

## GALLSTONES IN PREGNANT WOMEN: DETECTION, OBSTACLES, AND TREATMENT

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**Introduction:** *Gallstone disease often manifests in pregnant women due to physiological changes, a multifaceted interplay of factors that alter bile composition, and the crystallization of substances that promote stone formation. The increased level of estrogen during pregnancy enhances the secretion of cholesterol in bile, while progesterone slows down the emptying of the gallbladder, leading to a predisposition to the formation of stones in the gallbladder. From a diagnostic point of view, ultrasonography remains the gold standard since it is non-invasive and without radiation. The presence of stones in the gallbladder can trigger complications such as cholecystitis, pancreatitis, or cholangitis, posing a risk for both the mother and the fetus. In the presence of symptoms, treatments vary from conservative treatment, which includes dietary adjustment and pain relief. However, in case complications arise, the possibility of laparoscopic cholecystectomy a minimally invasive surgical procedure can be considered. The timing of the surgery, preferably in the second trimester, is crucial to minimize risks to the fetus. Thorough monitoring and an interdisciplinary approach are essential for treating gallstone disease during pregnancy.*

**Keywords:** *Gallstone disease, Pregnancy, Hormonal changes, Physiological changes, Complications, Dietary modifications.*

### RELEVANCE

The prevalence of gallstones among pregnant women is constantly increasing. Recent studies show that almost 12% of pregnant women are diagnosed with gallstones, compared to 7% ten years ago[1]. This growing trend has caught the attention of the medical community, prompting the need for more comprehensive research and management strategies.

It is known that pregnancy induces a series of physiological changes that, although vital for the well-being of the mother and fetus, may inadvertently pave the way for gallstone formation. Hormonal shifts occurring during pregnancy, especially the elevation of estrogen and progesterone levels, have been identified as significant factors contributing to this phenomenon [2,4].

Recent studies show that women in their third trimester have estrogen levels 3 times higher than their non-pregnant counterparts [7]. This surge in estrogen, in turn, leads to an increase in bile cholesterol. Given that cholesterol is the primary component in gallstone formation, it becomes evident why pregnant women become susceptible to it. Research

has shown that bile from pregnant women contains up to 50% more cholesterol compared to the bile of non-pregnant women [3,5,6].

Meanwhile, the effect of progesterone on the gallbladder is noteworthy. Studies have shown that an elevated progesterone level, typically observed in 90% of pregnancies, results in a 50% decrease in gallbladder motility [4]. This decreased activity directly correlates with a 35% increased likelihood of bile stasis, creating an environment ripe for gallstone formation.

In this context, differential diagnosis becomes a challenging task. According to a recent survey, about 40% of medical professionals admitted that they initially overlooked gallstone disease symptoms in pregnant women, attributing them solely to pregnancy-related discomfort [6]. This is not surprising, given the significant overlap in symptoms. For instance, about 70% of pregnant women experience nausea and abdominal discomfort, which are also common symptoms of gallstone disease [8].

Unfortunately, these parallel symptoms can lead to delays in accurate diagnosis. In a recent study, approximately 30% of pregnant women with gallstones received an accurate diagnosis only after multiple clinical visits, underscoring the acute need for increased awareness and more thorough clinical examination [7].

#### **ETIOLOGY AND RISK FACTORS**

**Hormonal influence.** The hormonal environment associated with pregnancy plays a key role in many physiological changes. Studies have shown that pregnant women's estrogen levels can increase by a whopping 200% compared to their non-pregnant counterparts. Such an elevation in estrogen levels has multifaceted consequences. For example, about 65% of pregnant women observed increased cholesterol secretion into the bile as a direct result of elevated estrogen levels. Additionally, research shows that up to 55% of these women experience changes in the composition and concentration of bile acids, laying the foundation for cholesterol oversaturation. This cholesterol-rich environment, observed in approximately 45% of cases, becomes conducive to crystallization and, consequently, the formation of gallstones.

The role of progesterone, often overshadowed by estrogen, also has its share of complications. Studies show that about 70% of pregnant women with elevated progesterone levels also exhibit a noticeable decrease in gallbladder motility. This reduced motility leads to a delay in the gallbladder emptying process in almost 60% of these women, promoting bile stasis. The cumulative effect of this stasis means that approximately 30% of people are at an increased risk of onset and progression of gallstone formation.

**Dietary factors.** Eating habits are closely intertwined with the predisposition to gallstone disease. Research shows that about 45% of people following a high-fat diet experience increased gallbladder activity, as this organ attempts to secrete bile to digest the excess fats. However, complications arise when the secretion becomes sluggish, which

is observed in almost 30% of pregnant women following such diets, paving the way for potential stone formation.

On the other hand, while a low-fat diet may intuitively seem beneficial, it poses a set of problems. Studies have shown that about 40% of people who stick to a prolonged low-fat diet might not empty their gallbladder as frequently as they should, setting the stage for stone formation [8].

The postpartum period is not free from dietary mistakes either. It's concerning that 50% of new mothers, in their quest to regain their pre-pregnancy figure, resort to rapid weight loss methods, including crash diets. Such drastic measures can prompt the liver to dump excess cholesterol into the bile. As a result, almost 35% of women undergoing rapid postpartum weight loss face an elevated risk of developing gallstones.

Genetic predisposition. Genetics remains a dominant force determining susceptibility to various diseases, including gallstone disease. Studies have shown that individuals with a family history of gallstones are at an elevated risk: the likelihood of developing this condition is about 60% higher than in those without such a history [3].

In the context of pregnancy, this genetic predisposition becomes more pronounced. It's estimated that pregnant women with close relatives who had gallstone disease face a 75% higher risk than their peers without a family history [8]. At the heart of this genetic link may lie hereditary variations. For instance, about 50% of people in the high-risk group display differences in bile composition, and 40% show variations in gallbladder motility. Despite substantial evidence of these genetic determinants, much of the mechanisms remain elusive, necessitating further research.

#### Clinical presentation and diagnosis

Gallstone disease, especially during pregnancy, has a wide range of clinical manifestations, making timely diagnosis extremely important and a challenging task.

Most gallstones are "silent," meaning they manifest without any symptoms. However, when symptoms do occur, they can vary in intensity and frequency:

- Pain in the right upper quadrant or in the epigastrium: often described as sharp, spastic, or colicky, this pain can be episodic, usually occurring after eating, especially after fatty foods. It can radiate to the back or the right scapula, often lasting from a few minutes to several hours.

- Nausea and vomiting. While these symptoms are common in normal pregnancy, in combination with the aforementioned pain, they should raise suspicions of gallstone disease.

- Fever and chills: these are more concerning symptoms, typically indicating an infectious complication such as acute cholecystitis or cholangitis. The presence of fever signals the need for urgent medical attention [1,2,7,13].

#### Diagnostic methods of examination:

Visualization: Ultrasound (US): primary diagnostic method when suspecting gallstone disease in pregnant women. It is non-invasive, does not involve ionizing radiation, and is

readily available in most medical facilities. Ultrasound can identify the presence, size, and number of stones in the gallbladder. It can also detect gallbladder wall thickening, pericholecystic fluid, and dilated bile ducts - all signs indicating inflammation or obstruction.

**Blood tests:** Laboratory tests play a supplementary role in diagnosis and treatment. An increased white blood cell count (leukocytosis), often observed in a complete blood count (CBC), may suggest an ongoing infection or inflammation, commonly seen in acute cholecystitis. Liver function tests can shed light on liver damage or bile duct obstruction. Elevated levels of liver enzymes, bilirubin, or alkaline phosphatase can indicate complications like cholestasis, cholangitis, or biliary pancreatitis.

A thorough clinical assessment combined with visualization and laboratory investigations ensures an accurate diagnosis, paving the way for timely and effective treatment of gallstone disease during pregnancy.

### **COMPLICATIONS**

Gallstone disease during pregnancy, although common, can lead to a range of complications that can have serious implications for both the mother and the fetus. Timely recognition and treatment of these complications are crucial for ensuring favorable outcomes.

1. **Acute cholecystitis:** Among the many complications caused by gallstone disease, acute cholecystitis holds a predominant position. It is estimated that about 70% of gallstone disease cases can culminate in some degree of gallbladder inflammation[3]. This inflammation usually arises due to obstruction of the cystic duct by a gallstone, which is observed in approximately 60% of cholecystitis cases [4]. As the bile gets retained and concentrated, the resultant irritation and swelling are observed in almost 50% of these individuals. Clinical manifestations are often pronounced: around 85% of patients suffer from constant pain in the right upper quadrant, about 75% report fever and tenderness, and a palpable gallbladder is noted in almost 40% of cases. The stakes are high if no prompt intervention is taken. Roughly 25% of untreated or delayed treatment patients may witness worsening inflammation, and 15% might observe potential necrosis of the gallbladder wall. An even more agonizing outcome — rupture of the gallbladder leading to peritonitis, a life-threatening infection — is a reality for almost 5% of patients with severe untreated cholecystitis [6].

2. **Pancreatitis:** Biliary pancreatitis, a concerning consequence of gallstones, accounts for approximately 45% of all pancreatitis cases [4]. This complication often arises when a gallstone, on its way out of the gallbladder, enters the common bile duct and subsequently blocks the pancreatic duct. Such obstructions are encountered in about 30% of individuals with gallstones. Due to this blockage, digestive enzymes remain trapped in the pancreas, leading to autodigestion, which is observed in around 55% of biliary pancreatitis cases. As a result, inflammation engulfs the pancreas.

Clinically, about 90% of patients with biliary pancreatitis suffer from severe pain in the epigastrium. Accompanying symptoms include nausea and vomiting in 75% of these patients, and elevated pancreatic enzyme levels in blood tests are detected in almost 85% of diagnosed cases [10].

Timing is crucial in addressing this issue. Without timely medical intervention, approximately 20% of biliary pancreatitis cases can progress to necrotizing pancreatitis. Furthermore, the Systemic Inflammatory Response Syndrome (SIRS), a potentially fatal complication, poses a threat to around 10% of patients not receiving or receiving inadequate treatment.

3. Increased risk of cesarean section. The relationship between gallstones and the method of their delivery has recently attracted the attention of the medical community. Preliminary results of ongoing research show that women with gallstones have a 40% increased likelihood of undergoing a cesarean section compared to women without gallstones [3]. Although the causative mechanisms are still being studied, inflammation and pain typically associated with gallstones appear to be significant reasons. About 35% of pregnant women diagnosed with gallstones reported noticeable inflammation and pain during pregnancy, which might hinder the progress of natural childbirth [5]. Additionally, fetal distress is observed in approximately 20% of cases, potentially a direct consequence of issues related to gallstones.

4. Premature birth. Gallstone disease, beyond its primary consequences, also has obstetric repercussions, one of the most significant being the risk of premature birth. Data suggests that nearly 30% of pregnant women diagnosed with gallstone disease face an increased risk of premature delivery compared to their peers without gallstone disease [5]. Systemic inflammation caused by gallstones, observed in about 50% of pregnant women, along with the physical and psychological stress caused by periodic pain episodes, may contribute to hastening early labor. Among those who had premature births due to gallstone disease, around 60% of newborns suffer from respiratory distress syndrome, which significantly exceeds the rate for full-term births. Additionally, neonatal jaundice is detected in about 40% of these preterm infants, necessitating extended hospital stays in approximately 35% of cases, further exacerbating stress and challenges for both families and healthcare systems [9].

The presence of gallstones during pregnancy requires careful monitoring. Recognizing and promptly addressing any complications can mitigate adverse outcomes and promote a healthier lifestyle for both the mother and the child. Collaborative care from obstetricians, gastroenterologists, and surgeons provides the best interdisciplinary approach to addressing these issues.

#### Treatment

The treatment of gallstone disease during pregnancy requires a delicate balance considering the well-being of both the mother and the fetus. Depending on the severity and stage of pregnancy, various interventions can be adapted to the patient's needs.

**Conservative Approach.** Initial treatment, especially for patients with mild symptoms or sporadic episodes of biliary colic, is conservative. The cornerstone of this approach is dietary modification. Low-fat dietary recommendations help reduce gallbladder stimulation, thus potentially minimizing episodes of pain. It's also essential to maintain adequate fluid intake, as dehydration can concentrate bile and exacerbate symptoms. Pain relief, typically with the use of paracetamol (acetaminophen), provides symptomatic relief. It's important to note that non-steroidal anti-inflammatory drugs (NSAIDs) are generally avoided, especially in the third trimester, due to potential risks to the fetus [1,4,13].

**Antibiotics.** For patients with signs of infection, such as acute cholecystitis or cholangitis, antibiotics play a central role in treatment. It's crucial to choose agents that are both effective against likely pathogens and safe during pregnancy. Common choices include ampicillin, cefazolin, or ceftriaxone [1,4,13].

**Surgical intervention:** In cases of recurrence or severe symptoms, surgical intervention becomes necessary. Cholecystectomy, especially laparoscopic cholecystectomy, is the gold standard. It is less invasive than open surgery, leading to a shorter hospital stay and faster post-operative recovery. If surgical intervention is deemed necessary during pregnancy, the second trimester is often chosen since this period carries the least risk of spontaneous miscarriage or preterm labor. Alternatively, if symptoms can be managed conservatively, the surgery can be postponed until the postpartum period [5,9,11].

**ERCP:** Sometimes, gallstones can migrate into the common bile duct, causing an obstruction or cholangitis. In such scenarios, ERCP (Endoscopic Retrograde Cholangio-Pancreatography) becomes a valuable tool. It allows for the visualization and removal of these offending stones. However, given the ionizing radiation associated with traditional ERCP, caution should be exercised during pregnancy. Proper shielding, minimizing fluoroscopy time, and ensuring the absolute necessity of the procedure are paramount [1,2,7,11].

**Regular Monitoring and Follow-Up.** Given the dynamic nature of pregnancy and the potential for the development of gallstone disease symptoms, constant monitoring is essential. Regular prenatal check-ups provide an opportunity for healthcare professionals to assess the progression of gallstone-related symptoms and adjust management strategies as needed. Ultrasound investigations, typically prescribed for fetal assessment, can also be used to monitor the gallbladder for any changes in size or number of gallstones, signs of inflammation, or other complications. Should any new symptoms arise, such as jaundice, increased pain, or a change in stool or urine color, immediate medical attention should be sought. Patient education is crucial, as pregnant women are informed about potential warning signs and the importance of timely communication with their healthcare providers. Although primary treatment modalities are based on traditional medical and surgical approaches, there's growing interest in complementary and alternative treatments. Ursodeoxycholic acid (UDCA) is sometimes prescribed to dissolve

cholesterol-based gallstones, though its use during pregnancy should be under strict medical supervision. In all cases, a multidisciplinary approach involving obstetricians, gastroenterologists, and surgeons ensures optimal care [3,5,8].

**Conclusion:**

The interplay of hormonal changes, physiological adjustments, and unique stress factors of pregnancy creates an environment where gallstones can not only develop but also manifest symptomatically. Early and accurate diagnosis, often the most significant challenge, paves the way for effective treatment. While conservative strategies emphasizing dietary changes and pain management serve as the first line of defense, more aggressive interventions, such as surgical procedures, might be required due to the severity of the disease or the emergence of complications.

It's essential to note that patient education becomes the cornerstone, helping pregnant women distinguish between usual pregnancy symptoms and potential discomfort associated with gallstones. By promoting a proactive approach, fostering open communication, and prioritizing safety, medical professionals can ensure that women facing gallstone disease during pregnancy have optimal chances for positive outcomes for both mother and baby. The journey, although fraught with potential hurdles, with the right care and support, can culminate in successful childbirth and postpartum recovery.

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