Safety and utility of ERCP during pregnancy CME

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Background: ERCP is an important diagnostic and therapeutic tool in patients with biliary and pancreatic disease. Its utility and safety during pregnancy is largely unknown because it is not often required and because its use has been only infrequently reported in the published literature.

Objective: Our purpose was to report the clinical experience with ERCP during pregnancy.

Design: Retrospective review, single academic center.

Patients: All (consecutive) pregnant women who underwent ERCP at Parkland Memorial Hospital from 2000 to 2006.

Main Outcome Measurements: History, clinical data, hospital course, procedure-related complication rates and outcomes, and delivery and fetal outcomes were abstracted from medical records.

Results: During the study period, 68 ERCPs were performed on 65 pregnant women. The calculated ERCP rate was 1 per 1415 births. The common indications for ERCP in pregnancy were recurrent biliary colic, abnormal liver function tests, and dilated bile duct on US. ERCP was technically successful in all patients. The median fluoroscopy time was 1.45 minutes (range 0-7.2 minutes). There was no perforation, sedation-related adverse event, postsphincterotomy bleeding, cholangitis, or procedure-related maternal or fetal deaths. Post-ERCP pancreatitis was diagnosed in 11 patients (16%). None of these 11 patients had local or systemic complications. Fifty-nine patients had complete follow-up. Endoscopic therapy at the time of ERCP was undertaken in all patients. Furthermore, 9 patients (32.1%) underwent cholecystectomy in the first and second trimesters for either acute cholecystitis (6) or symptomatic gallstones (3). Term pregnancy was achieved in 53 patients (89.8%). Patients having ERCP in the first trimester had the lowest percentage of term pregnancy (73.3%) and the highest risk of preterm delivery (20.0%) and low-birth-weight newborns (21.4%). None of the 59 patients with long-term follow-up had spontaneous fetal loss, perinatal death, stillbirth, or fetal malformation.

Limitation: Retrospective review.

Conclusions: ERCP can be performed safely during pregnancy. Further, ERCP performed in pregnancy leads to specific therapy in essentially all patients. However, ERCP may be associated with a higher rate of post-ERCP pancreatitis than in the general population. (Gastrointest Endosc 2009;69:453-61.)

ERCP has become an invaluable diagnostic and therapeutic tool for biliary and pancreatic disorders. Major ERCP complications include pancreatitis (2% to 9%), postsphincterotomy hemorrhage (0.2% to 5%), cholangitis (<1%), and perforation (<1%).[1,2] Known risk factors for post-ERCP pancreatitis include young age, female sex, history of pancreatitis, sphincter of Oddi dysfunction, pancreatic duct injection or pancreatic sphincterotomy, difficult cannulation, and precut sphincterotomy.[2] Although biliary tract disease appears to be relatively common during pregnancy, the available literature on the safety and efficacy of diagnostic and therapeutic ERCP in pregnancy is limited to a relatively small number of case reports and case series.[3-14] Parkland Memorial Hospital (PMH) is affiliated with the University of Texas Southwestern Medical Center and serves Dallas County's medical needs. There are approximately 16,000 deliveries annually, giving PMH the second highest birthing

Abbreviations: CBD, common bile duct; ED, emergency department; PMH, Parkland Memorial Hospital.

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rate in the United States.[15] In 2002, PMH's neonatal mortality rates—deaths that occur within the first 28 days of life—were far lower than the national average: 2.7 deaths per 1000 births (compared with 4.7 deaths per 1000 U.S. births).[15] In this report, we describe the outcome of 68 pregnant women who underwent ERCP between September 2000 and September 2006.

Capsule Summary

What is already known on this topic

- Pregnancy promotes gallstone formation and increases the risk of gallstone disease.
- The incidence of acute cholecystitis is between 1 and 8 per 10,000 pregnancies.
- Symptomatic choledocholithiasis occurs in 1 of 1200 pregnancies.

What this study adds to our knowledge

- In a retrospective review of 68 ERCPs performed in 65 pregnant women, no perforation, sedation-related adverse event, postsphincterotomy bleeding, cholangitis, or procedure-related maternal or fetal deaths occurred.
- Patients undergoing ERCP in the first trimester had the lowest percentage of term pregnancies (73.3%) but the highest risk of preterm delivery (20.0%) and low birth weight newborns (21.4%).

METHODS

Patients

This retrospective study was conducted over a 6-year period (September 2000 to September 2006) in the endoscopy unit at PMH. Through computerized diagnostic codes entered on discharge, we identified all consecutive pregnant patients who underwent ERCP and the annual birthing data during the same study period. A computerized database was established in 2000 at PMH. The patient history, hospital course, ERCP complications and outcomes, delivery, and fetal outcomes were retrieved through chart review. The University of Texas Southwestern Medical Center institutional review board of approved this retrospective study, and patient consent was not required.

All study subjects had been admitted to the obstetric service. Liver tests, serum lipase, amylase, and other basic blood tests were routinely obtained daily before and after ERCP on every patient. Transabdominal US was performed on all patients to detect the presence of gallstones, choledocholithiasis, extrahepatic biliary ductal dilation, and evidence suggestive of cholecystitis. Biliary ductal dilatation was defined as an extrahepatic bile duct diameter ≥ 7 mm. Biliary ductal dilation alone was not considered to be indication for ERCP. CT scan was avoided in all patients to avoid radiation. Short-term exposure to electromagnetic radiation from magnetic resonance imaging or MRCP does not produce harmful fetal effects.[4] MRCP has been available at PMH for the past 6 years, and it is usually performed in pregnant women who have low suspicion of choledocholithiasis and normal liver function tests.

ERCP was performed in the usual fashion with several minor modifications related to pregnancy. ERCP was routinely performed with moderate (conscious) sedation, administered by the endoscopy nurse, typically with intravenous midazolam, fentanyl, or meperidine. Maternal monitoring was achieved by continuous electrocardiography, continuous pulse oximetry, and periodic sphygmomanometry. Fetal monitoring was not performed during or after the procedure. Patients were positioned in the left lateral recumbent position to promote uterine perfusion. Additionally, fetal radiation was limited by lead shielding above and below the patient covering the abdomen and pelvis. Both sides of the abdomen were also covered with lead shielding.

ERCP was performed with a therapeutic duodenoscope (Olympus TJF 160F; Olympus, Tokyo, Japan). Biliary cannulation was attempted with a standard sphincterotome. Fluoroscopy was used briefly to confirm the deep biliary cannulation and to obtain contrast cholangiogram. Biliary cannulation was also confirmed by obtaining bile on aspiration. Excessive spot radiographs and continuous fluoroscopy were avoided to reduce radioactive energy. After successful biliary sphincterotomy, patients received the required therapeutic interventions as indicated by the findings. Biliary sphincterotomy was performed by exposing the opening of the distal bile duct with a Valleylab generator or ERBE ICC 200 generator (ERBE, Tubingen, Germany) with a pure cut mode. An endoscopic basket or a balloon was used to remove the stones. If the patient had a gallbladder and acute biliary pancreatitis developed, a prophylactic biliary sphincterotomy was performed to reduce the risk of recurrent biliary pancreatitis during the same pregnancy. When there was a biliary stricture, incompletely removed ductal stones, or bile leak, biliary stenting was performed, and a repeat ERCP was performed after delivery to remove the stent and any residual stones.

On completion of ERCP, patients were observed in the hospital on the obstetric service. Asymptomatic patients were routinely discharged the next day after being evaluated by the primary team and biliary consultation service. Elective cholecystectomy was routinely scheduled and performed within 6 months postpartum if the patient still had a gallbladder.

Post-ERCP complications were defined as any adverse clinical events such as hypotension, fever, pancreatitis, or unexpected clinical outcomes related to the procedure. We specifically assessed each patient for the presence of pancreatitis, bleeding, or perforation.[2] In this study, post-ERCP pancreatitis was defined as abdominal pain

TABLE 1. Baseline characteristics

	All ERCPs (n = 68)	First trimester (n = 17)	Second trimester (n = 20)	Third trimester (n = 31)
Patient age (y)	25.8 (6.1)	24.8 (5.1)	27.3 (7.8)	25.4 (5.2)
Race (Hispanic/African American/white)	58/6/4	13/3/1	15/3/2	30/0/1
No. of pregnancies	2.96 (1.7)	3.29 (1.7)	2.80 (1.4)	2.87 (1.9)
Parity	1.68 (1.4)	1.82 (1.2)	1.60 (1.2)	1.65 (1.7)
Prior ERCP with biliary sphincterotomy	5 (7.4%)	1 (5.9%)	3 (15.0%)	1 (3.2%)
Prior cholecystectomy	9 (13.2%)	4 (23.5%)	3 (15.0%)	2 (6.5%)
Indications for ERCP				
Abdominal pain ± nausea/vomiting	100%	100%	100%	100%
Current biliary pancreatitis	23 (33.8%)	2 (11.8%)	7 (35.0%)	14 (45.2%)
Recurrent biliary pancreatitis*	7 (10.3%)	0	1 (5.0%)	6 (19.4%)
Cholangitis	18 (26.5%)	6 (35.3%)	4 (20.0%)	8 (25.8%)
Abnormal liver test results	59 (86.8%)	17 (100%)	18 (90.0%)	24 (77.4%)
Dilated CBD on US	36 (52.9%)	9 (52.9%)	10 (50.0%)	17 (54.8%)
Choledocholithiasis on imaging studies (US and MRCP)	12 (17.6%)	1 (5.9%)	4 (20.0%)	7 (22.6%)
Prior diagnosis of gallstones	17 (25.0%)	4 (23.5%)	3 (15.0%)	10 (32.3%)
Cholelithiasis on US†	57/59 (96.6%)	12/13 (92.3%)	17/17 (100%)	28/29 (96.6%)
Significant comorbidities	5	1‡	0	4§

Quantitative data are summarized as mean (SD).
*During the same pregnancy.
†US examination was obtained during the same hospitalization. Multiple gallstones were noted in all but 1 patient whenever gallstones were reported.
‡Hyperthyroidism.
§Asthma (n = 2), epilepsy, and hypothyroidism.

with elevation in serum lipase levels at least 3 times the upper limit of normal.

In this study, a birth included all fetuses and infants born weighing at least 500 g, whether alive or dead. Term pregnancy was defined as at least 37 completed weeks of gestation. The first trimester corresponded to weeks 1 to 14, the second trimester to weeks 15 to 28, and the third trimester $\geq$29 weeks. Low birth weight was diagnosed when a newborn infant's first weight was less than 2500 g. Apgar scores were measured in all neonates at 1 and 5 minutes.

Statistical analysis

Descriptive statistics were used to characterize the study population. The mean and SD are presented as summary statistics in the format ''mean (SD).'' The number of subjects with post-ERCP pancreatitis was compared by use of a 2-tailed Fisher exact test in patients who did or did not receive a pancreatogram.

RESULTS

Study patients

During the study period, 68 ERCPs were performed in 65 pregnant women with 45.6% (31/68) of the ERCPs performed during the third trimester of pregnancy (Table 1). At PMH, the annual numbers of births were as follows: 16,504 (2001), 15,677 (2002), 15,549 (2003), 16,223 (2004), 15,972 (2005), and 16,307 (2006), and there were 96,232 deliveries during the study period (Fig. 1). The calculated rate of ERCP in pregnancy is one per 1415 births. Patients of Hispanic ethnicity composed 85% (55/65) of the study population. At PMH, the

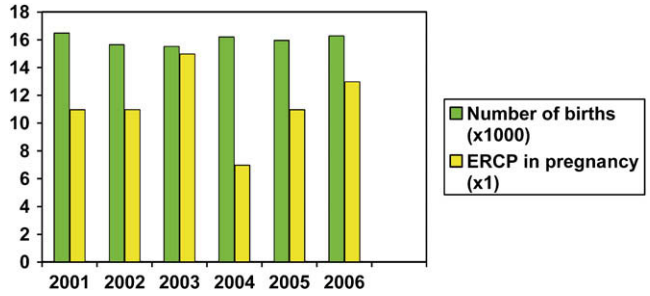

Figure 1. Annual number of births and number of ERCPs performed in pregnant patients at PMH.

demographics of patients seeking prenatal care are: 83% Hispanic, 12% African American, and 3% white.

Basic laboratory tests, such as complete blood cell count, liver tests, lipase, amylase, and chemistry panels were obtained in all patients in the emergency department (ED) (Table 2). In the ED or soon after admission, all patients underwent transabdominal US (Table 2). MRCP was performed in 6 patients: 2 in the first trimester, 1 in the second trimester, and 3 in the third trimester. Choledocholithiasis was diagnosed on MRCP in 4 patients. During ERCP, MRCP was found to be false positive in 1 of these 4 patients. MRCP was normal in 2 patients. ERCP was subsequently performed in 1 patient for recurrent biliary colic with abnormal liver function tests and in another patient for recurrent biliary pancreatitis within 2 weeks and for prophylactic sphincterotomy.

Outcomes

ERCP was technically successful in all patients. ERCP led to a diagnosis of choledocholithiasis in 51.5% of all patients. Multiple biliary stones were noted in 20.6% of all ERCPs and in 40% of ERCPs with choledocholithiasis. Successful clearance of biliary stones at the time ERCP was achieved in all but 1 patient (described above). Three patients (4.4%) had bile duct strictures: 2 patients had Mirrizi syndrome and the third patient had a short common bile duct (CBD) stricture associated with chronic stone disease. Biliary stenting was performed in 15 patients (22%, 2 in the first, 6 in the second, and 7 in the third trimester) for ductal decompression resulting from biliary strictures and potential residual stones.

In this study, 9 patients had prior cholecystectomies, and 3 of them did not have choledocholithiasis on cholangiogram before and after sphincterotomy. In our patients who had a sphincterotomy without choledocholithiasis, only 5 of 29 (18.5%) did not have stones in their gallbladders. Numerous gallstones were detected on US in all other patients. Cholecystectomy had been performed before pregnancy in 2 of these 5 patients.

Three patients underwent 2 ERCPs. In 2 of these 3 patients, both ERCPs were performed in the same trimester during the same pregnancy. The second ERCP in 1 patient was to rule out postcholecystectomy bile leak. In another patient, the first ERCP revealed a 15-mm stone impacted in the distal CBD. The stone could not be easily removed after biliary sphincterotomy. and biliary stenting was performed. She then underwent a second ERCP within 10 days for continued pain and the increasing serum bilirubin levels. The stone was removed after extended sphincterotomy and mechanical lithotripsy. The third patient underwent 2 ERCPs during the second trimester of different but consecutive pregnancies. During her first ERCP, multiple biliary stones were removed after biliary sphincterotomy. Biliary stenting with a double-pigtail stent was performed. She did not follow up with a scheduled ERCP for stent removal after delivery. She then underwent a second ERCP for biliary colic and abnormal liver function tests during a subsequent pregnancy. The old stent and several more stones were removed.

Complications

Complications were minimal in this patient cohort. There were no instances of perforation, oversedation, clinical postsphincterotomy bleeding, cholangitis, or procedure-related maternal or fetal complications (Table 3). The median fluoroscopy time was 1.45 minutes (range 0-7.2 minutes), and 75% of cases (52/68) required less than 3 minutes of fluoroscopy.

Post-ERCP pancreatitis was diagnosed in 11 patients (16%) on the basis of routinely obtained lipase and amylase levels after ERCP in combination with abdominal pain after the procedure. Sphincterotomy was performed in all but 1 patient. On cholangiograms in patients with post-ERCP pancreatitis, 7 were normal (no stones or strictures), 2 had stones, 1 had stricture, and 1 had stones and stricture. Four of these 11 patients were admitted with acute biliary pancreatitis before ERCP, and they all had normal cholangiograms. Three patients required hospitalization for more than 3 days after ERCP (5, 7, and 12 days). The others had mild pancreatitis and were discharged within 3 days after ERCP. None of these 11 patients had local or systemic complications such as pancreatic pseudocyst, necrosis, or organ failure. The rate of post-ERCP pancreatitis was not found to be significantly different in those who underwent contrast pancreatogram versus those who did not: 27.3% (3/11) versus 19.3% (11/57), respectively ($P = .68$, Fisher exact test). We admit that this observation could be due to a type II error. Indeed, these sample sizes would have less than 22% power to detect a significant difference even if the true rates would have been 30% versus 15% in those who did versus did not undergo a contrast pancreatogram, respectively.

There is an increased risk of post-ERCP pancreatitis and nonclinical bleeding with sphincterotomy in patients with normal cholangiograms without stones. In this study, the risk of post-ERCP pancreatitis was 11.4% (4/35) in patients with confirmed choledocholithiasis on ERCP with biliary sphincterotomy versus 20.7% (6/29) in patients without

TABLE 2. Baseline laboratory tests and US findings at presentation

	All ERCPs (n = 68)	First trimester (n = 17)	Second trimester (n = 20)	Third trimester (n = 31)
Laboratory tests				
AST (13-40 units/L)	96.2 (88.2)	154.0 (116.1)	108.2 (90.3)	55.5 (34.2)
ALT (10-40 units/L)	113.6 (120.2)	219.8 (141.6)	123.7 (117.0)	46.7 (39.7)
Total bilirubin (0.2-1.3 mg/dL)	2.01 (1.72)	2.44 (1.81)	2.38 (2.04)	1.52 (1.32)
Direct bilirubin (0.0-0.3 mg/dL)	1.02 (1.13)	1.24 (1.17)	1.31 (1.49)	0.70 (0.73)
AKP (38-126 units/L)	162.0 (74.7)	156.2 (122.2)	159.3 (51.8)	167.0 (50.5)
GGT (8-78 units/L)	125.8 (168.7)	296.1 (251.6)	84.6 (61.9)	53.0 (46.3)
White blood cell count (3.9-10.7 $\times$ 10^9/L)	11.95 (1.43)	9.72 (3.00)	12.29 (1.21)	11.27 (1.24)
Hemoglobin (13.2-16.9 g/L)	10.36 (3.01)	12.74 (1.48)	10.12 (2.89)	10.88 (3.09)
Platelet count (174-404 $\times$ 10^9/L)	242.6 (62.4)	235.2 (63.6)	247.3 (56.8)	244.0 (66.7)
Creatinine (0.6-1.2 mg/dL)	0.51 (0.10)	0.54 (0.10)	0.49 (0.08)	0.50 (0.12)
US findings				
Dilated CBD	36 (52.9%)	9 (52.9%)	10 (50.0%)	17 (54.8%)
Choledocholithiasis	8 (11.8%)	1 (5.9%)	2 (10.0%)	5 (16.1%)
Cholelithiasis on US*	57/59 (96.6%)	12/13 (92.3%)	17/17 (100%)	28/29 (96.6%)
Gallbladder wall thickening	3 (4.4%)	1 (5.9%)	1 (5%)	1 (3.2%)
Sonographic Murphy's sign	6 (8.8%)	1 (5.9%)	3 (15%)	2 (6.5%)

Quantitative data are summarized as mean (SD). *AST,* Aspartate aminotransferase; *ALT,* alanine aminotransferase; *AKP,* alkaline phosphatase; *GGT,* γ-glutamyltranspeptidase.
*US examination was obtained during the same hospitalization. Multiple gallstones were noted in all but 1 patient whenever gallstone was reported. A dilated CBD was defined as bile duct diameter ≥7 mm.

choledocholithiasis on ERCP with biliary sphincterotomy (P = .49, Fisher exact test). No patient in this cohort had another episode of acute biliary pancreatitis after biliary sphincterotomy. Before ERCP, 7 patients (10.3%) had a history of acute biliary pancreatitis before the ERCP, and 4 had 2 episodes of acute pancreatitis within 2 weeks of each other during pregnancy. Only 1 of these 7 patients was found with choledocholithiasis on ERCP with sphincterotomy. Only 1 of the 7 patients had a dilated bile duct on cholangiogram during ERCP. The risk of postsphincterotomy endoscopic bleeding was 5.7% (2/35) in patients with confirmed choledocholithiasis on ERCP with biliary sphincterotomy versus 10.3% (3/29) in patients without choledocholithiasis on ERCP with biliary sphincterotomy (P = .65, Fisher exact test).

Serum amylase was measured in all our patients in concordance with the lipase level. By use of only amylase elevations, 6 our 11 patients with post-ERCP pancreatitis would not be diagnosed with pancreatitis. These post-ERCP amylase levels were less than 2 times the upper normal limit (normal: 29-108 units/L) in 4 patients and were between 2× to 3× in the other 2 patients. However, these patients had abdominal pain with lipase increases between 400 and 640 units/L (normal: 7-59 units/L). We prefer using lipase in the diagnosis of post-ERCP pancreatitis.

Pregnancy and fetal outcomes

Medical records were available for 59 patients (90.8%) so as to allow complete follow-up through delivery (Tables 4 and 5). No patient had another episode of acute biliary pancreatitis after biliary sphincterotomy. Nine of the 28 patients with gallbladders undergoing ERCP in the first and second trimesters (32.1%) underwent cholecystectomy for either acute cholecystitis (n = 6, 21.4%) or symptomatic gallstones (n = 3, 10.7%). Only 1 patient (of 29, 3.4%) in the third-trimester group underwent cholecystectomy for acute cholecystitis during pregnancy. Term pregnancy was achieved in 53 of 59 patients (89.8%). Hepatobiliary diseases during the first trimester were associated with the lowest percentage of term pregnancy (73.3%), and with highest risks of preterm delivery (20.0%) and low birth weight (21.4%). Of 5 preterm deliveries in this study, only 1 woman had post-ERCP pancreatitis (requiring 12

TABLE 3. ERCP findings, outcomes, and complications

	All ERCPs (n = 68)	First trimester (n = 17)	Second trimester (n = 20)	Third trimester (n = 31)
ERCP findings and outcomes				
Total fluoroscopy time (median min)	1.45	1.70	1.55	1.00
Successful biliary cannulation	100%	100%	100%	100%
Wire-guided cannulation	12 (17.4%)	5 (29.4%)	2 (10.0%)	5 (16.1%)
Contrast pancreatogram obtained	14 (20.6%)	3 (17.6%)	6 (30.0%)	5 (16.1%)
Precutting	2 (2.9%)	1 (5.9%)	0	1 (3.2%)
Prophylactic pancreatic stenting	2 (2.9%)	2 (11.8%)	0	0
Biliary sphincterotomy	64 (94.1%)	16 (94.1%)	18 (90.0%)	30 (96.8%)
Biliary stones	35 (51.5%)	9 (52.9%)	12 (60.0%)	14 (45.2%)
Multiple stones (>1)	14 (20.6%)	3 (17.6%)	5 (25.0%)	6 (19.4%)
Mechanical lithotripsy	1 (1.5%)	0	1 (5.0%)	0
Successful stone removal	34 (97.1%)	9 (100%)	11 (91.7%)	14 (100%)
Biliary strictures*	3 (4.4%)	1 (5.9%)	1 (5.0%)	1 (3.2%)
Post-ERCP complications				
Pancreatitis	11 (16.2%)	3 (17.6%)	2 (10.0%)	6 (19.4%)
Perforation	0	0	0	0
Clinical bleeding	0	0	0	0
Oversedation	0	0	0	0
Cholangitis	0	0	0	0
Subclinical bleeding that needed epinephrine injection†	5 (7.4%)	0	3 (15.0%)	2 (6.5%)

*Two patients had Mirrizi syndrome and the third one had short stricture from chronic stone disease.
†Subclinical or endoscopic bleeding is not considered a post-ERCP complication.

days of hospitalization) and another woman required cholecystectomy during pregnancy. Both women were in the first trimester of pregnancy. All 4 pregnant women who were delivered of low-birth-weight neonates did not have post-ERCP complications and only 1 of them had undergone cholecystectomy during the same pregnancy (during the first trimester for symptomatic gallstones). Overall, none of these 59 patients had spontaneous fetal loss, perinatal death, stillbirth, or fetal malformation. Apgar scores at 5 minutes were 9 (0) in all neonates.

DISCUSSION

In this report, we have detailed our experience with ERCP in pregnancy since 2000. The rate of ERCP in pregnancy in current series (1/1415 deliveries) appears to be higher than that reported in some studies. This may be a result of more aggressive use of therapeutic ERCP in pregnancy, such as to perform biliary sphincterotomy. Other explanations include an increased incidence of gallstones and choledocholithiasis in our patient populations or more aggressive disease. In some reports, biliary stenting is performed for choledocholithiasis without coexisting biliary stricture or for limited cholangiograms. Currently, we try to remove biliary stones during ERCP and only place biliary stents if residual stones or fragments are present. However, biliary stenting is often performed if the stone removal is lengthy, to limit total fluoroscopy time. Unintentional long-term biliary stenting can cause stent-stone formation and biliary obstruction.[16]

In the current study, post-ERCP pancreatitis occurred in 16% of patients. This rate is higher than that in a recent review (5.5%) and in general populations (2%-9%). We speculate that this is due to one or more of the following: (1) modified diagnostic criteria for post-ERCP pancreatitis in this study. An increase in daily lipase levels associated with abdominal pain was considered to be consistent with post-ERCP pancreatitis. It is possible that some of our patients with increased lipase after ERCP and atypical

TABLE 4. Pregnancy and fetal outcomes

	All patients (n = 59)	First trimester (n = 15)	Second trimester (n = 15)	Third trimester (n = 29)
Complete follow-up (%)	90.8%	88.2%	83.3%	96.7%
Cholecystectomy during pregnancy*	10/57 (17.5%)	5/13 (38.5%)	4/15 (26.7%)	1/29 (3.4%)
For acute cholecystitis	7/10 (70.0%)	3/5 (60.0%)	3/4 (75.0%)	1/1 (100%)
Term pregnancy (≥37 wk)	53 (89.8%)	11 (73.3%)	14 (93.3%)	28 (96.6%)
Preterm delivery†	5 (8.5%)	3 (20.0%)	1 (6.6%)	1 (3.4%)
Elective abortion‡	1 (1.7%)	1 (6.7%)	0	0
Spontaneous abortion	0	0	0	0
Cesarean section	8/58 (13.8%)	1/14 (7.1%)	4 (26.6%)	3 (10.3%)
Apgar scores at 5 min	9 (0)	9 (0)	9 (0)	9 (0)
Low birth weight§	4/58 (6.9%)	3/14 (21.4%)	0	1 (3.4%)
Perinatal death and stillbirths	0	0	0	0
Fetal malformations	0	0	0	0

Quantitative data are summarized as mean (SD).
*Cholecystectomy in patients without prior gallbladder removal.
†Of 5 preterm pregnancies, only one woman had post-ERCP pancreatitis and another woman required cholecystectomy during pregnancy. Both women were in the first trimester for ERCP or surgery. Only 1 preterm delivery from the first-trimester group occurred before 34 weeks (at 32 weeks with a neonatal weight of 1710 g).
‡Elective abortion was performed outside the University of Texas Southwestern Medical Center.
§All 4 did not have any ERCP-related complications. Only 1 of them underwent cholecystectomy during the same pregnancy.

TABLE 5. Comparisons of liveborn infants between the study cohort and overall population during the same period

	Total liveborn infants (n = 96,232)	Study cohort (n = 58)
Preterm birth (wk)		
≤36	6.4%	8.6%
≤34	2.9%	0
≤32	1.5%	1.7%
Low birth weight (g)		
≤2500	6.8%	6.9%
≤1500	1.2%	0
≤1000	0.5%	0

abdominal pain did not have post-ERCP pancreatitis. They could simply have had post-ERCP elevations of lipase and amylase levels without pancreatitis, whereas the abdominal pain was related to pregnancy or resolving biliary pancreatitis. (2) The patient cohort was made of young and female patients who may have an increased risk of post-ERCP pancreatitis.[2] (3) Many patients (34%) had current and resolving acute biliary pancreatitis. (4) There could be ascertainment bias in previous studies because the case series were small. Almost all cases of post-ERCP pancreatitis in our study were mild and without systemic and local complications. Importantly, post-ERCP pancreatitis did not appear to adversely affect pregnancy-related outcomes. After biliary sphincterotomy, there was no recurrent biliary pancreatitis during the same pregnancy in our entire study cohort. (5) In this study, serum lipase levels, which are more sensitive, were used to diagnose pancreatitis. When only amylase elevations were considered, 6 of our 11 patients with post-ERCP pancreatitis would not be diagnosed with pancreatitis. We prefer using lipase levels in the diagnosis of post-ERCP pancreatitis.

Our data have suggested that ERCP with biliary sphincterotomy can effectively reduce the risks of recurrent cholangitis and biliary pancreatitis. Compared with that in patients with confirmed choledocholithiasis on ERCP with sphincterotomy, there is a small but insignificant increased risk of post-ERCP pancreatitis (20.7% vs 11.4%, $P = .49$) and nonclinical bleeding (10.3% vs 5.7%, $P = .65$) with sphincterotomy in patients with normal cholangiograms without stones. Importantly, no patient in this cohort had another episode of acute biliary pancreatitis after biliary sphincterotomy. These findings need to be confirmed in prospective randomized studies in this patient population before it is widely practiced. Before ERCP, 7 patients (10.3%) had a history of acute biliary

pancreatitis before the ERCP and 4 had 2 episodes of acute pancreatitis within 2 weeks of each other during pregnancy. Interestingly, only 1 of these 7 patients was found with choledocholithiasis on ERCP with sphincterotomy. Only 1 of the 7 patients had a dilated bile duct on cholangiogram during ERCP. In the entire cohort, there was no clinical bleeding after sphincterotomy that can be classified as a post-ERCP complication. Biliary stenting was performed in 15 patients (22%) for ductal decompression due to biliary strictures and potential residual stones. The stents were removed after delivery. This was our earlier experience and was practiced by attending endoscopists who had left our institution. Currently, we prefer not perform biliary stenting unless it is strongly indicated. We aim to remove all stones aggressively during the first ERCP and treat short strictures without stenting.

Data from our study suggest that development of hepatobiliary disease in the first trimester of pregnancy may be associated with preterm delivery or low birth weight. This conclusion is consistent with data from a previous study in which acute hepatitis A infection during pregnancy was associated with high risk of maternal complications and preterm labor; there was a significant correlation between gestational week at diagnosis of hepatitis and birth week.[17] Further, hepatitis B surface antigen carrier status appears to be associated with an increased risk of ''threatened'' preterm labor[18] and intrahepatic cholestasis of pregnancy, which often occurs early in pregnancy and has also been related to a high frequency of premature births and increased perinatal deaths.[19] Acute pancreatitis in pregnancy may also be associated with an increased risk of preterm delivery.[20] On the other hand, our data suggest that procedures themselves, such as ERCP, are not associated with an increased risk of preterm delivery or low birth weight. Further, cholecystectomy performed during pregnancy probably does not appear to lead to preterm delivery and low birth weight.[21] In aggregate, our data and these previous studies lead us to speculate that endoscopic or surgical interventions and even mild post-ERCP pancreatitis do not create a setting of prolonged physiologic dysfunction in pregnancy that would influence fetal growth. However, hepatobiliary diseases can result in maternal and fetal physiologic dysfunction leading to adverse pregnancy outcomes such as prematurity and low birth weight. Moreover, such detrimental effects are likely to be most pronounced when they occur during the first trimester, when fetal development is most vulnerable. Thus, it is particularly important to identify hepatobiliary disease early during pregnancy and to intervene appropriately as early as possible.

Various methods have been used to reduce or avoid medically related radiation during pregnancy.[3] CT scans are avoided in all patients when possible to prevent radiation. In the largest study measuring the fetal radiation exposure dose during ERCP, the mean (SD) fluoroscopy time was 14 (13) seconds. The fetal radiation exposure was 40 (SD, 46) mrad.[10] In another study, the mean (SD) fluoroscopy time was 3.2 (1.8) minutes and the estimated average (SD) fetal radiation dose was 310 (164) mrad.[9] The authors suggested that these fetal doses are substantially below the 5 to 10 rad level considered to be a risk for teratogenesis. Of note, there is a 2% to 3% incidence of major congenital malformations that exists in the general population.[4] MRCP can be performed in pregnant women with low suspicion of choledocholithiasis. EUS is another potential alternative imaging modality to detect biliary stone in this situation. However, our data have suggested that prophylactic sphincterotomy during ERCP can effectively reduce the risk of recurrent biliary pancreatitis during pregnancy. In many of our patients, we proceeded with ERCP and prophylactic biliary sphincterotomy. This explains a high biliary sphincterotomy rate (94.1%) in our study cohort although choledocholithiasis was diagnosed in 51.5% of study patients. EUS was not used at all in our patients to detect choledocholithiasis. In many of our patients, the pretest probability of choledocholithiasis is high. In addition, EUS adds extra costs, time, and special expertise.

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