A STUDY ON POSTNATAL OUTCOME OF FOETAL CHOLELITHIASIS
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ABSTRACT

BACKGROUND
The first prenatal diagnosis of cholelithiasis was done by Beretsky and Lankin in 1983. Foetal cholelithiasis is a rare finding during a third trimester of pregnancy. Despite the remarkable number of foetal scans performed annually worldwide, little is known about the pathogenesis and outcome of foetal cholelithiasis. We present the outcome of neonates with clinical and sonographic followup.

MATERIALS AND METHODS
We retrospectively analysed the data of neonates born between the periods of January 2012 to December 2016 in a tertiary hospital, diagnosed prenatally having echogenic material in the foetal gallbladder. Detailed maternal, medical, obstetric and foetal health was analysed. Follow up ultrasonographic and clinical findings till resolution of the echogenic foci were noted in the postnatal period. Postnatal complications of the neonate if any were also noted.

RESULTS
Over last five years, we detected 17 neonates with foetal diagnoses of echogenic focus in the gallbladder. Girl babies were affected more (58.8%). 64.7% cases were detected after 30 weeks of gestation. Mean gestational age of prenatal detection of echogenic foci was 34 weeks. Maternal obstetric complications associated with the cases were polyhydramnios, oligohydramnios, preeclamptic toxaemia and antepartum haemorrhage. Maternal medical illnesses were E-beta thalassaemia, gestational diabetes mellitus and hypothyroidism. Foetal and neonatal complications were prematurity, congenital anomaly (choledochal cyst), chromosomal anomaly (Down’s syndrome), polycythaemia, sepsis, neonatal hepatitis and haemolytic conditions. On follow-up, in 76.5% cases, resolution of echogenic material occurred within two months of postnatal age. There was persistence of echogenic material in 23.5% cases.

CONCLUSION
Biliary sludge and gallstones are uncommon in foetal life. The aetiopathogenesis of foetal cholelithiasis is currently unknown. Though, different maternal, obstetric and foetal predisposing risk factors are found to be associated, but there are no established correlations. In most of the cases, foetal cholelithiasis resolves spontaneously. Considering its high rate of spontaneous resolution, we recommend reassuring parents and closely observing the clinical evolution of the patients. However, it needs to be differentiated from the sinister pathologies and requires accurate diagnosis.

KEYWORDS
Foetal Cholelithiasis, Biliary, Ultrasonography, Echogenic.

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BACKGROUND
Potter described neonatal gallstones in 1928 and cited poorly-documented cases of foetal cholelithiasis diagnosed at the time of autopsy.1 The first prenatal diagnosis of cholelithiasis by Beretsky and Lankin occurred in 1983.2 Since then, there have been only few reports about the presence of gallstones in the foetus. The frequency of diagnosis has increased over the last few years probably due to both the improved accuracy and the increasing use of ultrasound examination in clinical practice. Despite the remarkable number of foetal scans performed annually worldwide, little is known about the pathogenesis and outcome of foetal cholelithiasis though maternal conditions, foetal or obstetrical predisposing risk factors have been proposed to have a causative role. Herein, we present the results of a retrospective study on foetal cholelithiasis.

Aims and Objectives
Aims of this study were to know the postnatal outcome of foetal cholelithiasis. Maternal and foetal conditions associated with foetal cholelithiasis were also analysed.
MATERIALS AND METHODS
We retrospectively analysed the data of neonates born between the periods of January 2012 to December 2016 in a tertiary hospital diagnosed prenatally having echogenic material in the foetal gallbladder. Gestational age at which echogenic foci were detected in the foetus was noted. Detailed maternal, medical, obstetric and foetal health was analysed. Follow up ultrasonographic and clinical findings till resolution of the echogenic foci were noted in the postnatal period. Postnatal complications of the neonate if any were also noted. The data collected was analysed statistically using descriptive statistics. Appropriate test of significance was used to analyse the data.

Inclusion Criteria
Neonates with prenatal diagnoses of echogenic focus in the gallbladder, and later after birth, the diagnoses had been confirmed by postnatal ultrasonography were included in the study.

Exclusion Criteria
Patients with prenatal diagnosis of echogenic focus in the gallbladder, but postnatal ultrasonography confirm hepatic calcification or perihepatic echogenic focus were excluded from the study. Seven cases of hepatic calcification was detected.

RESULTS
Details of the foetal and neonatal clinical profile and outcome of the babies with diagnoses of prenatal cholelithiasis are presented in table 1. Over last five years, we detected 17 neonates with foetal diagnoses of echogenic focus in the gallbladder. Girl babies were affected more (10 out of 17, 58.8%). All these had been detected in either second or third trimester of gestation. Eleven (64.7%) cases were detected after 30 weeks of gestation. Mean gestational age of prenatal detection of echogenic foci was 34 weeks. Eight (47%) of these babies were born prematurely. Other nine were term neonates. Biliary sludge was detected in 11 (64.7%) cases, and in rest of the cases, foetal gallstone was detected. Figure one showing echogenic material in the foetal gallbladder lumen in one of our patients. Figure two showing biliary sludge and calculous at gallbladder neck on second day of life in another baby of our study patients.

Maternal obstetric complications associated with the cases were polyhydramnios (one case, 5.8%), oligohydramnios (three cases, 17.6%), preeclamptic toxaemia (three cases, 17.6%) and antepartum haemorrhage (two cases, 11.7%). Maternal medical illnesses were E-beta thalassaemia and gestational diabetes mellitus and hypothyroidism (one in each case).

Foetal and neonatal complications were prematurity (eight cases, 47%), congenital anomaly (bilateral hydronephrosis, choledochal cyst, 11.7%), chromosomal anomaly (Down’s syndrome, three cases, 17.6%), polycythaemia (three cases, 17.6%), sepsis (two cases, 11.7%), neonatal hepatitis (three cases, 17.6%) and haemolytic conditions (three cases, 17.6%). Conjugated hyperbilirubinemia was present in cases of neonatal hepatitis, sepsicaemia and choledochal cyst. Hypercholesterolaemia was diagnosed in one neonate at the age of 7 months with unresolved cholelithiasis.

Follow-up was obtained in all seventeen neonates using serial postnatal ultrasonography scan. Maximum period of follow-up was up to one year. Followup ultrasonography scan showed resolution echogenic material within 2 weeks in eight (47%) cases. In two (11.7%) patients, there was resolution of echogenic material within first month. In one patient, resolution of biliary sludge occurred within two months. So, in about 76.5% cases, resolution of echogenic material occurred within two months of postnatal age. One patient died on second day of age due to perinatal asphyxia.

There was persistence of echogenic material in four (23.5%) cases. One of the four patients was with choledochal cyst. One of them was suffering from thalassaemia major. One was with congenital hypercholesterolaemia. One baby was with neonatal hepatitis due to congenital toxoplasmosis. Biliary sludge was detected in this cases, remained unresolved till its follow up period of 16 weeks of postnatal age. Then, the parents did not turn up for follow up.
<table>
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<td>Maternal medical profile</td>
<td>Gestational age of the foetus at diagnosis of echogenic foci</td>
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<tr>
<td>1.</td>
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<td>2.</td>
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<td>Oligohydramnios</td>
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<td>5.</td>
<td>PET, oligohydramnios and antepartum haemorrhage</td>
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<td>6.</td>
<td>PET</td>
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<td>9.</td>
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<td>16.</td>
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<tr>
<td>17.</td>
<td>Nil</td>
<td>Hypothyroidism</td>
<td>38 weeks</td>
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</tbody>
</table>

**Table 1. Foetal and Neonatal Clinical Profile and Outcome of Cholelithiasis**

**DISCUSSION**

Reported incidence of foetal cholelithiasis varies from 1 in 3000 to 5 in 1000 live newborns.\(^3,4,5\) According to some author, foetal cholelithiasis is more common in boys.\(^6\) But, in our study, 58.8% patients were girl baby.

Maternal conditions, foetal or obstetrical predisposing risk factors have been proposed to have a causative role, but the pathogenesis of foetal gallstones remains unknown. Fanaroff et al suggested that haemoglobin transformed in bilirubin passed through the placenta, increasing foetal serum levels of indirect bilirubin.\(^7\) Brown et al proposed that an increase in oestrogen serum levels could increase the risk of pigmented stone formation by increasing the cholesterol secretion and diminishing the bile acid synthesis.\(^8\)

Maternal haemolytic anaemia, ABO or Rh incompatibility, congenital biliary tract anomalies (choledochal cyst), ileum pathologies, Down’s syndrome, cholestasis related to septic states, prolonged total parenteral nutrition, diuretic therapy,
cerephalosporin use, phototherapy, etc. are the predisposing factors for foetal and neonatal cholelithiasis. Pregnancy-induced cholestasis has also been considered as a risk factor, which has not been confirmed. Narcotic use during pregnancy has also been suggested as another predisposing factor. In our present study, most of the reported predisposing conditions were seen to be present. Apart from the above-mentioned predisposing factors, we found neonatal polycythaemia in a good number of patients.

Foetal gallstones are seen by ultrasound examination as echogenic foci with or without distal shadowing or “comet tail” or V-shaped artifacts within the gallbladder lumen. However, echogenic foci without distal shadowing more likely represent biliary sludge. The sludge is made up of a precipitation of calcium, pigment and cholesterol element (calcium bilirubinate granules and cholesterol crystals) and is the precursor of gallstones. In our study, biliary sludge was detected in 64.7% cases, and in rest of the cases, foetal gallstone was detected.

The natural history of foetal gallstones is different from that of children and adults. Foetal gallstones have a tendency to form in the third trimester of pregnancy. In the series of Brown et al, the mean gestational age at the time of diagnosis was 36.2 weeks with a range of 28 to 42 weeks. In our study, prenatal detection of echogenic focus was done after 30 weeks of gestation in most of the cases (64.7%) with mean gestational age of 34 weeks.

The prognosis of foetal gallstones and biliary sludge is usually favourable as in our case. Careful follow-up ultrasound examinations are necessary for foetal cholelithiasis. With conservative management in most cases, foetal gallstones disappear spontaneously weeks or months after birth as the maternal predisposing factors disappear after delivery. In our study, resolution of echogenic focus was seen within two to eight weeks of postnatal age in most of the cases. Disappearance of foetal gallstones is probably due to spontaneous passage of the gallstones during early neonatal period or the dilution of cholesterol crystals with postnatal hydration. Brown et al (1992) observed spontaneous resolution in 40% cases of foetal gallstones associated with acoustic shadowing. Higher percentage of spontaneous resolution was noted when echogenic foci were without acoustic shadowing may have been because they were biliary sludge rather than true gallstones. In our study, there was resolution of echogenic foci in 76.5% of cases. Wendtland-Born A et al has reported persistence of foetal gallstones in one third of cases till 18 months of age. Persistence of gallstones was more likely with family history for gallstones. In our study, there was persistence of echogenic foci in 23.5% of cases.

Though according to some author, it is worthy to try to resolve them with ursodeoxycholic acid (15-20 mg/kg/day), some author has recommended only careful follow up of cases by serial ultrasound examination in which gallstones persist beyond 6 months.

Foetal gallstones should be differentiated from intrahepatic calcifications, calcified haemangioma or hamartomas in the liver or intra-abdominal calcifications due to meconium peritonitis and other echogenic bowel. Careful assessment is essential to localise the echogenic foci within the lumen of foetal gallbladder. In foetal life, gallbladder can be recognised as an anechoic, oblong, teardrop-like structure with a thin echogenic wall located at the inferior surface of the right lobe of the liver in ultrasonography examination. Accurate assessment and identification of the foetal gallbladder require prior visualisation of the umbilical vein, because they have a similar appearance. The foetal gallbladder can be visualised in 37.5% to 64.7% of the cases after 20 weeks of gestation.

Correct identification of foetal gallstones will allow for adequate counseling and will avoid unnecessary workup and maternal anxiety.

CONCLUSION

Biliary sludge and gallstones are uncommon in foetal life. The aetiopathogenesis of foetal cholelithiasis is currently unknown. Though, different maternal, obstetric and foetal predisposing risk factors are found to be associated, but there are no established correlations. In most of the cases, foetal cholelithiasis resolves spontaneously with hydration and feeding soon after birth. Considering its high rate of spontaneous resolution, we recommend reassuring parents and closely observing the clinical evolution of the patients without any medical or surgical treatment. However, clinical and ultrasonographic follow-up should continue until demonstration of resolution. It needs to be differentiated from the sinister pathologies and requires accurate diagnosis.

REFERENCES


