

## OBSTETRIC CHOLESTASIS IN FIRST TRIMESTER-UNUSUAL PRESENTATION OF THE DISEASE: CASE REPORT

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### ABSTRACT

Obstetric cholestasis (OC) presents mainly in the third trimester and uncommonly in the second trimester of pregnancy. It is characterised by pruritus, abnormal liver enzymes and raised total serum bile acids (TSBA). Cholestasis resolves after delivery. OC presenting in first trimester is rare, therefore the management guidelines are unclear. The present case is being reported as a case of first trimester OC, unresponsive to common treatment modalities. The patient was diagnosed with OC at 12 weeks. She didn't respond to the therapeutic doses of ursodeoxycholic acid (UDCA) and cholestyramine. Finally, rifampicin was added, which gave clinical relief, improved liver enzyme levels and allowed the pregnancy to continue till 32 weeks.

**KEYWORDS:** Obstetric Cholestasis, Ursodeoxycholic Acid, Rifampicin.

### INTRODUCTION

Obstetric cholestasis (OC) is a cholestatic disorder specific to pregnancy, characterised by unexplained pruritus without any dermatological cause, raised liver enzymes and elevated total serum bile acid (TSBA) level (1). The onset of the condition is usually in late pregnancy with most of the cases occurring in late second or third trimester. The diagnosis is confirmed with spontaneous resolution of disease following delivery (1). Raised TSBA levels have been implicated in maternal morbidity and adverse perinatal outcomes such as preterm delivery, meconium staining of liquor, fetal distress and rarely, stillbirth (2,3). Mothers are predisposed to postpartum haemorrhage due to impaired absorption of vitamin K from the small intestine and consequently, a prolonged prothrombin time (4). There are few case reports of OC presenting in early pregnancy, hence this case is being reported.

### CASE REPORT

A 26 year old, in her second pregnancy, presented at 12 weeks gestation with severe generalised itching and multiple episodes of vomiting. In her previous pregnancy she was diagnosed with OC at 30 weeks, and started on ursodeoxycholic acid. She had uncomplicated vaginal delivery at 37 weeks. There was no significant medical or surgical history. Her

blood investigations showed mildly raised liver enzymes and significantly raised TSBA. (Table 1) Routine antenatal investigations were normal. First trimester ultrasonography showed a 12 week pregnancy with normal nuchal translucency and other aneuploidy markers. Mild diffuse hepatic steatosis and gall bladder sludge were present.

Oral ursodeoxycholic acid (UDCA) was started in a dosage of 500mg twice a day. Following no improvement in clinical or biochemical parameters, expert consultation was taken from a hepatologist and cholestyramine was added in a dosage of 4gm twice a day. Despite two drugs, there was minimal improvement in the parameters at 2 weeks. (Table 1) Discontinuing cholestyramine, Rifampicin was added to the drug regimen as 600mg, oral, once a day. Within 2 days, the patient had significant improvement in her symptoms and TSBA decreased to 158  $\mu\text{mol/L}$ . She was continued on UDCA, and rifampicin.

At 25 weeks gestation, after 3 months, trial for discontinuation of rifampicin was done. UDCA was continued. However, though she remained asymptomatic, there was considerable derangement of biochemical parameters, and Rifampicin was re-started. She continued to be in remission for the next few weeks. At 31 weeks 4 days the patient presented with relapse of

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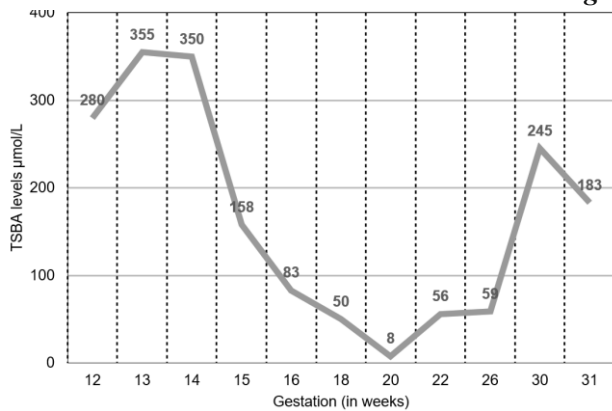
pruritis, disturbed sleep. TSBA levels rose sharply. Fig.1 shows the progression of TSBA levels. Growth scan and fetal Dopplers were normal. TSBA continued to rise, therefore, after steroid coverage, labour was induced. A 1.68 Kg baby girl was delivered at 32 weeks. The baby was discharged from Neonatal Intensive Care Unit (NICU) after 3 weeks. It took around 4 weeks for the liver enzymes and TSBA to normalise.

intrahepatic cholestasis. She was managed with UDCA, cholestyramine and S-Adenosyl-L-Methionine. The pregnancy continued till 32 weeks, with the delivery of a viable female baby weighing 1758g (8).

The primary aim of management is to overcome maternal symptoms and to reduce serum bile acids which might be helpful in preventing adverse

Drug	No drug	UDCA	UDCA + Cholestyramine	UDCA + Rifampicin	UDCA + Rifampicin	UDCA + Rifampicin
Gestation (weeks)	12	13	14	15	29	31+ 4
AST	45 IU/L	45 IU/L	50	44	27	33
ALT	82 IU/L	80 IU/L	127	51	43	42
ALP	127 IU/L	125 IU/L	119	180	250	237
TSBA	280 µmol/L	355 µmol/L	280 µmol/L	83 µmol/L	59 µmol/L	245 µmol/L

**Table 1: Showing Important Laboratory Values**



**Fig. 1: Showing Concentration of Total Serum Bile Acid Levels After Initiation of Treatment at Different Gestational Age**

**DISCUSSION**

Pruritus in pregnancy is common and mostly benign. Other causes could be pregnancy specific dermatoses which include atopic eruption, pemphigoid gestationis, OC and polymorphic eruption of pregnancy. OC is diagnosed when pruritis is associated with raised TSBA > 19 µmol/L in the absence of any hepatic disorders or dermatological problems (1). Levels of TSBA have been seen to be associated with adverse fetal outcomes and are used as a surrogate marker for obstetric surveillance.

Although cases have been reported, it is highly unusual for OC to present in the first trimester. A similar case was reported in a 26 year old pregnant lady. She developed OC in first pregnancy at 20 weeks and in the second at 10 weeks. The latter ended in stillbirth at 27 weeks. In her third pregnancy, TSBA at 13 weeks was 243.6 µmol/L. Liver biopsy at 22 weeks showed pure

perinatal outcomes. UDCA and antihistaminics have been used for clinical relief. A recent meta-analysis suggests that adverse pregnancy outcomes can be prevented by close monitoring and timely initiation of UDCA in the dose of 10-20 mg/kg/day.(9). UDCA is a hydrophilic bile acid with cyto-protective, immunomodulatory and choleric effect, acting through various complex and complementary mechanisms. Oral UDCA changes the hydrophobicity index of the bile acid pool by competitively displacing the endogenous hydrophobic or toxic bile acids at the absorption sites as well as increasing the absorption of hydrophilic bile acids. Cholestyramine and S-Adenosyl-L-Methionine have been found to have positive additive effect but are less effective as a standalone measure.

Addition of Rifampicin to UDCA has afforded dramatic relief in resistant cases. It enhances the activity of hepatic cytochrome P-450, promoting 6-alpha-hydroxylation and subsequent 6-alpha-glucuronidation of bile acids, thus decreasing the pool of toxic bile acids (10). A retrospective study of 28 women with severe OC showed that adding Rifampicin (300 to 1200 mg) to women with OC, refractory to UDCA resulted in improvement in pruritus and reduction in TSBA (11). We found remarkable improvement in symptoms and investigations when UDCA and Rifampicin were taken together.

The risk of stillbirth in mild OC ( peak bile acids 19-39 micromole/L) and moderate OC (peak bile acids 40-99 micromole/L) is 0.13% and 0.28% respectively which is comparable to background risk (12). However in moderate OC the risk appears to increase at around

38–39 weeks' gestation. (12). Delivery is therefore planned at 38-39 weeks in these cases.

For women with severe OC (peak bile acids 100 micromole/L or more) the risk of stillbirth is 3.44%, which is way higher than the normal population risk. Importantly, the risk appears to increase from 35–36 weeks' gestation. Hence, planned delivery 35-36 weeks gestation is considered as the standard of care.

## CONCLUSION

OC may present early in pregnancy, therefore the mere presence of first trimester should not bias one to miss the diagnosis. It has adverse effects on both mother and baby. Refractory cases may benefit from adding Rifampicin to the traditional UDCA regimen.

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