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AN OBSERVATIONAL RESEARCH ON OBSTETRIC CHOLESTASIS AND ITS IMPACT ON FOETAL OUTCOME

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Abstract

Background: Obstetric cholestasis (OC) is a hepatic disease distinctive to pregnancy which is classified as dermatoses of pregnancy with an initial presentation of pruritus. OC is different compared to the other dermatoses of pregnancy such that there are no lesions or primary rash but there is, however, a propensity for maternal morbidity and a substantial risk of morbidity and mortality of fetus, also there are implications about health of offspring in future. Increased foetal serum bile-acids viz. taurocholic and taurodeoxycholic acid are likely associated to foetal complications of Intra-hepatic cholestasis of pregnancy (ICP). It has been known that women suffering from OC have abnormal hormonal metabolism, genetic predisposition, altered immunity and they are subjected to environmental influences.

Aims & Objectives: To research the impact of obstetric cholestasis on foetal outcome.

Material & Methods: Patients who showed clinical symptoms of pruritus which was unidentified with other etiology along with elevated hepatic enzymes and who were presented between 30 to 40 weeks of gestation were identified as having clinical Obstetric cholestasis while few patients were excluded as they had other chronic hepatic disease or dermatological disease or choledocho-lithiasis and some of them had acute fatty hepatic of pregnancy.

Results: It was found that 20(40%) patients among 50 cases had bile-acid levels > 40 µmol/l while 30(60%) patients belonged to the group having bile-acid levels < 40 µmol/l. Among 20 cases in group 1, 18(90%) cases reported foetal complications which was very high compared to group 2 where among 30 cases only 4(13.3%) cases were found to have foetal complications. Among those 18 cases, majority of cases 10(55.6%) were observed to have respiratory distress followed by 4(22.2%) cases of low birth weight, 3(16.7%) cases with intrauterine foetal disease and 1(5.6%) still birth. While among 4 cases with bile-acid levels < 40 µmol/l, 3(75%) had respiratory distress followed by 25(%) low birth weight cases. There was no case of IFD as well as still birth in group 2.

Conclusion: Our research shows that there is a substantial risk of foetal morbidity and mortality in OC with clear consequences for the offspring's potential health. We also observed that in those with a higher bile-acid pool, most of the foetal complications occur. This indicates that bile-acid sensitivity can be used in OC as a predictive marker of foetal risk. This means that OC-affected pregnancies fall into the high-risk group and require foetal surveillance.

Keywords: obstetric cholestasis, foetal outcome, bile-acid levels, dermatoses, low birth weight

Introduction

Obstetric cholestasis (OC) is a hepatic disease distinctive to pregnancy which is classified as dermatoses of pregnancy with an initial presentation of pruritus. Due to the multifaceted and weakly understood etiology, pathology and physiology, intra-hepatic cholestasis of pregnancy has been classified as peculiar, complex and intriguing problem. OC is different compared to the other dermatoses of pregnancy such that there are no lesions or primary rash but there is, however, a propensity for maternal morbidity and a substantial risk of morbidity and mortality of fetus, also there are implications about health of offspring in future. The society of Medical-Foetal Medicine accord that obstetric cholestasis should be diagnosed when the total bile-acid levels or serum bile-acids are measured at 10 µmol/l. OC, pruritus gravidarum and recurrent idiopathic jaundice has also been referred as Intra-hepatic cholestasis of pregnancy. Jaundice, dysuria, pruritus, excoriations from scratching and steatorrhea are the clinical features of this disease[1]. The oral contraceptive pills which contains estrogen or only intake of estrogen is known to cause cholestasis which is due to inhibition of hepatocellular bile salt export pump. Increased foetal serum bile-acids viz. taurocholic and taurodeoxycholic acid are likely associated to foetal complications of Intra-hepatic cholestasis of pregnancy (ICP). It has been known that women suffering from OC have abnormal hormonal metabolism, genetic predisposition, altered immunity and they are subjected to environmental influences[2-5]. Meconium staining of amniotic fluid (MSAF) is considered to be an indication of foetal discomfort. In the normal term pregnancies the

incidence of MSAF is 15%. It has also been noted that about 16% to 58% of cases of ICP has MSAF and upto 100% cases are affected by intrauterine death[6,7]. ICP is reported to have associated with intrapartum as well as antepartum cardio-tocograpic abnormalities including decreased variability of foetal heart rate, tachycardia, decelerations and bradycardia8. There is an elevated risk of spontaneous preterm labour is present., which in some studies has been recorded in as many as 60 % of dehepaticies, but in ICP cases without active management, most studies report rates of 30 to 40%. In ICP pregnancies with maternal fasting serum bile-acid >40 μmol/l, the frequency of this complication was substantially higher. For either labour induction or elective caesarean section at 37 weeks 'gestation, there is an increased risk of respiratory distress syndrome. It occurs in around 22- 33% of patients[9-12]. In conjunction with the disease, there are clear records of adverse foetal outcomes. Many experiments have attempted to associate the biochemistry of maternal serum with foetal outcomes. In more recent research using active management policies, perinatal mortality in OC was reduced to 3.5% or less. Many different clinical strategies, including improved foetal management, can include the term active management. Monitoring, regular biochemical monitoring, ursodeoxycholic acid (UDCA) pharmacotherapy, or dehepaticy at 37 to 38 weeks gestation. These protocols of management are based on data showing that ICP stillbirths appear to cluster about 37-39 weeks[13-17]. Management: UDCA has been shown to have greater effectiveness in maternal pruritus and to enhance maternal pruritus than other treatment modalities, including the use of S-adenosyl-L-methionine, dexamethasone, cholestyramine and guar gum Serum transaminase and TBA levels[18]. A correlation between ICP and foetal growth has been seen in several studies, but the findings are inconsistent. A major, population-based longitudinal research recorded a substantial increase in the incidence of broad gestational age (LGA) infants after control for diabetes and preeclampsia in pregnancies complicated by ICP[19].

Material and Methods:

This research was done in the Tertiary healthcare Centre. Patients who showed clinical symptoms of pruritus which was unidentified with other etiology along with elevated hepatic enzymes and who was presented between 30 to 40 weeks of gestation were identified as having clinical Obstetric cholestasis. A total of 80 patients having itching were studied among which 50 were included in this research. Those 50 were clinically diagnosed with OC and 30 patients were excluded as they had other chronic hepatic disease or dermatological disease or choledocho-lithiasis and some of them had acute fatty hepatic of pregnancy. Examination details and history of patients was noted along with all investigations necessary for ANC especially bile-acid levels, non-stress test, hepatic function test and ultrasound. Pruritus coinciding with hepatic dysfunction and/or raised serum bile-acid levels > 10 μmol/l has been used as the criteria for diagnosing OC. The research patients have been classified into two groups categorized as below:

Group 1: Total bile-acid (TBA) levels > 40 μmol/l

Group 2: Total bile-acid (TBA) levels < 40 μmol/l

Babies weighing < 2.5 kg were considered as low birth weight babies. Any neonate who required continuous positive pressure of air, intubation, postpartum mask or bag ventilation, documentation of respiratory distress secondary to meconium aspiration, diagnosed for pneumonia was defined as respiratory distress.

Results:

Table 1: Foetal complications in ICP patients

Foetal complications in ICP patients	Number	Percentage
Present	20	40%
Absent	30	60%
Total	50	100%

It was observed that among 50 cases included in research, 20(40%) cases had foetal complications while foetal complication did not occur in 30(60%) cases.

Table 2: Distribution of foetal complications in classification of ICP patients according to total bile-acid (TBA) levels

Bile acid level	Number	Percentage
>40 micmol/l	20	40%
<40 micmol/l	30	60%
Total	50	100%

It was found that 20(40%) patients among 50 cases had bile-acid levels > 40 μmol/l while 30(60%) patients belonged to the group having bile-acid levels < 40 μmol/l.

Table 3: Distribution of foetal complications according to bile-acid levels.

Foetal complication	Group 1	Group 2
Intrauterine foetal death	3 (16.7%)	0(0%)
Low birth weight	4 (22.2%)	1 (25%)
Still birth	1 (5.6%)	0 (0%)
Respiratory distress	10 (55.6%)	3 (75%)

Among 20 cases in group 1, 18(90%) cases reported foetal complications which were very high compared to group 2 where among 30 cases only 4(13.3%) cases were found to have foetal complications. Among those 18 cases, majority of cases 10(55.6%) were observed to have respiratory distress followed by 4(22.2%) cases of low birth weight, 3(16.7%) cases with intrauterine foetal disease and 1(5.6%) still birth. While among 4 cases with bile-acid levels less than 40 µmol/l, 3(75%) had respiratory distress followed by 25(%) low birth weight cases. There was no case of IFD as well as still birth in group 2.

Discussion:

While OC is typically relatively benign to the mother, in pregnancies affected by OC, the risk of foetal abnormalities is known to be increased. These include elevated respiratory distress risks, amniotic fluid stained with meconium, low birth weight, stillbirth, and IUFD. Although ICP for mothers is a relatively non-threatening disease, there are significant risks to the foetus. It is associated with a higher risk of foetal death, amniotic fluid meconium staining, foetal distress and preterm birth[20,21]. In present research, foetal complications were observed in 20(40%) cases where as foetal complications were absent in 30(60%) cases among 50 cases included in the research. Also, 30(60%) cases had bile-acid levels <40 µmol/l and rest 20(40%) cases had bile-acid levels > 40 µmol/l. Majority of the foetal complications in our research were observed in the cases having higher bile-acid levels (>40 µmol/l) compared to those with lower bile-acid levels (< 40 µmol/l) which means that higher serum levels of bile-acid are associated with higher perinatal morbidity and mortality rates. The findings in our research are in agreement with a research done by Posh S et. al who showed that pregnancies complicated by meconium-stained liquor, cardiotocography anomalies, and foetal asphyxial events are more likely in ICP cases with higher maternal serum bile-acid levels (> 40 µmol/ l)[22]. A research done by Li et. al. showed that in ICP pregnancies, neonatal birth weight is lower than in normal pregnancies which is in agreement with present research[23]. In present research, 3(75%) among 4 cases of foetal complications had respiratory distress in group 2 while in group 1, 10(55.6%) among 18 cases were having respiratory distress. Zecca has recorded that in neonates born to mothers with ICP, the rate of respiratory distress syndrome is double that of the general population. This may be due in part to the earlier gestational age at birth, but on the basis of an examination of Broncho alveolar lavage fluid of neonates born to mothers with ICP, neonatal respiratory distress syndrome has been shown to be correlated with ICP[24].

Conclusion:

Our research shows that there is a substantial risk of foetal morbidity and mortality in OC with clear consequences for the offspring's potential health. We also observed that in those with a higher bile-acid pool, most of the foetal complications occur. This indicates that bile-acid sensitivity can be used in OC as a predictive marker of foetal risk. This means that OC-affected pregnancies fall into the high-risk group and require foetal surveillance.

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