Summary

Introduction. Obstetric cholestasis is the most common liver disease during pregnancy, which is predominantly associated with fetal complications.

Material and Methods. This retrospective study included a total of 44 pregnant women with obstetric cholestasis who gave birth at the Clinic of Obstetrics and Gynecology, Clinical Center of Vojvodina, Novi Sad, from January 1, 2014 to December 31, 2018.

Results. The average maternal age was 34 years. The mean gestational age at diagnosis of obstetric cholestasis was 31 weeks, and at the time of delivery 35 weeks of gestation. Abdominal pruritus was the main symptom of the disease affecting 72.72% of patients. The mean bile acid level in the blood at the time of diagnosis was 25.26 µmol/L. Twenty nine patients (65.90%) gave birth vaginally, while 15 (34.09%) underwent cesarean section. The main maternal complication was postpartum hemorrhage. The average blood loss was 567 ml. There were no maternal deaths or stillbirths. The average newborn birth weight was 2830 g. Respiratory distress syndrome was diagnosed in 8 newborns (15.09%).

Conclusion. Individual approach, continuous clinical and laboratory monitoring with adequate therapeutic treatment are necessary in patients with obstetric cholestasis.

Key words: Cholestasis; Infant, Newborn; Risk Factors; Perinatal Care; Pregnancy Outcome; Pregnancy Complications; Signs and Symptoms

Introduction

Obstetric cholestasis (OC) is the most common liver disease during pregnancy [1]. In the absence of other liver pathology, it is defined as pruritus with abnormal liver function which resolves following delivery [1]. The OC was first described in 1883 by Ahlfeld as jaundice in pregnancy that receded spontaneously after childbirth [2]. The OC is a multifactorial condition of pregnancy, but its pathogenesis is not well defined. A genetic predisposition, hormonal and environmental factors have a significant role in the etiology of OC [3]. Studies have shown that in patients with familial OC, there are variations in several genes encoding hepatobiliary transport proteins, as well as in the major bile acid receptor, farnesoid X receptor [4]. This condition may repeat in subsequent pregnancies [5].

Sažetak.

Uvod. Opstetrička holestaza je najčešća bolest jetre u trudnoći, koja je povezana sa komplikacijama prvenstveno po plod. Material i metode. Retrospektivna studija obuhvatila je 44 trudnice sa opstetričkom holestazom, porođene na Klinici za ginekologiju i akušerstvo Kliničkog centra Vojvodine u Novom Sadu, u periodu od 1. januara 2014. do 31. decembra 2018. godine. Rezultati. Prosečna starost majki iznosila je 34 godine. Prosečna gestacijska starost trudnoća u vreme postavljanja dijagnoze bila je 31 nedelja, a u vreme porođaja 35 gestacijskih nedelja. Svrab je bio dominantan simptom bolesti i najčešće se pojavljivao u predelu trbuha (72,72%). Prosečna vrednost žučnih kiselina u krvi u momentu postavljanja dijagnoze bila je 25,26 µmol/L. Dvadeset devet pacijentkinja (65,90%) porođeno je vaginarnim putem, dok je 15 (34,09%) trudnica porođeno carskim rezom. Glavna maternalna komplikacija bila je postpartum hemorrhage. Prosečan gubitak krvi bio je 567 ml. Nije bilo maternalnih smrti ni mrtvorođene dece. Prosečna telesna masa na rođenju iznosila je 2.830 g. Respiratorijski disters syndrom dijagnostikovan je kod osmoro novorođendu (15,09%).}

PERINATAL FOLLOW UP AND NEONATAL OUTCOMES OF PREGNANCIES WITH OBSTETRIC CHOLESTASIS

PERINATALNO PRAĆENJE I NEONATALNI ISHODI U TRUDNOĆAMA SA OPSTETRIČKOM HOLESTAZOM

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Sažetak.

Uvod. Opstetrička holestaza je najčešća bolest jetre u trudnoći, koja je povezana sa komplikacijama prvenstveno po plod. Material i metode. Retrospektivna studija obuhvatila je 44 trudnice sa opstetričkom holestazom, porođene na Klinici za ginekologiju i akušerstvo Kliničkog centra Vojvodine u Novom Sadu, u periodu od 1. januara 2014. do 31. decembra 2018. godine. Rezultati. Prosečna starost majki iznosila je 34 godine. Prosečna gestacijska starost trudnoća u vreme postavljanja dijagnoze bila je 31 nedelja, a u vreme porođaja 35 gestacijskih nedelja. Svrab je bio dominantan simptom bolesti i najčešće se pojavljivao u predelu trbuha (72,72%). Prosečna vrednost žučnih kiselina u krvi u momentu postavljanja dijagnoze bila je 25,26 µmol/L. Dvadeset devet pacijentkinja (65,90%) porođeno je vaginarnim putem, dok je 15 (34,09%) trudnica porođeno carskim rezom. Glavna maternalna komplikacija bila je postpartum hemorrhage. Prosečan gubitak krvi bio je 567 ml. Nije bilo maternalnih smrti ni mrtvorođene dece. Prosečna telesna masa na rođenju iznosila je 2.830 g. Respiratorijski disters syndrom dijagnostikovan je kod osmoro novorođendu (15,09%).
Characteristics/Karakteristike

| Characteristics/Karakteristike | 34 |
|--------------------------------|----|
| Age (years, mean)              | 34 |
| Parity (range)                 | 1−4 |
| Mode of conception/Način začeća| 31 (70.45%) |
| Spontaneous/Spontani           | 13 (29.55%) |
| In vitro fertilization/In vitro oplodnja | 31 (70.45%) |
| Gestational age at diagnosis (weeks, mean) | 31 |
| Mode of delivery/Način porodaja| 29 (65.90%) |
| Vaginal/Vaginalni              | 15 (34.09%) |
| Cesarean section/Carski rez    | 3 (6.81%) |
| Blood transfusion/Transfuzija krvi | 3 (6.81%) |
| Intrauterine growth retardation/Intrauterini zastoč u rastu | 2 (4.54%) |
| Gestational age at delivery (weeks, mean) | 35.86 |
| Delivery ≤ 37 weeks of gestation/Porodaj ≤ 37. gestacijske nedelje | 18 (40.9%) |
| Delivery < 34 weeks of gestations/Portaj < 34. gestacijske nedelje | 6 (13.63%) |

Abbrications

OC – obstetric cholestasis
IUGR – intrauterine growth restriction
RDS – respiratory distress syndrome

and environmental factors in the etiology of OC has also been described. The role of estrogen and progesterone in the etiology of OC has been proven, so this condition is more common in women with multifetal pregnancies and after oral progesterone treatment [6]. Special caution and monitoring is needed in patients with OC because of the risk of poor perinatal outcome such as: premature birth, meconium in the amniotic fluid, fetal bradycardia, fetal distress, and unfortunately intrauterine fetal death and stillbirth [7]. Intrahepatic cholestasis in pregnancy may be associated with significant vitamin K deficiency, severe coagulopathy and consequent life-threatening bleeding [8, 9]. The risk of adverse perinatal outcomes can be reduced by active treatment, including medications, antenatal fetal monitoring and elective early delivery. The aim of our study was to determine the maternal and neonatal outcomes in pregnancies with OC.

Material and Methods

This observational, descriptive cross-sectional retrospective study reviewed clinical outcomes of pregnant women with OC who gave birth at the Department of Obstetrics and Gynecology, Clinical Center of Vojvodina, Novi Sad in the period of five years (2014 – 2018). In the absence of other liver diseases, the diagnosis of OC was confirmed based on the presence of pruritus with abnormal liver function test results. The disease was diagnosed in pregnant women with pruritus and elevated bile acid levels (≥ 14 μmol/L) and/or elevated liver enzymes, without a chronic liver disease or dermatological diseases. The following maternal parameters were analyzed: age, mode of conception, gestational age at the time of OC diagnosis, mode of delivery, and gestational age at delivery. The following fetal and neonatal parameters were examined: intrauterine growth restriction (IUGR), stillbirth, gestational age at delivery, birth weight, Apgar score, and respiratory distress syndrome (RDS). We also evaluated complications (hemorrhage and blood transfusion) and laboratory parameters of liver function and bile acid values at the time of OC diagnosis. The time and mode of delivery depended on maternal complications and fetal condition. Exclusion criteria were: pruritus due to skin disorders, gall bladder and biliary disorder, pre-eclampsia, and patients with incomplete medical data. The collected data were presented in the form of median values and relative numbers (measure of variability). Statistical data processing was performed using the programs Microsoft Excel 2013.

Results

During the study period, 44 pregnant women with OC gave birth to 53 live babies after 24 weeks of gestation. The mean maternal age was 34 years (range 20 – 39 years) (Table 1). The average gestational age at diagnosis of OC and at the time of delivery was 31 and 35 gestational weeks. There were 31 (70.45%) spontaneous pregnancies and 13 (29.55%) pregnancies conceived by in vitro fertilization. Pruritus was the main symptom of the disease and it most commonly affected the abdomen (72.72%). The mean values of alanine transaminase, aspartate transaminase and alkaline phosphatase were 249.32 U/L; 154,53 U/L and 241,06 µmol/L, respectively (Table 2). The mean value of bile acid at the time of diagnosis was 25, 26 µmol/L. The mean total serum bilirubin level was 22,4 µmol/L. In terms of the mode of delivery, 29 patients (65.90%) underwent vaginal delivery, while 15 (34.09%) pregnancies were completed by cesarean section. Six patients (13.63%) gave birth after 34 weeks by emergency cesarean section and 18 patients (40.90%) gave birth after 34 weeks, but still prematurely (before 37 weeks of gestation). The main maternal complication was postpartum hemorrhage. The average blood loss during delivery was 567 ml. Two
patients (4.54%) had a blood loss over 1500 ml. Three patients (6.81%) received blood transfusion. There were no maternal deaths or stillbirths. The average birth weight of newborns was 2830 g (Table 3). The mean Apgar score at 1 minute was 7, while at 5 minutes it was 9. There were 8 neonates (15.09%) with birth weight of less than 2500 g. There were 8 neonates (15.09%) with birth weight of less than 2500 g. The average gestational age at birth was 35.2 weeks. The average gestational age at birth was 35.2 weeks. Studies have shown that itching is most intense at night and it is associated with insomnia. Itching occurs between 25 – 32 weeks of gestation, which confirms the disease. It commonly occurs between 25 – 32 weeks of gestation, which confirms the disease. It commonly occurs between 25 – 32 weeks of gestation, which confirms the disease. There were no intrauterine fetal deaths.

**Discussion**

In this study, we presented the outcomes of 44 pregnancies complicated by OC during a five year period. The mean maternal age in our study was 34 years. Few studies have shown that older maternal age is a risk factor for OC [10]. The majority of the patients were primigravida (65.9%). Symptoms of OC appeared between 27 and 39 weeks of gestation, which confirms the claims that the disease is most often diagnosed in the second and third trimesters of pregnancy [8, 11]. All patients had pruritus as the dominant symptom of the disease. In relation to location, patients mostly reported abdominal pruritus (72.72%), 8 patients (18.18%) said that palms and soles were the places of the most intense itching and only 4 patients (9.09%) reported itching all over the body. Our results are consistent with results found in other studies [12]. In the absence of other skin changes, skin excoriations from scratching were most often observed. After the diagnosis of OC, continuous monitoring (active management) of these patients is required, which includes pharmacological therapy, antenatal monitoring with a decision on the type and time of delivery. Ursodeoxycholate, which decreases maternal symptoms and serum bile acid levels, is widely used for the treatment of OC [13]. It is currently the most effective treatment for pruritus in OC [14]. The patients were recommended a course of ursodeoxycholate, 10 – 15 mg/kg/d, taken orally and divided into 2 – 3 doses/day. Antihistamines (chlorpheniramine) and topical agents with menthol may be useful in the treatment of pruritus. The average gestational age at birth was 35 weeks of gestation, which is in accordance with the literature data [15]. Active management is usually rec-
ommended to prevent the risk of intrauterine death and routine delivery at 37 to 38 weeks of gestation [16, 17]. There are still different recommendations about the time of delivery of patients with OC. It is believed that the time of delivery should be decided individually, taking into account the risk of premature birth, on the one hand, and the risks posed by continued pregnancy on the other hand [18]. The Department of Obstetrics and Gynecology (Clinical Centre of Vojvodina) has a specific protocol (continuous monitoring, therapy and postpartum control) (Graph 1). During the process of decision making, special attention is paid to the level of bile acids because the concentration ≥ 40 μmol/L may be associated with higher chance of poor outcome [19]. The dominant mode of delivery in our study was vaginal (65.9%) and 15 patients underwent cesarean section (34.1%); 9 elective and 6 emergency cesarean sections. There were 3 patients with postpartum hemorrhage (6.8%), which is low in comparison with study of Pokrnel et al. [11]. Out of 53 neonates, RDS was diagnosed in 8 (15.09%). In terms of prematurity, 52.83% of babies were born before 37 weeks, and 14 babies (26.41%) were born before 34 weeks of pregnancy. Much higher incidence of preterm deliveries was reported in the studies of Dodampahala et al. (76.4%) and Bacq et al. (60%) [20, 21]. Adverse pregnancy outcomes and fetal complications are most common with elevated bile acids ≥ 40 μmol/L [12]. There were no intrauterine deaths or stillbirths in our study. Studies from the literature data also show no intrauterine deaths or stillbirths [22, 23].

Conclusion

The diagnosis of obstetric cholestasis is a significant problem, primarily due to potential fetal complications. Careful monitoring, individual approach, and timely response are necessary to avoid adverse outcomes in pregnancies with obstetric cholestasis.

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