Article

Successful ERCP Application in Pregnant Women with Cholestasis

Lecturer Hülya Aladağ [1,*], Murat Aladağ [2,*]

[1] Malatya Turgut Özal University, Faculty of Medicine, Department of Obstetrics and Gynecology
[2] Malatya Turgut Özal University, Faculty of Medicine, Division of Gastroenterology
* Correspondence: hulya.aladag@ozal.edu.tr; murat.aladag@ozal.edu.tr

Abstract: Purpose: We aimed to present successful endoscopic retrograde cholangiopancreatography (ERCP) applications and results in our pregnant cases. Method: The data of 14 successful ERCP applications in our pregnant patients between 2016 and 2022 were evaluated retrospectively. ERCP procedure was performed by endoscopists experienced in biliary endoscopy while the patients were on the left decubitus position. Fluoroscopy was performed using methods to reduce fetal radiation exposure. Short-term fluoroscopy were used during the procedure. Fluoroscopy times applied to the patient were recorded. Results: ERCP and sphincterotomy were applied to 14 pregnant women who presented with cholestasis findings. Two of the procedures were performed aproprate trimesters in whole patients. The mean maternal age in our pregnant women was 24.8±5.6 (19-38), mean gestational age was 17.8 weeks (10-34w). The fluoroscopy time was 0.16 min (0-35sec). Fetal radiation exposure was negligible in 10 pregnant women (10 sec) and between 10-14 seconds in 4 pregnant women. The estimated fetal radiation exposure of the two women was between 30 and 35 seconds. Procedure-related complications were one minimal bleeding after sphincterotomy, two hyperamylasemia after ERCP, and one acute respiratory distress syndrome. Cholecystitis developed in one pregnant woman two days after ERCP. Conclusion: When necessary precautions are taken under the control of a multidisciplinary team, ERCP can be safely applied during pregnancy, and successful results can be obtained.

Keywords: Pregnancy; cholesistitis; pancreatitis; ERCP

1. Introduction

Physiological changes during pregnancy prone to biliary illness (1,2). High estrogen arouse hepatic cholesterol produce and cholesterol secretion (3,4). Increased progesterone during pregnancy delays the evacuation of the gallbladder, causing bile stasis and slowing the discharge of bile acids (3,4). This risk increases as the number of pregnancies increases, and multigravid mothers are more prone to bring out biliary complications (4). In a prospective study of 3,200 pregnant women without gallstones on initial abdominal ultrasonography (US), new cholelithiasis increasis in the next period and up to 10.2% in the sixth week after delivery (4,6). Complications for instance cholangitis, symptomatic choledocholithiasis, biliary stenosis and biliary pancreatitis require urgent treatment (6,7)

Physiological changes during pregnancy prone to biliary disease (1,2). High estrogen levels stimulate hepatic cholesterol production and cholesterol secretion (3,4). Increased progesterone during pregnancy delays the emptying of the gallbladder, causing bile stasis and slowing the release of bile acids (3,4). This risk increases as the number of pregnancies increases, and multiparous women are more likely to develop biliary complications (4). In a prospective study of 3,200 pregnant women without gallstones on initial abdominal ultrasonography (US), new cholelithiasis increasis in the next period and up to 10.2% in the sixth week after delivery (4, 6). Complications for instance acute cholesistitis, cholan-

 doi:10.20944/preprints202212.0548.v1

gitis, symptomatic choledocholithiasis, biliary stenosis and biliary pancreatitis require urgent treatment (6,7). These complications related to cholelithiases are relatively rare and can be treated conservatively (1-4).

Endoscopic retrograde cholangiopancreatography (ERCP) is most commonly required for gallstone pancreatitis or choledocholithiasis or. Major concerns relate to fetal radiation exposure. Pregnant patients with gallstone disease complicated by cholangitis or choledocholithiasis can be safely and successfully treated under the guidance of endoscopic retrograde cholangiopancreatography (ERCP) (9-11).

A general principle in caring for women with acute biliary tract disorders during pregnancy is to delay intervention until post-pregnancy or the second trimester. Since the complication rates will increase as the procedure is delayed, ERCP should be performed in these pregnant women without losing time in severe cases.

Table 1. Laboratory results of the patients.

Mean Age	**24,8±5,6 (19-38),**
BK:	**14300 ± 670 (11000-16000)**
ALT	**124 (75-420)**
AST	**130 (65-390)**
GGT	**220 (160-430)**
Bilirubin	**9.5 (2.5-16)**
MRCP	**Stone and debris in 13 cases, 1 case normal**
USG	**choledochal stones in 11 cases, IHBD dilatation in 2 cases, 1 case normal**

Table 2. Treatment results.

Number of patients	**14**
Diagnosis	**Ten choledocholithiasis, 2 IHBD dilatation, one biliary pancreatitis, one jaundice enzyme elevation**
Procedure	**Decompression with endoscopic sphincterotomy balloon in 13 cases** **Stent in 1 case, was removed after delivery.**
Choledochal content:	**Stone in 10 cases** **Debris in 2 cases** **Nothing in 2 cases**
Gestational age (week)	**18-35 weeks**
Delivery time (week)	**Ten term** **2 cases 36 weeks** **1 case 34 weeks, 1 case 35 weeks**

2. Materials and Methods

We aimed to present the results of the ERCP procedure in 14 pregnant patients with cholecystitis, choledocholithiasis, and cholangitis due to biliary pancreatitis after blood tests and imaging procedures.

3. Results

Our cases in which gallbladder stones, choledocholithiasis, and cholangitis due to acute pancreatitis were detected in the ultrasonography of our pregnant women with right upper quadrant pain, fever, jaundice, and laboratory examinations of elevated white

 doi:10.20944/preprints202212.0548.v1

blood cells, liver enzymes, ALT, AST, GGT, elevated bilirubin were evaluated by the multidisciplinary team. Pregnants were consulted by the obstetrics and gynecology before the procedure. The condition of the mother and fetus was evaluated and recorded in detail by experienced physicians.

Our patients results evaluated retrospectively. Magnetic resonance cholangiopancreatography was used to diagnose choledocholithiasis in cases with high bilirubin levels and intrahepatic bile duct dilatation on abdominal ultrasonography. A diagnosis of acute cholangitis due to choledocholithiasis was made in pregnant women with fever, abdominal pain, jaundice, and radiological findings.

The benefits, risks, and alternatives of ERCP-related treatment procedures were explained to all pregnant women and their family members in detail, and their verbal and written consents were obtained. Before the ERCP procedure, laboratory results were checked and recorded. Experienced obstetricians checked fetus and mother before the procedure. Pethidine HCl (≤100mg) and midazolam (≤3mg) were used for analgesia and sedation by an anesthesiologist experienced in the ERCP procedure. The patients were placed in appropriate position to prevent the vena cava or abdominal aorta from compressing the uterus in pregnant women. In order to decrease the radiation exposure of the fetus, a lead pate was placed under the pregnant woman before the mother was placed on the C-arm machine.

The ERCP procedure was performed by senior biliary endoscopists with experience in at least 200 procedures per year. After the appropriate duodenoscope was placed in the lumen, the bile duct was cannulated along the papilla with guide-wire cannulation of the bile duct, and attention was paid to seeing the bile leaking around the guide wire to confirm easy cannulation. Endoscopic sphincterotomy was performed after the bile duct anatomy, and the stone inside was visualized with the film taken after cannulation with very little opaque material. Stones and debris were removed by rapidly sweeping at least twice with a bile balloon. Appropriate endoscopic biliary stents were placed in cases where it was unclear whether the stones were cleared entirely.

Confirmation of successful therapeutic ERCP was achieved with clinical improvement of pregnant women and improvement of laboratory results. After ERCP procedures, ultrasonographic evaluation of the biliary tract was performed by a radiologist experienced in bile ducts. Afterward, all pregnants were followed up until discharge.The mean fluoroscopy time was 0.16 min (0-35 sec). Fetal radiation exposure was negligible in 10 pregnant women (< 0.0001 Gy), and it was between 0.0001-0.0002 Gy in 4 pregnant women. The estimated fetal radiation exposure of the two women was between 0.0002 and 0.0005 Gy.

3. Results

Our patients mean maternal age was 24.8±5.6 (19-38), and the mean gestational age was 24 weeks (8-35 weeks). Patients laboratory data are shown in Table 1. Treatment results findings are shown in Table 2. Successful cannulation was achieved in all pregnant women. No procedure-related complications were observed in the mother and fetus. Following endoscopic sphincterotomy with the bipolar flow during the ERCP procedure, stones and debris in the biliary tract were removed with biliary balloons. Six mm balloon was used in 10 patients and 8 mm balloon was used in 4 patients. The removal of stones in the biliary tract was confirmed with ultrasonography in all patients. Procedure-related complications were one minimal bleeding after sphincterotomy, two hyperamylasemia after ERCP, and one acute respiratory distress syndrome. Cholecystitis developed in one pregnant woman two days after ERCP. All patients delivered at term, and none of them had a recurrence during the 6-month follow-up. After ERCP, no preterm delivery or any other complication was observed. The clinical follow-ups continued without any problems and the patients were discharged

4. Discussion

Estrogen and progesterone irregularity in pregnancy increase the lithogenicity of bile and impair the emptying of the gallbladder causes gallstone formation. Acute cholecystitis is the second most common non-obstetric emergency in pregnant women. Choledocho-

 doi:10.20944/preprints202212.0548.v1

lithiasis and its consequent complications, such as pancreatitis are potentially fatal diseases for the fetus and mother (4,10,11). Biliary pancreatitis has serious maternal and fetal mortality (4). As in all patients, the treatment of gallstone-related diseases in pregnant women should be adjusted according to the patient. However, in pregnant women, the condition of the mother and the fetus and the gestational age should be considered when deciding during treatment. Asymptomatic gallstone patients do not need treatment. In patients with biliary colic but for whom complications such as cholecystitis of gallstones, cholangitis, biliary tract obstruction, and biliary pancreatitis are not considered, treatment is generally started with conservative methods (4,11-13).

For most patients with suspected gallstone disease and choledocholithiasis, preprocedural evaluation includes radiographic imaging (e.g., abdominal ultrasonography, magnetic resonance cholangiopancreatography (MRCP)) to confirm the diagnosis typically (4,14-16). Endoscopic ultrasound (EUS) is a reasonable alternative if the diagnosis of choledocholithiasis remains uncertain and/or MRCP cannot be performed or is doubtful (4,17). EUS can be done just before ERCP, and ERCP may not be necessary if gallstones are not detected. In addition, stone characteristics (e.g., size, number, location) can be evaluated to facilitate the ERCP procedure in patients with confirmed choledocholithiasis with EUS (4,18). Pre-procedural preparation for pregnant patients undergoing ERCP is the same as for non-pregnant patients undergoing ERCP.

Cholangitis in pregnancy has serious mortality rates for mother and fetus. The most effective treatment method for cholangitis and pancreatitis caused by choledocholithiasis is ERCP (4,5). However, the use of ERCP in pregnancy is limited due to the use of radiation. The risks associated with ERCP may include fetal death, intrauterine growth retardation, malformations, and childhood cancer (4). It has been recommended to use imaging methods that do not contain ionizing radiation during pregnancy (9). Therefore, attempts to completely exclude radiation in ERCP are of great importance. The literature has shown that ERCP can be safely performed in experienced hands without fluoroscopic use (9-12). Therapeutic ERCP is routinely used during pregnancy with definite indications in clinical practice (12,13). Although the literature on radiation exposure in ERCP has shown that ERCP is safe and effective early after the procedure, the long-term adverse effects of children's exposure to radiation are unknown (13-18). Late side effects such as cancer can take years to develop after delivery. To overcome this radiation problem, ERCP without radiation should be the first choice during pregnancy (4,5,19, 20)

In a meta-analysis by Azab et al., in which they evaluated 27 studies involving 1307 pregnant patients, the overall event rate for general adverse outcomes was found to be 15.9%, adverse events were found to be 17.6% in the ERCP group without radiation, and 21.6% in the ERCP group with radiation. Fetal side effects were found at 6.2% in the group without radiation and 5.2% in the ERCP group with radiation, and the difference was not statistically significant ($p>0.05$). As for the side effects in pregnant mothers, it was found to be 8.4% in the ERCP group without radiation and 7.6% in the ERCP group with radiation, and there was no significant difference between the groups ($p>0.05$). While the rate of non-pregnancy adverse events in pregnant mothers was 7.6% in those with ERCP without radiation, it was lower than 14.9% in those with ERCP with radiation, and there was a statistically significant difference between the two groups ($p<0.05$). These results showed that the ERCP procedure performed by experts experienced in biliary endoscopy is effective and safe in pregnancy, and it reduces the rates of non-pregnancy-related complications but does not reduce fetal and pregnancy-related complications (4,11,17). Despite the increased risk of preterm birth and low birth weight, ERCP was relatively safe on the fetus, without any reported fetal congenital malformation (4, 18,19). However, the risk of preterm delivery and intrauterine growth retardation was increased in both groups.

We applied ERCP with radiation in our study. In order to shorten the fluoroscopy time and to reduce the radiation exposure of the mother and especially the fetus, lead shields were placed under the mother during the ERCP procedure, and lead shields were

 doi:10.20944/preprints202212.0548.v1

placed in the front when necessary. Fluoroscopy was not used in any patient without control; only a film was taken for viewing at baseline. Experienced biliary endoscopists provided cannulation in all cases in one go. Then, by performing endoscopic sphincterotomy, the bile ducts were swept with 6 and 8 mm biliary balloons, stones and debris were removed, and no more than two balloon sweeps were performed. In our study, procedural complications were one minimal bleeding after sphincterotomy, two hyperamylasemia after ERCP, and one acute respiratory distress syndrome. Cholecystitis developed in one pregnant woman two days after ERCP. Our pregnant women were followed up and recorded for six months after delivery, and no complications such as malformation, miscarriage, or stillbirth were observed during this period. Our results were consistent with the literature.

5. Conclusions

In conclusion, our findings suggest that ERCP is a method that should be applied without delay for bile duct decompression during pregnancy to prevent potentially life-threatening complications for both mother and fetus. Non-radiation techniques can reduce the risk of non-pregnancy outcomes but do not affect fetal or pregnancy outcomes.

In conclusion, few studies have been conducted worldwide and in our country regarding ERCP without radiation during pregnancy (4,5,10,19,20). Therapeutic ERCP without radiation with guide-wire cannulation may be an effective treatment strategy for pregnant women with strong indications for ERCP. Laboratory and ultrasonographic follow-up of patients after the procedure can be a safe, simple, and cost-effective strategy to monitor the procedure's effectiveness. Stent placement should be considered when clearing the choledoch has failed. More extensive studies are needed to draw firm conclusions about ERCP with or without radiation.

References

1. Ibiebele I, Schnitzler M, Nippita T, Ford JB. Outcomes of Gallstone Disease during Pregnancy: a Population-based Data Linkage Study. Paediatr Perinat Epidemiol 2017; 31:522.
2. Luthra AK, Patel KP, Li F, et al. Endoscopic intervention and cholecystectomy in pregnant women with acute biliary pancreatitis decrease early readmissions. Gastrointest Endosc 2019; 89:1169.
3. Smith I, Gaidhane M, Goode A, Kahaleh M. Safety of endoscopic retrograde cholangiopancreatography in pregnancy: Fluoroscopy time and fetal exposure, does it matter? World J Gastrointest Endosc 2013; 5:148.
4. Azab M, Bharadwaj S, Jayaraj M, et al. Safety of endoscopic retrograde cholangiopancreatography (ERCP) in pregnancy: A systematic review and meta-analysis. Saudi J Gastroenterol 2019; 25:341.
5. Ersoz G, Turan I, Tekin F, et al. Nonradiation ERCP with endoscopic biliary sphincterotomy plus papillary balloon dilation for the treatment of choledocholithiasis during pregnancy. Surg Endosc 2016; 30:222.
6. Fine S, Beirne J, Delgi-Esposti S, Habr F. Continued evidence for safety of endoscopic retrograde cholangiopancreatography during pregnancy. World J Gastrointest Endosc 2014; 6:352.
7. Liao C, Thosani N, Kothari S, et al. Radiation exposure to patients during ERCP is significantly higher with low-volume endoscopists. Gastrointest Endosc 2015; 81:391.
8. Magno-Pereira V, Moutinho-Ribeiro P, Macedo G. Demystifying endoscopic retrograde cholangiopancreatography (ERCP) during pregnancy. Eur J Obstet Gynecol Reprod Biol 2017; 219:35.
9. Huda A, Garzón WJ, Filho GC, et al. Evaluation of staff, patient and foetal radiation doses due to endoscopic retrograde cholangiopancreatography (ERCP) procedures in a pregnant patient. Radiat Prot Dosimetry 2016; 168:401.
10. Annals of the International Commission on Radiological Protection. Pregnancy and Medical Radiation. 2000. https://journals.sagepub.com/doi/pdf/10.1177/ANIB_30_1 (Accessed on April 25, 2022).
11. Radiation and Pregnancy: A Fact Sheet for Clinicians. Centers for Disease Control and Prevention. Available at: https://emergency.cdc.gov/radiation/prenatalphysician.asp (Accessed on November 08, 2017).
12. Laudanno O, Garrido J, Ahumarán G, et al. Long-term follow-up after fetal radiation exposure during endoscopic retrograde cholangiopancreatography. Endosc Int Open 2020; 8:E1909.
13. Kwok K, Hasan N, Duloy A, et al. American Society for Gastrointestinal Endoscopy radiation and fluoroscopy safety in GI endoscopy. Gastrointest Endosc 2021; 94:685.
14. Brewer Gutierrez OI, Godoy Brewer G, Zulli C, et al. Multicenter experience with digital single-operator cholangioscopy in pregnant patients. Endosc Int Open 2021; 9:E116.
15. Ludvigsson JF, Lebwohl B, Ekbom A, et al. Outcomes of Pregnancies for Women Undergoing Endoscopy While They Were Pregnant: A Nationwide Cohort Study. Gastroenterology 2017; 152:554.
16. Inamdar S, Berzin TM, Sejpal DV, et al. Pregnancy is a Risk Factor for Pancreatitis After Endoscopic Retrograde Cholangiopancreatography in a National Cohort Study. Clin Gastroenterol Hepatol 2016; 14:107.

 doi:10.20944/preprints202212.0548.v1

17. Annals of the International Commission on Radiological Protection. Pregnancy and Medical Radiation. 2000. https://journals.sagepub.com/doi/pdf/10.1177/ANIB_30_1 (Accessed on April 25, 2022).
18. Radiation and Pregnancy: A Fact Sheet for Clinicians. Centers for Disease Control and Prevention. Available at: https://emergency.cdc.gov/radiation/prenatalphysician.asp (Accessed on November 08, 2017.
19. Cappell MS, Stavropoulos SN, Friedel D. Systematic review of safety and efficacy of therapeutic endoscopic-retrograde-cholangiopancreatography during pregnancy including studies of radiation-free therapeutic endoscopic-retrograde-cholangiopancreatography. World J Gastrointest Endosc 2018; 10:308.
20. Ünal HÜ, Saruç M. Gebelikte safra taşları ve akut pankreatit. Kutsal NE, editör. Gebelikte Gastrointestinal Sistem ve Karaciğer Hastalıkları. 1. Baskı. Ankara: Türkiye Klinikleri; 2021. p.14-23.