstetric cholestasis as 0.7 _ 1.8%[8]. Prevalence of OC in a population of the South Birmingham area reported an overall prevalence of 0.7% [9].

In our study prevalence was 1.6%. Mean age was 28.6±4.64, mean parity 2.1±1.43, mean POG at diagnosis of OC 33.46±2.67, and mean POG at delivery was 37.4 ±2.76. In a study on obstetric cholestasis Asma Afzal found out that the mean age of patients was 24.79 years, the mean POG at delivery was 38.4 and 2/3rd patients were primi gravidas [9]. In another study by Nira Singh mean age of patients was 26.59 years and the mean POG was 32.53 weeks at diagnosis.

Obstetric cholestasis usually presents in the second trimester with a history of pruritis which is typically worst at night, pale stools, dark urine, and jaundice may also occur. Nira Singh found that 89.25% of patients had itching over the abdomen and over palms and soles [10]. In another study, itching was noted over the abdomen by 75% of patients and over the palms and soles by 25% of patients[11]. Factors which increase the risk of OC are personal or family history of OC, multiple pregnancies, hepatitis carriers, presence of gall stones, and women of Indian and Pakistani descent are a twofold increase in risk[11]. In our study history of pruritis in previous pregnancies was present in 17(20.7%) and a family history of OC was present in 6(7.31%) patients

In a study by Chloe Arthius 11.4% had a positive family history, 8.6% of patients had a history of OCPs intake, and 2.8% cases had gall stones[12]. In a study on OC patients Nira Singh observed that OC was complicated by Diabetes in 17.85% cases, hypertensive disorders of pregnancy in 15.47%, 13% cases delivered preterm, 10% had twin delivery and PPH occurred in 4% of patients.[10]

The preterm labour mechanism in OC is not well defined. However, an increased response of myometrial strips is found to oxytocin and when incubated with cholic acid there was increased oxytocin receptor expression. [13] Prevalence of OC was significantly higher among women with morbid obesity, Gestational Diabetes Mellitus (GDM), and preeclampsia[14,15] There is a relationship between bile acid, cholesterol, and glucose homeostasis. Primary bile acid receptor Fernicsoid X receptor (FXR) influences normal glucose homeostasis. Martineau and Rakor compared the effect of metformin versus Ursodeoxy Cholic Acid (UA) and advocated the use of both medicines for improving neonatal outcomes[16]. In our study coexistent diabetes was present in 4(4.87%) patients, associated with mild hypertension seen in 7(8.5%) cases, and both diabetes and hypertension are seen in one patient only.

Naga found an association between mild preeclampsia 31.6% GDM 20%, Pregnancy Induced Hypertension (PIH) 6.6%, hyperbilirubinemia 5% preterm delivery 23%, and PPH in 1.6% of cases of OC [8]. Women with obstetric cholestasis should have their liver function tests (LFTs) monitored weekly. Clotting studies should also be carried out. The pregnancy-specific reference range of liver function tests is 20% lower than the non-pregnant range[16,17]. In our study mean bilirubin was 1.06±56.72 and mean SGPT was 26.79 ±37.46 iU/ml. Naga also found out that transaminase was mostly elevated in 85% of cases of OC. Urine bile salts and pigments were detected in 8.3% of case[8.]

Ruth reported a significant relationship between OC and multiple births. In the study, multiple births were found in 4(4.87%) cases. Various studies suggested that estrogens are involved in pathogeneses of OC. Also, the predominant appearance of OC in the 3rd trimester is correlated with high estrogen production. OC is four times higher in twin pregnancy and also in women using oral contraceptives with high estrogen content [14].

Medical therapies such as the use of Vitamin K, topical emollients, anti-histamines, and Ursodeoxycholic Acid (UDA) are advised. A low-fat diet is also advised. UDA is highly effective in decreasing liver enzymes and bile acid concentration. With the use of UDA, Shultz and Chappel found fewer occurrences of premature births reduced fetal distress and fewer admissions in ICU.[18,19]

Regarding mode of delivery Shirestha found out that 60.69% of patients delivered via C section, 39.27% delivered vaginaly [10]. 51.15% of labour induction was carried out at 38 weeks of gestation. Indications of cesarean section were failed induction 33% fetal distress and non-progress of labour 26%. Perinatal complications were MSL 25%, fetal distress, and abnormal CTG 70%, and 30% of babies were admitted to NICU. In another study, spontaneous delivery was (28.3%) and 71.7% were induced. Out of which 41.7% had an emergency cesarean section. Indications of cesarean section were fetal distress 71.6%, cephalopelvic disproportion (CPD) 16%, failed induction 16%, and non-progress of labour 12% [8]. Chloe Arthius observed that 82.9% had term vaginal delivery, 22.9% had cesarean section and 50% of cases were associated with adverse neonatal outcomes. Fetal distress occurred in 20% of cases. Preterm delivery was found in 12.8% cases[2.4]

In Gabzedyl's study intrauterine death occurred in 0.4% of cases[20]. Asma Afzal's observations were sponta-

neous onset of labour in 50.67% of cases of OC [9].

In this study of 82 patients with obstetric cholestasis 53 (64.63%) cases were of normal vaginal delivery, 6(7.31%) instrumental delivery and 23 (28.04%) patients underwent cesarean sections. Out of 23 patients who had caesarian sections main indications were fetal distress in 11 cases, failure to progress in 5, and failed induction in 3 patients.

The newborn risk of respiratory distress syndrome was found 2.5 times higher than in control infants (28.6 vs 14%). Raised bile acid level has a direct effect on neonatal lungs which could be a bile acid pneumonia.[20]

Prevalence of OC was significantly higher among women with morbid obesity, Gestational Diabetes Mellitus (GDM), and preeclampsia[14,15] There is a relationship between bile acid, cholesterol, and glucose homeostasis. Primary bile acid receptor Fernicsoid X receptor (FXR) influences normal glucose homeostasis. Martineau and Rakor compared the effect of metformin versus Ursodeoxy Cholic Acid (UA)and advocated the use of both medicines for improving neonatal outcomes[16]. In our study coexistent diabetes was present in 4(4.87%) patients, associated with mild hypertension seen in 7(8.5%) cases, and both diabetes and hypertension are seen in one patient only.

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CONCLUSION

Intrahepatic cholestasis of pregnancy has a significant association with increased perinatal morbidity and mortality. In our study, MSL was found in 16(19.51%) cases and fetal distress was encountered in 13(15.85%) cases. 14(16.27%) newborns got admitted to nursery and NICU. Close monitoring in the antenatal period and induction of labour at 37- 38 weeks can improve the perinatal outcome. Various studies advocate delivery at 38 weeks of gestation except in cases of deranged liver biochemical parameters where early delivery is advised.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Mazhar T,: Data collection, literature search, writing up.

Niaz H: Data analysis

Bukhari N: Conceived the idea

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.