Laparoscopic bile duct exploration during pregnancy: a multi-centre case series and literature review

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Abstract

Background

The physiological changes of pregnancy increase the risk of gallstone formation and choledocholithiasis. Traditionally, endoscopic retrograde cholangiopancreatography (ERCP) has been the main approach for managing choledocholithiasis during pregnancy, but recent progress in laparoscopic bile duct exploration (LBDE) has demonstrated this technique as a safe and effective alternative option.

Methods

A retrospective multicenter study of all patients who underwent LBDE during pregnancy from five centers with proven experience in LBDE between January 2010 and June 2020 was performed. The primary endpoint was to analyze the role of LBDE during pregnancy and to further characterize its position as a safe and effective alternative for the management of choledocholithiasis. A systematic review of the published literature relating to LBDE during pregnancy until February 2022 was also performed.

Results

Five from 17 centers, with a total of 3950 LBDEs reported performing LBDE during pregnancy with a cumulative experience of eight patients (0.2%). Median surgical time was 75 minutes (range: 60-140 minutes). The bile duct was cleared successfully in all patients and the median hospital stay was 2 days (range: 1-3 days). The literature review identified a total of seven patients with a successful CBD clearance rate of 86%. There were no major maternal, fetal or pregnancy-related complications in any of the total 15 patients included.

Conclusion

The limited available data suggests that LBDE during pregnancy is a safe and effective. More evidence reporting outcomes of LBDE during pregnancy is needed before any strong recommendations can be made.

Introduction

The physiological changes of pregnancy increase the risk of gallstone formation and choledocholithiasis(1, 2). The management of symptomatic cholelithiasis, with or without choledocholithiasis, during pregnancy is challenging(3, 4). Complications of choledocholithiasis, such as obstructive jaundice, cholangitis and pancreatitis, are uncommon during pregnancy(5). However, when it occurs, it poses significant risk to the mother and fetus(6).

Traditionally, endoscopic retrograde cholangiopancreatography (ERCP) has been the main approach to this pathology during pregnancy(7–10). The main concern for this modality, together with the risk of post-ERCP pancreatitis, cholangitis, bleeding, and perforation, is the radiation exposure to the fetus during fluoroscopy. To avoid fetal irradiation, there are some alternatives such as endoscopic or transabdominal ultrasound, but their role has not been clearly defined in pregnancy.

In the last decade, laparoscopy has allowed development of a minimally invasive approach to the bile duct, namely Laparoscopic Bile Duct Exploration (LBDE). Current guidelines consider it the preferred treatment provided that local expertise is available(11–13). Widespread evidence exists on the use of laparoscopy during pregnancy(14), however, to date there are no case series demonstrating the role of LBDE during pregnancy. The aim of this multi-institutional review was to analyze the role of LBDE during pregnancy and to further characterize its position as a safe and effective alternative to ERCP for the management of choledocholithiasis.

Methods

Study design

A retrospective review of all patients who underwent LBDE during pregnancy from five centers with proven experience in LBDE between January 2010 and June 2020 was performed. Participating centers were in Spain, United Kingdom, Finland and Italy. A cross-sectional survey was distributed by email collecting the experience in LBDE during pregnancy in groups with experience in LBDE. Authors who provided us data on their experience and perioperative outcomes were included in the study. Ethical approval for this study was obtained from the Clinical Research and Ethics Committee at the Virgen de la Arrixaca Clinic and University Regional Hospital Murcia, Spain (Internal Protocol Code: 2021-12-10-HCUVA).

Data collected included demographic and patient-related factors (gestational age, maternal age and medical co-morbidity, American Society of Anesthesiology (ASA) score, body mass index (BMI), previous cholecystectomy), indication for LBDE (pancreatitis, jaundice, deranged liver function tests (LFTs) or dilated CBD (≥ 8 mm)), pre-operative imaging (ultrasound (US), magnetic resonance cholangiopancreatography (MRCP) or ERCP), use of intra-operative imaging (intra-operative cholangiography (IOC) or laparoscopic intra-operative ultrasound (LiOUSI)), intra-operative findings (access to CBD (transcystic or transducal), closure of choledochotomy, type of choledochoscope, successful clearance of the CBD, operative time) and post-operative outcomes (post-operative morbidity, pregnancy-related complications to mother or fetus and length of hospital stay). Data was also collected on surgeon-related factors including seniority of operating surgeon and annual volume of LBDE.

Literature review
A systematic strategy was used to search the published literature using electronic databases of Medline/PubMed and Scopus till August 2021. Medical subject headings and keywords used for the search included: “laparoscopic bile duct exploration”; “LBDE”; “LCBDE”; “choledocholithiasis”; “pregnancy”; with the use of ‘AND’ or ‘OR’ conjunctions. The reference lists of selected articles were manually scrutinized to ensure inclusion of all relevant studies. The list of articles obtained was then checked to exclude duplicates. The search was limited to studies published in the English language, using standard limitations provided by the respective databases.

**Statistical analysis**

Data was analyzed using SPSS 25.0 (IBM Corp., New York, US). Student’s t, Mann Whitney U, Chi-square, or Fisher’s exact tests were used as appropriate. Categorical data was presented as proportions, and continuous data was presented as either mean and standard deviation or median and inter-quartile-range as appropriate.

**Results**

**Multicenter demographic and peri-operative outcomes**

Seventeen centers responded to the survey, with a total of 3950 LBDEs being undertaken. Only five institutions reported performing LBDE during pregnancy with a cumulative experience of eight patients (0.2%). Demographic and pre-operative data have been summarized in Table 1. Two patients were ASA grade 1 and six were ASA grade 2. The median age and BMI were 32 years (range: 24–38 years) and 29 kg/m² (range: 24–38 kg/m²), respectively. One patient had previously undergone open gastric bypass. The indications for LBDE were pancreatitis (n = 1), jaundice (n = 1), deranged LFTs (n = 4) and cholecystitis (n = 2). Pre-operative abdominal US was performed in all patients, whereas MRCP and LIOUS were performed selectively in five and one patient, respectively.

<table>
<thead>
<tr>
<th>Surgeon qualification (years)</th>
<th>LDPE per year</th>
<th>Total cases</th>
<th>Maternal age (years)</th>
<th>Gestation (months)</th>
<th>BMI (kg/m²)</th>
<th>ASA</th>
<th>Comorbidities</th>
<th>Indication for LBDE</th>
<th>Bilirubin (mg/dL)</th>
<th>Pre-op US</th>
<th>Pre-op MRCP</th>
<th>LIOL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>25</td>
<td>60</td>
<td>515</td>
<td>31</td>
<td>5</td>
<td>30</td>
<td>2</td>
<td>Gastric bypass</td>
<td>0.6</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Case 2</td>
<td>25</td>
<td>60</td>
<td>515</td>
<td>38</td>
<td>6</td>
<td>35</td>
<td>2</td>
<td>Obesity</td>
<td>0.1</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Case 3</td>
<td>6</td>
<td>20</td>
<td>30</td>
<td>38</td>
<td>3</td>
<td>28</td>
<td>2</td>
<td>Cholecystitis</td>
<td>0.1</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Case 4</td>
<td>25</td>
<td>25–30</td>
<td>&gt;400</td>
<td>30</td>
<td>3</td>
<td>24</td>
<td>1</td>
<td>No</td>
<td>0.8</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Case 5</td>
<td>12</td>
<td>20</td>
<td>70</td>
<td>28</td>
<td>4</td>
<td>27</td>
<td>2</td>
<td>Asthma</td>
<td>0.2</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Case 6</td>
<td>4</td>
<td>65</td>
<td>160</td>
<td>38</td>
<td>3</td>
<td>27</td>
<td>1</td>
<td>No</td>
<td>3.6</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Case 7</td>
<td>4</td>
<td>65</td>
<td>160</td>
<td>32</td>
<td>7</td>
<td>34</td>
<td>2</td>
<td>Obesity</td>
<td>0.36</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Case 8</td>
<td>4</td>
<td>65</td>
<td>160</td>
<td>24</td>
<td>7</td>
<td>38</td>
<td>2</td>
<td>Hypothyroidism, diabetes, obesity</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Intra-operative and post-operative outcomes have been summarized in Table 2. The median surgical time was 75 minutes (range: 60–140 minutes). The bile duct was cleared successfully in all patients. The 5 and 3 mm choledochoscopes were used in six and two patients respectively. In three patients, a transduetal approach to the bile duct was used and primary closure of the choledochotomy was performed in all cases. Of those, two developed low-output bile leak (International Study Group of Liver Surgery grade A). Both patients were managed conservatively, one with oral antibiotics and the other with clinical observation alone and were discharged on the 2nd and 3rd post-operative day respectively. There were no other post-operative complications. The median hospital stay was 2 days (range: 1–3 days). Intra-operative and post-operative fetal monitoring was normal in all cases. There were no maternal or fetal pregnancy-related complications related to LBDE.
Table 2
Intra-operative data and post-operative outcomes (including pregnancy and fetal events).

<table>
<thead>
<tr>
<th>Case</th>
<th>Technique for LBDE</th>
<th>Diameter of scope (mm)</th>
<th>CBD closure technique</th>
<th>Operative time (mins)</th>
<th>CBD clearance</th>
<th>Morbidity (within 90 days)</th>
<th>Clavien-Dindo</th>
<th>Pregnancy events</th>
<th>Fetal events</th>
<th>Hospital stay (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Transductal</td>
<td>5</td>
<td>Primary closure</td>
<td>60</td>
<td>Yes</td>
<td>No</td>
<td>-</td>
<td>No</td>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>Transcystic</td>
<td>3</td>
<td>N/A</td>
<td>60</td>
<td>Yes</td>
<td>No</td>
<td>-</td>
<td>No</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Transductal</td>
<td>3</td>
<td>Primary closure</td>
<td>140</td>
<td>Yes</td>
<td>Bile leak</td>
<td>2</td>
<td>No</td>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>Transductal</td>
<td>5</td>
<td>Primary closure</td>
<td>110</td>
<td>Yes</td>
<td>Bile leak</td>
<td>2</td>
<td>No</td>
<td>No</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>Transcystic</td>
<td>5</td>
<td>N/A</td>
<td>110</td>
<td>Yes</td>
<td>No</td>
<td>-</td>
<td>No</td>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>Transcystic</td>
<td>5</td>
<td>N/A</td>
<td>70</td>
<td>Yes</td>
<td>No</td>
<td>-</td>
<td>No</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>Transcystic</td>
<td>5</td>
<td>N/A</td>
<td>60</td>
<td>Yes</td>
<td>No</td>
<td>-</td>
<td>No</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>Transcystic</td>
<td>5</td>
<td>N/A</td>
<td>80</td>
<td>Yes</td>
<td>No</td>
<td>-</td>
<td>No</td>
<td>No</td>
<td>2</td>
</tr>
</tbody>
</table>

Literature review: LBDE during pregnancy

A literature search of LBDE during pregnancy identified six case reports that included a total of 7 patients (Table 3)(17–22). Maternal age ranged between 19 and 38 years and gestational age between 8 and 32 weeks. The indication for LBDE was pancreatitis (n = 1), jaundice (n = 1), deranged LFTs (n = 3) and dilated CBD (n = 2). A pre-operative diagnosis of CBD stones was made in four patients by US (n = 2), MRCP (n = 2) and ERCP (n = 1). In one patient, US and MRCP were both diagnostic of CBD stones. Overall, the successful CBD clearance rate after LBDE was 86% (6/7). A transcystic approach to the bile duct was performed in five patients including one patient who received therapeutic transcystic saline lavage without formal choledochoscopy. One patient had failed laparoscopic transcystic stone extraction and was managed with placement of a transcystic drain with CBD clearance achieved 6 weeks post-partum with ERCP(17). Two patients underwent transductal stone extraction and the choledochotomy was closed primarily with a transcystic drain in one patient and closure over a T-tube in the other. There were no post-operative complications, adverse effects on pregnancy, or fetal complications reported in any of the patients and the hospital stay ranged between 2 and 6 days.

Table 3
Peri-operative outcomes for LBDE during pregnancy described in the literature. *Pre-operative investigation was diagnostic of CBD stone(s). US, ultrasound; MRCP, magnetic resonance cholangiopancreatography; ERCP, endoscopic retrograde cholangiopancreatography; ES, endoscopic sphincterotomy; IOC, intra-operative cholangiogram; INtra-operative ultrasound; NS, not stated.
Discussion

To our knowledge, this is the first reported case series for the management of choledocholithiasis with concomitant gallstones during pregnancy using a single-stage approach with LBDE at the time of laparoscopic cholecystectomy. The outcomes from this study suggest that LBDE during pregnancy is safe and effective, avoiding the general risks of ERCP and radiation to the fetus.

Gallstone-related complications are relatively common during pregnancy and the second most common indication for non-obstetric-related surgical intervention. Previous reports have found the incidence of biliary sludge and cholelithiasis in pregnancy to be 5–31% and 2–11%, respectively, although only 0.05–0.1% of them will present with symptoms(2, 23). Traditionally, the indications for surgery for symptomatic gallstones diagnosed during pregnancy were limited to acute cholecystitis, obstructive jaundice and pancreatitis. Whilst maternal and fetal death as a consequence of complications from choledocholithiasis is rare, readmissions for symptom relapse are common and occur in 58–72% of patients(24, 25). The finding that unfavorable maternal-fetal outcomes are more closely related to the pathological process than to the surgery has caused a paradigm shift in management. As with the non-pregnant population, acute gallstone pancreatitis remains a serious complication of choledocholithiasis during pregnancy. Maternal and fetal mortality of 15% and 60% respectively have been reported in gallstone pancreatitis during pregnancy(26).

The diagnosis of choledocholithiasis in a pregnant woman can be made pre-operatively with abdominal US and/or MRCP, but not being recommended in the first trimester. Intra-operatively, the diagnosis is made with LIOUS or IOC. In addition, transcystic choledochoscopy using ultra-thin scopes is increasingly becoming a diagnostic tool, which can also be therapeutic with stone extraction if necessary.

Complicated choledocholithiasis remains the most common indication for ERCP during pregnancy. Different authors have analyzed the outcomes of ERCP in pregnancy. Tang et al. retrospectively identified all ERCPs performed in pregnant patients over a 6-year period and found their rate of ERCPs in pregnancy to be 1 in 1,415 births(24). They concluded that hepatobiliary diseases during the first trimester were associated with the highest risk of preterm delivery (20%). Tiware et al. reviewed 214 ERCPs in 302 patients and the reported complications included spontaneous miscarriage (0.9%), fetal distress (0.6%), post-procedure pancreatitis (4.6%) and preterm birth (4.6%)(27). Immnadar et al. performed a retrospective matched-cohort study and compared data of pregnant women who underwent ERCP (n = 907) with those from non-pregnant women (controls, n = 2721)(28). They concluded that pregnancy is an independent risk factor for pancreatitis and is more prevalent in community hospitals when compared to tertiary care centers.

One of the main drawbacks of ERCP is the radiation which is considered teratogenic. However, the radiation dose used in pregnancy is significantly lower than the threshold dose likely to result in fetal malformations, otherwise known as the deterministic effect. Laudanno et al. analyzed long-term outcomes of 15 babies born after radiation exposure to mothers who underwent ERCP during pregnancy and did not find any evidence of developmental delay, poor school performance, or malignancy. To avoid radiation, EUS-guided ERCP is an alternative that has also been used in the management of choledocholithiasis during pregnancy. Same session EUS immediately prior to scheduled ERCP may eliminate the need for unnecessary ERCP and its related risks in pregnant patients when the EUS is negative. In patients with confirmed choledocholithiasis, EUS provided additional information regarding the location, number and size of stones, which enabled the successful clearance of the bile duct without the use of fluoroscopy. Some physicians are reluctant to perform EUS during pregnancy because it involves an invasive procedure. Another alternative management strategy to conventional ERCP is real-time transabdominal ultrasound guided ERCP. Li et al. described this approach in four pregnant adult patients with resolution of clinical symptoms but two patients suffered adverse events later in their pregnancy(29).

Single-stage laparoscopic management of choledocholithiasis appears in most international clinical guidelines as one of the recommended options for the treatment of common bile duct stones with gallbladder in situ(30). This approach allows the surgeon to perform the cholecystectomy together with the bile duct exploration in the same sitting with a low rate of complications(13, 31). One of the main complications is biliary leakage, but this is mainly associated with the transuductal approach, and it can be minimized by increasing the use of the transcystic route(32, 33). This has been reported to be facilitated using the leveraging access to technology and enhanced surgical technique (LATEST) approach(34). In the present series, the only two complications were related to self-limiting bile leakage related to the transuductal approach. Experience of this approach from the wider literature is very limited, with a total of just seven case reports published to date. In all patients but one, the bile duct was cleared laparoscopically without maternal or fetal complication and the transcystic approach was mainly used (~ 70%).

Nowadays, the benefits of a laparoscopic approach in pregnant patients are similar to non-pregnant patients, especially during the second trimester, in which the risk of premature delivery is close to 0% and that of spontaneous miscarriage is 5.6%. During the third trimester, the risk of preterm birth reaches 40% while that of spontaneous miscarriage approaches 0%. A recent meta-analysis concluded that laparoscopic cholecystectomy is a safe procedure in pregnancy, despite some technical limitations, particularly during the third trimester(35). This is related to the risk of uterine manipulation, the poor vision obtained and limited laparoscopic access due to the gravid uterus. The non-technical limitation during any trimester is the uncertain physiological effects of the pneumoperitoneum and hypercapnia in the fetus. Glucagon can also be used, if necessary, without added risk to the pregnancy or the fetus.

Conclusion

The evidence from this study is very limited due to the scarce experience that exists on this topic. The limited available data suggests that LBDE during pregnancy is a safe procedure with high efficacy. Advantages of LBDE over ERCP include avoidance of radiation and the related complications. More evidence reporting on outcomes of LBDE during pregnancy is needed before any firm conclusions or strong recommendations can be made.

Declarations

Disclosure: The authors have no relevant financial or non-financial interests to disclose.
Funding: The authors declare non financial support

Conflicts of interest: The authors declare that they have no conflicts of interest.

Ethics approval: All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication: Informed consent was obtained from all individual participants included in the study.

Consent for publication: The authors affirm that human research participants provided informed consent for publication.

Availability of data and material: The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials

Code availability: The data for this project are confidential, but may be obtained with Data Use Agreements with the Massachusetts Department of Elementary and Secondary Education (DESE). Researchers interested in access to the data may contact Víctor Lopez-Lopez at victorrelopez@gmail.com. It can take some months to negotiate data use agreements and gain access to the data. The author will assist with any reasonable replication attempts for two years following publication.

References


