

# Acute cholecystitis in pregnancy

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## ABSTRACT

Acute cholecystitis is the most common non-obstetric abdominal emergency in pregnant patients. It is a consequence of increased formation of cholelithiasis, and occurs due to inflammation of the gallbladder, usually caused by the blockage of the cystic duct. There is also described the appearance of cholecystitis without the presence of gallstones, and this is named as acalculous cholecystitis.

Elevated levels of estrogen and progesterone are thought to be a cause of women's increased predisposition to this condition. In pregnancy, literature describe the appearance of gallstones in 1% to almost 3% pregnancies, and it is known that pregnancy by itself affects the contractility of gallbladder.

For sludge and gallstones, even if there is a large range of symptoms, almost up to 50% of patients are asymptomatic. Acute cholecystitis is suspected in a patient with continuous pain in the right upper quadrant, alongside anorexia, vomiting, and fever.

Laboratory findings in acute cholecystitis show leukocytosis, an elevated level of bilirubin, up to 4 mg/dl and elevated liver tests. The most useful imaging tool in diagnosing gallstones and further acute cholecystitis is an abdominal ultrasound.

Any pregnant women with upper right quadrant pain should be hospitalized to exclude other differential diagnoses and for pain management, usually done with acetaminophen. Supportive care treatment includes administration of intravenous fluids and when necessary antibiotic therapy.

Recent studies have showed that interventional surgery by itself brings some associated risks during pregnancy, but with an experienced team of surgeon, anesthesia specialist, and obstetrician, outcomes are better, no matter the trimester of pregnancy.

**Keywords:** acute cholecystitis, gallstones, sludge, pregnancy, gallbladder disease

## INTRODUCTION

During pregnancy, acute cholecystitis (AC) is a common consequence of increased formation of cholelithiasis and occurs due to inflammation of the gallbladder, usually caused by the blockage of the cystic duct. The most common etiology for cystic duct obstruction is the presence of the gallstones or biliary sludge [1,2].

There is also described the appearance of cholecystitis without the presence of the gallstones, and this is noted as acalculous cholecystitis. In developing countries such as Asia or southern Africa, the

most common reason for cholecystitis is found to be helminthic infection (ascariasis) [1,2].

Incidence of gallstones appearance during pregnancy is between 0.05-0.8% and treating pregnant patients with gallbladder disease has always been a challenge [2].

North American statistics have showed that every year more than 20 million of Americans are affected by cholelithiasis, the majority of them being asymptomatic, 1-4% of patients develop biliary colic, and up to 20% of them will suffer from AC without treatment [2,3].

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## MATERIALS AND METHODS

We conducted a PubMed research for primary articles, reviews and guidelines. Search words were “acute cholecystitis”, “gallstones”, “sludge” and “cholecystectomy in pregnancy”. We used only English publications. All the publications used can be found in the reference section.

## EPIDEMIOLOGY AND ETIOLOGY

Race, weight, diet, serum lipid levels and genetic predisposition are some of the factors that are liable for appearance of cholecystitis. Elevated levels of estrogen and progesterone are thought to be a cause of women increased predisposition to this condition [3].

In pregnancy, literature describe the appearance of gallstones in 1% to almost 3% pregnancies, and it is known that pregnancy by itself affects the contractility of gallbladder. Besides pregnancy, obesity and a large body mass index adds as risk factors for gallbladder disease [2,3].

Even though there is a susceptibility for biliary sludge in pregnancy, AC is not described more frequently than in general population, and it only occurs in 0.1% of pregnant women [1-3].

## PATHOPHYSIOLOGY

Inflammation of the gallbladder usually caused by obstruction of the cystic duct, leads to acute cholecystitis. Even when the cystic duct is blocked, gallbladder mucosa still continues to produce mucus, and without having a way out, the pressure in the gallbladder will rise and subsequent to arterial stasis, ischemia and later on necrosis will install [1].

Prostaglandins I and E synthesis, which intervene in inflammatory response, is stimulated because of the trauma caused by the gallstones. In some cases, in women who had multiple pregnancies or in patients having received total parenteral nutrition, sludge can persist and that can lead to microlithiasis. Usually patients with sludge are asymptomatic [4].

Also, pregnancy generates modifications in bile acid synthesis, that lead to a slower capacity of bile to solubilize cholesterol, because of an excess production of hydrophobic bile acids like chenodeoxycholate [5].

These changes return to normal in one or two months after delivery.

## CLINICAL MANIFESTATIONS

During pregnancy, there are no important changes regarding anatomy of the gallbladder, and so clinical manifestations are comparable to

non-pregnant patients, and diagnosis is forthright [6].

For sludge and gallstones, even if there is a large range of symptoms, almost up to 50% of patients are asymptomatic. AC is suspected in a patient with continuous pain in the right upper quadrant, alongside anorexia, vomiting, and fever [7].

Laboratory findings in AC show leukocytosis, an elevated level of bilirubin, up to 4 mg/dl and elevated liver tests. Sometimes even if frank jaundice usually does not appear, when present, it should raise the suspicion of Mirizzi's syndrome, simultaneous choledocholithiasis or gallbladder perforation. Mirizzi's syndrome is defined by the obstruction of the common hepatic duct resulted from an impacted stone in the cystic duct or antrum of the gallbladder that cause external compression [4-7].

The apprehension of breath during inspiration while palpating the gallbladder is called Murphy's sign and is a useful indication, alongside tenderness in the right upper quadrant [7].

## DIAGNOSIS

With an almost 90% specificity rate, the most useful imaging tool in diagnosing gallstones and further AC is an abdominal ultrasound. Findings that enhance the suspicion for AC are the thickening of the gallbladder wall larger than 3 mm, pericholecystic fluid, and a positive sonographic Murphy's sign [8].

Magnetic resonance imaging (MRI) scan can also be useful for detecting gallstones, however, is not so sensitive in diagnosis of AC. Other investigations such as magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatogram (ERCP) are rarely used in pregnancy because of the risk of exposure the fetus to ionizing radiation and to magnetic fields during these procedures [8,9].

However, since 1990 literature describe 9 cases of ERCP during pregnancy, and none of them reported any serious harm on both the mother and the fetus, because the quantity of radiation during procedure was between 18 and 314 mrad, smaller than damaging dose between 5 to 10 rad. Nevertheless, throughout the first trimester radiation risk is higher [9,10].

## DIFFERENTIAL DIAGNOSIS

Epigastric pain or right upper quadrant pain during pregnancy must be differentiated from other severe pregnancy related conditions such as preeclampsia, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), abruptio placentae or uterine rupture [11]. While hypertension

is the required indicator for preeclampsia, thrombocytopenia is mandatory in HELLP syndrome. Neither hypertension nor thrombocytopenia are found in gallbladder disease [12,13].

Clinical symptoms like uterine sensitivity, uterine contractions or vaginal bleeding make difference between abruption and gallbladder disorder but pain is not limited to epigastrium or right upper quadrant [14].

Majority of uterine ruptures are at patients that had a vaginal birth after a previous cesarean section. Patients presents with clinical symptoms like an unusual fetal heart rate or even fetal death, uterine tenderness, vaginal bleeding, and shock. Usually, uterine rupture happens after the beginning of the labor [15].

## MANAGEMENT

Most patients diagnosed with gallstones are asymptomatic and do not require treatment. In the past, in cases of AC, nonoperative treatment was preferred particularly in the first and third trimester [16].

Any pregnant women with upper right quadrant pain should be hospitalized to exclude other differential diagnoses and for pain management, usually done with acetaminophen. Supportive treatment includes administration of intravenous fluids and when necessary antibiotic therapy [16].

Nonsteroidal anti-inflammatory medication is usually not recommended in pregnancy, particularly after 32 weeks gestational age, since potential bad outcomes can happen after more than 48 hours of using it, such as premature closure of ductus arteriosus [17].

Patients suffering from AC, cholangitis, or severe gallstone pancreatitis, are in need for antibiotic therapy, even though AC is mainly an inflammatory disease, because of the bile stasis and obstruction of the cystic duct, infection of the gallbladder can take place. *Escherichia coli*, *Enterococcus*, *Klebsiella*, and *Enterobacter* are the most common bacteria found in the gallbladder [18,19].

In 1882 Carl Langenbuch in Berlin performed the first open cholecystectomy, and it was gold standard procedure for cholecystitis until 1987, when a French surgeon first performed a laparoscopic cholecystectomy [18].

In a nationwide analysis of morbidity, comparing cholecystectomy treatment with non-operative treatment for pregnant women with AC, 6,390 pregnant women were included having AC: 38.2% undergo cholecystectomy and results showed that patients with non-operative treatment were at higher risk for maternal-fetal complications. Regarding readmission rates after 30 days, in the non-operative treatment group rates were superior [18-20].

Another large prospective study made between 2001-2015 in Lund and Malmo, included all pregnant women admitted in hospital between that period, with diagnosis of biliary colic or cholecystitis or acute pancreatitis. A total of 35 women undergo surgical intervention as treatment and 62 cases went for conservative treatment. Results showed that regarding readmission, group of intervention had better outcomes compared to group of conservative treatment where 24 patients were readmitted, and also regarding safety, results were superior in intervention group [20].

When it comes to surgical treatment for cholelithiasis in pregnancy, literature is divided in two phases, pre- and post-laparoscopic cholecystectomy period. Two case report studies in Los Angeles have sustained different opinions on this issue in pre-laparoscopic cholecystectomy period. During the second trimester of the pregnancy, or even prior to planned pregnancy, Dixon et al, suggested surgical treatment for women with biliary symptoms. Contrary, Hiatt et al. recommend continuing medical management until delivery, because of the high fetal mortality reported in the surgical group [17].

Most studies showed that in cases of recurrent symptomatic biliary colic, further relapses are more serious than previous episodes and for that reason cholecystectomy should be considered [21].

A study made between January 2003 and September 2015, including 23,939 pregnant women with AC, tried to identify the trends in management of AC. Comparing laparoscopic cholecystectomy with opened cholecystectomy, they demonstrated that opened cholecystectomy loses in favor of the laparoscopic one, with an increased risk of preterm labor, delivery or abortion. On the other hand, laparoscopic cholecystectomy was associated with a reduced risk of amniotic infection and antepartum hemorrhage [2].

Same study showed that postponement of surgery for pregnant woman with AC is related to an increased risk for complications for both mother and fetus [2].

## DISCUSSION

Most common non-obstetric abdominal emergency in pregnant women are disorders of the gallbladder, mostly symptomatic gallstone. Because of the affected contractility of the gallbladder during pregnancy, women during this period of time are at higher risk for developing gallstones. Also, another risk factor for this condition that sometimes may lead to AC is modification in bile acid synthesis, which causes a slower capacity of bile to solubilize cholesterol [1-5].

Criteria for diagnosis of the gallstones has no differences than in non-pregnant patients, and the

most useful and certain method for identifying stones remains ultrasonography. Current literature showed that magnetic resonance cholangiopancreatography and cholescintigraphy are safe during pregnancy, as an alternative option for diagnosis when ultrasonography is unclear [6-7].

In cases of uncomplicated biliary colic, laboratory findings usually are in normal range, but in cases of AC or other complicated gallbladder disease, can be an important tool, showing elevated levels of direct bilirubin, hepatic enzymes and alkaline phosphatase. But physicians should always have in mind the normal range for pregnant patients, which sometimes may differ from non-pregnant patients [4-7].

In this review we emphasize recommendations from past and present literature regarding the safety of surgical intervention in pregnancy in cases of AC. As showed, concerns about risk for fetal harm during surgical procedure are diminished, and even if actual recommendations for performing cholecystectomy necessity is applied through every trimester of the pregnancy, some studies raised the idea that, if possible, to postpone it until second trimester [10].

The idea to defer surgical procedure came from the fact that at the end of the first trimester, organogenesis is complete, and uterus still has moderate dimensions and do not obturate the surgical view [10,11].

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## CONCLUSIONS

Acute cholecystitis is the second most common non-obstetric cause of abdominal pain demanding surgery during pregnancy.

Appearance of gallstones and later on AC is dependent on a number of risk factors, such as race, weight, diet, serum lipid levels and genetic predisposition. Because of changes that take place during pregnancy, pregnant women are at a greater risk of having gallstones.

Right upper quadrant or epigastric abdominal pain are the main symptoms for patients presenting with AC. Usually, pain appears postprandial, especially after having a fat meal. But the majority of patients with gallstones are asymptomatic and there is no need for further treatment. Otherwise, symptomatic pregnant woman with biliary colic requires admission into hospital for intravenous fluid therapy and pain control.

Recent studies have showed that interventional surgery by itself brings some associated risks during pregnancy, but with an experienced team of surgeon, anesthesia specialist, and obstetrician, outcomes are better, no matter the trimester of pregnancy.