INTRODUCTION

Hormonal changes during pregnancy contribute to elevated cholesterol levels and a delay in gallbladder emptying, both of which can increase the risk of gallstone formation, the incidence of which is between 3-12% during pregnancy. The majority of pregnant patients with cholelithiasis are asymptomatic and do not require therapy. However, 1.2% of pregnant women with cholelithiasis may exhibit symptoms, including right upper quadrant discomfort, nausea, or symptoms of cholecystitis. Symptomatic gallstone disease is in fact the second most common abdominal emergency during pregnancy.

After acute appendicitis, and may require surgical intervention.

On occasion, a stone or sludge may escape the gallbladder and lodge in the common bile duct (CBD) causing biliary colic, gallstone pancreatitis and/or obstructive jaundice. Although uncommon, choledochoolithiasis during pregnancy is a challenging dilemma for treating gastroenterologists, given its complications including pancreatitis and cholangitis, which can be life threatening for both the mother and the fetus, and often necessitate immediate intervention. Endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy and stone extraction is the standard of care for management of choledochoolithiasis. Aside from the inherent risks of the ERCP procedure, pregnant patients face additional concerns due to the potential harm that
ionizing radiation could have on the fetus.\textsuperscript{5} There have been strategies implemented to relegate the radiation risk to the fetus, such as reducing fluoroscopy time or adopting non-radiation ERCP (NR-ERCP) techniques whenever possible.

Overall, ERCP is now considered relatively safe and effective during pregnancy, and this article intends to discuss the various nuances of this clinical scenario.

\textbf{Indications}

Advances in imaging modalities, including abdominal ultrasound (USG), magnetic resonance imaging/cholangiopancreatography (MRI/MRCP), and endoscopic ultrasound (EUS), have generally obviated diagnostic ERCP in non-pregnant and pregnant patients. Prior to undertaking an ERCP, a strong suspicion of the presence of a CBD stone, as well as radiological assessment is essential.

ERCP should be avoided for weak indications such as preoperative cholangiography in patients with a low probability of having choledocholithiasis. Intraoperative cholangiography (IOC) during laparoscopic cholecystectomy (CCY) should be done in patients thought to have an intermediate probability of a retained CBD stone, and if definite filling defect/s seen, a postoperative ERCP can be performed, thereby avoiding unnecessary preoperative ERCP.

The most common indications for performing therapeutic ERCP during pregnancy are symptomatic choledocholithiasis, obstructive jaundice, biliary pancreatitis, cholangitis or less commonly biliary or pancreatic ductal injury.
ERCP has also been utilized in pregnant patients for management of choledochal cysts, pancreatic adenocarcinoma, and parasitic infestation of the biliary tree according to a few reports. ERCPs are considered therapeutic when one or more of the following procedures are performed: endoscopic sphincterotomy, stone removal, stent placement, and/or stricture dilation. Pancreatic endotherapy generally requires relatively lengthy fluoroscopy time, can be technically challenging, and may be associated with increased risk, and hence, it should preferentially be avoided unless absolutely indicated.

Contraindications
In serious obstetric complications such as placental abruption, imminent delivery, ruptured membranes, or eclampsia, endoscopy is generally contraindicated.

Concerns and Risks Associated with ERCP in Pregnancy

Radiation Risk to the Fetus
Exposure to ionizing radiation prenatally can have an impact on embryonic and fetal development, depending on the dose and gestational age at which the exposure occurs. Potential radiation exposure risks to the fetus can be divided into four categories: intrauterine fetal death; malformations and disturbances of growth and development; mutagenic; and carcinogenic effects.

Radiation-induced damage can result in fetal growth restriction and congenital malformations, often associated with intellectual disability, as well as the possibility for increased cancer risk. Although the risk of developing cancer from radiation is low, it is a stochastic effect with no clear radiation threshold level defined. Fetal radiation exposure is not routinely assessed, and hence total fluoroscopy time is the most suitable alternative surrogate, although they do not directly correlate well. A thermoluminescent dosimeter (TLD) placed on the upper back in the line of primary radiation beam has been shown to best correlate with fetal radiation exposure.

Maternal Outcomes
Pancreatitis, post-sphincterotomy bleeding, perforation, and cholecystitis are among the maternal non-pregnancy related post-ERCP adverse events. The data on patients being more susceptible to post-ERCP pancreatitis (PEP) during pregnancy versus the general population are conflicting. The literature, however, is limited by a small sample size and its retrospective nature.

A national cohort study compared data from pregnant women (n=907) to non-pregnant women (controls, n=2721) who underwent ERCP and found that PEP occurred in 12% of pregnant women and in 5% of controls (P<0.001). This higher rate was attributed to the avoidance of fluoroscopy to verify wire and catheter position, as well as time constraints to perform ERCP as soon as possible during pregnancy.

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Fetal Outcomes
ERCP is also associated with a higher risk of preterm labor, especially when performed during the first trimester. Tang et al., observed in the same study that following ERCP, 53 patients (90%) had a full–term pregnancy, but patients who underwent ERCP during the first trimester had only 73% of deliveries at term, but a higher risk of preterm delivery (20%), and an increased risk of low-birth-weight infants (21%). However, in 2019, a systematic review and meta-analysis by Azab et al. (27 studies, 1307 pregnant patients who underwent ERCP) noted that, despite the increased risk of preterm labor and low birth weight, ERCP was deemed relatively safe on the fetus without any reported cases of fetal congenital malformation or stillbirth. Another systematic review in 2018 showed that therapeutic ERCP has a very high rate of technical success in clearing the bile duct of gallstones, and has a relatively low and acceptable rate of maternal and fetal complications.

Special Considerations and Modifications of ERCP During Pregnancy
A general principle in the care of women with an acute biliary tract disorder during pregnancy is to provide the most conservative management possible with the hope of delaying intervention only when
Figure 2. 37 year-old G3P2 with acute pancreatitis (suspected gallstone) and obstructive jaundice. 2(A and B): EUS demonstrates 6-7 mm stone in distal CBD (with shadowing); 2(C): Successful cannulation with aspiration technique and advancement of guidewire; 2(D): Confirmation of guidewire position and minimal contrast injection with minimal use of fluoroscopy; 2(E and F): Completion of ERCP endoscopically with sphincterotomy and stone removal, without further use of fluoroscopy.
ERCP During Pregnancy: A Review of Safe Practices

absolutely indicated, until after pregnancy or until the second trimester, when surgical intervention is relatively safest.

As previously stated, ERCP should not be used as a diagnostic procedure and instead non-invasive imaging modalities (USG, MRI/MRCP) are relied upon to achieve a diagnosis. MRCP does not require the use of paramagnetic contrast agents like gadolinium, which has been shown to cross the placenta, and is hence safe. Because of the risk of radiation exposure and low sensitivity for choledocholithiasis, computed tomography (CT) scans are generally avoided in pregnant patients,\textsuperscript{6,8,17-19} but may become necessary in rare malignancy related circumstances, or to assess severe pancreatitis.

If ERCP is planned for a pregnant patient, there are some special considerations and strategies that need to be deliberated. The primary goal of these approaches is to improve overall safety of ERCP for pregnant patients, and reducing the amount of radiation exposure to the fetus. It may be reasonable to manage asymptomatic and mildly symptomatic choledocholithiasis patients expectantly, with the understanding that there is still a risk of cholangitis and gallstone pancreatitis if stones are left untreated.\textsuperscript{6,9}

Timing of ERCP

When possible, ERCP should be postponed to until after delivery or at least until the second trimester, which is regarded a relatively safer trimester to perform surgical interventions, although ERCP has been performed safely throughout all trimesters of pregnancy. To avoid fetal exposure to ionizing radiation during the period of organogenesis and the risk of spontaneous abortion, ERCP during the first trimester should be avoided, recognizing that this may not always be the case. Similarly, during the late third trimester, elective ERCP should be deferred to after delivery, if possible, to minimize fetal loss and birth related complications.\textsuperscript{6-7,17}

Informed Consent, Position, Radiation Shielding, Medications and Sedation

Informed Consent: The patient and family should be extensively counseled about the indication and steps of the ERCP procedure, along with detailed discussion of expected benefits, and risks for the mother and the fetus, as well as alternatives, and obtain written informed consent from the patient.\textsuperscript{15}

Involving patient’s spouse/significant other and additional family members (of patient’s choice) is essential to build trust as well as to relieve their anxiety. Although the perceived risk of radiation exposure is much greater than the actual risk, the importance of full explanation of these risks to the woman and her family prior to the exposure cannot be overemphasized.

Patient Position: During the ERCP, the patient should be placed in a left pelvic tilt or left lateral position to avoid vena cava or aortic compression. Supine position is also equally acceptable. The patient may be placed in the standard prone position if the procedure is performed early in the pregnancy or second trimester, but should be avoided in the later part of pregnancy.

Radiation Shielding: Lead shields ought to be employed to reduce radiation exposure to the fetus. They should be placed underneath the patient’s abdomen, keeping in mind that the x-ray beam originates from beneath the patient.\textsuperscript{6,20} The value of placing a second lead shield over the patient’s abdomen is unproven, and is practiced per endoscopist’s discretion.

Maternal-Fetal Monitoring: An astute monitoring is recommended during the ERCP procedure, with documentation of fetal heart tones prior to sedation and immediately upon completion of the procedure. In the first and second trimester, the procedure can be performed in GI endosuite, but in the third trimester, it is generally better to perform the procedure in Operating Room (OR) with presence of Obstetrics support, in an event of labor or other complications necessitating delivering of the baby.

Medications: Glucagon (category B) is used to reduce intestinal contraction during ERCP and has been shown to have no significant teratogenicity or other adverse effects on the mother or the fetus, so it can be used safely. Diatrizoate (category D) is a contrast agent used during ERCP to visualize the biliary tree. Because the contrast is iodine-based, transient fetal hypothyroidism is a theoretical risk; however, no convincing evidence prevents its use, especially when the risk of maternal cholangitis and its consequences on the fetus are weighed against the theoretical risk of fetal hypothyroidism. The use
Sedation: ERCP in pregnant patients should preferably be performed with anesthesia professionals, so that the patient is adequately sedated, and hemodynamics and airway are appropriately managed, while the endoscopist is able to concentrate solely on the procedure steps.\textsuperscript{9,15} Decision regarding monitored anesthesia care using Propofol versus general anesthesia with intubation should be per anesthesia professional’s prerogative, depending on patient comorbidities, clinical situation and procedural indication. Sedative medications for ERCP, such as meperidine (Category B), propofol (Category B), fentanyl (Category C), and midazolam (Category D), are thought to be generally safe during pregnancy. Meperidine alone can be used for procedural sedation during pregnancy (preferred over category C agents such as fentanyl and morphine), followed by small doses of midazolam as needed. Propofol can cause respiratory depression rapidly and should only be used in pregnant patients with the consultation of an anesthesiologist.\textsuperscript{9,21,22} In our anecdotal clinical experience at our centers, the majority of pregnant patients underwent safe and successful ERCP with use of propofol, administered by anesthesia professionals.

Rectal Indomethacin: Rectal indomethacin is considered standard of care for prevention of post-ERCP pancreatitis,\textsuperscript{36} however, there is lack of data
for its use in pregnant women for us to comment on its routine use. In pregnant women presenting with preterm labor or shortened cervix, which places them at risk for preterm labor and delivery, oral or vaginal or rectal indomethacin is often used as a tocolytic to prolong pregnancy by decreasing uterine contractions. However, increased neonatal complications including oligohydramnios, renal failure, necrotizing enterocolitis, intraventricular hemorrhage, and closure of the patent ductus arteriosus have been reported with the use of indomethacin.

Since the physiological effects of single dose of rectally administered indomethacin during ERCP (especially if done during second trimester) is unclear, and given these concerns, the authors endorse this decision to be made on a case-by-case basis considering the degree of difficulty of biliary cannulation, inadvertent pancreatic duct cannulation/injection and other procedural factors.

Multidisciplinary Approach

Obstetric support should be available in the event of any pregnancy-related complications. As stated before, anesthesia professionals should be preferably involved.

Modified ERCP Techniques in Pregnant Patients

A few modifications to ERCP technique could be considered in a pregnant patient, with an overall goal of minimizing procedure time and fluoroscopy time, in order to achieve best outcomes for both the mother and the fetus.

A) Techniques to Reduce Fluoroscopy Time and Exposure

The majority of our understanding of radiation effects on fetal outcomes is derived from epidemiological and observational studies from atomic radiation survivors or from animal studies. According to the American College of Obstetrics and Gynecology (ACOG), fetal growth restriction, fetal risk of anomalies, or abortion have not been reported with a dose of radiation less than 50 mGy (or 5 rad), which is much higher than the typical ERCP exposure range, which maybe as low as 0.1 – 3 mGy per procedure.\(^{14,23}\) Such complications may occur at radiation doses higher than 100-200 mGy, but such doses are not usual in general diagnostic radiology, especially with ERCP, where the fetus lies outside the primary beam.

During the fluoroscopy phase in an ERCP, radiation is used to visualize the anatomy of the biliary tract. It is also used to verify that the bile duct cannulation, stone extraction, and sphincterotomy are all done safely and successfully.\(^{14}\) Certain modifications in fluoroscopy should be employed, carefully communicated to the fluoroscopy technician assisting on the case, to reduce radiation exposure, as below:

- Minimizing the overall fluoroscopy time by using short taps of fluoroscopy and avoiding hard copy images, which emit between 25 to 2000 mrem of radiation per procedure.\(^{17}\)
- Utilizing the last-image hold feature to review images
- Avoiding the use of magnification
- Using low-dose-rate pulsed fluoroscopy and collimating the x-ray beam to the smallest field possible.\(^{6}\) (Figures 3A and 3B) Collimation prevents unnecessary exposure of anatomy outside the area of interest, and it also improves image quality by producing less scatter radiation from these areas.

For confirmed choledocholithiasis, sphincterotomy and stone extraction need be performed (Figure-1). Biliary strictures and leaks are generally treated with stenting.\(^{20,24}\) To further minimize radiation use in a pregnant patient, a two-stage approach can also be employed in complicated pancreatobiliary pathologies, wherein the initial ERCP is done as a temporary measure using minimal or no fluoroscopy, and typically includes biliary sphincterotomy and stent placement, and the subsequent ERCP is definitive in the post-partum period, with required detailed interventions.\(^{25}\)
**B) Techniques to Avoid Radiation**

Radiation-free ERCP for biliary stone removal in pregnant patients has been shown to be successful in various case reports and series.

### Radiation-Free ERCP Techniques

- In a pregnant patient with previous sphincterotomy, successful biliary cannulation can be performed without use of fluoroscopy, using a choledochoscope (Spyglass™), as reported by Girotra et al., with accurate localization of biliary calculi and successful removal. Complete clearance of the bile duct can also be confirmed using choledochoscopy (Figures 3C and 3D). Placement of a biliary stent is optional; to prevent recurrent biliary events during pregnancy, especially if the gallbladder is still in-situ with more confirmed stones/sludge. This stent can later be removed post partum, once CCY is accomplished.

- For pregnant patients with native papilla, an empirical bile aspirate guided technique is used, which includes biliary cannulation using a sphincterotome, followed by bile aspiration to confirm biliary access, and then sphincterotomy, and stone extraction with a balloon catheter. This technique may miss additional stones due to the lack of a clear definition of the ductal system. However, most residual stones, if present, should pass without difficulty with an adequate sphincterotomy. Alternately, a biliary stent can be placed temporarily until post-partum period, as discussed above.

### Imaging-Guided Techniques

Transabdominal ultrasound, EUS or choledochoscopy/cholangioscopy can be used to provide imaging guidance.

The use of trans-abdominal ultrasound during ERCP procedure has the benefit of allowing real-time visualization, wire placement confirmation, and observation of stone clearance.

EUS is now widely available and can be used to determine common bile duct diameter, as well as the number, morphology, and size of bile duct stones (Figure 2), and can sometimes eliminate the need for an ERCP, in cases where stones spontaneously pass. Choledochoscopy is a helpful tool, not only for visualizing calculi and confirming ductal clearance as previously discussed, but also for disrupting choledocholithiasis with laser therapy or electrohydraulic lithotripsy. Therefore, to confirm clearance of the common bile duct, one could consider using EUS or choledochoscopy, in order to minimize radiation use.

The potential disadvantages of not using radiation may include the possibility of a lengthier procedure time, difficulty with visually confirming bile duct cannulation, inadvertent cystic duct cannulation, remnant biliary stones and difficulty recognizing bile leak or stricture. As per the systematic review by Azab et al., radiation-free techniques do not appear to decrease the fetal and pregnancy related complications, but they seem to reduce the rates of non-pregnancy complications.

**CONCLUSION**

Therapeutic ERCP during pregnancy can be safely and effectively performed, when definitively indicated. A multidisciplinary approach should be adopted, wherein an experienced endoscopist performs the procedure, with assistance of anesthesia professionals, with a parallel active involvement of obstetricians and surgeons, to manage any potential peri-procedural pregnancy-related issues. The procedure should be scheduled during the second trimester, which is generally deemed safest for any surgical intervention. First trimester (early organogenesis period) and late third trimester (higher chances of obstetric complications) are generally avoided, if possible. The general principle while performing ERCP during pregnancy should be to minimize the amount of radiation that the fetus is exposed to, and as a result, radiation-avoidance strategies have been suggested and proven to be effective in smaller series.

**References**

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Answers to this month’s crossword puzzle:

1. GALL
2. LIVER
3. BLADDER
4. DODGER
5. DER
6. ER
7. E
8. A
9. O
10. I
11. L
12. O N
13. PET
14. STOOL
15. LINED
16. H A
17. T
18. S
19. E
20. GO
21. O O
22. E
23. R
24. EE
25. K I N
26. A T
27. S H
28. O O
29. O C
30. N A
31. T E
32. B U
33. D E S O N I D E
34. B
35. U S E
36. E E R
37. D G U T
38. L A
39. N O B E S I T Y
40. U N I
41. E
42. U D T
43. E A R
44. O
45. S U M
46. S Y S T E M
47. B U R N