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OBSTETRIC CHOLESTASIS

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ABSTRACT

Intrahepatic cholestasis of pregnancy {ICP} is a disorder characterised by pruritus with the onset in the second and third trimester of pregnancy. The serum bile acids and aminotransferases are raised. The incidence is higher in Chile and Bolivia. Around 5 to 15% genetic, environmental and hormonal factors contribute to the pathogenesis of ICP. Mother suffers from pruritus which is more in palms and soles. It causes difficulty in getting good sleep as this happens more at night. However the effect can be dangerous to the fetus. The risk of preterm delivery is 19 to 60%, meconium staining of amniotic fluid is 27%, fetal bradycardia is 14%, fetal distress 22 to 41% and unexplained fetal death 0.4 to 4.1%. If the bile acids are more than 40 micromol/litre the risk of fetal death is high. Hence it is recommended to deliver the fetus by 37 weeks of gestation.

KEYWORDS: Primary biliary cirrhosis, Intrahepatic cholestasis, Primary sclerosing cholangitis.

INTRODUCTION

SYNONYMS

RECURRENT JAUNDICE OF PREGNANCY

PRURITUS GRAVIDARUM

INTRAHEPATIC JAUNDICE OF PREGNANCY

DEFINITION

It is a cholestatic disorder characterised by pruritus without rash, elevated serum transaminases and bile acids without obvious jaundice, with the onset in the second or third trimester of pregnancy and spontaneous relief of symptoms within 2 to 3 weeks of delivery. It was first described by Ahlfeld in 1883.

Epidemiology

It is seen in all ethnic groups but there is a significant geographical variation in the incidence of ICP. The incidence is highest in Bolivia and Chile among Araucanos Indians. Of chile 27.6% and Aimara indians of Bolivia 13.8%. In europe, north america the incidence is <1%. It is more common in winter months and in twin and multiple pregnancy.

Clinical Manifestations

Pruritus is the primary clinical symptom. It can be mild or severe causing sleep deprivation. It usually presents after 30 weeks of gestation. jaundice develops after 1 to 4 weeks after the onset of pruritus. other manifestations are steatorrhoea, vitamin k deficiency, prolonged prothrombin time, gallstones and postpartum haemorrhage.

The biochemical features are elevation of serum bile acids and transaminases. The bile acids may exceed 10 - 100 times above the normal range.

There is reduced glycine to purine ratio<1.

Alkaline phosphatase is increased to 4. There is hyperbilirubinemia and ALT and AST are raised.

Etiopathogenesis

It is multifactorial involving hormonal, genetic and environmental factors are known to be the cause. Estrogen and progesterone have a role in impaired sulfation and transportation of bile acids. Family clustering, presence of ethnic and geographic variations and mutations in hepatobiliary transport proteins indicate a genetic predisposition in ICP.

Environmental factors like geographic and seasonal conditions may induce ICP in genetically susceptible individuals. Seasonal variations are attributed to high maternal levels of copper, low levels of zinc and selenium.

There is excess accumulation of hydrophobic bile acids that are hepatotoxic in the fetal compartment. impaired fetomaternal transport of bile acids across the placenta and inability of the fetus to excrete cholic acid leads to accumulation of bile acids and fetal cardiotoxicity. Bile acids induce vasoconstriction in chorionic veins and umbilical veins. It explains fetal hypoxia, meconium inhalation and neonatal death. Bile acid is a cause of increase in myometrial contractility and induces preterm

labour. So it is difficult to predict fetal outcome via standard fetal cardiac monitoring tests.

Differential Diagnosis
Viral hepatitis
Autoimmune liver disease
Gallstones
Preeclampsia
HELLP syndrome
AFLP

CASE HISTORY
From January 2018 six women with obstetric cholestasis {OC} were recruited from Dande hospital. Data was collected after the women gave consent to participate in the research. The diagnosis of ICHP was based upon persistent pruritus with abnormal LFT in the absence of other liver disease which resolved postnatal. Abnormal LFT was defined as abnormality in SGOT, TOTAL SERUM BILE ACIDS and SGPT. On detection of abnormal liver function, possible alternative causes of liver disease were sought like hepatitis A, hepatitis B, C on serology. Liver ultrasound and coagulation screen was done in all cases. Once identified the women were interviewed weekly regarding the nature and severity of pruritus and features like malaise, anorexia, dark urine, pale stool, right upper quadrant pain and urinary tract infection. Women were given Chlorpheniramine 4mg three times a day and topical emollients. Ursodeoxycholic acid was given to each patient. All were managed according to standard protocol which included delivery before 38 weeks. Obstetric outcome was recorded.

RESULTS

Age	**29**	**30**	**27**	**25**	**35**
Parity	G2 para 1	G3 para 2	G2para1	primi	G2 A1
Previous affected pregnancy	yes	Yes in second pregnancy NO MISCARRIAGE	Pruritus in previous pregnancy Not investigated	nil	nil
Rhesus group	B Rh +	A Rh+	O Rh +	0 Rh +	B Rh +
Maternal medical history	nil	nil	nil	GDM on metformin 500 mg BD	GDM on insulin and hypothyroidism
Cyclic pruritus	Yes	yes	yes	yes	yes
F/H/O pruritus in pregnancy	no	no	no	no	Sister had pruritus in pregnancy
Personal /family history of gallstones	nil	Mother had gallstones	yes	nil	yes
Liver USG	normal	normal	normal	normal	Gallstones seen
hepatitis	negative	negative	negative	negative	negative
Pale stools	no	no	no	no	no
Dry cough	no	yes	no	no	no
ROQ pain, uti	no	no	yes	no	no
GA at the onset of pruritus	31 weeks	18 weeks	30 weeks	32 weeks	28 weeks
Area of itching	Palms soles legs	Arms legs palms and soles	Whole body	Legs palms soles	generalised
Treatment with chlorpheniramine	yes	yes	yes	yes	yes

and ursodeoxycholic acid					
Vaginal delivery	no	no	no	no	no
Caesarean section	yes	yes	yes	Yes due to failed induction	yes
GA at delivery	37	37	38	37	34
Steroids	received	received	received	received	received
Blood loss at the time of delivery	No pph	No pph	No pph	No pph	no pph
NICU admission	Not needed	Not needed	Not needed	Baby was admitted	Twin babies were admitted in nicu
Weight of the newborns	2.5	2.4	2.3	2.5	Both babies weighing 1.5 kgs
Follow Up of mother and baby	Asymptomatic and LFT was normal	NORMAL	NORMAL	NORMAL	NORMAL

5 women of mean age 30 years were recruited in the study. Liver function normalised and pruritus ceased postnatal in all cases. The median gestational age at the onset of pruritus was 30 weeks. None reported rash. Bile acids and aminotransferases were raised in all cases. Liver ultrasound showed gallstones in only one patient. Other causes of abnormal LFT like hepatitis were negative in all. All were given medicines to treat the pruritus and relieve the cholestasis. All of them responded well symptomatically and with reduction in levels of AST and ALT. All women had maximum itching on palms and soles. They were monitored weekly for symptoms like pruritus, cough, right upper quadrant pain, pale stools. Two had gestational diabetes which was well controlled in one with metformin and in other with insulin. They were monitored with weekly LFT and fetal Doppler every two weeks. All of them received in betnesol at 36 weeks except the one with twin pregnancy. She was given betnesol injection 12 mg two doses 12 hours apart. They were delivered at 37 weeks and the twin pregnancy at 34 weeks by caesarean section the fetal weights ranged from 2 to 2.6 kg. The twin babies weighed 1.5 kg each.

We have to keep a high index of suspicion in diagnosing this condition clinically and biochemically. Prognosis of the baby should be explained to them that early delivery is desirable to reduce fetal morbidity and mortality. Steroid to the mother with early delivery around 37 weeks helps to reduce neonatal morbidity, meconium aspiration, respiratory distress and NICU admission. In my study all women had healthy babies and good neonatal and maternal outcome. Two cases needed NICU Admission. It was for respiratory support and the babies were shifted to the mother in 72 hours. All the babies received vitamin K.

DISCUSSION

This study describes the nature and outcome of obstetric cholestasis in 5 patients .4 out of 5 patients developed this condition after 30 weeks. This study confirms that generalised pruritus or pruritis of palms and soles may be particularly suggestive of the condition. Though they have mild pruritus at other sites pruritus always preceded the biochemical abnormality in the form of abnormal LFT by 2 weeks. Other abnormality like dry cough, was seen in only one patient.

A family history of gallstones or personal history is a recognised association with obstetric cholestasis. It is seen in three out of five patients.

One out of five patients had gallstones diagnosed seen on ultrasound. No patient was positive for hepatitis B or C.

It is known that Indian and Pakistani population has a higher incidence than Caucasian population.

Ursodeoxycholic acid was used in all 5 cases. No studies are available to establish whether it improves the obstetric outcome. However it is effective in reducing the pruritus and normalising the liver function tests. All women underwent CTG every week and an ultrasound study fortnightly. The birth weights were appropriate for gestational age in each case. Two patients were detected to be diabetic and one managed with insulin therapy and the other with metformin. All patients received steroids before delivery.

There was no stillbirth or early neonatal death. All patients were delivered at 37 weeks except the one with twin pregnancy. She was delivered at 34 weeks. There was no history of reduced fetal movements in these women. No one received vitamin k prophylaxis. No one landed up with postpartum haemorrhage. All women underwent caesarean section. NICU admission was needed in two patients just for respiratory support. Meconium staining of liquor was seen in one patient.

CONCLUSION

As there is historical evidence of adverse neonatal outcome, any reduced perinatal mortality as a result of active management must be balanced against increased intervention. Appropriate consideration and advice as to the iatrogenic risks involved should accompany policies of active management. Prediction of fetal compromise is the most difficult aspect of management of obstetric cholestasis. No effect has been demonstrated on the Doppler blood flow analysis in the uterine, umbilical or fetal cerebral arteries, even in severe cases of OC. The risk of given complications is higher if a woman has suffered that complication in a previous pregnancy.

Risk of developing OC in future pregnancies is approximately 90%. These women should avoid estrogen containing pill. If administered the liver function test must be monitored. In my case series all patients were diagnosed around 30 weeks, managed actively and delivered around 37 weeks. There was no neonatal or maternal complication.

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