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PREVALENCE AND ULTRASONOGRAPHIC PHENOTYPES OF BILIARY TRACT INJURY IN WOMEN OF REPRODUCTIVE AGE AND PREGNANT WOMEN WITH CHRONIC HEPATITIS B

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Abstract: Background: Pregnancy increases the risk of biliary stasis and gallbladder dysmotility, predisposing to biliary sludge and gallstones. A systematic review and meta-analysis reported a global prevalence of gallstones in pregnancy of approximately 3.6% (95% CI: 1.9–6.7). [1] Chronic hepatitis B (CHB) may modify hepatobiliary ultrasound patterns through inflammatory parenchymal changes and hepatitis-associated gallbladder wall edema, making interpretation challenging because gallbladder wall thickening is a common yet nonspecific finding also observed in viral hepatitis. [2]
Objective: To synthesize evidence on biliary abnormalities relevant to pregnant and reproductive-age women with CHB and to propose a standardized ultrasound reporting framework.
Methods: Narrative review integrating contemporary hepatology guidance for hepatitis B management and recent imaging literature on pregnancy-related liver and biliary disease and ultrasound criteria for cholecystitis and cholestasis. [3–5]
Conclusions: In CHB, pregnancy-related biliary stasis can coexist with hepatitis-associated gallbladder wall edema. A phenotype-based ultrasound report (stasis, lithogenic, inflammatory, obstructive, hepatitis-associated edema) combined with targeted laboratory tests supports safer and more specific clinical decision-making and improves comparability across studies.

Keywords: chronic hepatitis B; pregnancy; biliary sludge; cholelithiasis; ultrasound; gallbladder wall thickening; cholestasis; cholecystitis.

Introduction

Chronic hepatitis B (CHB) remains a major driver of chronic liver disease worldwide and has particular relevance in women of reproductive age due to pregnancy planning, prevention of mother-to-child transmission (MTCT), and monitoring for pregnancy-associated liver and biliary complications. Contemporary European guidance emphasizes early pregnancy screening and risk stratification based on virologic and host factors, with simplified algorithms to support care. [3]
Pregnancy promotes biliary stasis via hormonal effects (especially progesterone), increasing fasting gallbladder volume and reducing contractility. [4] Because abdominal ultrasound is safe and widely available, it is the first-line modality for evaluating hepatobiliary complaints during pregnancy. [5] However, interpretation becomes more complex in CHB because some ultrasound findings overlap with extra-biliary conditions. In particular, gallbladder wall thickening is a nonspecific sign that may occur in primary gallbladder disease as well as systemic and hepatic conditions, including viral hepatitis. [2]
This review summarizes actionable ultrasound patterns (phenotypes) relevant to CHB in pregnancy and proposes a practical, standardized reporting framework.

Pathophysiologic Rationale: Why CHB Plus Pregnancy Matters for the Biliary Tract

- **Pregnancy-related biliary stasis:** Pregnancy is associated with gallbladder dysmotility and larger fasting volumes, supporting a stasis-driven pathway to biliary sludge and gallstone formation. [4]
- **Hepatitis-associated gallbladder wall edema:** Diffuse gallbladder wall thickening may reflect inflammatory or systemic edema and can be seen in hepatitis; therefore, wall thickening alone should not be equated with acute cholecystitis. [2]
- **Cholestatic syndromes in pregnancy and differential diagnosis:** In pruritus-predominant presentations, intrahepatic cholestasis of pregnancy is primarily a biochemical diagnosis; imaging is used to exclude extrahepatic obstruction and other structural pathology. [5]

Epidemiology and Prevalence Signals

A meta-analysis of 31 studies (total sample size ~190,714) estimated the prevalence of gallstones in pregnancy at 3.6% (95% CI: 1.9–6.7), with high heterogeneity across regions and study designs. [1] In clinical cohorts, biliary sludge is often more frequent than definite stones and may be transient. In CHB cohorts, gallbladder wall thickening prevalence may be higher due to hepatitis-associated edema, creating misclassification risk if strict composite criteria are not used for diagnosing inflammatory biliary disease.

Ultrasound Phenotypes of Biliary Tract Injury (Proposed Classification)

To reduce misclassification and enable reproducible research outcomes, biliary ultrasound findings can be summarized into pragmatic phenotypes. Phenotypes should be assigned using explicit criteria and, whenever possible, interpreted in conjunction with symptoms and key laboratory markers.

Phenotype A: Stasis phenotype (sludge-dominant)

- Low-level echoes layering in the gallbladder lumen; typically mobile with position change (sludge).
- No definite posterior acoustic shadowing.
- May be associated with gallbladder overdistension depending on fasting state.
- Commonly asymptomatic or mild dyspepsia; pregnancy physiology contributes. [4]

Phenotype B: Lithogenic phenotype (stone-dominant)

- Echogenic foci with posterior acoustic shadowing; mobility supports intraluminal stones.
- May present with biliary colic; risk of acute cholecystitis or choledocholithiasis if symptomatic.

Phenotype C: Inflammatory phenotype (acute cholecystitis pattern)

- Use a composite rather than wall thickening alone: stone/sludge plus sonographic Murphy sign and supportive signs (overdistension, pericholecystic fluid, hyperemia when available).
- Gallbladder wall thickening supports but is not decisive. [2]

Phenotype D: Obstructive phenotype (bile duct dilation)

- Extrahepatic duct (CBD) dilation and/or intrahepatic ductal dilation.
- Correlate with jaundice and cholestatic labs (ALP/GGT, bilirubin). Imaging in pregnancy helps exclude obstruction. [5]

Phenotype E: Hepatitis-associated edema phenotype (GBWT without inflammatory/obstructive constellation)

- Diffuse wall thickening without Murphy sign, pericholecystic fluid, or ductal dilation.

- Reassess hepatitis activity and systemic edema states; avoid overdiagnosing cholecystitis. [2]

Standardized Ultrasound Reporting Checklist (Recommended)

For clinical consistency and research comparability, the ultrasound report should capture core variables related to the gallbladder, bile ducts, and CHB context. Below is a practical checklist that can be integrated into routine reporting.

Domain	Variables to record (minimum set)
Patient context	Gestational age/trimester; fasting duration; pain during exam; RUQ tenderness
Gallbladder	Wall thickness (mm); distension; sludge (yes/no; mobile/fixed); stones (yes/no; shadowing; mobility); pericholecystic fluid; sonographic Murphy sign; hyperemia if Doppler available
Bile ducts	CBD diameter (mm); intrahepatic ductal dilation (yes/no)
Liver/portal context (CHB)	Parenchymal echogenicity/heterogeneity; spleen size (if portal HTN suspected); ascites (if present)
Phenotype assignment	A/B/C/D/E with brief rationale and recommended next step

Integrating Ultrasound with CHB Pregnancy Care

Ultrasound findings should be interpreted alongside CHB management principles and pregnancy-specific differentials. When pruritus dominates, prioritize serum bile acids and use ultrasound primarily to exclude obstruction (phenotype D). [5] When gallbladder wall thickening is present, confirm an inflammatory phenotype using composite criteria rather than thickness alone. [2] CHB pregnancy care also requires MTCT prevention planning, guided by virologic markers and contemporary guidance. [3]

Clinical Implications and Suggested Diagnostic Pathway

1. **CHB pregnant woman with RUQ pain:** Perform ultrasound, assign phenotype, and correlate with clinical signs. If inflammatory phenotype is suspected, escalate for multidisciplinary evaluation (obstetrics, surgery/gastroenterology).
2. **CHB pregnant woman with pruritus and cholestatic labs:** Use ultrasound to exclude obstructive phenotype. If no ductal dilation, proceed with biochemical workup for intrahepatic cholestasis of pregnancy (e.g., bile acids) and obstetric monitoring. [5]
3. **Isolated gallbladder wall thickening (phenotype E):** Reassess hepatitis activity and systemic conditions; consider follow-up imaging if symptoms evolve. [2]

Limitations of Current Evidence

- Heterogeneity across pregnancy biliary studies (trimester distribution, fasting state, operator dependence).
- Limited CHB-specific biliary prevalence data in pregnancy; high risk of misclassification if gallbladder wall thickening is interpreted non-specifically.

- Future studies should report both raw ultrasound features and phenotype-based composite outcomes using standardized variables.

Conclusions

Biliary tract abnormalities in pregnancy often represent a spectrum from stasis (sludge) to lithiasis, with less frequent inflammatory or obstructive complications. In CHB, hepatitis-associated gallbladder wall edema may mimic inflammatory disease. A phenotype-based ultrasound report combined with targeted laboratory testing improves diagnostic specificity, supports safer triage, and standardizes research reporting.

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