

Management of biliary lithiasis in pregnancy – an updated overview

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ABSTRACT

It is estimated that 2% of pregnant women develop gallstones during pregnancy. Symptoms of biliary lithiasis may vary during pregnancy, from a slight added digestive discomfort to biliary colic of varying intensity, acute cholecystitis, or acute pancreatitis. Ultrasonography is the gold standard for diagnosis of sludge and gallstones, being both highly sensitive and specific. Initial management overlaps with the out-of-pregnancy management, initiating conservative, supportive care, as well as an adequate diet. Laparoscopic cholecystectomy is considered a safe intervention in pregnancy, being the second most common surgery after appendicectomy. If open laparoscopy is preferred, the major risk - perforation of the uterus - is avoided. Important complications of gallstones in pregnancy, jaundice and acute pancreatitis can be resolved safely and quickly by cholangiopancreatography (ERCP) techniques, with stone removal, sphincterotomy or stent mounting. After remission of pancreatic symptoms, laparoscopic cholecystectomy can be performed. Recent scientific data and current practice suggest an increase of biliopancreatic emergencies during pregnancy (probably due to rising incidence of obesity, age of gravida, prolonged use of oral combined contraceptives, dyslipidemia, etc.). Surgeons, as well as obstetricians, should be aware of the prompt modern management of these cases.

Keywords: biliary lithiasis, pregnancy, acute cholecystitis, jaundice

INTRODUCTION

Maternal physiology is subject to significant adaptive changes in pregnancy, which can lead to diseases that require therapeutic attitude. Such an example is the genesis of biliary stones in pregnancy, with the most varied manifestations: biliary sludge, gallstones, and migration of these stones, with complex pathological consequences (from biliary colic to acute cholecystitis, cholangitis, cholelithiasis and even pancreatitis) (1).

MATERNAL PHYSIOLOGY AND LITHOGENESIS

Biliary lithogenesis and its pathology in pregnancy are stimulated by the following mechanisms: changes in maternal lipid metabolism (serum hyperlipidemia) and biliary stasis. The adaptations of lipid metabolism, in the sense of favoring lipolysis, are most often manifested in the second half of pregnancy. Thus, by resetting the maternal hypothalamic lipostat, the storage of lipids in the central deposits and the transfer of essential fatty acids

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Article History:

Received: 20 November 2021

Accepted: 27 November 2021

transplacental toward the fetus are favored. Circulating levels of all lipidic fractions increase: total serum cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, reaching the following values: 265 +/- 30 mg/dl, 135 +/- 30 mg/dl, 80 +/- 15 mg/dl, and 245 +/- 75 mg/dl.

The gallbladder contractility is reduced during pregnancy. Under the direct influence of progesterone (which inhibits the contractility of the biliary smooth muscle mediated by cholecystokinin), biliary stasis occurs, with increasing volume of residual bile (twice the non-pregnant state). Being hyper-saturated with cholesterol crystals, the bile initially constitutes the biliary sludge (in 30% of pregnant women), and then the gallstones are formed (1). It is estimated that 2% of pregnant women develop gallstones during pregnancy. The risk of developing gallstones increases proportionate to the increase in parity, the incidence being much higher in multiparous.

Additional risk factors are: older age (nowadays, when more and more patients choose to delay the time of conception), pre-pregnancy obesity, long-term treatments with estrogen-progestin oral contraceptives.

THE CLINICAL PICTURE

Symptoms of biliary lithiasis may vary during pregnancy, from a slight added digestive discomfort (nausea, occasional vomiting, intermittent right upper quadrant or epigastric pain, headache) to biliary colic of varying intensity, acute cholecystitis, or acute pancreatitis. These more serious complications of gallstones develop in less than ten percent of symptomatic patients. The biliary colic occurs postprandially (usually one to three hours after a fat rich meal), having the same characteristics as in non-pregnant patients (progressive pain, then plateau in different ranges -sometimes very intense, and dissolution after several hours).

Acute cholecystitis has as a precipitating factor the obstruction of the cystic duct, with consecutive bacterial superinfection. The most frequent isolated germs are *Escherichia coli*, *Klebsiella* and *Enterobacter*. The incidence of acute cholecystitis is 1 in 1000 pregnant women (2).

Clinical manifestations occur in pregnant women who already have experienced pain in the hypochondrium or were known to have gallstones, but can also appear as a lightning in a clear sky, in a pregnant woman without a significant history. Pregnant women complain of pain in the right upper quadrant, radiating to the right shoulder or back, loss of appetite, nausea and vomiting, fever. The positive Murphy sign is present during abdominal examination, as well as guarding.

Ultrasonography is the gold standard for diagnosis of sludge and gallstones, being both highly sensitive and specific. Acute cholecystitis is recognized due to gallbladder distension, thick walls, pericholecystic fluid and the sonographic Murphy sign.

Common bile duct stones are sometimes difficult to visualize by transabdominal ultrasonography, which is less sensitive. More accurate diagnosis is provided by endoscopic ultrasound and endoscopic retrograde cholangiopancreatography (ERCP). Non-contrast magnetic resonance cholangiopancreatography (MRCP) is useful in complicated cases, when other diagnostic procedures failed. It appears to be safe for the fetus, during the second and third trimester (3).

Other imaging modalities (computed tomography, plain radiography or cholescintigraphy with 99mTC-hepatic iminodiacetic acid HIDA scan) are usually not recommended during pregnancy.

All patients with biliary complaints should have a thorough laboratory test evaluation (complete blood count, liver, and hepatic tests). In patients with acute cholecystitis, leukocytosis is moderate. If complications occur, elevated liver aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase and pancreatic (amylases, lipases) enzymes, or elevated total bilirubin levels may be observed.

Differential diagnosis of right upper quadrant and/ or epigastric pain in pregnant patients must be made with severe acute complications of pregnancy - HELLP syndrome, severe preeclampsia, acute fatty liver, abruptio placentae, uterine rupture or chorioamnionitis.

THERAPEUTIC CONDUCT IN SYMPTOMATIC PATIENTS

Initial management overlaps with out-of-pregnancy management, initiating conservative, supportive care (nasogastric aspiration, vigorous intravenous hydration, antispasmodic medication – butylscopolamine, pain control - acetaminophen or intravenous opioids and antibiotic therapy, initially empiric (acute cholecystitis or cholangitis) – amoxicillin plus potassium clavulanate or clavulanate), as well as an adequate diet (3).

In over 50% of cases, the symptoms remit, but the recurrence rate is high, and some patients will also reach the need for a surgical gesture. These recurrences will occur during pregnancy and especially in the third trimester of pregnancy, when the intervention associated risks are high (the impossibility of performing a laparoscopy and the need for laparotomy, the higher risk of premature birth, etc.). This is the reason why most organizations with concerns in the field (ACOG, ACS) recommend early surgical treatment (during the second trimester).

ter, if possible), giving preference to minimally invasive techniques - laparoscopic cholecystectomy (3,4).

Laparoscopic cholecystectomy is considered a safe intervention in pregnancy, being the second most common surgery after appendectomy (5). If open laparoscopy is preferred, the major risk - perforation of the uterus - is avoided (6). Insufflation is performed slowly, until a pneumoperitoneum of 10 mmHg is obtained. Also, the other trocars are introduced under direct laparoscopic visual control (7). If the pregnancy is more advanced, the peritoneal cavity may be entered directly through the Palmer point (left hypochondrium, on the midclavicular line, 2 cm below the costal rim). Another accepted variant is gas-free laparoscopy, with the use of a special abdominal retractor-elevator (8). Studies published in the literature of the last decade show that peritoneal insufflation with CO₂ has similar effects in pregnant women compared to non-pregnant women. A slight increase in pCO₂ and a slight decrease in pH may occur, due to absorption of CO₂. Maternal-fetal effects may include hypercarbia and acidosis. For this reason, throughout the intervention, end-tidal CO₂ (ET CO₂) is monitored, which must be maintained between 30-35 mmHg (9).

Through hypercarbia and increased intra-abdominal pressure, as well as decreased venous return, there are some changes in the cardiovascular system: increased heart rate, increased systemic vascular resistance, increased lung pressure, central venous pressure, and arterial pressure. Maternal-fetal consequences may be placental hypoperfusion, with possible fetal hypoxia and acidosis. These changes are well controlled if the insufflation pressure values are not exceeded over 15 mmHg. Except for the uterus perforation with the Verres needle or the central trocar, no other specific complications are noticeable (6).

Choledochal lithiasis is a rare manifestation in pregnancy. The clinical picture can sometimes be very acute, with epigastralgia, pain in the right hypochondrium or covering the whole abdomen, fever, jaundice, vomiting. Leukocytosis is marked, bilirubin levels are significantly increased. The association of the pancreatic reaction will complete the paraclinical picture with increases in serum amylase levels. Ultrasonography and MRI document the lithiasis and its location.

Jaundice and acute pancreatitis may be important complications of biliary lithiasis during pregnancy, but they can be resolved safely and quickly by ERCP techniques, with stone removal, sphincter-

otomy or stenting (10). After remission of pancreatic symptoms, laparoscopic cholecystectomy must be performed (11). If this gesture is not performed, acute pancreatitis may recur. Compared to other conditions, acute pancreatitis carries the highest risk of premature birth. Mild sedation-analgesia (pethidine and midazolam) is recommended, which has the advantage of mild tocolysis (12,13).

The specialized literature has presented in the last years the successful solution of the pathology of the bile ducts through ERCP without the use of radiological exploration, using complementary techniques to confirm the correctness of the procedure. Another recommended option is rechecking – final ERCP – during the postpartum period (14).

Also, MRI retrograde cholecystography (MRCP), with the advantages of lack of irradiation, but with particularly high costs, can be considered a good alternative in pregnancy (15).

OBSTETRIC FEATURES

The favorable evolution of the pregnant woman with acute biliary pathology can be ensured only by the perfect teamwork of the surgeon, anesthesiologist, and obstetrician. The latter has the task of controlling two of the associated risks: the risk of the threat of abortion or premature birth (due to increased uterine contractility) and the neonatal risks - respiratory distress and cerebral hemorrhage of the newborn (16).

The risk of uterine contractility increases with the age of pregnancy. Ideally, continuous cardiotocography monitoring allows the precise timing of need of tocolytic medication (antispasmodics, beta-mimetic IV for up to 48 hours or of an oxytocin receptor inhibitor - tractocile - Atosiban). After 28 weeks of amenorrhea, fetal lung maturation is accelerated by the administration of betamethasone or dexamethasone, and the prophylaxis of neonatal cerebral hemorrhage is achieved by the administration of phytomenadione.

CONCLUSIONS

Recent scientific data and current practice suggest an increase of biliopancreatic emergencies during pregnancy (probably due to the rising incidence of obesity, age of gravida, prolonged use of oral combined contraceptives, dyslipidemia etc.). Surgeons, as well as obstetricians, should be aware of the prompt modern management of these cases, including ERCP and MRCP.

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