



CLDF

Chronic Liver Disease Foundation

3RD ANNUAL
LIVER C³ONNECT
CONFERENCE

Accredited by:



Presented by:





CLDF

Chronic Liver Disease Foundation

3RD ANNUAL

LIVER C  **NNECT**

CONFERENCE

WISE

A Pregnant Pause: It's Time to Revisit the Guidelines

Ani Kardashian, MD
Assistant Professor of Medicine
University of Southern California
March 24, 2023



Disclosures

- None

Topics We Will Cover Today: A Potpourri

- Available guidelines for pregnancy and liver disease
- Discrepancies between guidelines
 - Intrahepatic cholestasis of pregnancy (ICP) diagnosis
 - Risk-based vs universal screening for HCV
 - Aspirin prophylaxis for preeclampsia
- Gaps in data and recommendations



What Current Guidelines Exist?

CME

ACG Clinical Guideline: Liver Disease and Pregnancy

Tram T. Tran, MD, FACP, FAASLD¹, Joseph Ahn, MD, MS, FACP² and Nancy S. Reau, MD, FAASLD, FAGA³



Society for
Maternal • Fetal
Medicine
High-risk pregnancy experts

HEPATOLOGY



PRACTICE GUIDANCES | HEPATOLOGY, VOL. 73, NO. 1, 2021

Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases



ACOG
The American College of
Obstetricians and Gynecologists

Clinical



Royal College of
Obstetricians &
Gynaecologists



GUIDELINE



Guidelines for endoscopy in pregnant and lactating women

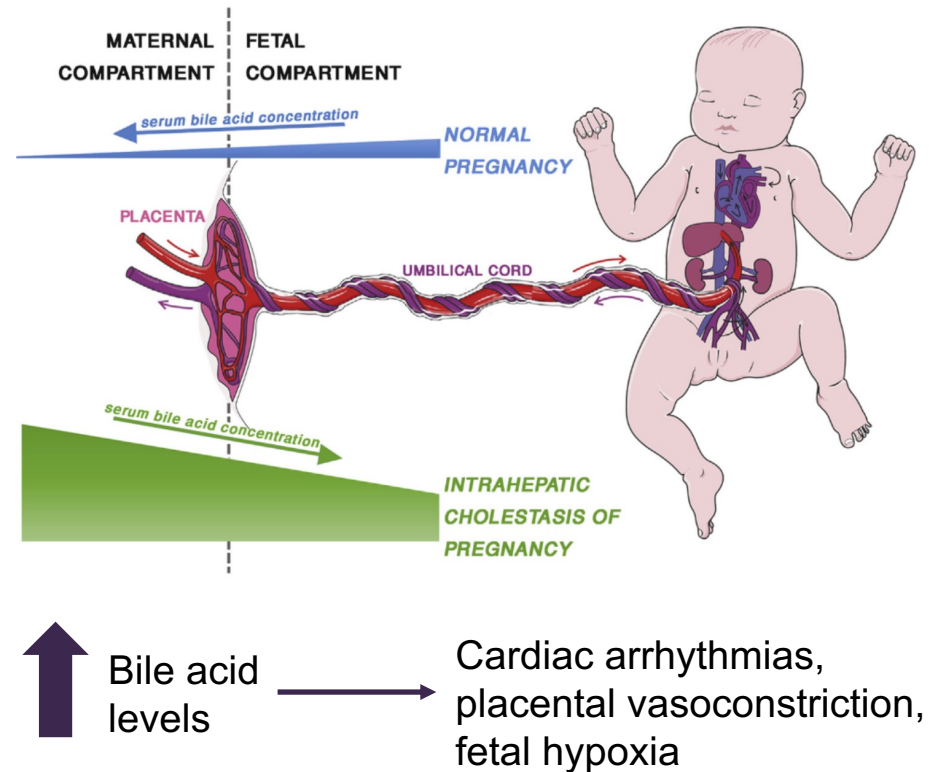
NICE National Institute for
Health and Care Excellence

What Do the Guidelines Cover?

Pregnancy topic	Guideline coverage
Pregnancy-associated liver diseases	American College of Gastroenterology (ACG), American Association for the Study of Liver Diseases (AASLD); Royal College of Gastroenterology (RCOG), National Institute for Health and Care Excellence (NICE)
Chronic liver disease in pregnancy	ACG, AASLD, American College of Gynecology (ACOG...but more of a review than guideline)
Cholestasis in pregnancy	ACG, AASLD, RCOG, European Association for the Study of the Liver (EASL), Society of Maternal Fetal Medicine (SMFM)
Endoscopy in pregnancy	American Society for Gastrointestinal Endoscopy (ASGE)

Intrahepatic Cholestasis of Pregnancy (ICP)

- Most common gestational liver disease
- Pruritus of palms and soles of feet
 - Less common: jaundice, steatorrhea
- Presents @ ~32-34 weeks gestation
- Risk factors: hepatitis C, multifetal pregnancy, in vitro fertilization
- Adverse fetal outcomes:
 - Preterm birth
 - Stillbirth
 - Prolonged neonatal ICU admission
- Treatment: ursodeoxycholic acid 10-15mg/kg/day, delivery prior to 37 weeks

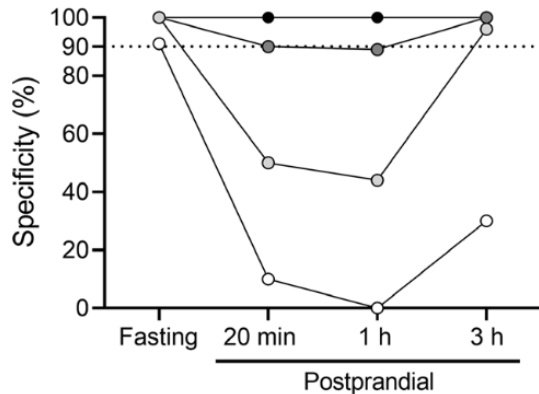


ICP Diagnostic Discrepancies

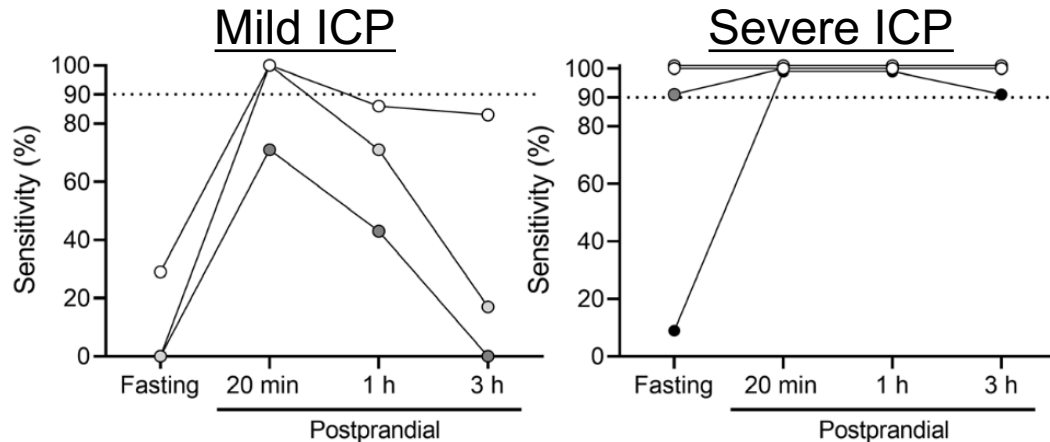
Diagnostic criteria	Society of Maternal Fetal Medicine	AASLD	ACG	EASL	Royal College of Obstetricians and Gynaecologists
Presence of pruritus	Yes	Yes	Yes	Yes	Yes
Total serum bile acid levels	>10 $\mu\text{mol/L}$	>10 $\mu\text{mol/L}$	>10 $\mu\text{mol/L}$	>11 $\mu\text{mol/L}$	$\geq 19 \mu\text{mol/L}$
Fasting/non-fasting specified?	Fasting	No	No	No	Postprandial
AST/ALT elevations required?	Not necessary	Not necessary	Not necessary	Not necessary	Not necessary
Ruling out other liver diseases recommended?	Yes	Yes	Not specified	Yes	No, unless symptoms are atypical or in early onset severe ICP

Fasting or Peak Bile Acid Concentrations?

Specificity of bile acids for women without ICP



Sensitivity of bile acids to detection of ICP



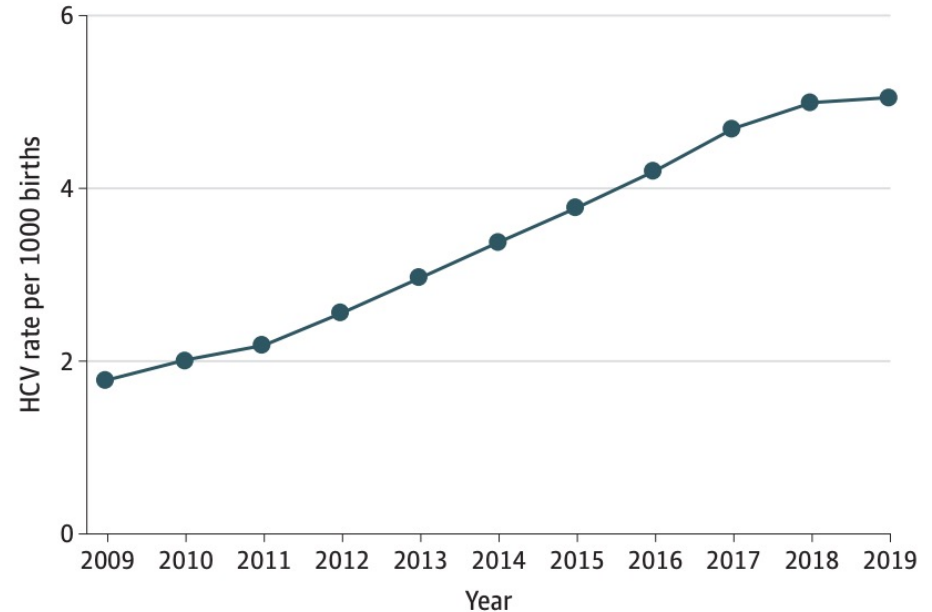
Threshold

- $\geq 6 \mu\text{mol/l}$
- $\geq 11 \mu\text{mol/l}$
- $> 15 \mu\text{mol/l}$
- $\geq 40 \mu\text{mol/l}$

Controversies in HCV Screening in Pregnancy

- Hepatitis C virus (HCV) is becoming more common in pregnancy due to rising rates of people who inject drugs
- Rates of new HCV infections increased by more than 60% from 2015 to 2019
- In 2019, 63% of new HCV infections occurred among adults 20-39 years old
- ~1700 HCV-infected infants are born to 29,000 HCV-positive women every year
- Pregnancy is a unique opportunity to engage young women in HCV care

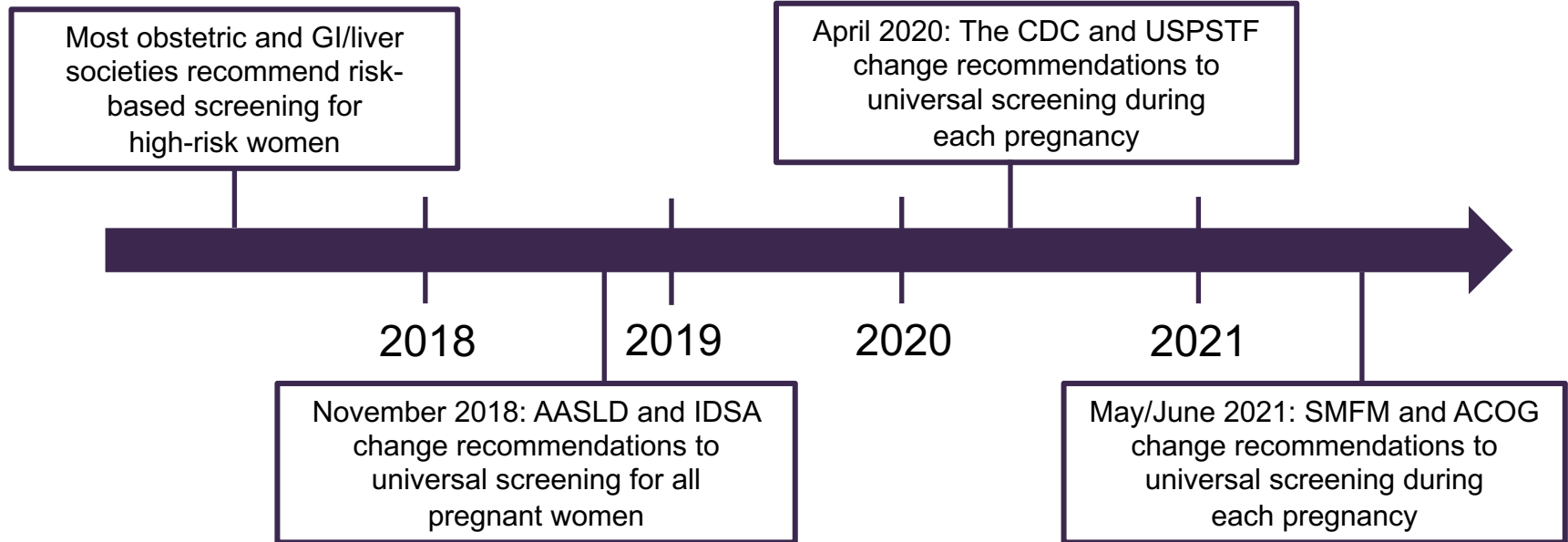
HCV Infections Among Pregnant People Delivering Live Births in the US



Risk-Based vs Universal HCV Screening

Risk-based screening	Universal screening
<p>Only women at high risk for HCV should receive HCV antibody testing, including:</p> <ul style="list-style-type: none">• History of injection or nasal drug use (current or past)• History of blood-borne viral infections (HIV, HBV, HDV)• History of receiving blood products• History of organ/tissue transplantations• Tattoos, piercings• Occupational risk• Other risk behavior – sexual transmission	<p>All pregnant women should receive HCV antibody testing at initial prenatal visit</p>

Universal vs Risk-Based HCV Screening



AASLD: American Association for the Study of Liver Diseases; ACOG: American College of Gastroenterology; CDC: Centers for Disease Control; IDSA: Infectious Diseases Society of America; SMFM: Society of Maternal Fetal Medicine; USPSTF: US Preventive Services Task Force. AASLD-IDSA HCV Guidance Panel. *Clin Infect Dis*. 2018; CDC. Test for Hep C During Pregnancy 2020; USPSTF Task Force. *JAMA*. 2020. SMFM Consult Series. *AJOG* 2021.




Increases in HCV Screening Since Policy Changes

- Retrospective analysis of HCV screening and case detection during risk-based vs universal screening among pregnant women in Western Pennsylvania

	Risk-Based Screening	Universal Screening
Pregnant people	N=12,142	N=12,588
HCV IgG tested	2749 (23%)	10167 (81%)
HCV IgG positive	148 (1.2%)	237 (1.9%)
HCV RNA tested	33 (22% of HCV IgG+)	225 (95% of HCV IgG+)
HCV RNA positive	11 (0.091%)	85 (0.68%)

7.5-fold increase in detection of active HCV infection

Medication Prophylaxis for Preeclampsia

- Aspirin has been the most rigorously studied for prophylaxis in at-risk pregnant women
- Doses have ranged from 50 to 150 mg/day in randomized controlled trials
- Aspirin use is associated with:
 - ↓ Preeclampsia 
 - ↓ Perinatal mortality 
 - ↓ Preterm birth 
 - ↓ Intrauterine growth restriction
- No significant associations with postpartum hemorrhage, other bleeding-related harms
- No established role for magnesium, antioxidants, or other nutritional supplements

Aspirin Prophylaxis for Preeclampsia

Aspirin prophylaxis	RCOG (UK)	NICE (UK)	ACOG and USPSTF (US)
Recommended?	Yes	Yes	Yes
Dosage	81mg daily	75-150mg daily	81mg daily
Duration	12 weeks until birth	12 weeks until birth	12 weeks gestation until birth
Indications	<p>Women with ≥ 1 high risk factors:</p> <ul style="list-style-type: none"> • HTN during prior pregnancy • CKD • Autoimmune disease such as lupus, APLS • Type 1 or 2 diabetes • Chronic hypertension <p>Women with >1 moderate risk factor:</p> <ul style="list-style-type: none"> • Nulliparity • Age ≥ 40 • Pregnancy interval of >10 years • BMI of 35 kg/m² or more at first visit • Family history of pre-eclampsia • Multi-fetal pregnancy 	<p>Women with ≥ 1 high-risk factors:</p> <ul style="list-style-type: none"> • Previous pregnancy with preeclampsia • Multifetal gestation • Renal disease • Autoimmune disease • Type 1 or type 2 diabetes mellitus • Chronic hypertension <p>Women with >1 moderate risk factor:</p> <ul style="list-style-type: none"> • Nulliparity • Age ≥ 35 • BMI of 30 kg/m² or more • Family history of pre-eclampsia • Personal history factors 	

ACOG: American College of Gastroenterology; NICE: National Institute for Health and Care Excellence; RCOG: Royal College of Gastroenterology; USPSTF: US Preventive Services Task Force.

US Preventive Services Task Force. *JAMA*. 2021; *ACOG Committee Opinion*. 2018; *NICE*. Guideline. 2019.

Additional Gaps and Areas for Future Research

Liver diseases unique to pregnancy

- Use of genetic testing to identify women at risk for ICP
- Define risk groups and efficacy of UDCA in patients with ICP
- Comparative effectiveness trials for preeclampsia prevention to identify specific aspirin dosing, length of continuation and which populations are most likely to benefit

Chronic liver disease in pregnancy

- Larger-scale clinical trials of DAA therapy in pregnant women with chronic HCV
- Studies determining safety/efficacy of TAF in pregnant women with chronic HBV
- Incidence, natural history, outcomes in mothers with chronic liver disease or cirrhosis and their children
- Pregnancy outcomes among patients with fatty liver (i.e. long-term cardiometabolic and liver-related risks to mothers and children)



Thank You!