

---

Miroslav Cvetanović<sup>1</sup>, Jasmina Cvetanović<sup>2</sup>, Rastko Živić<sup>1</sup>,  
Miljan Milanović<sup>1</sup>, Djordje Miladinović<sup>1</sup>

## HEPATOBIILIARY DISEASES IN PREGNANCY

**Abstract:** Non-obstetric surgery during pregnancy is estimated to have a frequency of 0.3–2.2%. Laparoscopy due to gynecological indications is the most common procedure in the first trimester (34%), while appendectomy is the most common procedure during the second and third trimesters. Acute cholecystitis is the second highest incidence of acute abdomen in pregnancy with an incidence range of 1 to 1600–3000. Cholelithiasis is the cause of cholecystitis in 90% of cases. Differential diagnosis includes: myocardial infarction, acute liver disease in pregnancy, HELLP syndrome, etc. Hepatobiliary ultrasound is the diagnostic method of choice. Two diagnostic and therapeutic procedures in pregnancy have not yet been fully defined: ERCP and perioperative cholangiography.

AP appears to occur most commonly in the advanced stage of pregnancy, more commonly in the second or third trimester. Typical symptoms are the same as in the general population. Ultrasound is the initial method of choice for both the confirmation of pancreatitis and the exclusion of other diseases. Although there is no consensus, in severe and unclear cases, abdominal CT is used. Early surgery for patients with necrotizing AP is not recommended and should be delayed as much as possible. Antibiotics are not indicated.

The goals of treatment are to avoid organ failure and infectious complications that have an impact on fetal development and maternal survival. There is still a dilemma as to whether pregnant patients with gallstones should be treated conservatively. The outcome of the disease depends, as in the general population, on the severity of the disease, the cause, and the fetal outcome depends in part on the trimester of pregnancy in which AP occurred.

The number of non-obstetric surgeries during pregnancy is relatively high, and surgical procedures may be necessary at any stage of pregnancy.

**Key words:** pregnancy, non-obstetric surgery, cholecystitis, pancreatitis

---

<sup>1</sup> CH „Dr Dragiša Mišović”

<sup>2</sup> City Council for Medical Emergency, Belgrade

## ***Introduction***

Non-obstetric surgery during pregnancy is estimated to have a frequency of 0.3–2.2%.

So as many as 87,000 pregnant women in the United States and 115,000 pregnant women in the European Union annually need some sort of non-birth anaesthesia surgery. These figures may be higher as more recent studies have shown that as many as 0.35% of women had outpatient interventions, then 2.6% of women who had laparoscopic interventions and 1.2% of adolescents had positive pregnancy test results during surgery. (1)

If the patient's history indicates that she may be pregnant, it may be advisable to test her for pregnancy, although this is not routine practice. Surgery may be necessary at any stage of pregnancy.

A study conducted in Sweden on 5405 patients who had surgery during pregnancy showed that 42% had surgery during the first trimester of pregnancy, 35% during the second trimester, and 23% during the third trimester.

Laparoscopy due to gynecological indications is the most common procedure in the first trimester (34%), while appendectomy is the most common procedure during the second and third trimesters. The indications may be related to current pregnancy, or not related to pregnancy at all. Indications regarding current pregnancy are most commonly associated with cervical incompetence or the existence of ovarian cysts. (2) The most common indications for non-current pregnancy surgical procedures are acute abdominal conditions (most commonly appendicitis and cholecystitis), trauma and malignancies.

Two recent studies examining maternal mortality in the UK indicate that maternal mortality is also present in early pregnancy and that the most common causes are bleeding, sepsis, thromboembolic complications and anesthesiologic reasons.

Fetal mortality risks are associated with:

1. the effects of the disease on the fetus;
2. teratogenicity of anesthetic agents and other medicines used in the perioperative period;
3. intraoperative disorders of uteroplacental perfusion and fetal oxygenation
4. risks of preterm birth. (1,2)

## ***Acute cholecystitis in pregnancy***

Acute cholecystitis is the second highest incidence of acute abdomen in pregnancy with an incidence range of 1 to 1600–3000. Cholelithiasis is the cause of cholecystitis

in 90% of cases. Progesterone-induced smooth muscle relaxation causes a bile duct, and elevated estrogen levels increase bile lithogenicity. Both agents contribute to the increased incidence of gallstones.

The symptomatology is the same as in the general population: nausea, vomiting, dyspepsia, fatty food intolerance as well as pain in the epigastrium or below the right rib arch that can spread in the back to the right shoulder blade. A positive Murphy's sign is less common in pregnancy.

Differential diagnosis includes: myocardial infarction, acute liver disease in pregnancy, HELLP syndrome, preeclampsia, acute hepatitis, pancreatitis, gastroduodenal ulcer disease (with or without perforation), pyelonephritis, lower right lobe pneumonia and the first stage of herpes zoster. (3)

Hepatobiliary ultrasound is the diagnostic method of choice. Ultrasound findings suggestive of acute cholecystitis in which surgery was induced are thickening (>5mm) with stratification of the gallbladder wall, pericholecystitis, congestive cystic contraction, and a positive sonographic Murphy sign. If there is evidence of enlarged extra and / or intrahepatic bile ducts, MR cholangiography is indicated.

Such ultrasound finding also suggests an absolute indication for emergency surgery.

Emergency or early surgery is sometimes recommended for acute cholecystitis without the following signs: a) the total amount of medication is reduced, b) the recurrence of the disease is 44–92% depending on the trimester of presentation, c) the hospitalization is shorter overall – in the case of medical therapy the patient requires repeated hospitalizations for elective cholecystectomy and d) avoid potentially life-threatening complications for the mother and fetus, including: biliary peritonitis, biliary sepsis and biliary pancreatitis. (4)

Incisions include a right subcostal incision or upper median laparotomy, that is, an open method laparoscopic approach (Hasson technique). The laparoscopic approach was not induced in the third trimester due to difficulty in manipulating the instruments.

Two diagnostic and therapeutic procedures in pregnancy have not yet been fully defined, although there are guidelines from the American Society for Gastrointestinal and Endoscopic Surgery. The first is the use of cholangiography in patients with intraoperative cholecystitis

with choledocholithiasis (stones in choledochus). Cholecystectomy is always performed with choledochotomy and extraction of concretions from the choledochus. (5)

The follow-up recommendations are as follows:

- in the case of advanced pregnancy, no intraoperative cholangiography is performed, but only secondary cholangiography after delivery;
- in the case of early pregnancy, secondary cholangiography is performed after the stage of fetal organogenesis with the protection of the pelvis with a lead apron. (6)

Another issue is the use of ERCP (endoscopic retrograde cholangiopancreatography).

If absolutely indicated, it is performed with the minimum amount of radiation that can be achieved:

- a) complete papillotomy and calculus extraction and choledochus flushing, then contrasting evidence of neat choledochus filling with contrast,
- b) by taking fluoroscopic images and subsequently re-examining them instead of repeatedly repeating them using radiation;
- c) using ultrasound during papillotomy.

In highly specialized centers, MR cholangiography is used instead of ERCP. (7)

### *Acute pancreatitis*

The incidence is the same as the incidence of cholecystitis in pregnancy. AP appears to occur most commonly in the advanced stage of pregnancy, more commonly in the second or third trimester. 19% of AP occurred in the first, 26% in the second, 53% in the third (consistent with the potential lithogenic effect of estrogen during pregnancy) and 2% in the postpartum period, most commonly occurring in the third trimester and early postpartum.

One of the causes is increased intra-abdominal pressure and direct uterine pressure on the bile ducts as well as an increased incidence of gallstones. (1,3)

The second most common cause is alcohol pancreatitis, and the more common causes are: previous abdominal surgery, blunt abdominal trauma, hyperparathyroidism, perforated ulcer. Hyperlipidemic pancreatitis is represented by 4–6%.

**Clinical presentation.** AP is reflected in the same clinical presentation as during pregnancy. However, it is difficult to diagnose it on the basis of physical examination and medical history due to many other abdominal conditions and maternal changes during pregnancy.

Typical symptoms are the same as in the general population:

- sudden and severe epigastric or gingival pain with spread in the back in 40% of cases, followed by frequent vomiting and fever;
- peristalsis is weakened by secondary paralytic ileus;
- the abdomen is extremely painful for palpation in the projection of the pancreas;
- symptoms can last from 1 to 3 weeks;
- In severe cases, tachycardia, hyperventilation and odor of acetone in the breath may be present.

The differential diagnosis is the same as in acute cholecystitis. A triple or greater increase in amylase as well as an increase in serum lipase have been shown to have the same diagnostic significance as in the general population. Lipase growth is a better predictor of pancreatitis than in the general population. Because other diseases in the area (cholecystitis, peptic ulcer, etc.) can cause a temporary increase in these enzymes, serial monitoring of the enzyme may sometimes be necessary for diagnosis.

The laboratory parameter that facilitates diagnosis is the ratio of amylase to creatinine clearance, calculated according to the formula  $\sim 100 \times [\text{amylase (urine)} \times \text{creatinine (serum)}] / [(\text{amylase (serum)} \times \text{creatinine (urine)})] \sim$ . A ratio  $> 5\%$  suggests to acute pancreatitis in pregnancy. (4,8)

Ultrasound is the initial method of choice for both the confirmation of pancreatitis and the exclusion of other diseases. Although there is no consensus, in severe and unclear cases, abdominal CT is used. Ranson criteria for pancreatitis that have not been systematically analyzed in the pregnant population can be used to orient the severity of the disease.

The therapy is conservative and involves parenteral nutrition (initially), analgesics, oxygen, fluid and electrolyte supplementation, and the introduction of antibiotic therapy if the temperature rises or sepsis develops.

The patient should be placed in the intensive care unit. Analgesics use tramadol or meperidine, which, unlike morphine, does not cause spasm of the Oddi sphincter, which could worsen pancreatitis. Surgical therapy is induced in cases of disease progression, as well as the occurrence of complications: infected pancreatic necrosis, peripancreatic abscess, or ruptured / infected pancreatic pseudocyst (occurs in a later course of the disease). All infected material should be removed with the introduction of flow drainage. In the case of biliary pancreatitis, ERCP was induced with papillotomy and extraction of choledochus stones, or papilla Vateri, within 48 hours of the onset of the disease, unless with conservative therapy.

there is improvement. Mortality from the available data is not defined, however, it is probably similar to that in the general population, meaning that it can be as high as 30% in severe pancreatitis.

Early surgery for patients with necrotizing AP is not recommended and should be delayed as much as possible. Antibiotics are not indicated.

The indications for surgery and antibiotics are the following:

- pancreatic necrosis 3–4 weeks after the onset of symptoms;
- large intra-abdominal exudates;
- clinical deterioration. (1,4,9)

In some cases, percutaneous drainage may delay necessary surgery, and is necessary in patients with pancreatic abscesses. A necrectomy should be done as late as possible, and can be performed after a caesarean section.

It is recommended to prevent uterine contractions if they occur prematurely, but if worsening occurs, it is sometimes necessary to complete the pregnancy.

Indications for completion of pregnancy:

- 1) obvious signs of abortion;
- 2) fetal distress or intrauterine death;
- 3) if the fetus is mature for extrauterine life, a caesarean section is induced, and if intrauterine death is involved, the birth is induced.

**Treatment.** When diagnosed with AP in pregnancy, it is necessary to evaluate the severity of the disease according to clinical signs, analysis of blood, urine and other methods, to determine the appropriate treatment method for each patient. Treatment of AP is not standardized and the more severe form of AP continues to be a major problem for treatment.

The goals of treatment are to avoid organ failure and infectious complications that have an impact on fetal development and maternal survival. With the advancement of diagnostic and treatment methods, the outcome for both mother and fetus has improved significantly in recent decades.

**Principles of surgical treatment.** Surgical treatment has two aspects that include the invasive treatment of AP and the cause that led to its occurrence. There is still a dilemma as to whether pregnant patients with gallstones should be treated conservatively. There is also a risk of the fetus from repeated attacks, complications related to gallstones, risk of malnutrition due to reduced oral food intake.

On the other hand, there is a risk of surgery for the fetus, primarily because of anesthesia and the specificity of laparoscopic surgery. However, laparoscopic cholecystectomy is the method of choice in patients who have not responded to conservative therapy or recurrent seizures. The benefits of laparoscopic surgery are the same as in the non-pregnant population, less postoperative pain, less postoperative ileus, significantly shortened hospitalization period, less use of analgesics, and faster return to normal diet. There is also less manipulation of the uterus and a reduced risk of deep vein thrombosis due to faster motility.

**Outcome and prognosis.** The outcome of the disease depends, as in the general population, on the severity of the disease, the cause, and the fetal outcome depends in part on the trimester of pregnancy in which AP occurred. Perinatal and maternal mortality varies from 20-60% most commonly in the third trimester. On the other hand, fetal mortality is reduced, primarily due to good neonatal care in the case of preterm delivery. It is extremely important to monitor the condition of the fetus, so decide in a timely manner for childbirth if there is a worsening of the mother's condition. (10)

The number of non-obstetric surgeries during pregnancy is relatively high, and surgical procedures may be necessary at any stage of pregnancy.

## References

1. Practice ACoO ACOG Committee Opinion No. 474: nonobstetric surgery during pregnancy. *Obstet Gynecol.* 2011; 117: 420–421.
2. Pearl J., Price R., Richardson W., Fanelli R. Society of American Gastrointestinal Endoscopic S (2011) Guidelines for diagnosis, treatment, and use of laparoscopy for surgical problems during pregnancy. *Surg Endosc.* 25: 3479–3492.
3. de Bari O., Wang TY., Liu M., Paik CN., Portincasa P., Wang DQ. Cholesterol cholelithiasis in pregnant women: pathogenesis, prevention and treatment. *Ann Hepatol.* 2014; 13(6): 728–45.
4. Cappell MS., Friedel D. Abdominal pain during pregnancy. *Gastroenterol Clin North Am* 2003; 32: 1–58.
5. Cox TC., Huntington CR., Blair LJ., Prasad T., Lincourt AE., Augenstein VA., Heniford BT. Laparoscopic appendectomy and cholecystectomy versus open: a study in 1999 pregnant patients. *Surg Endosc.* 2016; 30: 593–602.
6. Brent RL. Protection of the gametes embryo/fetus from prenatal radiation exposure. *Health Phys.* 2015; 108: 242–274.
7. Capecomorin S. Pitchumoni and Balaji Yegneswaran. Acute pancreatitis in pregnancy. *World J Gastroenterol.* 2009; 15(45): 5641–5646.
8. Ainsworth AP., Rafaelsen SR., Wamberg PA., Durup J., Pless TK., Mortensen MB. Is there a difference in diagnostic accuracy and clinical impact between endoscopic ultrasonography and magnetic resonance cholangiopancreatography? *Endoscopy.* 2003; 35: 1029–1032.
9. Pitchumoni CS., Yegneswaran B. Acute pancreatitis in pregnancy. *World J Gastroenterol.* 2009; 15: 5641–6.
10. Hernandez A., Petrov MS., Brooks DC., Banks PA., Ashley SW., Tavakkolizadeh A. Acute pancreatitis and pregnancy: A 10-year single center experience. *J Gastrointest Surg.* 2007; 11: 1623–7.