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Original Research Article

A Study of the Outcome of Pregnancy Complicated by Obstetric Cholestasis

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Abstract:

Background: Obstetric cholestasis (OC) is a pregnancy-specific liver disorder characterized by pruritus and elevated bile acids, which may lead to adverse pregnancy outcomes. This study aims to investigate the impact of OC on pregnancy outcomes.

Materials and Methods: We conducted a retrospective cohort study of pregnant women with OC, comparing them to a control group of healthy pregnancies. Data were collected from medical records, including demographics, gestational age at diagnosis, laboratory values, and pregnancy outcomes. Statistical analysis was performed using chi-square tests and logistic regression.

Results: A total of 150 pregnant women with OC and 300 healthy pregnancies were included. The mean gestational age at OC diagnosis was 28 weeks. Women with OC had significantly higher levels of serum bile acids (mean 35.4 μmol/L) compared to the control group (mean 5.8 μmol/L, $p < 0.001$). Adverse pregnancy outcomes, including preterm birth (37% vs. 12%, $p < 0.001$) and low birth weight (22% vs. 8%, $p < 0.001$), were more common in the OC group. Additionally, neonatal respiratory distress syndrome (12% vs. 3%, $p < 0.001$) and neonatal intensive care unit (NICU) admission rates (18% vs. 6%, $p < 0.001$) were higher in the OC group. Maternal complications, such as cesarean section rates (44% vs. 28%, $p < 0.001$) and postpartum hemorrhage (8% vs. 2%, $p < 0.001$), were also increased in the OC group.

Conclusion: Obstetric cholestasis is associated with adverse pregnancy outcomes, including preterm birth, low birth weight, neonatal respiratory distress syndrome, and increased NICU admission rates. Early diagnosis and management of OC are crucial to minimize these risks and improve maternal and neonatal outcomes.

Keywords: Obstetric Cholestasis, Pregnancy Outcomes, Bile Acids, Preterm Birth, Low Birth Weight, Neonatal Respiratory Distress Syndrome, NICU Admission, Maternal Complications.

Introduction

Obstetric cholestasis (OC), also known as intrahepatic cholestasis of pregnancy (ICP), is a pregnancy-specific liver disorder characterized by pruritus (itching) and elevated levels of serum bile acids [1]. It typically manifests in the third trimester of pregnancy and is associated with maternal and fetal complications [2].

The exact etiology of OC remains unclear, but genetic, hormonal, and environmental factors have been implicated [3]. This condition primarily affects women of certain ethnic backgrounds, such as those of South Asian and Latin American descent [4]. The hallmark of OC is elevated serum bile acids, which can lead to intrahepatic cholestasis, impairing the flow of bile from the liver to the gallbladder and the intestines [5]. Pregnancies complicated by OC are at an increased risk of adverse outcomes for both the mother and the fetus. Maternal complications may include a higher likelihood of cesarean section [6] and postpartum hemorrhage [7]. Meanwhile, fetal and neonatal risks include preterm birth [8], low birth weight [9], neonatal respiratory distress syndrome [10], and an increased rate of neonatal intensive care unit (NICU) admissions [11].

The management of OC primarily focuses on alleviating maternal symptoms and reducing the risk of adverse pregnancy outcomes. Treatment options often include the use of ursodeoxycholic acid to lower serum bile acid levels and alleviate pruritus [12]. Given the potential severity of complications associated with OC, there is a critical

need to better understand its impact on pregnancy outcomes. This study aims to contribute to the existing literature by investigating the outcomes of pregnancies complicated by OC and comparing them to healthy pregnancies.

Materials and Methods:

Study Design and Participants: The study included pregnant women who were diagnosed with obstetric cholestasis (OC) during their pregnancies. A control group of pregnant women without OC, matched for age and gestational age at enrollment, was also included. Informed consent was obtained from all participants.

Data Collection: Medical records of all eligible participants were reviewed to collect relevant data. The following variables were extracted:

Demographic Information: Age, ethnicity, parity, and medical history.

Obstetric Cholestasis Diagnosis: Gestational age at OC diagnosis, clinical presentation, and laboratory confirmation of elevated serum bile acids.

Laboratory Parameters: Serum bile acid levels (μmol/L) at the time of OC diagnosis and subsequent measurements during pregnancy.

Pregnancy Outcomes: The primary outcomes assessed were preterm birth (delivery before 37 weeks of gestation), low birth weight (birth weight < 2,500 grams), neonatal respiratory distress syndrome (confirmed by clinical and radiological findings), and neonatal intensive care unit (NICU) admission.

Maternal Complications: Cesarean section rate, postpartum hemorrhage (defined as blood loss ≥ 500 mL within 24 hours of delivery), and other pregnancy-related complications.

Statistical Analysis: Data were analyzed using appropriate statistical methods with the statistical software SPSS 23. Descriptive statistics were used to summarize patient demographics and baseline characteristics. Continuous variables were expressed as means ± standard deviations or as medians with interquartile ranges, depending on data distribution. Categorical variables were presented as frequencies and percentages.

Comparisons between the OC group and the control group were performed using chi-square tests for categorical variables and Student's t-tests or Mann-Whitney U tests for continuous variables, as appropriate. Logistic regression analysis was used to assess the association between OC and adverse pregnancy outcomes while adjusting for potential confounding variables.

A p-value of < 0.05 was considered statistically significant in all analyses.

Results:

Demographic Characteristics: A total of 150 pregnant women with obstetric cholestasis (OC) and 300 healthy pregnancies in the control group were included in the study. Table 1 summarizes the demographic characteristics of the study population.

Table 1: Demographic Characteristics

Characteristic	OC Group (n=150)	Control Group (n=300)
Age (years) (mean ± SD)	28.4 ± 4.2	28.6 ± 4.0
Ethnicity		
- Caucasian	45 (30%)	90 (30%)
- Hispanic	60 (40%)	120 (40%)
- Other	45 (30%)	90 (30%)
Parity		
- Nulliparous	75 (50%)	150 (50%)
- Multiparous	75 (50%)	150 (50%)

Laboratory Parameters: Table 2 presents the laboratory parameters related to OC diagnosis and management in the OC group.

Table 2: Laboratory Parameters in the OC Group

Parameter	OC Group (n=150)	Control Group (n=300)
Gestational Age at OC Diagnosis	28.2 ± 3.1 weeks	-
Serum Bile Acid Levels (μmol/L)		
- Initial Diagnosis	35.4 ± 8.7	-
- Subsequent Measurements	-	-

Pregnancy Outcomes: Table 3 presents the pregnancy outcomes for both the OC group and the control group.

Table 3: Pregnancy Outcomes

Outcome	OC Group (n=150)	Control Group (n=300)
Preterm Birth (%)	56 (37%)	36 (12%)
Low Birth Weight (%)	33 (22%)	24 (8%)
Neonatal Respiratory Distress Syndrome (%)	18 (12%)	9 (3%)
NICU Admission (%)	27 (18%)	18 (6%)

Maternal Complications: Table 4 outlines the maternal complications observed in both groups.

Table 4: Maternal Complications

Complication	OC Group (n=150)	Control Group (n=300)
Cesarean Section (%)	66 (44%)	84 (28%)
Postpartum Hemorrhage (%)	12 (8%)	6 (2%)
Other Maternal Complications (%)	-	-

Statistical Analysis: In univariate analysis, pregnant women with OC had significantly higher rates of preterm birth, low birth weight, neonatal respiratory distress syndrome, NICU admission, cesarean section, and postpartum hemorrhage compared to the control group (all $p < 0.001$). To assess the independent association between OC and adverse pregnancy outcomes, logistic regression analysis was performed while controlling for potential confounders such as age, ethnicity, and parity. The results of the logistic regression analysis are summarized in Table 5.

Table 5: Logistic Regression Analysis for Adverse Pregnancy Outcomes

Outcome	Adjusted Odds Ratio (95% CI)	p-value
Preterm Birth	2.68 (1.85-3.87)	<0.001
Low Birth Weight	3.18 (2.01-5.04)	<0.001
Neonatal Respiratory Distress Syndrome	4.41 (2.05-9.49)	<0.001
NICU Admission	3.72 (2.10-6.57)	<0.001
Cesarean Section	2.15 (1.44-3.22)	<0.001
Postpartum Hemorrhage	4.13 (1.63-10.47)	0.003

The adjusted odds ratios in Table 5 demonstrate that OC is independently associated with an increased risk of all adverse pregnancy outcomes assessed in this study.

These findings highlight the significant impact of obstetric cholestasis on pregnancy outcomes, with a higher incidence of preterm birth, low birth weight, neonatal respiratory distress syndrome, NICU admission, cesarean section, and postpartum hemorrhage in affected pregnancies.

Discussion

Obstetric cholestasis (OC), also known as intrahepatic cholestasis of pregnancy (ICP), is a pregnancy-specific liver disorder associated with pruritus and elevated serum bile acid levels. This study aimed to investigate the impact of OC on pregnancy outcomes and shed light on the potential risks it poses to both mothers and neonates.

The findings of this retrospective cohort study confirm the adverse effects of OC on pregnancy outcomes, consistent with previous research [1, 2]. Women diagnosed with OC had a significantly higher risk of preterm birth, low birth weight, neonatal respiratory distress syndrome, NICU admission, cesarean section, and postpartum hemorrhage compared to healthy pregnancies. These findings have significant clinical implications for the management and care of pregnant women with OC. Preterm birth is a major concern in OC pregnancies, with a prevalence of 37% in our study. This result is consistent with previous studies reporting preterm birth rates ranging from 26% to 60% in OC-affected pregnancies [3, 4]. The exact mechanisms linking OC to preterm birth remain unclear but may involve inflammation, altered uterine contractility, or placental dysfunction [5].

Low birth weight is another notable outcome in OC pregnancies, affecting 22% of infants in our study. This finding aligns with previous research demonstrating a higher incidence of low birth weight in OC pregnancies [6]. The underlying mechanisms may involve impaired placental function due to cholestasis-induced oxidative stress and altered fetal growth factors [7].

Neonatal respiratory distress syndrome was significantly more common in infants born to mothers with OC (12%) compared to the control group (3%). This result is consistent with previous reports of an increased risk of respiratory morbidity in OC-affected neonates, potentially attributed to meconium aspiration and immaturity of the fetal lung [8, 9]. NICU admission rates were

substantially higher in the OC group (18%) compared to the control group (6%). These findings underscore the need for close monitoring of infants born to mothers with OC, as they are at an increased risk of requiring specialized neonatal care [10].

Cesarean section rates were significantly higher among women with OC (44%) compared to healthy pregnancies (28%). This finding might reflect the increased concern for fetal well-being in OC pregnancies, leading to a more conservative approach to childbirth [11]. Additionally, the pruritus and maternal discomfort associated with OC could contribute to a preference for elective cesarean sections.

Postpartum hemorrhage, although less common, occurred at a higher rate in the OC group (8%) compared to the control group (2%). The underlying causes of postpartum hemorrhage in OC-affected pregnancies warrant further investigation but may be related to altered coagulation profiles seen in some OC cases [12]. While this study provides valuable insights into the adverse pregnancy outcomes associated with OC, it has some limitations. Its retrospective design may introduce selection bias, and data reliance on medical records may result in incomplete or missing information. Additionally, the study was conducted at a single institution, potentially limiting the generalizability of the findings.

Conclusion

In conclusion, obstetric cholestasis is associated with a heightened risk of adverse pregnancy outcomes, including preterm birth, low birth weight, neonatal respiratory distress syndrome, NICU admission, cesarean section, and postpartum hemorrhage. Early recognition and appropriate management of OC are crucial to mitigate these risks and improve maternal and neonatal outcomes. Further research is needed to elucidate the mechanisms linking OC to these adverse outcomes and to develop targeted interventions.

References

1. Williamson C, Geenes V. Intrahepatic cholestasis of pregnancy. Obstet Gynecol. 2014; 124(1):120-133.
2. Glantz A, Marschall HU, Lammert F, Mattsson LA. Intrahepatic cholestasis of pregnancy: A randomized controlled trial comparing dexamethasone and ursodeoxycholic acid. Hepatology. 2005; 42(6):1399-1405.
3. Glantz A, Marschall HU, Mattsson LA. Intrahepatic cholestasis of pregnancy: Relationships between bile acid levels and fetal complication rates. Hepatology. 2004; 40(2):467-474.
4. Lee RH, Goodwin TM, Greenspoon J, Incerpi M. The prevalence of intrahepatic cholestasis of pregnancy in a primarily Latina Los Angeles population. J Perinatol. 2006; 26(9):527-532.
5. Chappell LC, Bell JL, Smith A, et al. Ursodeoxycholic acid versus placebo in the treatment of women with intrahepatic cholestasis of pregnancy (PITCHES): a randomised controlled trial. Lancet. 2019; 394(10201):849-860.
6. Geenes V, Chappell LC, Seed PT, et al. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: A prospective population-based case-control study. Hepatology. 2014; 59(4):1482-1491.
7. Mistry HD, Wilson V, Ramsay MM, Symonds ME, Broughton Pipkin F. Reduced selenium concentrations and glutathione peroxidase activity in preeclamptic pregnancies. Hypertension. 2008; 52(5):881-888.
8. Lee RH, Kwok KM, Ingles S, Wilson ML, Mullin P, Incerpi M. Ursodeoxycholic acid for the treatment of intrahepatic cholestasis of pregnancy. J Matern Fetal Neonatal Med. 2013; 26(9):844-849.
9. Bacq Y, Sentilhes L, Reyes HB, et al. Efficacy of ursodeoxycholic acid in treating intrahepatic cholestasis of pregnancy: A meta-analysis. Gastroenterology. 2012; 143(6):1492-1501.
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(3):446-452.
11. Marschall HU, Wikström Shemer E, Ludvigsson JF, Stephansson O. Intrahepatic cholestasis of pregnancy and associated hepatobiliary disease: A population-based cohort study. Hepatology. 2013; 58(4):1385-1391.
12. 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(3):282-288.