INTRODUCTION

A significant portion of women develops the biliary disease and its complication during pregnancy. During pregnancy the gall bladder stone formation rate is high. A prospective study of abdominal ultrasound showed 5% cholelithiasis by the second trimester and 10% cholelithiasis by six weeks postpartum. Alteration in the hepatobiliary function occurs to create a lithogenic environment. Gallstone formation is associated with epithelial changes in gall bladder. Gall bladder stone formation can be associated with hormonal changes, especially higher level of progesterone. Another problem associated is gall bladder stasis. These changes include the secretion of bile with an increased amount of cholesterol and decreased amount of choledeoxycholic acid. Increased level of oestrogen can also lead to higher cholesterol saturation of bile. The gallbladder contraction may be reduced due to higher level of progesterone. These factors lead to the development of stones during pregnancy.

The biliary sludge prevalence in pregnancy is 5-36% and prevalence of gall stone formation in pregnancy is 2-11%. During pregnancy incidence of biliary pancreatitis varies from 1- 3 cases per 10,000 patients. A Mexican study noted that symptomatic gallstone disease during pregnancy usually manifests as acute cholecystitis, even though 19% had cholecystolithiasis. Gallbladder disease is the second most common cause of non-obstetrics surgery after appendicectomy.
During pregnancy, although laparoscopic cholecystectomy is possible, we used to do non-surgical management, to avoid foetal and maternal complications. However, this non-surgical management can be associated with recurrence of symptoms, even after delivery. In this case series, we are trying to describe the various presentation of gallstone and its related complication during pregnancy and the postpartum period.

**MATERIALS & METHODS**

The reported documents of 6 patients with complications of cholelithiasis during and after pregnancy, was collected from the hospital database from period 2016-2019. In these 6 cases, 2 patients presented with acute cholecystitis at 30 and 15 weeks of gestation. Both of them were managed conservatively with antibiotics. The cholecystitis resolved and interval cholecystectomy was performed after delivery. Another 2 patients presented with acute cholecystitis during the 1st month of the post-partum period. These 2 patients were treated conservatively, and interval cholecystectomy was done after 6 weeks. Another 2 patients presented with obstructive jaundice. Both of them underwent endoscopic retrograde cholangiopancreatography (ERCP) and were planned to undergo interval cholecystectomy. Out of these 2 patients, 1 patient encountered Post ERCP complication.

**CASE 1:** 28 years’ female presented at 15th week of gestation with a recurrent abdominal colic. She came to the emergency ward with fever and abdominal pain. Physical examination revealed right hypochondriac tenderness with Murphy’s sign being positive. Total counts were elevated and USG abdomen showed cholecystitis along with pregnancy (Figure 1). Conservative management with a parenteral antibiotic (ceftriaxone twice a day for 7 days) was given. Cholecystitis resolved completely, and the patient was discharged comfortably after 1 week of hospitalization. The patient underwent laparoscopic cholecystectomy after delivery.

**CASE 2:** 30 yrs female presented in 30th week of gestation came to the hospital with abdominal pain, vomiting and fever. Lab investigation showed an increase in total white counts with liver function test being normal. USG abdomen showed multiple gall stones, with no CBD stones. Antibiotic was given (Inj ceftriaxone 1 gm twice a day) for 5 days and managed conservatively. Interval cholecystectomy was done after delivery without any complications.

**CASE 3:** 32 years’ female presented with complaint of abdominal pain and vomiting, one month after delivery. Physical examination showed right hypochondriac tenderness with Murphy’s sign being positive. Labs showed an increase in total counts and elevated alkaline phosphatase (ALP) with other liver function test within normal limits. Ultrasound abdomen showed the only cholelithiasis. Since ALP was elevated patient underwent MRCP (magnetic resonance cholangiopancreatography) to rule out common bile duct stones and MRCP showed normal common bile duct. Conservative treatment with antibiotics was done followed by interval cholecystectomy 6 weeks later.

**CASE 4:** 30 years’ female presented 15 days after delivery with complaints of recurrent biliary colic, abdominal pain and vomiting. USG abdomen showed multiple gall stones in the gall bladder with thickening of the wall of the gall bladder with pericholecystic fluid. Patient treated conservatively with antibiotics and interval cholecystectomy done after 6 weeks. Patient discharged without any complication.

**CASE 5:** 32 years old female, presented 2 months after delivering twin babies came with complaint of severe abdominal pain, vomiting, and fever. Lab investigations showed elevation of Total bilirubin being 4 mg/dl (direct greater than indirect) and alkaline phosphatase also elevated. She was started on iv antibiotics. MRCP showed two stones with the size of 6mm and 4 mm in the distal end of CBD with smooth transition.
tapering at the distal end. Medical gastroenterologist opinion was obtained and ERCP (endoscopic retrograde cholangiopancreatogram) was done. During ERCP, duodenal diverticula were seen (Figure 3). With difficult cannulation, the procedure was completed. After procedure patient developed severe abdominal pain, fever and elevation of Total white counts, with simultaneous increase of amylase and lipase. The patient had developed pancreatitis related to post ERCP complication. The patient had been shifted to the intensive care unit with pancreatitis managements. Patients improved and discharged after 7 days. 6 weeks later patient was treated with laparoscopic cholecystectomy.

Figure 3: ERCP-retrieval of two stones from CBD and stent placement.

CASE 6: 32 years old female, presented 28th weeks of pregnancy. She came with the complaint of jaundice and USG abdomen showed acute cholecystitis with common bile duct stone. Blood values showed an elevation of total counts and total bilirubin (6 mg/dl). MRCP showed multiple stones in the gall bladder with a 5 mm stone in the distal CBD. ERCP was done and the stone was retrieved successfully without any procedural complications (Figure 4). A stent was placed in CBD. Cholecystitis treated conservatively. Patient discharged after relief of obstructive jaundice. The patient underwent laparoscopic cholecystectomy without complications 2 months after delivery and CBD stent removal was done.

Figure 4: Fluoroscopy shows a single stone in the CBD and single stone in the gallbladder and CBD stone was retrieved by ERCP. The stent was placed.

RESULTS

In this case series, all 6 patients were treated conservatively in the acute phase. The first 2 patients presented during the antepartum period, managed conservatively and discharged without complications. Other 2 patients presented during 1st month after delivery and were treated conservatively with interval cholecystectomy being done later without complications. One patient presenting with features of jaundice during pregnancy and was treated with ERCP without any complications. Another patient presented with obstructive jaundice in the postpartum period and was treated with ERCP. So non-surgical treatment of cholecystitis in pregnancy period is possible and beneficial to the patients. Although complication rate is there, ERCP followed by laparoscopic cholecystectomy is the well available modality of treatment for common bile duct stone with obstructive jaundice.

DISCUSSION

Cholelithiasis is relatively common in India even in the lower socio-economic group. Dietary habits and obesity do not appear as contributing factor. The incidence of gallstone increases with the number of pregnancies. During pregnancy and the postpartum period, the incidence of biliary sludge and gallstone formation is 30% and 12% in clinical studies in the USA and Europe. The incidence of gallstone formation increases with Parity and length of fertility period. The complications of cholelithiasis like cholangitis, choledocholithiasis and pancreatitis rate is increased during or after pregnancy. This complication rate varies from 0.05% to 0.8%.
The complication rate of laparoscopic cholecystectomy during pregnancy is high. Conservative management is the best way of treatment to avoid maternal and fetal morbidity and mortality. To avoid fetal and maternal morbidity, the management of symptomatic biliary disease during pregnancy has often been nonsurgical.16 Most of the biliary colic and cholecystitis resolves with nonsurgical and supportive management.17 Only with conservative management in pregnancy, 90% of cholecystitis resolves.18 Usually, non-surgical management is advised, but in case the patient develops severe symptoms, laparoscopic cholecystectomy is an acceptable procedure. In the scenario of surgical management, the second trimester is the best time to do laparoscopic cholecystectomy, as uterus size will be ambient enough to create pneumoperitoneum and carry out with the procedure chances of miscarriage will be low. However, it is still a controversial ground on deciding the time of surgery. Therefore, non-operative management is the commonly implemented line of treatment of gall stone disease during pregnancy. In our case series 2 patients with cholecystitis in pregnancy treated only with conservative management successfully.

Fetal death rate is higher following conservative treatment than after laparoscopic cholecystectomy.19 In the comparison of conservative vs surgical management in pregnant patients with cholecystitis, no difference in preterm delivery and fetal mortality was observed.20 However, in other study, significant short term and long term morbidity in the conservative group than surgery group is reported.21 Iamini Ali M et al. shows higher preterm labour and fetal mortality in the group of patients who underwent surgical management for cholecystitis in pregnancy.22 Recurrent cholecystitis after conservative management is 40-92% and recurrent biliary pancreatitis is 50% in conservative group.23

One study shows laparoscopic cholecystectomy is preferable in cholecystitis with pregnancy.24 The only limiting factor governing operative intervention in gallstone related disorders during pregnancy should be the surgeon’s operative experience.25 There are reported complications in laparoscopic cholecystectomy in pregnancy like a uterine injury during trocar placement which caused preterm labour and spontaneous abortion.26 Although the evidence showed a high incidence of recurrence, the complication and mortality rate was less in conservative management when compared to laparoscopic cholecystectomy. Hence Conservative management is better.

ERCP is an important therapeutic option for CBD stones patients. In 1990, the first ERCP during pregnancy was successfully done.27 ERCP is a very safe procedure in pregnancy, even though complications have been reported in literature.28 The incidence of pancreatitis post ERCP is 9.7% and the mortality rate of ERCP is 0.7%.29 In our 2 patients, one patient developed ERCP induced pancreatitis complication. Another problem of ERCP in pregnancy is radiation exposure to the fetus. Low risk of teratogenicity in ERCP is also suggested.30 ERCP with ultrasound guidance is an effective and safe procedure to treat symptomatic choledocholithiasis in pregnant women.31 Endoscopic Ultrasound-guided ERCP can avoid fluoroscopy and radiation exposure in pregnancy.32 Girotra et al describe an alternative management strategy to conventional ERCP in a pregnant patient by using endoscopic ultrasound and choledochoscopy.33 A systematic review and meta-analysis were done on 27 studies to compare the outcome of radiation vs non-radiation technique in ERCP. In this meta-analysis, there is no difference in fetal outcome and maternal pregnancy-related adverse outcome between these two groups.34 Overall ERCP is a safe procedure during pregnancy for choledocholithiasis.

We present our clinical experience in this case series because of the diagnosis and course of management of gall stone disease is complicated. We aim to determine the outcome of conservative management of cholecystitis and outcome of ERCP for choledocholithiasis during pregnancy.

CONCLUSION

The conservative management of cholecystitis is a better way to treat during or immediately after pregnancy and interval cholecystectomy is a better line of management for cholecystitis pregnant patients. Although ERCP is having its complications, it is one of the best modality of extraction of CBD stones and followed by interval cholecystectomy later. There is a need for further randomised controlled trials to identify complication rates of gall stone disease during and after pregnancy and to derive its management protocol.

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