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Bile Tract Emergencies: An Updated Data for Emergency Healthcare Professionals, Nursing, and Clinical Pathologists

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Abstract

Background: Gallbladder disease, including acute cholecystitis (AC) and biliary colic, is a common condition that primarily affects women, especially during pregnancy. It is influenced by various factors, including hormonal changes, multiparity, and obesity, which contribute to gallstone formation and complications. The prevalence of gallstones varies across regions and populations, with higher rates observed among certain ethnic groups and during pregnancy.

Aim: The aim of this study is to provide an updated overview of gallbladder-related emergencies, including the epidemiology, risk factors, pathophysiology, and clinical management, particularly focusing on emergency healthcare professionals, nurses, and clinical pathologists.

Methods: A review of current literature and clinical data was conducted to analyze the incidence, risk factors, pathogenesis, and clinical presentation of gallbladder disease, with a particular emphasis on pregnant women. The role of hormones such as estrogen and progesterone in gallstone formation and the effects of insulin resistance were also explored.

Results: Gallstones are more common in women, particularly during pregnancy, with incidence rates increasing with multiparity and obesity. Hormonal changes, especially elevated estrogen levels, contribute to gallstone formation, while insulin resistance further exacerbates the risk. The study also found that gallbladder disease in pregnancy may remain asymptomatic but can progress to acute cholecystitis, pancreatitis, or cholangitis, often requiring surgical intervention.

Conclusion: Gallbladder disease remains a significant health issue, particularly in pregnant women, and requires prompt diagnosis and management. Emergency healthcare professionals, including nurses and clinical pathologists, should be aware of the risk factors and clinical manifestations to provide effective care and reduce complications. Preventive measures, including lifestyle changes and careful monitoring in high-risk populations, are essential for managing this condition.

Keywords: Gallstones, Acute Cholecystitis, Biliary Colic, Pregnancy, Hormonal Changes, Obesity, Insulin Resistance, Emergency Healthcare, Clinical Pathology.

Introduction:

Acute Cholecystitis/Biliary Colic

Friedrich Daniel von Recklinghausen (1833–1910) discovered that 90% of women with gallstones had experienced at least one pregnancy. Later, Ludwig Georg Courvoisier (1843–1918), through autopsy studies, demonstrated that gallstones were three times more common in women than men, implicating pregnancy as a major risk factor for cholelithiasis [1]. The prevalence of gallbladder disease varies widely across populations and geographic regions. William Mayo highlighted that gallstones occur three times more frequently in women than men [2]. In the United States, approximately 10–15% of adults have gallstones, with notable variations by ethnicity. For instance, 70% of Native American women over 30 develop cholelithiasis, while the prevalence is 14% in Mexican American women, compared to 4% in Caucasian women and 5% in Black women [3]. Chilean and Latin American women are at particularly high risk, with prevalence rates of up to 50% in some regions [5]. In Mexico, gallstone prevalence reaches 14.3%, increasing with age to 25% by age 60 and 33% by age 70 [6]. Gallstone-related complications are the second most common non-gynecologic conditions requiring surgery during pregnancy. The incidence of gallbladder disease during pregnancy ranges from 0.05–0.3% [7–12]. Asymptomatic gallstones are observed

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in 2.5–10% of pregnancies and 12% during the early puerperium, compared to 1.3% in non-pregnant women [4, 13–15]. Approximately 60–69% of pregnant women with gallstones remain asymptomatic [4, 14]. Acute cholecystitis (AC) occurs at a rate of 1/1,000–1/10,000 pregnancies [16–20], and about 40% of pregnant women with symptomatic cholelithiasis require cholecystectomy during pregnancy [21–23]. Postpartum, 0.8% of women with gallbladder disease undergo cholecystectomy within the first year, with over 32,000 young women in the U.S. requiring this procedure annually [24, 25]. Notably, 81% of women with gallbladder disease symptoms experienced their first attack within one year of pregnancy [26]. In Saudi Arabia, the incidence of gallbladder disease during pregnancy is higher (0.39%), attributed to frequent pregnancies and genetic predisposition, as 7.5% of pregnant women harbor silent gallstones compared to 3.5% in Western countries [27]. The distribution of surgical gallstone disease during pregnancy includes biliary colic and AC (62.7–86.3%), biliary acute pancreatitis (3–25.4%), choledocholithiasis (6.8–7.0%), and acute cholangitis (2.6–5%) [22, 29, 30].

Risk Factors

Biliary sludge, characterized as a mixture of cholesterol granules and calcium bilirubinate crystals within viscous bile, is the precursor to gallstone formation and the earliest identifiable stage of lithogenesis [34]. During pregnancy, biliary sludge forms in 11–31% of women, while gallstones develop in 2–6% [4, 35–37]. Postpartum resolution of sludge occurs in 61% of cases, and gallstones resolve in 28% [37]. The accuracy of ultrasound for detecting microscopic sludge is limited to 50–60% [24]. Multiparity is a significant risk factor for gallstone formation due to hormonal changes during pregnancy [35, 38]. The prevalence of gallbladder disease increases from 1.3% in nulliparous women to 12.2% in multiparous women [39]. The risk of gallbladder disease rises with the number of pregnancies and decreases slightly with breastfeeding due to reduced estrogen levels [43, 44]. However, other hormonal changes associated with lactation may also contribute to this protective effect. Early marriage and frequent pregnancies until menopause further elevate the risk [31, 47]. Obesity and insulin resistance significantly increase the risk of gallbladder disease during pregnancy, with obese women (BMI ≥30 kg/m²) exhibiting a higher incidence of sludge and stones (2.3% vs. 0.4% in non-obese women) [7, 24, 50]. Insulin resistance associated with higher BMI contributes to gallstone formation [51–57]. Bariatric surgery also increases the risk, with symptomatic cholelithiasis reported in up to 15% of cases post-surgery, depending on the procedure type [60, 61].

Gallbladder Volume and Function

Gallstone and biliary sludge formation during pregnancy is closely associated with increased fasting gallbladder volume [62] and elevated postprandial gallbladder volume [63, 64]. Another contributory factor is impaired gallbladder motility, which has been implicated in the pathogenesis of gallstone and biliary sludge formation [65, 66]. Studies involving healthy pregnant women have demonstrated a direct correlation between gallbladder hypomotility and the development of gallstones and biliary sludge [35].

Pathogenesis

Estrogen and Progesterone:

Cholesterol gallstones are significantly more prevalent in women than men, with this disparity becoming evident from puberty and persisting throughout the childbearing years [5, 67]. Pregnancy induces various physiological changes, including an increased proportion of colic acid, heightened cholesterol secretion, enlarged bile acid pool size, reduced enterohepatic circulation, and diminished levels of chenodeoxycholic acid [68]. Progesterone, known for its smooth muscle relaxation properties, reduces gallbladder motility, thereby slowing gallbladder emptying and promoting bile stasis [69, 70]. This hormone also suppresses bile acid secretion, heightening the risk of cholelithiasis and acute cholecystitis (AC) [71]. Ultrasound findings in pregnant women reveal reduced gallbladder emptying rates alongside increased fasting and residual gallbladder volumes during the second and third trimesters. Additionally, incomplete postprandial gallbladder emptying is prevalent during pregnancy [63, 66, 72]. Estrogen plays a pivotal role in cholesterol gallstone formation by enhancing hepatic secretion of biliary cholesterol, which increases bile cholesterol saturation [73-76]. Elevated estrogen levels significantly activate 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, a critical enzyme in hepatic cholesterol biosynthesis, even under conditions of high dietary cholesterol [76, 77]. Furthermore, estrogen augments dietary cholesterol absorption and facilitates its conversion into supersaturated bile, predisposing to cholesterol precipitation and gallstone formation [77, 78]. Consequently, yellow cholesterol stones are the most prevalent type during pregnancy [5, 24]. Estrogen also induces gallbladder and sphincter of Oddi hypomotility [79, 80]. As plasma estrogen levels rise progressively during pregnancy, the risk of gallstone formation peaks in the third trimester. Estrogen reduces plasma low-density lipoprotein (LDL) cholesterol and increases high-density lipoprotein (HDL) cholesterol by upregulating hepatic LDL receptor expression, which accelerates LDL clearance and boosts biliary cholesterol secretion. This process contributes to increased hepatic output of biliary cholesterol derived from plasma lipoproteins [81, 82]. Notably, there is a high dissolution rate of gallstones and biliary sludge postpartum, with resolution rates ranging from 15–28% for gallstones and 39–68% for biliary sludge within the first month after delivery [37, 86]. Spontaneous gallstone resolution is more frequent in older women, where reduced gallbladder contractility leads to lithogenic bile dissolution. Conversely, younger postpartum women experience acute pancreatitis (AP) due to gallstones, as gallbladder contraction resumes as early as two weeks postpartum, expelling smaller gallstones [64].

Insulin

Insulin resistance plays a significant role in gallstone formation, although its exact mechanisms remain unclear. Cholesterol, the principal component of gallstones during pregnancy, forms due to various pathogenic factors, including hepatic bile supersaturation with cholesterol and impaired gallbladder motility. Hyperinsulinemia, characteristic of insulin resistance, stimulates cholesterol synthesis through HMG-CoA reductase [87] and enhances hepatic LDL cholesterol uptake [88]. Furthermore, insulin resistance is associated with reduced serum HDL cholesterol levels, a known contributor to gallstone risk

[89]. Insulin administration in diabetes mellitus (DM) has been shown to elevate biliary cholesterol saturation [90]. Patients with type II DM exhibit higher biliary cholesterol saturation compared to controls [91, 92]. Insulin inhibits both basal and cholecystokinin (CCK)-stimulated gallbladder motility, frequently causing gallbladder dysmotility in type II DM [93, 94]. Animal studies indicate that non-obese diabetic mice experience decreased gallbladder contractility and accelerated cholesterol crystal formation [95].

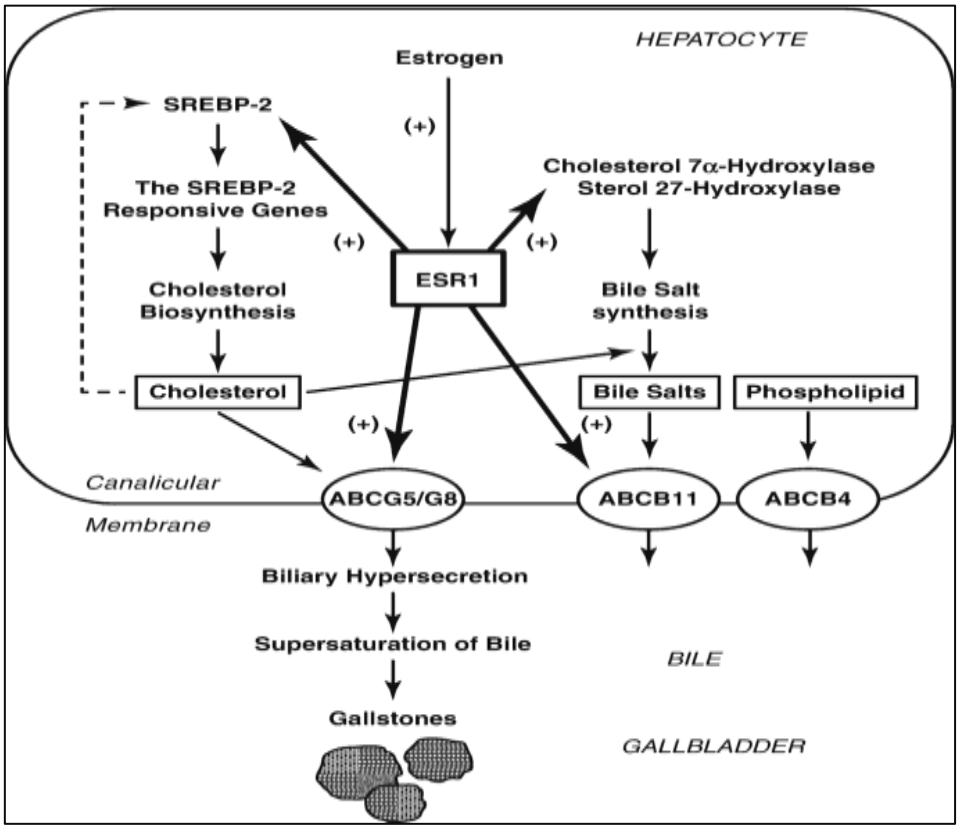

Figure 1: Gallstone and Estrogen Hormones.

Similarly, gallbladder contractility inversely correlates with glucose and insulin levels in obese animals [96]. In non-obese, non-diabetic humans, insulin resistance is linked to gallbladder dysmotility, potentially leading to gallbladder sludge and stone formation by impairing gallbladder motility or altering biliary lipid secretion [97]. Insulin resistance may act as a proxy for other unidentified pathophysiological mechanisms contributing to gallstone development [58]. Diabetic individuals exhibit increased cholesterol saturation indices in bile compared to non-diabetics [98], along with larger fasting gallbladder volumes and reduced motility in non-insulin-dependent DM patients [99, 100]. Hyperinsulinemia, a hallmark of non-insulin-dependent DM, is associated with an increased prevalence of gallbladder disease [51, 53, 54]. Both hyperglycemia and euglycemic hyperinsulinemia inhibit CCK-stimulated gallbladder motility [93]. Insulin may influence gallbladder function by regulating the Na^+-K^+ pump, which impacts ionic and osmotic homeostasis in smooth muscle cells, including gallbladder myocytes [101]. Decreased Na^+-K^+ pump activity elevates intracellular Na^+, triggering Na^+-Ca^{2+} exchange and increasing intracellular calcium. This calcium elevation affects smooth muscle tone and neurotransmitter release. Additionally, gallbladder myocytes from obese diabetic mice demonstrate reduced responsiveness to CCK [102]. Insulin resistance or DM may alter acetylcholine or CCK receptor density or sensitivity and interfere with neurotransmitter receptor interactions. Advanced glycation end products formed via non-enzymatic sugar-protein reactions cause covalent cross-linking in collagen and protein matrices [103]. Such cross-linking stiffens the gallbladder wall, impairing contraction and potentially hindering CCK diffusion through vascular basement membranes, limiting its interaction with neural or myocyte receptors.

Diabetes Mellitus, Obesity, and Bariatric Surgery

Gallbladder dynamics differ between obese and lean individuals, potentially due to variations in serum and gallbladder wall lipid content [104]. Elevated smooth muscle cell cholesterol-to-phospholipid ratios in obese individuals reduce membrane fluidity, impairing gallbladder function. Moreover, rapid weight loss following bariatric surgery exacerbates gallstone risk through impaired gastric emptying and increased bile stasis [105, 106]. Women of reproductive age who undergo laparoscopic sleeve gastrectomy experience a fourfold increased risk of cholecystectomy during pregnancy, with over one-fourth undergoing the procedure post-surgery [61]. Lower gestational weight gain is a significant factor associated with cholecystectomy following laparoscopic sleeve gastrectomy [61]. Prophylactic ursodeoxycholic acid administration and rigorous postoperative monitoring are recommended for these patients.

Other Factors

Pregnancy-associated hormonal changes, including a 50% increase in bile acid pool size and steroid-induced cholesterol secretion, contribute to gallstone development. Additionally, the replacement of deoxycholic and chenodeoxycholic acids with cholic acid, combined with gallbladder enlargement and reduced motility, further promotes biliary stone formation [26].

Clinical Presentation

The association between gallstones and pregnancy has been recognized for over a century, with William Mayo in 1911 identifying that asymptomatic gallstones may become symptomatic during gestation [2]. The symptoms of gallstone disease in pregnant women mirror those experienced by nonpregnant individuals [4, 107]. Typically, biliary pain manifests as sharp discomfort in the right upper quadrant or mid-epigastric area, often intensifying in severity. This pain, known as biliary colic, arises suddenly and may radiate to the interscapular region, the right scapular angle, or the right shoulder. Precipitating factors include consumption of fatty meals or large meals following fasting. A distinct diurnal pattern is noted, with pain peaking near midnight. Approximately half of patients experience nausea and vomiting during colic episodes, and 70–80% report a history of gallstones, colic attacks, or intolerance to fatty foods [16]. Escalating severity of pain, fever, or chills (rigors) often signifies complications such as acute cholecystitis (AC), acute pancreatitis (AP), or cholangitis. Persistent jaundice is indicative of common bile duct (CBD) stones.

Physical Examination

Physical examination can reveal several indicative signs:

- **Abdominal tenderness:** Tenderness localized to the right upper quadrant, with minimal symptom blunting despite the uterine enlargement displacing the gallbladder.
- **Murphy's sign:** Although less frequently elicited in pregnancy, this sign (cessation of inspiration during palpation of the gallbladder) suggests AC [108].
- **Muscle rigidity:** Associated with gallbladder perforation and biliary peritonitis, although abdominal wall laxity in late pregnancy may obscure classic signs of peritonitis [109].
- **Fever and tachycardia:** These symptoms are inconsistently present and become more pronounced in advanced disease stages.
- **Other symptoms:** Vomiting and dyspepsia may mimic peptic ulcers, while pruritus suggests liver disease or biliary obstruction.

Notably, biliary pain is experienced exclusively by women with preexisting gallstones [37].

Differential Diagnosis

Hyperemesis Gravidarum

Hyperemesis gravidarum is characterized by unrelenting nausea and persistent vomiting, leading to a weight loss exceeding 5% of prepregnancy body weight and the presence of ketonuria [110]. Occurring in 0.5–1.5% of pregnancies [110], this condition is more frequent among nulliparous women with predisposition to cholelithiasis or cholecystitis [111]. Severe dehydration often necessitates hospitalization for intravenous fluid therapy [111]. Symptoms predominantly appear in the first trimester and resolve before mid-pregnancy irrespective of treatment. Jaundice, although rare, is not accompanied by abdominal pain or fever. Elevated liver enzymes, especially ALT levels exceeding AST, are common, though their frequency is not well-documented. Abnormal ALT levels may assist in distinguishing hepatitis from drug-induced liver injury when jaundice is present. Liver biopsy is typically unnecessary. Hyperthyroidism secondary to this condition is transient and generally requires no specific intervention [111].

Perihepatitis (Fitz-Hugh–Curtis Syndrome)

Perihepatitis, resulting from early dissemination of *Chlamydia trachomatis* or gonococcal infections, is frequently observed in young women, particularly during the second and third trimesters or postpartum [113]. It manifests as sharp, pleuritic pain in the right upper quadrant, occasionally accompanied by nausea or hiccups. Physical findings include tenderness under the right costal margin, hepatic friction rub, and fever. A history of recent pelvic infection supports the diagnosis, which can be further confirmed by cervical cultures identifying gonococcus and symptomatic improvement following antibiotic therapy [113].

Costal Margin Pain

Described by Alexander Tietze in 1921, this syndrome involves pain at the costochondral cartilages, likely caused by irritation of intercostal nerves rather than synovitis [114]. During pregnancy, costal margin pain is common due to muscular stretching. The diagnosis can be confirmed through maneuvers like Carnett's sign, where abdominal muscle tensing reproduces the pain. Diagnostic blocks using long-lasting local anesthetics, such as 0.5% bupivacaine, provide relief. Postpartum management may involve a combination of local anesthesia and triamcinolone, with repeated blocks required for persistent symptoms.

Diagnosis

Pregnancy-related jaundice is relatively rare. Although jaundice often resolves spontaneously without intervention, its prognosis should not always be considered benign, as it can occasionally signify the onset of acute yellow atrophy of the liver, as noted by John Whitridge Williams in 1903.

Laboratory Findings

When biliary colic or acute cholecystitis (AC) is clinically suspected, hospital evaluation is essential. The presence of granulocytosis with a left shift typically indicates bacterial infection. Elevated C-reactive protein (CRP) levels above 40 mg/L strongly suggest bacterial etiology. In pregnant women, serum bilirubin and transaminase levels may rise similarly to those in nonpregnant women. However, serum alkaline phosphatase levels are less reliable due to the natural estrogen-induced elevation, which can double during pregnancy. Transient elevations in serum amylase are observed in up to 33% of cases. Additionally, postprandial plasma bile acid levels progressively increase throughout pregnancy.

Transabdominal Ultrasound

Transabdominal ultrasonography (US) achieves a 95–98% success rate in visualizing the gallbladder during pregnancy [47, 115, 116]. Patients whose gallbladders are not initially visualized often present with chronic cholecystitis, characterized by a contracted gallbladder and thickened walls upon subsequent scans [47]. Gallbladder sludge, noted as bile accumulation, is detected in up to 30% of pregnant patients, with similar postpartum prevalence [24]. Early pregnancy US often confirms physiological gallbladder expansion and the presence of stones, debris, or bile. The gallbladder of healthy pregnant women typically shows decreased emptying rates and increased residual volumes post-emptying. Isolated gallstones are classified as biliary colic. Diagnostic US criteria for AC include gallbladder calculi, wall thickening exceeding 3 mm, pericholecystic fluid, and a positive sonographic Murphy's sign (localized tenderness under the US probe). For therapeutic considerations, common bile duct (CBD) obstruction must be excluded. Diagnostic indicators for CBD obstruction include:

- CBD diameter exceeding 7 mm,
- Dilation of intra- and extrahepatic ducts,
- Gallstones are smaller than the cystic duct diameter.

Suspected urolithiasis-related abdominal pain is better evaluated using US. Although pregnancy-related hydronephrosis complicates calculus diagnosis, combining bladder color Doppler US to identify ureteral jets and transvaginal US for detecting distal ureter stones enhances diagnostic accuracy [117]. Magnetic resonance cholangiopancreatography (MRCP) is a valuable diagnostic tool for distinguishing CBD stones from intrahepatic cholestasis of pregnancy, given their overlapping clinical and biochemical profiles [118]. MRCP is particularly useful when transabdominal US reveals dilation of intrahepatic and extrahepatic ducts. It also aids in differentiating CBD stones from external compression caused by Mirizzi syndrome. MRCP provides superior visualization of the pancreas, pancreatic duct obstructions, and peripancreatic inflammation in biliary acute pancreatitis (AP), areas often obscured by bowel gas in US assessments.

Treatment

Historical Perspective

In 1890, Robert Barnwell Rhett, Jr. documented a cholecystotomy performed on a pregnant woman, marking a pivotal moment in the history of treating biliary disorders during pregnancy. Subsequently, in 1893, Boorse highlighted a case where pregnancy exacerbated biliary calculi, and Willien reported a cholecystotomy in the first trimester. By 1895, Vineberg and Davis AB contributed cases involving AC during the puerperium and successful cholecystectomy during advanced pregnancy, respectively, demonstrating the complexities and potential safety of surgical interventions. Ploger (1910) and Peterson extensively documented cases correlating pregnancy with biliary colic and gallstone formation, emphasizing the influence of gestation on biliary physiology [122, 31]. Grube's comprehensive findings outlined five pregnancy-induced biliary changes: bile stasis, increased bile cholesterol, protein breakdown, epithelial desquamation, and mucosal hyperemia, which, alongside bacterial infection, were deemed critical in gallstone pathogenesis [126]. Peterson noted that gallstone complications often coincided with critical gestational stages, including late pregnancy and the immediate postpartum period, due to mechanical and physiological factors such as uterine pressure and postpartum biliary trauma. These findings were supported by other notable researchers like M'Nee and Ashoff, who identified aseptic gallstone formation as a pregnancy-associated phenomenon [127, 128]. The interplay between pregnancy and gallstone pathology has been linked to both direct physiological effects and mechanical changes resulting from gestation.

Conservative Treatment

Conservative management strategies were traditionally endorsed until 1997 for symptomatic cholelithiasis, with current approaches favoring nonoperative measures in 82–92.5% of cases [129, 130, 131]. Medical therapy is frequently implemented during early pregnancy to mitigate complications such as premature contractions and fetal demise, emphasizing continuous monitoring and hospitalization for high-risk cases. Delayed cholecystectomy until the second trimester has historically been practiced to minimize abortion risks, although this may lead to advanced complications like AC, maternal malnutrition, and fetal growth impairment [107, 134, 135]. Surgery in the third trimester presents heightened risks, including prolonged hospital stays, increased costs, and higher preterm delivery (PTD) rates [137, 138]. Postpartum cholecystectomy remains a preferable approach for advanced pregnancy cases, as delaying surgery often results in recurrent symptoms or complications postpartum [129, 145].

Total Parenteral Nutrition

Total parenteral nutrition (TPN) has been validated as an effective alternative to surgical intervention during the second and third trimesters, promoting maternal and fetal health without adverse effects on weight gain or fetal development [146, 147]. Essential fatty acids and amino acids provided through TPN support vital organ development in the fetus, with peripherally inserted central catheters (PICCs) being a safer and more convenient option compared to central venous catheters [148, 149]. Dietary adjustments play a pivotal role in conservative management. A low-fat, cholesterol-minimized diet

supplemented with fruits, fibers, and natural remedies like beetroot and apple juice can prevent gallstone formation and support bile acid regulation. Specific compounds, such as malic acid in apple juice and betaine in beetroot juice, enhance liver function and bile composition, offering therapeutic benefits. Dicyclomine, categorized as FDA class B, may suppress lactation and adversely affect nursing infants. Its use in nursing mothers requires careful consideration. Ursodeoxycholic acid, a bile acid agent used to dissolve gallstones in nonpregnant patients, lacks established safety and efficacy for gallstone management during pregnancy, though it has been utilized for other pregnancy-related liver conditions like intrahepatic cholestasis [150]. In high-risk pregnant patients or those with recurrent gallbladder colic, percutaneous transhepatic gallbladder aspiration offers a temporary management option. This procedure, guided by ultrasound and local anesthesia, involves inserting a pigtail drainage tube into the gallbladder to alleviate symptoms. Despite its utility, risks include bile leakage, bile duct injury, abdominal abscess formation, necessitating subsequent laparoscopic cholecystectomy (LC).

Operative Treatment

Early surgical intervention for acute cholecystitis (AC) is strongly advised in the general population [153], as it does not elevate the risk of bile duct injury [154, 155]. Early open cholecystectomy (OC), compared to delayed OC, is associated with reduced blood loss, shorter operative duration, lower complication rates, and decreased hospitalization time [46]. Similarly, laparoscopic cholecystectomy (LC) during the initial hospital admission results in faster recovery, shorter hospital stays, and lower overall costs compared to OC [154, 155].

According to the Tokyo Guidelines [153], AC severity is categorized into three grades:

- **Mild (Grade I):** Early LC is the preferred intervention.
- **Moderate (Grade II):** Early cholecystectomy is typically performed, but severe local inflammation necessitates early gallbladder drainage (percutaneous or surgical). When early cholecystectomy is impractical, delayed intervention coupled with medical management is recommended.
- **Severe (Grade III):** Initial management involves addressing organ dysfunction and severe local inflammation through gallbladder drainage or cholecystectomy. Elective cholecystectomy may be performed later when clinically indicated.

Pregnant Population

The most frequent indication for biliary surgery during pregnancy is recurrent biliary colic (37–70%), followed by AC (20–40%), common bile duct (CBD) stones (7%), and biliary acute pancreatitis (AP) in 3% of cases [22, 135, 156]. Pregnant women with biliary AP undergo surgical treatment more often compared to other gallbladder diseases (32.5% vs. 11.9%) [12]. Challenges arise in comparing nonoperative and operative management groups. The nonoperative group typically presents with complex obstetric issues, such as higher incidences of hypertension, preeclampsia, eclampsia, and gestational diabetes, which predispose to worse outcomes. Conversely, operatively managed patients often present with higher disease severity, including peritonitis and sepsis. Even after adjusting for these disparities using propensity scores, nonoperative management is associated with increased maternal-fetal complications and unplanned readmissions [142, 157]. Recurrence rates following nonoperative management vary by trimester, reaching 92% in the first trimester, 64% in the second, and 44% in the third [10, 132, 134, 142, 156, 158]. Some studies suggest the highest relapse rates occur in the second trimester [130, 159]. Pregnancies experience an average of 2–6 relapses, each lasting 5–8 days [10, 30, 130, 132, 158, 160], with increasing severity at each recurrence [130]. Despite these risks, most pregnant women in the US with AC are managed nonoperatively, contrary to current guidelines [157]. While cholecystectomy during the first trimester carries a heightened risk of maternal and fetal complications compared to the second trimester [139–142], some evidence suggests LC can be safely performed in the first trimester without increasing such risks, eliminating the need to delay surgery [161]. In advanced pregnancy, conservative management is preferred; however, when surgical intervention is essential, LC and OC are performed with comparable frequency [162]. LC reduces the risks of spontaneous abortion and premature labor in the first and third trimesters, respectively [133, 163]. Historically, LC was predominantly performed postpartum, while OC was preferred during pregnancy [50]. Presently, LC is recognized as a safe option even in the third trimester, with over 90% of procedures in the US performed laparoscopically [143, 157].

Maternal and neonatal benefits of operative management include:

- Reduced medication use, hospital stays, and readmissions,
- Lower rates of severe complications (perforation, biliary sepsis, peritonitis),
- Reduced incidences of biliary AP, spontaneous abortions, preterm labor (PTL), and preterm delivery (PTD) [132].

LC offers superior outcomes compared to OC and is performed significantly earlier in pregnancy [21, 168, 169]. High-volume surgeons yield better results in pregnant populations, with conversion rates to OC as low as 13% in Australia [171].

Contraindications for Laparoscopic Surgery

Absolute contraindications for laparoscopy include hypovolemic shock, massive bleeding, severe cardiorespiratory disease, and uncontrolled coagulopathy [173]. Relative contraindications encompass peritonitis, portal hypertension, extensive intra-abdominal adhesions, and advanced third trimester.

Specific Considerations

- **Diabetic Pregnant Patients:** Diabetic patients demonstrate higher rates of symptomatic gallstones during pregnancy, warranting proactive surgical management to prevent complications.
- **IVF Pregnancies:** Increased exposure to female hormones in IVF pregnancies heightens the risk of biliary sludge and stones. Limited case studies show favorable outcomes with LC in this subgroup [175, 176].

Surgical Procedures

- **Open Cholecystectomy:** Standard techniques emphasize minimal uterine manipulation to reduce PTL risk.
- **Laparoscopic Cholecystectomy:** Although earlier recommendations discouraged third-trimester laparoscopy due to technical challenges and uterine injury risks, advancements have made LC viable during all trimesters [179].

Gallstone-Related Hospitalization During the First Postpartum Year

Gallbladder disease remains one of the primary non-obstetric reasons for hospitalization within the initial postpartum year. A total of 76% of cases were identified as uncomplicated cholelithiasis, 16% as acute pancreatitis (AP), 9% as acute cholecystitis (AC), and 8% as cholangitis. Among these, 73% of hospitalized patients underwent cholecystectomy, while 5% received endoscopic retrograde cholangiopancreatography (ERCP). Key risk factors for hospitalization included maternal ethnicity, age, pre-pregnancy overweight or obesity status, gestational weight gain, and gestational age [7].

Fetal Outcomes

Earlier investigations into pregnancy-associated gallbladder disease reported fetal loss rates ranging from 12% to 15% [31, 158, 191], escalating to 24% following cholecystectomy [192]. During that era, 10% of pregnancies culminated in spontaneous abortion [193]. Non-surgical management exhibited a fetal mortality rate of approximately 7%. Older studies indicated a fetal death rate of up to 5.2% post-laparoscopic cholecystectomy (LC) [36, 130, 133, 168, 190], which later declined to 2.5% [142] and is now reported at 0% [30, 156, 171]. The association between surgery and adverse outcomes was inconclusive due to variable time intervals between surgical intervention and abortion. Notably, cholecystectomy during pregnancy does not elevate risks of preterm labor (PTL), fetal complications, or mortality [143, 169, 186, 187, 189]. For AC management, LC demonstrates no adverse fetal outcomes [190, 194, 195], with second-trimester biliary colic surgeries yielding positive outcomes [171]. These findings underscore the severity of the underlying disease, rather than the surgical intervention, as the determinant of fetal prognosis. However, progression to AP significantly elevates fetal loss risk. First-trimester ERCP has been linked with heightened rates of preterm delivery (PTD) and low birth weight [171, 196].

Common Bile Duct Stones and Acute Cholangitis

Incidence

Common bile duct (CBD) stones affect 1 in 1,200 pregnancies [197], occurring in 10–12.5% of pregnant individuals undergoing cholecystectomy [159, 198], and account for 7% of jaundice cases during pregnancy [9]. Certain studies highlight biliary AP as the predominant form, affecting up to 70% of AP cases during pregnancy [199]. Variations in prevalence are influenced by etiological differences, including gallstone disease, hypertriglyceridemia, and alcohol consumption. For instance, biliary AP incidence was recorded at 1 in 3,300 pregnancies in Dallas, Texas [200], compared to 1 in 1,500 in Southern California [199].

Risk Factors

Due to limited data, specific risk factors for CBD stones in pregnancy remain unidentified. However, the etiopathogenesis mirrors that observed in non-pregnant populations. Most risk factors align with those associated with gallbladder stones in pregnancy.

Clinical Presentation

Pregnant patients with CBD stones exhibit clinical symptoms akin to those in the general population. Typical manifestations include abdominal pain, jaundice, nausea, vomiting, and pruritus. Painless jaundice without fever suggests CBD stones or periampullary tumors, while painful jaundice accompanied by fever and chills indicates acute cholangitis. AC may concurrently develop with CBD stones. The abdominal pain may present as colicky or stabbing, radiating to the right flank, scapula, or shoulder. Pain onset is abrupt, with peak intensity reached within 10–20 minutes. The pain is typically steady and ranges from moderate to severe. In 50% of cases, pain may exhibit a band-like radiation toward the back. Additional symptoms include anorexia, dyspepsia, low-grade fever, tachycardia, and intolerance to fatty foods [200]. Some of these symptoms overlap with those of AP, making differential diagnosis essential. Biliary AP presents similarly to AP of other etiologies.

Differential Diagnosis

Abdominal ultrasound (US) or magnetic resonance cholangiopancreatography (MRCP) is crucial for differential diagnosis. Two conditions, intrahepatic cholestasis of pregnancy (ICP) and acute fatty liver of pregnancy (AFLP), warrant detailed evaluation for precise diagnosis.

Incidence and Risk Factors

ICP typically manifests after 25 weeks of gestation and resolves spontaneously postpartum. Its prevalence varies significantly across regions [201], with the highest rates reported in Bolivia and Chile, ranging from 11.8% to 27.7% during 1974–1975 [202]. More recent studies indicate a decline in prevalence to 4.0–6.5% [202, 203]. The condition is more prevalent in twin pregnancies [206], winter months [207], and pregnancies following in vitro fertilization (2.7% versus 0.7%) [208].

Diagnosis

Pregnant women with biliary acute pancreatitis (AP) often exhibit normal liver function test results. Transaminase levels typically remain below five times the upper normal limits in 89% of cases and under three times the upper limits in 80%. This phenomenon may result from the placental metabolism of maternal transaminases, which leads to seemingly normal maternal enzyme levels [43]. Ultrasound (US) serves as the primary diagnostic modality for assessing the biliary system, offering a diagnostic accuracy of 97% for cholelithiasis [47, 115]. However, its effectiveness decreases for detecting common

bile duct (CBD) abnormalities (50%) and pancreatic conditions, where only 60% of the pancreas is visualized with inconclusive results [120]. When abdominal ultrasound fails to provide definitive results, MRCP emerges as the superior diagnostic imaging tool for biliary disorders during pregnancy. Although rarely employed due to disease rarity, emergent presentations, and limited access, MRCP effectively distinguishes CBD stones from Mirizzi syndrome. Preoperative diagnosis through MRCP circumvents the need for endoscopic retrograde cholangiopancreatography (ERCP) and radiation exposure. Advanced 3D MRCP techniques enhance diagnostic accuracy to nearly 100% by reconstructing overlapping slices of less than 1 mm, making it the preferred imaging choice over diagnostic ERCP [120, 244, 245].

Endoscopic Retrograde Cholangiopancreatography (ERCP)

ERCP has been employed since 1990 to manage complicated gallstone disease [246]. Current guidelines advocate urgent therapeutic ERCP within 72 hours of symptom onset for biliary AP, cholangitis, or dilated CBD. Endoscopic sphincterotomy is necessary for severe cases, with emerging evidence suggesting its application in mild and idiopathic gestational biliary AP [247]. ERCP should ideally be avoided during the first trimester unless critically indicated, given its association with increased risks of preterm delivery (PTD) and low birth weight [196, 248]. To ensure fetal safety, procedural precautions include adjusting the placement of grounding pads and favoring bipolar electrocautery [248, 249]. Despite the risks, ERCP remains the safest therapeutic option compared to surgery or percutaneous techniques for managing bile duct obstructions during pregnancy [250, 251]. ERCP during pregnancy, while generally safe, requires expert execution due to heightened risks such as post-ERCP pancreatitis (6–16%) [131, 196, 253], preterm labor (PTL), and bleeding [255]. Pregnancy-specific physiological changes may exacerbate these complications, necessitating cautious procedural planning [255, 256].

Endoscopic Ultrasound (EUS)

EUS, a semi-invasive diagnostic approach, is rarely employed during pregnancy except when MRCP is unavailable or inconclusive. This modality offers near-perfect predictive accuracy for small CBD stones or sludge, surpassing MRCP in sensitivity [257, 258]. However, its reliance on specialized equipment and expertise limits its widespread use [259].

Treatment

Laparoscopic Cholecystectomy (LC) After ERCP

Although conservative management following ERCP has been associated with healthy pregnancies, studies in nonpregnant populations highlight higher conversion rates to open cholecystectomy (OC) when LC is delayed, emphasizing the importance of early intervention [68]. Prompt LC, ideally within 24–48 hours of ERCP, minimizes hospital stays, recurrent symptoms, and subsequent complications [154, 262, 263]. The procedure is particularly beneficial in pregnancy for mitigating maternal morbidity [68, 159, 196, 261]. A simultaneous hybrid ERCP and LC (rendezvous technique) is feasible during pregnancy, offering reduced procedural risks and hospital stays while lowering treatment costs [264]. This method, successful in 80–90% of cases, avoids fetal radiation exposure. Factors influencing this approach include small stone size (<0.8 cm), limited stone number (≤5), and favorable biliary anatomy [262]. Reserved for cases where the transcystic approach is contraindicated or unsuccessful, choledochotomy involves more invasive intervention while maintaining safety for both mother and fetus [262]. This paraphrased content maintains the original structure and clinical details while employing a more formal and academic tone.

Symptomatic Choledochal Cysts

The pathological description of choledochal cysts was first made by Vater in 1723 [273], followed by the clinical description by Douglas in 1852 [274]. Since then, over 400 cases have been documented in the general population. In 1888, Seyffert reported the first symptomatic case during pregnancy, with jaundice developing post-partum [275]. The first documented rupture of a choledochal cyst in the puerperium following a normal vaginal delivery was presented by Friend in 1958 [276], and Saunders and Jackson reported the first rupture during pregnancy in 1969 [277]. Choledochal cysts represent a rare congenital abnormality of the biliary tract, with a notably higher incidence in Japan and Korea compared to Europe and the United States. Approximately one-third of cases are from Japan [278]. Incidence rates range from 1 in 100,000–150,000 live births [279], with a higher frequency of 1 in 13,000 births in Japan [280]. While typically diagnosed in childhood, choledochal cysts present for the first time in adulthood in 25% of patients. The condition is four times more common in females [279]. By 1944, 14 cases of choledochal cysts during pregnancy and puerperium had been published [281], and by 1978, approximately 50 cases of ruptured cysts were reported, including those in pregnancy and puerperium [282]. As of 2007, 21 cases were diagnosed during pregnancy, with a significant number occurring during labor and early puerperium [275, 276, 281, 283-312]. Most affected patients were nulliparous [303], and 82% exhibited the Todani I type [303].

Pathophysiology

Although choledochal cysts are a rare cause of obstructive jaundice, they are more likely to present during pregnancy [281, 283]. The expansion of the cyst, along with associated pain and jaundice, may be attributed to hormonal influences (e.g., progesterone-induced stasis and relaxin), compression of the bile duct and cyst by the gravid uterus, and increased intra-abdominal pressure during pregnancy and labor [286, 303, 305, 309].

Clinical Presentation

The clinical presentation of choledochal cysts is nonspecific and variable. Symptoms may intensify during late pregnancy due to hormonal effects and compression of the common bile duct (CBD) by the enlarging uterus [304]. Charcot's triad—comprising right upper quadrant abdominal pain, jaundice, and fever—occurs infrequently in adults and in only one-third of pregnant patients [285, 309]. The cyst may not be easily detected due to anatomical changes during pregnancy,

particularly in advanced stages [306]. If asymptomatic, it may go unnoticed or be discovered incidentally during routine abdominal ultrasound. The majority of patients (75%) present with upper right quadrant abdominal pain, jaundice (50%), and nausea or vomiting (50%) [303]. Complications include cholangitis, acute pancreatitis [284, 306], cyst rupture with biliary peritonitis [285], and malignancy within the cyst [287]. When biliary obstruction is present, symptoms resemble those of CBD stones. Cyst perforation most commonly occurs in the late third trimester or during labor, due to the elevated intra-abdominal pressure. Another possibility is the destruction of the cyst wall caused by inflammation (cholangitis) associated with biliary obstruction.

Differential Diagnosis

The differential diagnosis of choledochal cysts varies depending on the clinical presentation. In cases of obstructive jaundice during pregnancy, viral hepatitis or intrahepatic cholestasis of pregnancy (ICP) are more commonly implicated.

Diagnosis

Diagnosis during pregnancy can be challenging due to the overlap of symptoms with normal pregnancy conditions. Routine hematological and liver function tests are of limited diagnostic value. Radiographic studies are constrained by fetal exposure to radiation. Transabdominal ultrasound serves as the initial screening tool for abdominal masses, acute abdomen, or hepatobiliary conditions. However, it may be hindered by distortion of abdominal anatomy caused by the gravid uterus. The cyst may be misidentified as an ovarian tumor or mucocele [311]. While endoscopic retrograde cholangiopancreatography (ERCP) or CT may provide more accurate information, ionizing radiation should generally be avoided in pregnancy [288]. Magnetic resonance imaging (MRI) is preferred due to its high-resolution imaging of the biliary tree without exposing the mother or fetus to ionizing radiation [312]. MRI can also define the type of choledochal cyst.

Treatment

Though choledochal cysts are rare during pregnancy, clinicians must be vigilant, as delayed or inappropriate treatment can lead to severe consequences for both mother and child. Once diagnosed, patients should be referred to specialized centers where treatment can be meticulously planned due to the potential for cyst-related complications in both the short and long term. The timing of the operation depends on the presentation type (elective or emergent), and the surgical approach varies according to the cyst type, as classified by Todani. Surgical principles remain the same in the postpartum period as during pregnancy, with emergent cases requiring urgent surgery [307]. Otherwise, elective surgery during puerperium or after breastfeeding cessation reduces postoperative complications and minimizes the need for medication therapy related to the newborn.

Asymptomatic Choledochal Cyst

Asymptomatic choledochal cysts, when palpable but without other symptoms, should be monitored regularly. Several treatment strategies are available. The first involves postponing definitive treatment until after labor and puerperium to reduce the operational impact on the mother and fetus. The second option involves performing definitive surgery during elective cesarean section (CS). The first approach is recommended as it minimizes potential complications during pregnancy, including prolonged recovery, hemostasis difficulties due to the hyperemic state, and obstructed surgical views due to the gravid uterus. There is no consensus on the optimal timing for surgery following CS, with some recommending surgery six weeks post-delivery [304, 309], or postponing surgery until the patient's physiological condition normalizes after elective CS [304]. Indications for semi-urgent surgical intervention during pregnancy include (a) symptomatic cysts, (b) increased cyst size on serial ultrasound, or (c) suspected/confirmed cholangiocarcinoma. In elective settings, the recommended surgical technique for both pregnant and nonpregnant women involves complete excision of the extrahepatic duct, cholecystectomy, and Roux-en-Y hepaticojejunostomy. Cyst excision eliminates the risk of malignant degeneration, which may be as high as 30% [314], or cyst inflammation. For large cysts, a bilateral Roux-en-Y hepaticojejunostomy may be considered [311]. Complete excision of the extrahepatic bile duct, from the hepatic hilum to the pancreaticobiliary junction, is the most radical solution. In some instances, pancreaticoduodenectomy or hepatic resection may be necessary if the porta hepatis structures are not identifiable, particularly following repeated cholangitis episodes leading to adhesion formation. In such cases, choledochocystoduodenostomy is performed, involving a side-to-side anastomosis between the choledochal cyst's most dependent part and the second part of the duodenum. For type III cysts, endoscopic sphincterotomy is the preferred method. Treatment for type IVa cysts (combined extra and intrahepatic biliary dilation) remains controversial, but total cyst excision, including hepatectomy, is generally recommended for both the general and pregnant populations [288, 315]. For type V cysts, hepatic resection is often recommended in cases of unilobar Caroli's disease [316].

Role of Emergency Professionals:

The role of emergency professionals in managing symptomatic choledochal cysts during pregnancy and puerperium is crucial, given the potential for life-threatening complications and the complex interplay between the condition and pregnancy-related physiological changes. Emergency physicians and paramedics must be adept at identifying these rare but serious conditions, as well as providing timely interventions to optimize outcomes for both the mother and fetus. Choledochal cysts are congenital malformations of the biliary tract that, though rare, can lead to significant clinical challenges when they present during pregnancy. These cysts, when symptomatic, often manifest as obstructive jaundice, abdominal pain, fever, and nausea, symptoms that overlap with common pregnancy complaints. Emergency professionals must therefore be skilled in differentiating choledochal cysts from more common conditions like viral hepatitis, intrahepatic cholestasis of pregnancy (ICP), and gallstones, which can also present with similar clinical manifestations. As the condition is often diagnosed in childhood, presenting it during pregnancy or puerperium poses a diagnostic challenge. Therefore, the ability to quickly assess and order appropriate diagnostic tests, such as ultrasound or MRI, is crucial. Once a choledochal cyst is suspected, emergency professionals must be prepared to manage complications such as rupture, cholangitis, or biliary peritonitis, which are potential sequelae of untreated or undiagnosed cysts. A ruptured choledochal cyst, for example, can lead to severe infection and

abdominal sepsis, both of which pose immediate threats to maternal health. Timely recognition of these complications and prompt surgical intervention is essential. The role of emergency professionals extends beyond diagnosis to include stabilizing the patient and preparing for the necessary surgical interventions, which may require coordination with surgical teams and other specialists. Additionally, during pregnancy, physiological changes, such as increased intra-abdominal pressure and hormonal effects like progesterone-induced bile stasis, can exacerbate symptoms of choledochal cysts. Emergency professionals need to recognize these pregnancy-specific changes and understand how they may impact the biliary tract. This knowledge helps in managing patient care by considering both the cyst's impact and the physiological demands of pregnancy.

Emergency physicians must also be aware of the timing of intervention. While some choledochal cysts may be asymptomatic and not require immediate surgical action, others may present with acute symptoms or complications that require urgent intervention. For example, in cases where a cyst causes biliary obstruction or rupture, immediate surgery may be necessary. The timing of surgery is critical, as it is typically recommended after childbirth or once the mother's physiological state is stabilized. Therefore, emergency professionals need to coordinate with obstetricians and surgical teams to determine the most appropriate time for surgical intervention to minimize risks for both the mother and child. Furthermore, emergency medical services (EMS) play a vital role in the pre-hospital setting. Paramedics may be the first to encounter patients with choledochal cysts or complications arising from them. They must be able to assess the patient's clinical presentation and provide supportive care, such as intravenous fluids and pain management, while transporting the patient to an appropriate facility for further evaluation and treatment. During transport, communication with the receiving hospital can ensure that the emergency department is prepared for the patient's arrival, particularly if surgical intervention is likely. In conclusion, emergency professionals play an integral role in the early identification, stabilization, and management of symptomatic choledochal cysts during pregnancy and puerperium. Their ability to swiftly diagnose, manage complications, and coordinate care with other specialists is key to optimizing outcomes for both the mother and fetus.

Role of Nursing Intervention Protocols:

Nursing intervention protocols are essential in managing symptomatic choledochal cysts during pregnancy and puerperium, as they provide a structured approach to patient care, ensuring safety, timely intervention, and optimal outcomes for both the mother and fetus. Given the complexity of the condition and the potential for serious complications, such as rupture or cholangitis, nurses play a crucial role in early identification, management, and coordination of care. This article discusses the significance of nursing intervention protocols for managing symptomatic choledochal cysts during pregnancy and puerperium, focusing on assessment, monitoring, collaboration, and education.

Early Identification and Assessment

One of the primary functions of nursing intervention protocols is to guide the early identification and assessment of symptoms suggestive of choledochal cysts. Since choledochal cysts can be asymptomatic or present with nonspecific symptoms, early diagnosis is challenging. Nurses are often the first healthcare professionals to assess patients and must be skilled in identifying risk factors and symptoms indicative of choledochal cysts, such as right upper quadrant abdominal pain, jaundice, fever, and nausea. The nursing protocol should include a thorough history-taking, focusing on past medical history, obstetric history, and any previous biliary tract conditions that could raise suspicion for choledochal cysts. Early identification enables timely intervention and prevents progression to more severe complications like cyst rupture or biliary peritonitis. Moreover, nursing protocols should incorporate the regular monitoring of patients with known or suspected choledochal cysts. Routine assessments, including vital signs, abdominal examination, and laboratory tests such as liver function tests, are necessary to track any changes in the patient's condition. Nurses must be vigilant in monitoring for signs of complications such as infection, sepsis, or hepatic dysfunction, which may require immediate intervention. For instance, monitoring for fever or signs of infection (e.g., increased white blood cell count) can prompt further diagnostic tests and ensure timely medical interventions. Protocols should also provide guidance on when to escalate care to physicians or surgical teams, particularly when the condition worsens, or complications develop.

Pain and Symptom Management

Pain management is a critical aspect of nursing interventions for patients with choledochal cysts, especially when they experience abdominal pain or discomfort. Effective pain control is essential for patient comfort and overall well-being. Nursing protocols should outline appropriate pharmacological and non-pharmacological interventions based on the patient's condition and stage of pregnancy. Non-pharmacological methods, such as relaxation techniques, positioning for comfort, and applying heat or cold, can be utilized to manage mild pain. In cases of severe pain, pharmacological interventions such as analgesics (e.g., acetaminophen) or opioids (under careful supervision) may be necessary, with close monitoring to avoid adverse effects, especially during pregnancy. Nurses should also be aware of the risks associated with medication use during pregnancy and adjust their interventions accordingly, taking into account fetal safety. Symptom management is not limited to pain; it extends to managing other symptoms associated with choledochal cysts, such as nausea and vomiting. Nursing protocols should specify the use of antiemetics when appropriate, and also emphasize non-pharmacological interventions, including dietary modifications and hydration, to help alleviate these symptoms. Nurses play an important role in providing emotional support to patients, especially those who may experience anxiety related to their condition and the potential risks to their pregnancy. A compassionate and holistic approach can improve patient outcomes and enhance the overall patient experience.

Collaboration and Coordination of Care

The management of symptomatic choledochal cysts requires interdisciplinary collaboration. Nursing intervention protocols should outline clear communication strategies to ensure seamless coordination among obstetricians, surgeons, radiologists, and other specialists involved in the care of the patient. Nurses are essential in facilitating communication between

the healthcare team and the patient, ensuring that the patient understands the plan of care, and advocating for the patient's needs. This is particularly important when planning for diagnostic tests, such as ultrasound or MRI, or coordinating surgical intervention. In cases where choledochal cyst rupture or other complications arise, the nursing protocol must emphasize the importance of timely escalation to the surgical team for emergent interventions. Nurses should also be prepared to support patients through pre-operative and post-operative care, including patient education on expected recovery and potential complications. Clear documentation of patient assessments, care plans, and any changes in the patient's condition is also crucial for maintaining continuity of care.

Patient Education and Emotional Support

Patient education is a core component of nursing intervention protocols for managing symptomatic choledochal cysts. Nurses must provide clear, accurate information to patients and their families regarding the nature of the condition, potential complications, and treatment options. This includes educating the patient about the risks and benefits of surgery, the potential impact of the condition on pregnancy, and what to expect during the postoperative recovery period. Nurses should tailor their education to the individual patient's needs, ensuring that the information is delivered in a way that is easy to understand and culturally appropriate. Furthermore, emotional support plays a key role in nursing care for pregnant patients with choledochal cysts, as the diagnosis and the prospect of surgery can be overwhelming. Nurses should provide a supportive environment where patients can express their concerns and receive reassurance. Offering emotional support through active listening and providing psychological counseling resources, such as access to social workers or counseling services, can alleviate anxiety and improve patient outcomes. Nursing intervention protocols are a vital component of the comprehensive care plan for managing symptomatic choledochal cysts during pregnancy and puerperium. These protocols guide nurses in early identification, symptom management, and coordination of care, ensuring that patients receive timely, appropriate interventions. By focusing on pain management, patient education, collaboration with other healthcare professionals, and emotional support, nurses can play a significant role in improving patient outcomes and minimizing complications. The application of structured nursing protocols ensures a systematic approach to care, enhancing both maternal and fetal well-being in the context of a challenging and complex medical condition.

Conclusion:

Gallbladder disease, particularly in pregnant women, remains a significant concern for healthcare providers, including emergency healthcare professionals, nurses, and clinical pathologists. The prevalence of gallstones varies across different populations, with notable variations linked to ethnicity, hormonal changes, and obesity. Pregnancy itself is a major risk factor for gallstone formation due to increased levels of estrogen and progesterone, which promote bile stasis and reduce gallbladder motility, thereby enhancing the likelihood of gallstone development. Moreover, insulin resistance plays a crucial role in the pathogenesis of gallstones, especially in obese and diabetic populations. In pregnant women, gallstones can often be asymptomatic but may lead to complications such as acute cholecystitis (AC), pancreatitis, and cholangitis, particularly when exacerbated by certain risk factors such as obesity or multiple pregnancies. Symptoms of gallbladder disease include right upper quadrant pain, biliary colic, and jaundice, which can escalate into more severe conditions, requiring immediate medical intervention. Early identification of symptoms and timely management are critical to preventing serious complications and improving patient outcomes. Surgical intervention, such as cholecystectomy, is often necessary for symptomatic cases, particularly in those experiencing recurrent pain or complications. Additionally, the resolution of gallstones postpartum is a noteworthy factor, as many women experience the spontaneous resolution of gallstones within a few months after delivery. Preventive measures are crucial for managing gallbladder disease in high-risk populations, especially among obese individuals and those undergoing bariatric surgery. Prophylactic treatments and close monitoring during and after pregnancy can help mitigate the risks of gallstone formation. Overall, a multidisciplinary approach involving healthcare professionals at all levels is essential to address this complex and prevalent condition.

References:

1. Gerdes MM, Boyden EA. The rate of emptying of human gallbladder in pregnancy. Surg Gynecol Obstet. 1938;66:145–56.
2. Mayo W. "'Innocent'" gall-stones a myth. JAMA. 1911;56:1021–4.
3. Grundy SM, Kalser SC. Highlights of the meeting on prevention of gallstones. Hepatology. 1987;7:946–51.
4. Valdivieso V, Covarrubias C, Siegel F, Cruz F, et al. Pregnancy and cholelithiasis: pathogenesis and natural course of gallstone diagnosed in early puerperium. Hepatology. 1993;17:1–4.
5. Diehl A. Epidemiology and natural history of gallstone disease. Gastroenterol Clin N Am. 1991;20:1–19.
6. Méndez-Sánchez N, Jessurun J, Ponciano-Rodríguez G, Alonso-De-Ruiz P, Uribe M, Hernández-Avila M. Prevalence of gallstone disease in Mexico - a necropsy study. Dig Dis Sci. 1993;38:680–3.
7. Ko C. Risk factors for gallstone-related hospitalization during pregnancy and the postpartum. Am J Gastroenterol. 2006;101:2263–8.
8. McKellar DP, Anderson CT, Boynton CJ, et al. Cholecystectomy during pregnancy without fetal loss. Surg Gynecol Obstet. 1992;174:465–8.
9. Printen KJ, Ott RA. Cholecystectomy during pregnancy. Am J Surg. 1978;44:432–4.
10. Swisher SG, Schmit PJ, Hunt KK, et al. Biliary disease during pregnancy. Am J Surg. 1994;168:576–81.
11. Hill LM, Johnson CE, Lee RA. Cholecystectomy in pregnancy. Obstet Gynecol. 1975;46:291–3.
12. Ibiebele I, Schnitzler M, Nippita T, Ford JB. Outcomes of gallstone disease during pregnancy: a population-based data linkage study. Paediatr Perinat Epidemiol. 2017;31:522–30.
13. Stauffer RA, Adams A, Wygal J, Lavery JP. Gallbladder disease in pregnancy. Am J Obstet

14. Basso L, McCollum PT, Dariling MR, et al. A study of cholelithiasis during pregnancy and its relationship with age, parity, menarche, breastfeeding, dysmenorrheal, oral contraception and a maternal history of cholelithiasis. Surg Gynecol Obstet. 1992;175:41–6.
15. Chesson RR, Gallup DG, Gibbs RL, et al. Ultrasonographic diagnosis of asymptomatic cholelithiasis in pregnancy. J Reprod Med. 1985;30:920–2.
16. Friley MD, Douglas G. Acute cholecystitis in pregnancy and the puerperium. Am Surg. 1972;38:314–7.
17. Landers D, Carmona R, Crombleholme W, Lim R. Acute cholecystitis in pregnancy. Obstet Gynecol. 1987;69:131–3.
18. Elerding S. Laparoscopic cholecystectomy in pregnancy. Am J Surg. 1993;165:625–7.
19. Kammerer W. Nonobstetric surgery during pregnancy. Med Clin North Am. 1979;63:1157–64.
20. Morrell DG, Mullins JR, Harrison PB. Laparoscopic cholecystectomy during pregnancy in symptomatic patients. Surgery. 1992;112:856–9.
21. Graham G, Baxi L, Tharakan T. Laparoscopic cholecystectomy during pregnancy: a case series and review of the literature. Obstet Gynecol Surv. 1998;53:566–74.
22. Ghumman E, Barry M, Grace PA. Management of gallstones in pregnancy. Br J Surg. 1997;84:1646–50.
23. Wishner JD, Zolfaghari D, Wohlgemuth SD, et al. Laparoscopic cholecystectomy in pregnancy. A report of 6 cases and review of the literature. Surg Endosc. 1996;10:314–8.
24. Ko CW, Beresford SAA, Schulte SJ, et al. Incidence, natural history, and risk factors for biliary sludge and stones during pregnancy. Hepatology. 2005;41:359–65.
25. Hamilton BE, Martin JA, Osterman MJK, Curtin SC, Matthews TJ. Births: final data for 2014. Natl Vital Stat Rep. 2015;64(12):1–64.
26. Casey BM, Cox SM. Cholecystitis in pregnancy. Infect Dis Obstet Gynecol. 1996;4:303–9.
27. Honoré L. Cholesterol cholelithiasis in adolescent females. Arch Surg. 1980;115:62–8.
28. Hansen GC, Duerinckx AJ, Fymat A, et al. Cholelithiasis in the gravid Hispanic population. J Clin Ultrasound. 1994;22:187–91.
29. Akhter N, Mir IN, Manzoor SV. Course and outcomes of complicated gallstone disease in pregnancy: a single Centre experience. Int J Res Med Sci. 2019;7:2686–9.
30. İlhan M, İlhan G, Gök AFK, Günay K, Ertekin C. The course and outcomes of complicated gallstone disease in pregnancy: experience of a tertiary center. Turk J Obstet Gynecol. 2016;13:178–82.
31. Peterson R. Gallstones during pregnancy and the puerperium. Surg Gynecol Obstet. 1910;11:1–11.
32. Buchanan TA, Xiang AH, Kjos SL, et al. Antepartum predictors of the development of type 2 diabetes in Latino women 11-26 months after pregnancies complicated by gestational diabetes. Diabetes. 1999;48:2430–6.
33. Marín R, Gorostidi M, Portal CG, et al. Long-term prognosis of hypertension in pregnancy. Hypertens Pregnancy. 2000;19:199–209.
34. Lee SP, Maher K, Nicholls JF. Origin and fate of biliary sludge. Gastroenterology. 1988;94:170–6.
35. Bolukbas FF, Bolukbas C, Horoz M, et al. Risk factors associated with gallstone and biliary sludge formation during pregnancy. J Gastroenterol Hepatol. 2006;21:1150–3.
36. Cosenza CA, Saffari B, Jabbour N, et al. Surgical management of biliary gallstone disease during pregnancy. Am J Surg. 1999;178:545–8.
37. Maringhini A, Ciambra M, Baccelliere P, et al. Biliary sludge and gallstones in pregnancy: incidence, risk factors and natural history. Ann Intern Med. 1993;119:116–20.
38. Scott L. Gallstone disease and pancreatitis in pregnancy. Gastroenterol Clin N Am. 1992;21:803–15.
39. Mendez-Sanchez N, Chavez-Tapia NC, Uribe M. Pregnancy and gallbladder disease. Ann Hepatol. 2006;5:227–30.
40. Thijs C, Knipschild P, Leffers P. Pregnancy and gallstone disease: an empiric demonstration of the importance of specification of risk periods. Am J Epidemiol. 1999;134:186–95.
41. Barbara L, Sama C, Morselli Labate AM, et al. A population study on the prevalence of gallstone disease: the Sirmione study. Hepatology. 1987;7:913–7.
42. Everhart JE, Khare M, Hill M, et al. Prevalence and ethic differences in gallbladder disease in the United States. Gastroenterology. 1999;117:632–9.
43. Liu B, Beral V, Balkwill A, Million Women Study Collaborators. Childbearing, breastfeeding, other reproductive factors and the subsequent risk of hospitalization for gallbladder disease. Int J Epidemiol. 2009;38:312–8.
44. Petrakis NL, Wrensch MR, Ernster VL, et al. Influence of pregnancy and lactation on serum and breast fluid estrogen levels: implications for breast cancer risk. Int J Cancer. 1987;40:587–91.
45. Khan MK, Jalil MA, Khan SU. Pregnancy causing gallstone disease. Mymensingh Med J. 2008;17:S91–6.
46. Järvinen HJ, Hästbacka J. Early cholecystectomy for acute cholecystitis: a prospective randomized study. Ann Surg. 1980;191:501–5.
47. Rambal S, Manhas K, Sharma S, Gupta S. Ultrasound evaluation of gallbladder disease in pregnancy. JK Sci. 2001;3:78–83.
48. Khuroo MS, Mahajan R, Zargar SA, et al. Prevalence of biliary tract disease in India: a sonographic study in adult population in Kashmir. Gut. 1989;30:201–5.
49. Walcher T, Haenle MM, Kron M, et al. Pregnancy is not a risk factor for gallstone disease: results of a randomly selected population sample. World J Gastroenterol. 2005;11:6800–6.
50. Álvarez-Villaseñor AS, Mascareño-Franco HL, Agundez-Meza JJ, Cardoza-Macías F, Fuentes-Orozco C, Rendón-Félix J, et al. Cholelithiasis during pregnancy and postpartum: prevalence, presentation and consequences in a referral hospital in Baja California Sur. Gac Med Mex. 2017;153:146–52.

51. Haffner SM, Diehl AK, Mitchell BD, et al. Increased prevalence of clinical gallbladder disease in subjects with non-insulin-dependent diabetes mellitus. Am J Epidemiol. 1990;132:327–35.
52. Misciagna G, Guerra V, Di Leo A, et al. Insulin and gall stones: a population case control study in southern Italy. Gut. 2000;47:144–7.
53. Ruhl CE, Everhart JE. Association of diabetes, serum insulin, and C-peptide with gallbladder disease. Hepatology. 2000;31:299–303.
54. Scragg RK, Calvert GD, Oliver JR. Plasma lipids and insulin in gallstone disease: a case-control study. BMJ. 1984;289:521–5.
55. De Santis A, Attili AF, Ginanni Corradini S, et al. Gallstones and diabetes: a case-control study in a free-living population sample. Hepatology. 1997;25:787–90.
56. Kono S, Shinchi K, Ikeda N, et al. Prevalence of gallstone disease in relation to smoking, alcohol use, obesity, and glucose tolerance: a study of self- defense officials in Japan. Am J Epidemiol. 1992;136:787–94.
57. Maurer KR, Knowles JE, Everhart WD, et al. Risk factors for gallstone disease in the Hispanic populations of the United States. Am J Epidemiol. 1990;96:487–92.
58. Ko CW, Beresford SAA, Schulte SJ, Lee SP. Insulin resistance and incident gallbladder disease in pregnancy. Clin Gastroenterol Hepatol. 2008;6:76–81.
59. Mokdad AH, Ford ES, Bowman BA, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. JAMA. 2003;289:76–9.
60. Tucker O, Fajnwaks P, Szomstein S, Rosenthal R. Is concomitant cholecystectomy necessary in obese patients undergoing laparoscopic gastric bypass surgery? Surg Endosc Other Interv Tech. 2008;22(11):2450–4.
61. Rottenstreich A, Kleinstern G, Levin G, Mintz Y, Elchalal U, Elazary R. Does pregnancy increase the risk of cholecystectomy following bariatric surgery? A cross-sectional cohort study. Surg Obes Relat Dis. 2019;15(10):1822–8.
62. Van Bodegraven AA, Böhmer CJ, Manoliu RA, et al. Gallbladder contents and fasting gallbladder volumes during and after pregnancy. Scand J Gastroenterol. 1998;33:993–7.
63. Braverman DZ, Johnson ML, Kern F Jr. Effects of pregnancy and contraceptive steroids on gallbladder function. N Engl J Med. 1980;302:362–4.
64. Kapicioglu S, Gürbüz S, et al. Measurement of gallbladder volume with ultrasonography in pregnant women. Can J Gastroenterol. 2000;14:403–5.
65. Everson GT, Fennessey P, Kern F Jr. Contraceptive steroids alter the steady-state kinetics of bile acids. J Lipid Res. 1988;29:68–76.
66. Everson GT, McKinley C, Lawson M, et al. Gallbladder function in the human female: effect of the ovulatory cycle, pregnancy, and contraceptive steroids. Gastroenterology. 1982;82:711–9.
67. Lammert F, Sauerbruch T. Mechanisms of disease: the genetic epidemiology of gallbladder stones. Nat Clin Pract Gastroenterol Hepatol. 2005;2:423–33.
68. Sungler P, Heinerman PM, Steiner H, et al. Laparoscopic cholecystectomy and interventional endoscopy for gallstone complications during pregnancy. Surg Endosc. 2000;14:267–71.
69. Ryan JP, Pellecchia D. Effect of progesterone pretreatment on Guinea pig gallbladder motility in vitro. Gastroenterology. 1982;83:81–3.
70. Davis M, Ryan JP. Influence of progesterone on Guinea pig gallbladder motility in vitro. Dig Dis Sci. 1986;31:513–8.
71. Behar J. Clinical aspects of gallbladder motor function and dysfunction. Curr Gastroenterol Rep. 1999;1:91–4.
72. Kern F Jr, Everson GT, DeMark B, et al. Biliary lipids, bile acids, and gallbladder function in the human female. Effects of pregnancy and the ovulatory cycle. J Clin Invest. 1981;68:1229–42.
73. Angelin B, Olivecrona H, Reihner E, Rudling M, Stahlberg D, Eriksson M, et al. Hepatic cholesterol metabolism in estrogen-treated men. Gastroenterology. 1992;103(5):1657–63.
74. Henriksson P, Einarsson K, Eriksson A, et al. Estrogen-induced gallstone formation in males. Relation to changes in serum and biliary lipids during hormonal treatment of prostatic carcinoma. J Clin Invest. 1989;84:811–6.
75. Uhler ML, Marks JW, Voigt BJ, Judd HL. Comparison of the impact of transdermal versus oral estrogens on biliary markers of gallstone formation in postmenopausal women. J Clin Endocrinol Metab. 1998;83(2):410–4.
76. Wang HH, Afdhal NH, Wang DQH. Overexpression of estrogen receptor alpha increases hepatic cholesterogenesis, leading to biliary hypersecretion in mice. J Lipid Res. 2006;47(4):778–86.
77. Everson GT, McKinley C, Kern F Jr. Mechanisms of gallstone formation in women. Effects of exogenous estrogen (Premarin) and dietary cholesterol on hepatic lipid metabolism. J Clin Invest. 1991;87:237–46.
78. Coyne MJ, Bonorris GG, Chung A, et al. Estrogen enhances dietary cholesterol induction of saturated bile in the hamster. Gastroenterology. 1978;75:76–9.
79. Portincasa P, Di Ciaula A, Wang HH, et al. Coordinate regulation of gallbladder motor function in the gut-liver axis. Hepatology. 2008;47:2112–26.
80. Tierney S, Qian Z, Burrow C, Lipsett PA, Pitt HA, Lillemoe KD. Estrogen inhibits sphincter of Oddi motility. J Surg Res. 1994;57(1):69–73.
81. Brown MS, Goldstein JL. A receptor-mediated pathway for cholesterol homeostasis. Science. 1986;232:34–47.
82. Kozarsky KF, Donahee MH, Rigotti A, Iqbal SN, Edelman ER, Krieger M. Overexpression of the HDL receptor SR-BI alters plasma HDL and bile cholesterol levels. Nature. 1997;387:414–7.
83. Wang HH, Liu M, Clegg DJ, Portincasa P, Wang DQ. New insights into the molecular mechanisms underlying effects of estrogen on cholesterol gallstone formation. Biochim Biophys Acta. 2009;1791(11):1037–47.
84. Maringhini A, Ciambra M, Baccelliere P, et al. Sludge, stones, and pregnancy. Gastroenterology. 1988;95:1160–1.
85. Maringhini A, Marcenò MP, Lanzarone F, et al. Sludge and stones in gallbladder after pregnancy. J Hepatol. 1987;5:218–23.

86. Gangwar R, Dayal M, Dwivedi M, Ghosh UK. Gallbladder disease in pregnancy. J Obstet Gynaecol India. 2011;61:57–61.
87. Ness GC, Zhao Z, Wiggins L. Insulin and glucagon modulate hepatic 3-hydroxy-3-methylglutaryl-coenzyme A reductase activity by affecting immunoreactive protein levels. J Biol Chem. 1994;269(46):29168–72.
88. Chait A, Bierman EL, Albers JJ. Low-density lipoprotein receptor activity in cultured human skin fibroblasts. Mechanism of insulin-induced stimulation. J Clin Invest. 1979;64(5):1309–19.
89. Petitti DB, Friedman GD, Klatsky AL. Association of a history of gallbladder disease with a reduced concentration of high-density-lipoprotein cholesterol. N Engl J Med. 1981;304:1396–8.
90. Bennion LJ, Grundy SM. Effects of diabetes mellitus on cholesterol metabolism in man. N Engl J Med. 1977;296(24):1365–71.
91. de Leon MP, Ferenderes R, Carulli N. Bile lipid composition and bile acid pool size in diabetes. Am J Dig Dis. 1978;23(8):710–6.
92. Haber GB, Heaton KW. Lipid composition of bile in diabetics and obesity-matched controls. Gut. 1979;20(6):518–22.
93. Gielkens HA, Lam WF, Coenraad M, et al. Effect of insulin on basal and cholecystokinin-stimulated gallbladder motility in humans. J Hepatol. 1998;28:595–602.
94. Hahm JS, Park JY, Park KG, Ahn YH, Lee MH, Park KN. Gallbladder motility in diabetes mellitus using real time ultrasonography. Am J Gastroenterol. 1996;91:2391–4.
95. Graewin SJ, Kiely JM, Lee KH, Svatek CL, Nakeeb A, Pitt HA, et al. Nonobese diabetic mice have diminished gallbladder motility and shortened crystal observation time. J Gastrointest Surg. 2004;8(7):824–30.
96. Tran KQ, Goldblatt MI, Swartz-Basile DA, Svatek C, Nakeeb A, Pitt HA. Diabetes and hyperlipidemia correlate with gallbladder contractility in leptin-related murine obesity. J Gastrointest Surg. 2003;7(7):857–63.
97. Nakeeb A, Comuzzie AG, Al-Azzawi H, Sonnenberg GE, Kissebah AH, Pitt HA. Insulin resistance causes human gallbladder dysmotility. J Gastrointest Surg. 2006;10(7):940–9.
98. Stone BG, Gavaler JS, Belle SH, Shreiner DP, Peleman RR, Sarva RP, et al. Impairment of gallbladder emptying in diabetes mellitus. Gastroenterology. 1988;95(1):170–6.
99. Chapman BA, Chapman TM, Frampton CM, Chisholm RJ, Allan RB, Wilson IR, et al. Gallbladder volume: comparison of diabetics and controls. Dig Dis Sci. 1998;43(2):344–8.
100. Güliter S, Yilmaz S, Karakan T. Evaluation of gallbladder volume and motility in non-insulin-dependent diabetes mellitus patients using real-time ultrasonography. J Clin Gastroenterol. 2003;37(4):288–91.
101. Sweeney G, Klip A. Mechanisms and consequences of Na+, K+-pump regulation by insulin and leptin. Cell Mol Biol (Noisy-le-grand). 2001;47(2):363–72.
102. Graewin SJ, Lee K-H, Kiely JM, et al. Gallbladder myocytes are short and cholecystokinin-resistant in obese diabetic mice. Surgery. 2004;136:431–6.
103. Bucala R. Lipid and lipoprotein modification by AGEs: role in atherosclerosis. Exp Physiol. 1997;82:327–37.
104. Chen Q, Amaral J, Biancani P, Behar J. Excess membrane cholesterol alters human gallbladder muscle contractility and membrane fluidity. Gastroenterology. 1999;116(3):678–85.
105. Altieri MS, Yang J, Nie L, Docimo S, Talamini M, Pryor AD. Incidence of cholecystectomy after bariatric surgery. Surg Obes Relat Dis. 2018;14(7):992–6.
106. Wanjura V, Sandblom G, Österberg J, Enochsson L, Ottosson J, Szabo E. Cholecystectomy after gastric bypass—incidence and complications. Surg Obes Relat Dis. 2017;13(6):979–87.
107. Davis VL, Cox RAK. Gallbladder disease in pregnancy. J Reprod Med Obstet Gynecologist. 1995;40:759–62.
108. Augustin G, Majerovic M. Non-obstetrical acute abdomen during pregnancy. Eur J Obstet Gynecol Reprod Biol. 2007;131:4–12.
109. DeVore G. Acute abdominal pain in the pregnant patient due to pancreatitis, acute appendicitis, cholecystitis, or peptic ulcer disease. Clin Perinatol. 1980;7:349–69.
110. Goodwin TM. Hyperemesis gravidarum. Obstet Gynecol Clin N Am. 2008;35:401–17.
111. Bottomley C, Bourne T. Management strategies for hyperemesis. Best Pract Res Clin Obstet Gynaecol. 2009;23(4):549–64.
112. Morali GA, Braverman DZ. Abnormal liver enzymes and ketonuria in hyperemesis gravidarum. A retrospective review of 80 patients. J Clin Gastroenterol. 1990;12(3):303–5.
113. Reichert JA, Valle RF. Fitz-Hugh-Curtis syndrome. A laparoscopic approach. JAMA. 1976;236(3):266–8.
114. Tietze A. Über eine eigenartige Häufung von Fallen mit Dystrophie der Rippenknorpel. Kln Wochenschr (Berlin). 1921;58:829–31.
115. Deutchman ME, Connor P, Hahn RG, Rodney WM. Maternal gallbladder assessment during obstetric ultrasound: results, significance, and technique. J Fam Pract. 1994;39(1):33–7.
116. Chang T, Lepanto L. Ultrasonography in the emergency setting. Emerg Med Clin North Am. 1992;10(1):1–25.
117. Loughlin KR. Urologic radiology during pregnancy. Urol Clin North Am. 2007;34:23–6.
118. Hepburn IS. Pregnancy-associated liver disorders. Dig Dis Sci. 2008;53:2334–58.
119. Paspulati R. Imaging of the nonobstetric acute abdomen during pregnancy and puerperium. Contemp Diagn Radiol. 2008;31:1–6.
120. Oto A, Ernst R, Ghulmiyyah L, Hughes D, Saade G, Chaljub G. The role of MR cholangiopancreatography in the evaluation of pregnant patients with acute pancreaticobiliary disease. Br J Radiol. 2009;82(976):279–85.
121. http://www.findagrave.com/cgi-bin/fg.cgi?page=gr&GRid=55489857.
122. Ploger R. Die Gallegsteinkrankheit in ihrer Beziehung zur Schwangerschaft und zum Wochenbett. Beitr z klin Chir. 1910;69:275–95.

123. Green R. Cholecystitis and cholelithiasis associated with pregnancy. Boston Med Surg J. 1913;160:679–81.
124. Branson L. Cholecystitis and cholelithiasis in their relation to pregnancy. JAMA. 1911;57:1690–4.
125. Graham J. Gallstones complicating pregnancy and the puerperium. South Med J. 1914;7:389–92.
126. Grube K. Ueber die Bedeutung der Schwangerschaft für die Entstehung der Gallensteinkrankheit. Veroffentl d balneol Gesellsch. 1912;23:13–6.
127. Hoffbauer J. über Relationen weiblicher Generatiensvorgange zur Klinik der Cholelithiasis. Med Klin. 1909;5:239–41.
128. M'Nee J. Recent work on the etiology of gallstones. Glasgow Med J. 1914;81:106–15.
129. Jorge A, Gawron AJ, Veerappan A, Soper NJ, Keswani RN. Nonoperative management of symptomatic cholelithiasis in pregnancy is associated with frequent antepartum and early postpartum hospitalizations. Gastroenterology. 2015;19:598–603.
130. Lu EJ, Curet MJ, El-Sayed YY, Kirkwood KS. Medical versus surgical management of biliary tract disease in pregnancy. Am J Surg. 2004;188:755–9.
131. Othman MO, Stone E, Hashimi M, et al. Conservative management of cholelithiasis and its complications in pregnancy is associated with recurrent symptoms and more emergency department visits. Gastrointest Endosc. 2012;76:564–9.
132. Dixon NP, Faddis DM, Silberman H. Aggressive management of cholecystitis during pregnancy. Am J Surg. 1987;154(3):292–4.
133. Curet MJ, Allen D, Josloff RK, Pitcher DE, Curet LB, Miscall BG, et al. Laparoscopy during pregnancy. Arch Surg. 1996;131(5):546–50.
134. Glasgow RE, Visser BC, Harris HW, Patti MG, Kilpatrick SJ, Mulvihill SJ. Changing management of gallstone disease during pregnancy. Surg Endosc. 1998;12(3):241–6.
135. Muench J, Albrink M, Serafini F, et al. Delay in treatment of biliary disease during pregnancy increases morbidity and can be avoided with safe laparoscopic cholecystectomy. Am Surg. 2001;67:539–42.
136. Visser BC, Glasgow RE, Mulvihill KK, Mulvihill SJ. Safety and timing of nonobstetric abdominal surgery in pregnancy. Dig Surg. 2001;18(5):409–17.
137. Fong ZV, Pitt HA, Strasberg SM, Molina RL, Perez NP, Kelleher CM, et al. Cholecystectomy during the third trimester of pregnancy: proceed or delay? J Am Coll Surg. 2019;228:494–502.e1.
138. Hong J, Yang J, Zhang X, Su J, Tumati A, Garry D, et al. Considering delay of cholecystectomy in the third trimester of pregnancy. Surg Endosc. 2021;35(8):4673–80.
139. Cheng V, Matsushima K, Ashbrook M, Matsuo K, Schellenberg M, Inaba K, et al. Association between trimester and outcomes after cholecystectomy during pregnancy. J Am Coll Surg. 2021;233(1):29–37.e1.
140. Upadhyay A, Stanten S, Kazantsev G, Horoupian R, Stanten A. Laparoscopic management of a nonobstetric emergency in the third trimester of pregnancy. Surg Endosc Other Interv Tech. 2007;21(8):1344–8.
141. Holthausen UH, Mettler L, Troidl H. Pregnancy: a contraindication? World J Surg. 1999;23:856–62.
142. Jelin EB, Smink DS, Vernon AH, Brooks DC. Management of biliary tract disease during pregnancy: a decision analysis. Surg Endosc. 2008;22(1):54–60.
143. Kuy S, Roman SA, Desai R, Sosa JA. Outcomes following cholecystectomy in pregnant and nonpregnant women. Surgery. 2009;146:358–66.
144. Reedy MB, Källén B, Kuehl TJ. Laparoscopy during pregnancy: a study of five fetal outcome parameters with use of the Swedish Health Registry. Am J Obstet Gynecol. 1997;177:673–9.
145. Veerappan A, Gawron AJ, Soper NJ, Keswani RN. Delaying cholecystectomy for complicated gallstone disease in pregnancy is associated with recurrent postpartum symptoms. J Gastrointest Surg. 2013;17:1953–9.
146. Lockwood C, Stiller RJ, Bolognese RJ. Maternal total parenteral nutrition in chronic cholecystitis. A case report. J Reprod Med. 1987;32:785–8.
147. Levine MG, Esser D. Total parenteral nutrition for the treatment of severe hyperemesis gravidarum: maternal nutritional effects and fetal outcome. Obstet Gynecol. 1988;72:102–7.
148. Ogura JM, Francois KE, Perlow JH, Elliott JP. Complications associated with peripherally inserted central catheter use during pregnancy. Am J Obstet Gynecol. 2003;188:1223–5.
149. Russo-Stieglitz KE, Levine AB, Wagner BA, Armenti VT. Pregnancy outcome in patients requiring parenteral nutrition. J Matern Fetal Med. 1999;8:164–7.
150. Ward A, Brogden RN, Heel RC, et al. Ursodeoxycholic acid: a review of its pharmacologic properties and therapeutic efficacy. Drugs. 1984;27:95–131.
151. Caliskan K. The use of percutaneous cholecystostomy in the treatment of acute cholecystitis during pregnancy. Clin Exp Obstet Gynecol. 2017;44(1):11–3.
152. Allmendinger N, Hallisey MJ, Ohki SK, et al. Percutaneous cholecystostomy treatment of acute cholecystitis in pregnancy. Obstet Gynecol. 1995;86:653–4.
153. Takada T, Strasberg SM, Solomkin JS, et al. Updated Tokyo guidelines for the management of acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci. 2013;20:1–7.
154. Chandler CF, Lane JS, Ferguson P, Thompson JE, Ashley SW. Prospective evaluation of early versus delayed laparoscopic cholecystectomy for the treatment of acute cholecystitis. Am Surgeon. 2000;66:896–900.
155. Kiviluoto T, Sirén J, Luukkonen P, Kivilaakso E. Randomized trial of laparoscopic versus open cholecystectomy for acute and gangrenous cholecystitis. Lancet. 1998;351:321–5.
156. Chiappetta Porras LT, Napoli ED, Canullan CM, Quesada BM, Roff HE, Alvarez Rodriguez J, et al. Minimally invasive management of acute biliary tract disease during pregnancy. HPB Surg. 2009;2009:829020.
157. Rios-Diaz AJ, Oliver EA, Bevilacqua LA, Metcalfe D, Yeo CJ, Berghella V, et al. Is it safe to manage acute cholecystitis nonoperatively during pregnancy?: a nationwide analysis of morbidity according to management strategy. Ann Surg. 2020;272(3):449–56.

158. Jackson H, Granger S, Price R, et al. Diagnosis and laparoscopic treatment of surgical disease during pregnancy: an evidence-based review. Surg Endosc. 2008;22:1917–27.
159. Al-Akeely MH. Management of complicated gallstone disease during pregnancy. Saudi J Gastroenterol. 2003;9(3):135–8.
160. Ali ME, Al-Shehri MY, Abu-Eshy S, et al. Is surgical intervention in acute cholecystitis in pregnancy justified? J Obstet Gynaecol. 1997;17:435–8.
161. Pearl J, Price R, Richardson W, et al. Guidelines for diagnosis, treatment, and use of laparoscopy for surgical problems during pregnancy. Surg Endosc. 2011;25:3479–92.
162. Sedaghat N, Cao AM, Eslick GD, Cox MR. Laparoscopic versus open cholecystectomy in pregnancy: a systematic review and meta-analysis. Surg Endosc. 2017;31(2):673–9.
163. Barone JE, Bears S, Chen S, et al. Outcome study of cholecystectomy during pregnancy. Am J Surg. 1999;177:232–6.
164. Machado NO, Machado LS. Laparoscopic cholecystectomy in the third trimester of pregnancy: report of 3 cases. Surg Laparosc Endosc Percutan Tech. 2009;19:439–41.
165. Meshikhes A. Successful laparoscopic cholecystectomy in the third trimester of pregnancy. Saudi Med J. 2008;29:291–2.
166. Eichenberg BJ, Vanderlinden J, Miguel C, et al. Laparoscopic cholecystectomy in the third trimester of pregnancy. Am Surg. 1996;62:874–7.
167. Halkic N, Tempia-Caliera AA, Ksontini R, et al. Laparoscopic management of appendicitis and symptomatic cholelithiasis during pregnancy. Langenbecks Arch Surg. 2006;391:467–71.
168. Rollins MD, Chan KJ, Price RR. Laparoscopy for appendicitis and cholelithiasis during pregnancy: a new standard of care. Surg Endosc. 2004;18:237–41.
169. Affleck DG, Handrahan DL, Egger MJ, Price RR. The laparoscopic management of appendicitis and cholelithiasis during pregnancy. Am J Surg. 1999;178:523–9.
170. Balinskaite V, Bottle A, Sodhi V, Rivers A, Bennett PR, Brett SJ, et al. The risk of adverse pregnancy outcomes following nonobstetric surgery during pregnancy. Ann Surg. 2017;266(2):260–6.
171. Paramanathan A, Walsh SZ, Zhou J, Chan S. Laparoscopic cholecystectomy in pregnancy: an Australian retrospective cohort study. Int J Surg. 2015;18:220–3.
172. Pearl JP, Price RR, Tonkin AE, Richardson WS, Stefanidis D. SAGES guidelines for the use of laparoscopy during pregnancy. Surg Endosc. 2017;31(10):3767–82.
173. Hart RO, Tamadon A, Fitzgibbons RJ Jr, Fleming A. Open laparoscopic cholecystectomy in pregnancy. Surg Laparosc Endosc. 1993;3:13–6.
174. Chiedozi LC, Al-Hady FH. Antimicrobial prophylaxis for cholecystectomy in diabetes. Ann Saudi Med. 1993;13:498–500.
175. Pezzolla A, Lattarulo S, Disabato M, Barile G, Primiceri G, Paradies D. [Laparoscopic cholecystectomy for acute cholecystitis in pregnancy: a case report in woman with situs viscerum inversus]. Recenti Prog Med. 2012;103(12):578–80.
176. Augustin G, Vrcic H, Zupancic B. Laparoscopic cholecystectomy due to acute calculous cholecystitis in 16 weeks' in vitro fertilization and embryo transfer pregnancy: report of the first case. J Postgrad Med. 2012;58(4):298–300.
177. Lyall S, Jayakar J, Prasath G. Innovative technique for cholecystectomy in twin pregnancy complicated with biliary pancreatitis. J Surg Pak. 2012;17:43–5.
178. Pucci RO, Seed RW. Case report of laparoscopic cholecystectomy in the third trimester of pregnancy. Am J Obstet Gynecol. 1991;165:401–2.
179. https://www.mountnittany.org/wellness-article/abdominal-pain-in-pregnancy-gallstones.
180. NIH consensus development panel on gallstones and laparoscopic cholecystectomy. Gallstones and laparoscopic cholecystectomy. Surg Endosc. 1993;7:271–9.
181. Fatum M, Rojansky N. Laparoscopic surgery during pregnancy. Obstet Gynecol Surv. 2001;56:50–9.
182. SAGES guidelines for laparoscopic surgery during pregnancy. SAGES publication 0023.
183. Lemaire BM, van Erp WF. Laparoscopic surgery during pregnancy. Surg Endosc. 1997;11:15–8.
184. Topgül K, Yürüker SS, Kuru B. Single-incision laparoscopic cholecystectomy in a 6-month pregnant woman: a report of a case. Surg Laparosc Endosc Percutan Tech. 2011;21:e100–3.
185. Behera R, Salgaonkar H, Bhandarkar D, Gupta T, Desai S. Laparoendoscopic single-site cholecystectomy in a pregnant patient. J Minim Access Surg. 2013;9(4):183–6.
186. Athwal R, Bhogal RH, Hodson J, Ramcharan S. Surgery for gallstone disease during pregnancy does not increase fetal or maternal mortality: a meta-analysis. Hepatobiliary Surg Nutr. 2016;5:53–7.
187. Date RS, Kaushal M, Ramesh A. A review of the management of gallstone disease and its complications in pregnancy. Am J Surg. 2008;196:599–608.
188. Silvestri MT, Pettker CM, Brousseau EC, Dick MA, Ciarleglio MM, Erekson EA. Morbidity of appendectomy and cholecystectomy in pregnant and nonpregnant women. Obstet Gynecol. 2011;118:1261–70.
189. Palanivelu C, Rangarajan M, Senthilkumaran S, Parthasarathi R. Safety and efficacy of laparoscopic surgery in pregnancy: experience of a single institution. J Laparoendosc Adv Surg Tech A. 2007;17:186–90.
190. Abuabara SF, Gross GW, Sirinek KR. Laparoscopic cholecystectomy during pregnancy is safe for both mother and fetus. J Gastrointest Surg. 1997;1:48–52.
191. Peterson R. Gallstones during pregnancy. Trans Am Gynecol Soc. 1910;35:84–120.
192. Greene A, Rubin LJR. Fetal loss after cholecystectomy during pregnancy. CMAJ. 1963;88:576–7.
193. King A. Threatened and repeated abortion: present status of therapy. Obstet Gynecol. 1953;1:104.
194. Amos JD, Schorr SJ, Norman PF, et al. Laparoscopic surgery during pregnancy. Am J Surg. 1996;171:435–7.

195. Jamal A, Gorski TF, Nguyen HQ, Davis R. Laparoscopic cholecystectomy during pregnancy. Surg Rounds. 1997;20:408–15.
196. Tang S-J, Mayo MJ, Rodriguez-Frias E, et al. Safety and utility of ERCP during pregnancy. Gastrointest Endosc. 2009;69:453–61.
197. McKay AJ, O'Neill J, Imrie CW. Pancreatitis, pregnancy and gallstones. BJOG. 1980;87:47–50.
198. Glenn F, McSherry CK. Gallstones and pregnancy among 300 young women treated with cholecystectomy. Surg Gynecol Obstet. 1968;127:1067–72.
199. Swisher SG, Hunt KK, Schmit PJ, et al. Management of pancreatitis complicating pregnancy. Am Surg. 1994;60:759–62.
200. Ramin SM, Richey SD, Cunningham FGKR. Acute pancreatitis in pregnancy. Am J Obstet Gynecol. 1995;173:187–91.
201. Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. World J Gastroenterol. 2009;15:2049–66.
202. Reyes H, Gonzalez MC, Ribalta J, et al. Prevalence of intrahepatic cholestasis of pregnancy in Chile. Ann Intern Med. 1978;88:487–93.
203. Rioseco AJ, Ivankovic MB, Manzur A, et al. Intrahepatic cholestasis of pregnancy: a retrospective case-control study of perinatal outcome. Am J Obstet Gynecol. 1994;170:890–5.
204. Laifer SA, Stiller RJ, Siddiqui DS, et al. Ursodeoxycholic acid for the treatment of intrahepatic cholestasis of pregnancy. J Matern Fetal Med. 2001;10:131–5.
205. Lee RH, Goodwin TM, Greenspoon J, Incerpi M. The prevalence of intrahepatic cholestasis of pregnancy in a primarily Latina Los Angeles population. J Perinatol. 2006;26:527–32.
206. Gonzalez MC, Reyes H, Arrese M, et al. Intrahepatic cholestasis of pregnancy in twin pregnancies. J Hepatol. 1989;9:84–90.
207. Brites D, Rodrigues CMP, Van-Zeller H, Brito A, Silva R. Relevance of serum bile acid profile in the diagnosis of intrahepatic cholestasis of pregnancy in an high incidence area: Portugal. Eur J Obstet Gynecol Reprod Biol. 1998;80:31–8.
208. Koivurova S, Hartikainen AL, Karinen L, Gissler M, Hemminki E, Martikainen H, et al. The course of pregnancy and delivery and the use of maternal healthcare services after standard IVF in Northern Finland 1990-1995. Hum Reprod. 2002;17:2897–903.
209. Glantz A, Marschall H-U, Mattsson L-A. Intrahepatic cholestasis of pregnancy: relationships between bile acid levels and fetal complication rates. Hepatology. 2004;40:467–74.
210. Reyes H. Review: intrahepatic cholestasis. A puzzling disorder of pregnancy. J Gastroenterol Hepatol. 1997;12:211–6.
211. Brites D, Rodrigues CM, Oliveira N, et al. Correction of maternal serum BA profile during ursodeoxycholic acid therapy in cholestasis of pregnancy. J Hepatol. 1998;28:91–8.
212. Borum M. Hepatobiliary diseases in women. Med Clin North Am. 1998;82:51–75.
213. Reyes H. The spectrum of liver and gastrointestinal disease seen in cholestasis of pregnancy. Gastroenterol Clin N Am. 1992;21:905–21.
214. Bacq Y, Sapey T, Brechot MC, Pierre F, Fignon A, Dubois F. Intrahepatic cholestasis of pregnancy: a French prospective study. Hepatology. 1997;26(2):358–64.
215. Egerman RS, Riely CA. Predicting fetal outcome in intrahepatic cholestasis of pregnancy: is the bile acid level sufficient? Hepatology. 2004;40:287–8.
216. Dann AT, Kenyon AP, Seed PT, et al. S-transferase and liver function in intrahepatic cholestasis of pregnancy and pruritus gravidarum. Hepatology. 2004;40:1406–14.
217. Goulis DG, Walker IAL, de Swiet M, et al. Preeclampsia with abnormal liver function tests is associated with cholestasis in a subgroup of cases. Hypertens Pregnancy. 2004;23:19–27.
218. Vanjak D, Moreau R, Roche-Sicot J, et al. Intrahepatic cholestasis of pregnancy and acute fatty liver of pregnancy. An unusual but favorable association? Gastroenterology. 1991;100:1123–5.
219. Rolfes DB, Ishak KG. Liver disease in pregnancy. Histopathology. 1986;10:555–70.
220. Ropponen A, Sund R, Riikonen S, Ylikorkala O, Aittomäki K. Intrahepatic cholestasis of pregnancy as an indicator of liver and biliary diseases: a population-based study. Hepatology. 2006;43:723–8.
221. Sheehan H. The pathology of acute yellow atrophy and delayed chloroform poisoning. J Obstet Gynaecol. 1940;47:49–62.
222. Castro MA, Fassett MJ, Reynolds TB, et al. Reversible peripartum liver failure: a new perspective on the diagnosis, treatment, and cause of acute fatty liver of pregnancy, based on 28 consecutive cases. Am J Obstet Gynecol. 1999;181:389–95.
223. Knight M, Nelson-Piercy C, Kurinczuk JJ, et al. A prospective national study of acute fatty liver of pregnancy in the UK. Gut. 2008;57:951–6.
224. Meng J, Wang S, Gu Y, Lv H, Jiang J, Wang X. Prenatal predictors in postpartum recovery for acute fatty liver of pregnancy: experiences at a tertiary referral center. Arch Gynecol Obstet. 2016;293:1185–91.
225. Malone FD, Kaufman GE, Chelmow D, et al. Maternal morbidity associated with triplet pregnancy. Am J Perinatol. 1998;15:73–7.
226. Cruciat G, Stamatian F, Puscas M, Cruciat C, Ispasoiu F, Mureşan D. Acute pancreatitis in a pregnant woman with acute fatty liver dystrophy. A case report. J Gastrointestin Liver Dis. 2007;16(2):193–6.
227. Treem WR, Shoup ME, Hale DE, et al. Acute fatty liver of pregnancy, hemolysis, elevated liver enzymes, and low platelets syndrome, and long chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency. Am J Gastroenterol. 1996;91:2293–300.
228. IJlst L, Oostheim W, Ruiter JP, Wanders RJ. Molecular basis of long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency: identification of two new mutations. J Inherit Metab Dis. 1997;20:420–2.
229. Bacq Y. Acute fatty liver of pregnancy. Semin Perinatol. 1998;22:134–40.
230. Bacq Y, Constans T, Body G, et al. La stéatose hépatique aiguë gravidique. Gynecol Obstet Biol Reprod (Paris). 1986;15:851–61.
231. Riely C. Acute fatty liver of pregnancy. Semin Liver Dis. 1987;7:47–54.

232. de Oliveira CV, Moreira A, Baima JP, et al. Acute fatty liver of pregnancy associated with severe acute pancreatitis: a case report. World J Hepatol. 2014;6:527–31.
233. Castro MA, Ouzounian JG, Colletti PM, et al. Radiologic studies in acute fatty liver of pregnancy. A review of the literature and 19 new cases. J Reprod Med. 1996;41:839–43.
234. Rolfes DB, Ishak KG. Acute fatty liver of pregnancy: a clinicopathologic study of 35 cases. Hepatology. 1985;5:1149–58.
235. Prakash J, Ganiger V. Acute kidney injury in pregnancy-specific disorders. Indian J Nephrol. 2017;27(4):258.
236. Papafragkakis H, Singhal S, Anand S. Acute fatty liver of pregnancy. South Med J. 2013;106:588–93.
237. Yu CB, Chen JJ, Du WB, Chen P, Huang JR, Chen YM, et al. Effects of plasma exchange combined with continuous renal replacement therapy on acute fatty liver of pregnancy. Hepatobiliary Pancreat Dis Int. 2014;13:179–83.
238. Martin JN, Briery CM, Rose CH, Owens MT, Bofill JA, Files JC. Postpartum plasma exchange as adjunctive therapy for severe acute fatty liver of pregnancy. J Clin Apher. 2008;23:138–43.
239. Eddy JJ, Lynch GE, Treacy DE. Pancreatic pseudocysts in pregnancy: a case report and review of the literature. J Perinatol. 2003;23:69–72.
240. Kaplan MM. Acute fatty liver of pregnancy. N Engl J Med. 1985;313:367–70.
241. Knox TA, Olans LB. Liver disease in pregnancy. N Engl J Med. 1996;335:569–76.
242. Mjahed K, Charra B, Hamoudi D, Noun M, Barrou L. Acute fatty liver of pregnancy. Arch Gynecol Obstet. 2006;274:349–53.
243. Dwivedi S, Runmei M. Retrospective study of seven cases with acute fatty liver of pregnancy. ISRN Obstet Gynecol. 2013;27:730569.
244. Tuech JJ, Binelli C, Aube C, et al. Management of choledocholithiasis during pregnancy by magnetic resonance cholangiography and laparoscopic common bile duct stone extraction. Surg Laparosc Endosc Percutan Tech. 2000;10:323–5.
245. Bagci S, Tuzun A, Erdil A, et al. Treatment of choledocholithiasis in pregnancy: a case report. Arch Gynecol Obstet. 2003;267:239–41.
246. Baillie J, Cairns SR, Putman WS, Cotton PB. Endoscopic management of choledocholithiasis during pregnancy. Surg Gynecol Obstet. 1990;171:1–4.
247. Working Party of the British Society of Gastroenterology, Association of Surgeons of Great Britain and Ireland, Pancreatic Society of Great Britain and Ireland, Association of Upper GI Surgeons of Great Britain and Ireland. UK guidelines for the management of acute pancreatitis. Gut. 2005;54(Suppl 3):iii1–9.
248. Shergill AK, Ben-Menachem T, Chandrasekhara V, Chathadi K, Decker GA, Evans JA, et al. Guidelines for endoscopy in pregnant and lactating women. Gastrointest Endosc. 2012;76:18–24.
249. Kahaleh M, Hartwell GD, Arseneau KO, et al. Safety and efficacy of ERCP in pregnancy. Gastrointest Endosc. 2004;60:287–92.
250. Tham TCK, Vandervoort J, Wong RCK, et al. Safety of ERCP during pregnancy. Am J Gastroenterol. 2003;98:308–11.
251. Azab M, Bharadwaj S, Jayaraj M, Hong A, Solaimani P, Mubder M, et al. Safety of endoscopic retrograde cholangiopancreatography (ERCP) in pregnancy: a systematic review and meta-analysis. Saudi J Gastroenterol. 2019;25(6):341–54.
252. Barthel JS, Chowdhury T, Miedema BW. Endoscopic sphincterotomy for the treatment of gallstone pancreatitis during pregnancy. Surg Endosc. 1998;12:394–9.
253. Gupta R, Tandan M, Lakhtakia S, et al. Safety of therapeutic ERCP in pregnancy-an Indian experience. Indian J Gastroenterol. 2005;24:161–3.
254. Jamidar PA, Beck GJ, Hoffman BJ, et al. Endoscopic retrograde cholangiopancreatography in pregnancy. Am J Gastroenterol. 1995;90:1263–7.
255. Inamdar S, Berzin TM, Sejpal DV, Pleskow DK, Chuttani R, Sawhney MS, et al. Pregnancy is a risk factor for pancreatitis after endoscopic retrograde cholangiopancreatography in a National Cohort Study. Clin Gastroenterol Hepatol. 2016;14:107–14.
256. Gawrychowski J, Drózdz M, Olejek A, Zamłyński J. Treatment of mild acute pancreatitis during pregnancy using retrograde cholangiography and endoscopic sphincterotomy. Int J Gynaecol Obstet. 2007;99:147–9.
257. Pitchumoni BCY. Acute pancreatitis in pregnancy. World J Gastroenterol. 2009;45:5641–6.
258. Lee YT, Chan FKL, Leung WK, et al. Comparison of EUS and ERCP in the investigation with suspected biliary obstruction caused by choledocholithiasis: a randomized study. Gastrointest Endosc. 2008;67:660–8.
259. Roumieu F, Ponchon T, Audra P, Gaucherand P. Acute pancreatitis in pregnancy: place of the different explorations (magnetic resonance cholangiopancreatography, endoscopic ultrasonography) and their therapeutic consequences. Eur J Obstet Gynecol Reprod Biol. 2008;140:141–2.
260. Chong VH, Jalihal A. Endoscopic management of biliary disorders during pregnancy. Hepatobiliary Pancreat Dis Int. 2010;9:180–5.
261. Simmons DC, Tarnasky PR, Rivera-Alsina ME, et al. Endoscopic retrograde cholangiopancreatography (ERCP) in pregnancy without the use of radiation. Am J Obstet Gynecol. 2004;190:1467–9.
262. de Vries A, Donkervoort SC, van Geloven AA, Pierik EG. Conversion rate of laparoscopic cholecystectomy after endoscopic retrograde cholangiography in the treatment of choledocholithiasis: does the time interval matter? Surg Endosc. 2005;19:996–1001.
263. Polydorou A, Karapanos K, Vezakis A, et al. A multimodal approach to acute biliary pancreatitis during pregnancy: a case series. Surg Laparosc Endosc Percutan Tech. 2012;22:429–32.
264. Valadez-Caballero D, González-Santamaría R, Soto-Mendoza H, Blanco-Figueroa JA, Flores-Pantoja JM. Choledocholithiasis and pregnancy. Hybrid laparo-endoscopic treatment in one step. Cir Cir. 2014;82:158–63.

265. Patel SG, Veverka TJ. Laparoscopic cholecystectomy in pregnancy. Curr Surg. 2002;59:74–8.
266. Reyes-Tineo R. Laparoscopic cholecystectomy in pregnancy. Bol Asoc Med P R. 1997;89:9–11.
267. Girotra M, Jani N. Role of endoscopic ultrasound/SpyScope in diagnosis and treatment of choledocholithiasis in pregnancy. World J Gastroenterol. 2010;16:3601–2.
268. Shelton J, Linder JD, Rivera-Alsina ME, Tarnasky PR. Commitment, confirmation, and clearance: new techniques for nonradiation ERCP during pregnancy (with videos). Gastrointest Endosc. 2008;67:364–8.
269. Uradomo L, Pandolfe F, Aragon G, Borum ML. SpyGlass cholangioscopy for management of choledocholithiasis during pregnancy. Hepatobiliary Pancreat Dis Int. 2011;10:107.
270. Diettrich NA, Kaplan G. Surgical considerations in the contemporary management of biliary tract disease in the postpartum period. Am J Surg. 1998;176:251–3.
271. Zhou Y, Zhang X, Zhang X, et al. ERCP in acute cholangitis during third trimester of pregnancy. Hepato-Gastroenterology. 2013;60:981–4.
272. Chan CHY, Enns RA. ERCP in the management of choledocholithiasis in pregnancy. Curr Gastroenterol Rep. 2012;14:504–10.
273. Vater A. Dissertation in auguralis medica, poes diss. Qua Scirris viscerum dissert, C.S. Ezlerus, 70;1723.
274. Douglas A. A case of dilatation of the common bile duct. Monthly J Med Sci (London). 1852;14:97–100.
275. Seyffert R. Zur Pathologie der Gallengänge, Zyste des Ductus choledochus, operativ behandelt; 1888.
276. Friend W. Rupture of choledochal cyst during confinement. Br J Surg. 1958;46:155–7.
277. Saunders BTPJ. Rupture of choledochus cyst in pregnancy. BMJ. 1969;3:573–4.
278. Louw J. Choledochal cysts. S Afr J Surg. 1975;13:199–205.
279. O'Neill JA Jr, Templeton JM Jr, Schnaufer L, et al. Recent experience with choledochal cyst. Ann Surg. 1987;205:533–40.
280. Jones PG, Smith ED, Clarke AM, Kent M. Choledochal cysts: experience with radical excision. J Pediatr Surg. 1971;6:112–20.
281. Chesterman J. Choledochus cyst complicating pregnancy and the puerperium. BJOG. 1944;51(6):512–8.
282. Spitz L. Choledochal cyst. Surg Gynecol Obstet. 1978;147:444–52.
283. Fleming R. Cyst of the common bile duct in a case of pregnancy of 8 months causing pyloric obstruction. S Afr Med J. 1947;21:778–82.
284. Beattie GJ, Keay S, Muir BB, Boddy K. Acute pancreatitis with pseudocyst formation complicating pregnancy in a patient with a co-existent choledochal cyst. BJOG. 1993;100:957–9.
285. Diamond T, Panesar KJ. Biliary peritonitis due to choledochal cyst presenting in late pregnancy. Ulster Med J. 1986;55:190–2.
286. Pai Dhungat PB, Pai Dhungat N, Gothil S. Choledochal cyst in twin gestation pregnancy. Bombay Hosp J. 2010;52:436–7.
287. Binstock M, Sondak VK, Herd J, et al. Adenocarcinoma in a choledochal cyst during pregnancy: a case report and guidelines for management. Surgery. 1988;103:588–92.
288. Aszodi A, Ponsky JL, Kiwi R, Parulekar SG. Choledochal cyst in a pregnancy adult. Am J Gastroenterol. 1990;85:1048–9.
289. Joseph P, Raju RS, Vyas FL, Sitaram V. Spontaneous perforation of choledochal cyst and hyperemesis gravidarum. Trop Gastroenterol. 2008;29:46–7.
290. Nassar AH, Chakhtoura N, Martin D, et al. Choledochal cysts diagnosed in pregnancy: a case report and review of treatment options. J Matern Fetal Med. 2001;10:363–5.
291. Taylor TV, Brigg JK, Russell JG. Choledochal cyst of pregnancy. J R Coll Surg Edinb. 1977;22:424–7.
292. Russell JG, Taylor V, Torrance B. Ultrasonic diagnosis of choledochal cyst in pregnancy. Br J Radiol. 1976;49:425–6.
293. Angel JL, Knuppel RA, Trabin J. Choledochal cyst complicating a twin gestation. South Med J. 1985;78:463–6.
294. Grotz RL, MacDermid RG, Orlando R, Pyrtek LJ. Choledochal cyst diagnosed in pregnancy. Conn Med. 1991;55:262–6.
295. Nasu K, Matsuki S, Kawano Y, et al. Choledochal cyst diagnosed and conservatively treated during pregnancy. Am J Perinatol. 2004;21:463–8.
296. Kaponis A, Vitsas C, Decavalas GO. Conservative management of a choledochal cyst during a twin pregnancy. J Obstet Gynaecol. 2015;35:646–7.
297. Wong AM-C, Cheung Y-C, Liu YH, et al. Prenatal diagnosis of choledochal cyst using magnetic resonance imaging: a case report. World J Gastroenterol. 2005;11:5082–3.
298. Anderl P, Hetzenauer A. Pregnancy complications caused by choledochus cyst. Geburtshilfe Frauenheilkd. 1985;45:731–4.
299. Benchellal ZA, Simon E, d'Altéroche L, et al. Choledochal cyst rupture during pregnancy. Gastroenterol Clin Biol. 2009;33:390–1.
300. Pal S, Simon EG, Koshy AK, et al. Spontaneous choledochal cyst rupture in pregnancy with concomitant chronic pancreatitis. Indian J Gastroenterol. 2013;32:127–9.
301. Purohit R, Singh A, Kant K. Spontaneous rupture of choledochal cyst during pregnancy: a case report. J Dent Med Sci. 2015;14:51–3.
302. Conway WC, Campos GMR, Gagandeep S. Choledochal cyst during pregnancy: the patient's first pregnancy was complicated by a congenital anomaly. Am J Obstet Gynecol. 2009;200:588.e1–2.
303. Prochazka R, Ojeda M, Cedron H, et al. Choledochal cyst in pregnancy and puerperium: report on two cases and review of literature. Rev Gastroenterol Peru. 2007;27:79–84.
304. Wu YK, Chang YJ, Lee YT, et al. Choledochal cyst in pregnancy – report of two cases. Tzu Chi Med J. 2005;17:261–3.
305. Hewitt PM, Krige JEJ, Bornman PC, Terblanche J. Choledochal cyst in pregnancy: a therapeutic dilemma. J Am Coll Surg. 1995;181(3):237–40.

306. Wig JD, Goenka MK, Chawla YK, Nagi B. Cholangitis secondary to choledochal cyst in pregnancy and puerperium. J Clin Gastroenterol. 1997;25:489–91.
307. Oncü M, Alhan E, Calik A. Rupture of a choledochal cyst during postpartum period. Z Gastroenterol. 1990;28:396–8.
308. Wu DQ, Zheng LX, Wang QS, et al. Choledochal cysts in pregnancy: case management and literature review. World J Gastroenterol. 2004;10:3065–9.
309. Gmijović D, Stojanović M, Radojkovic M. Complicated choledochal cysts in pregnancy. Facta Universitatis. 2006;13:90–3.
310. Kitahama A, Harkness SO, Moynihan PO, Webb WR. A large choledochal cyst with impending rupture post partum. Br J Surg. 1984;71:156.
311. Fok WY, Yip S-K, Leung TN, et al. Large choledochal cyst present through 2 pregnancies. A case report. J Reprod Med. 2003;48:482–4.
312. Shanley DJ, Gagliardi JA, Daum-Kowalski R. Choledochal cyst complicating pregnancy: antepartum diagnosis with MRI. Abdom Imaging. 1994;19:61–3.
313. Martínez-Ordaz JL, Morales-Camacho MY, Centellas-Hinojosa S, Román-Ramírez E, Romero-Hernández T, De La Fuente-Lira M. Quiste de colédoco y embarazo. Reporte de 3 casos y revisión de la bibliografía. Cir Cir. 2016;84(2):144–53.
314. Nagorney DM, McIlrath DC, Adson MA. Choledochal cysts in adults: clinical management. Surgery. 1984;96:656–63.
315. Todani T, Watanabe Y, Toki A, et al. Reoperation for congenital choledochal cyst. Ann Surg. 1988;207:142–7.
316. Büyükyavuz I, Ekinci S, Çiftçi AÖ, et al. A retrospective study of choledochal cyst: clinical presentation, diagnosis and treatment. Turk J Pediatr. 2003;45:321–5.