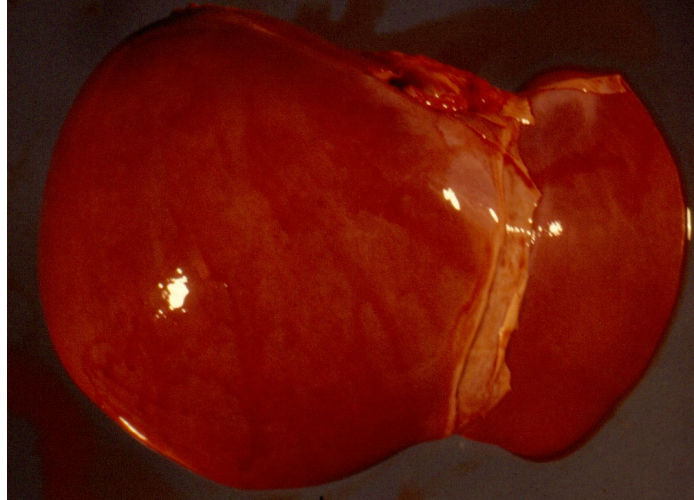


Liver Disease in Pregnancy



David B. Nelson MD

Gillette Professorship of Obstetrics and Gynecology

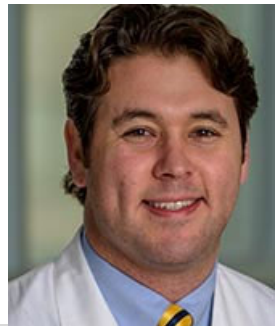
Dedman Family Scholar in Clinical Care

Chief, Division of Maternal-Fetal Medicine

Associate Professor, Maternal-Fetal Medicine

Department of Obstetrics & Gynecology

University of Texas Southwestern Medical Center



Disclosures

- *Author of Williams Obstetrics 26th edition and Senior Editor for Williams Obstetrics 27th edition.*
- *National Institute of Health (NIH). National Heart, Lung, and Blood Institute (NHLBI). RO1 HL142605-01*
- *PCORI. Improving Maternal Postpartum Access to Care through Telemedicine (IMPACT) Study.*
- *HemoSonics- UTSW OBGYN, CTA 202408-0061, Clinical Study Number: HEMCS-048*
- *UTSW CTSA-TPP-YR4-D. Intrahepatic cholestasis in pregnancy.*

Objectives

1. Review physiologic changes of pregnancy
2. **Acute fatty liver of pregnancy**
 - a. Describe the pathogenesis
 - b. Characterize clinical features and differentiate between HELLP syndrome
 - c. Review management and the anticipated recovery
3. **Intrahepatic Cholestasis of Pregnancy**
 - a. Outline diagnosis
 - b. Describe antepartum testing strategies
 - c. Review management strategies
4. **Hepatitis C**
 - a. Outline current national rates and trends
 - b. Review risk factors
 - c. Define testing algorithms



Physiologic changes of pregnancy

■ Physiologic changes of pregnancy

- Liver size does not enlarge during pregnancy.

Williams Obstetrics 26th ed.

Physiologic changes of pregnancy

- Liver size does not enlarge during pregnancy.

Portal vein blood flow

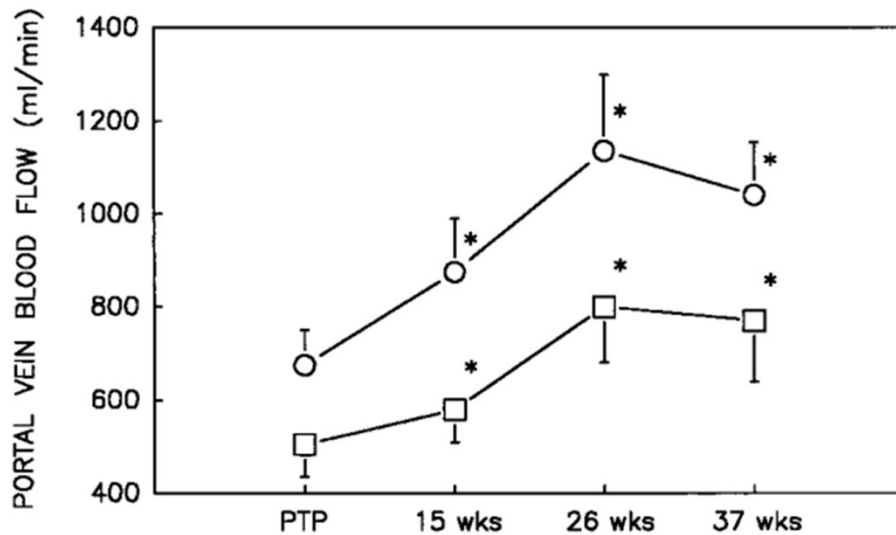


Fig 1. Effects of pregnancy and position on portal vein blood flow. Asterisks, Significant change from pre-pregnancy levels ($P < .05$ to $P < .001$); open circles, left lateral recumbent position; open squares, at standing rest.

Clapp 3rd JF, et al. *Am J Obstet Gynecol.* 2000 Jul;183(1):167-72.

Williams Obstetrics 26th ed.

Physiologic changes of pregnancy

- Liver size does not enlarge during pregnancy.

Portal vein blood flow

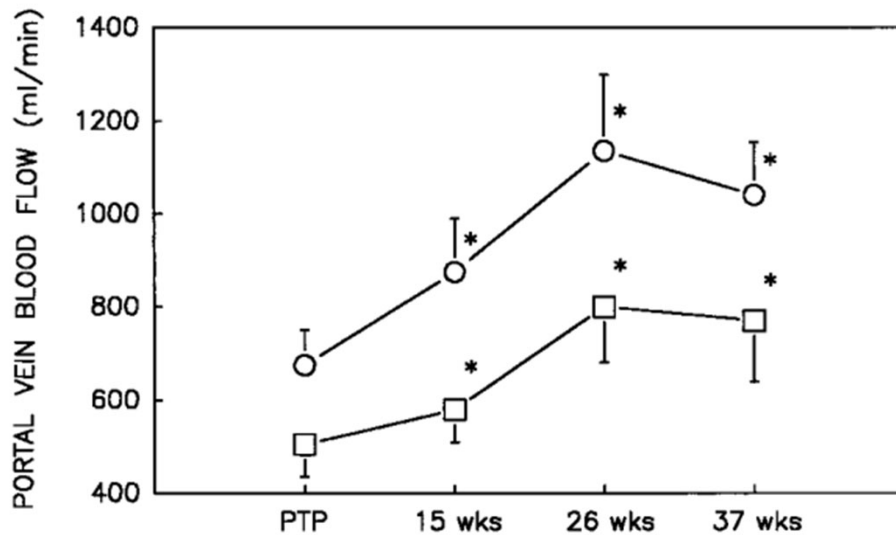
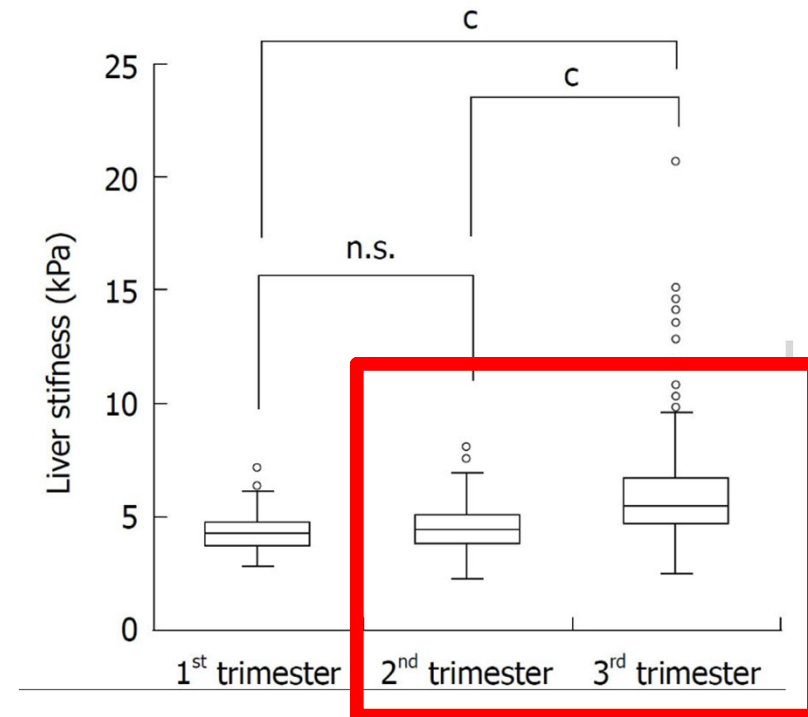


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Clapp 3rd JF, et al. *Am J Obstet Gynecol.* 2000 Jul;183(1):167-72.

Liver stiffness



Ammon FJ et al. *Observational Study World J Gastroenterol.* 2018 Oct 14;24(38):4393-4402.

Williams Obstetrics 26th ed.

Physiologic changes of pregnancy

Some laboratory test results of hepatic function are altered in normal pregnancy that differ when compared to non-pregnant individuals:

- Total alkaline phosphatase activity 
- Aspartate transaminase (AST), alanine transaminase (ALT) 
- Bilirubin levels 
- Serum albumin concentration 

Williams Obstetrics 26th ed.

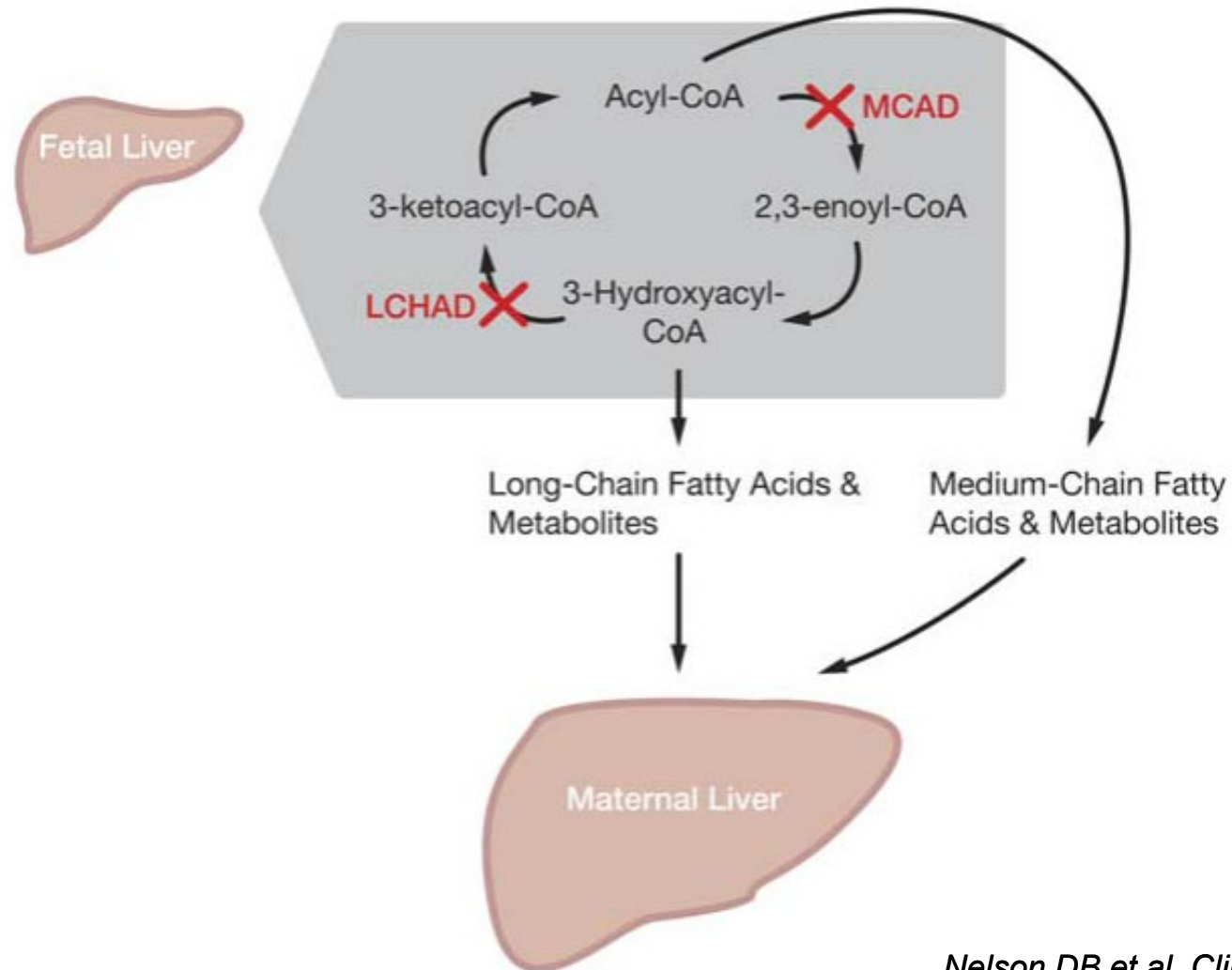
	Nonpregnant Adult ^A	First Trimester	Second Trimester	Third Trimester	References ^B
COAGULATION					
Antithrombin III, functional (%)	70–130	89–114	88–112	82–116	15, 16
D-dimer (μg/mL)	0.22–0.74	0.05–0.95	0.32–1.29	0.13–1.7	16, 25, 35, 51
Factor V (%)	50–150	75–95	72–96	60–88	40
Factor VII (%)	50–150	100–146	95–153	149–211	16
Factor VIII (%)	50–150	90–210	97–312	143–353	16, 40
Factor IX (%)	50–150	103–172	154–217	164–235	16
Factor XI (%)	50–150	80–127	82–144	65–123	16
Factor XII (%)	50–150	78–124	90–151	120–194	16
Fibrinogen (mg/dL)	233–496	244–510	291–538	373–619	16, 25, 42, 51
Homocysteine (μmol/L)	4.4–10.8	3.34–11	2.6–20.3	3.2–21.4	43, 45, 46, 53, 72
International Normalized Ratio	0.9–1.04 ^G	0.89–1.05	0.85–0.97	0.80–0.94	15
Partial thromboplastin time, activated (sec)	26.3–39.4	24.3–38.9	24.2–38.1	24.7–35.0	15, 16, 42

Beware that electronic medical records and referent laboratory values are often registered for non-pregnant adults wherein **“normal” registered values (eg. Fibrinogen) may be profoundly abnormal in pregnancy!!!**

Ababassi-Ghnaavati M et al. Obstet Gynecol. 2009

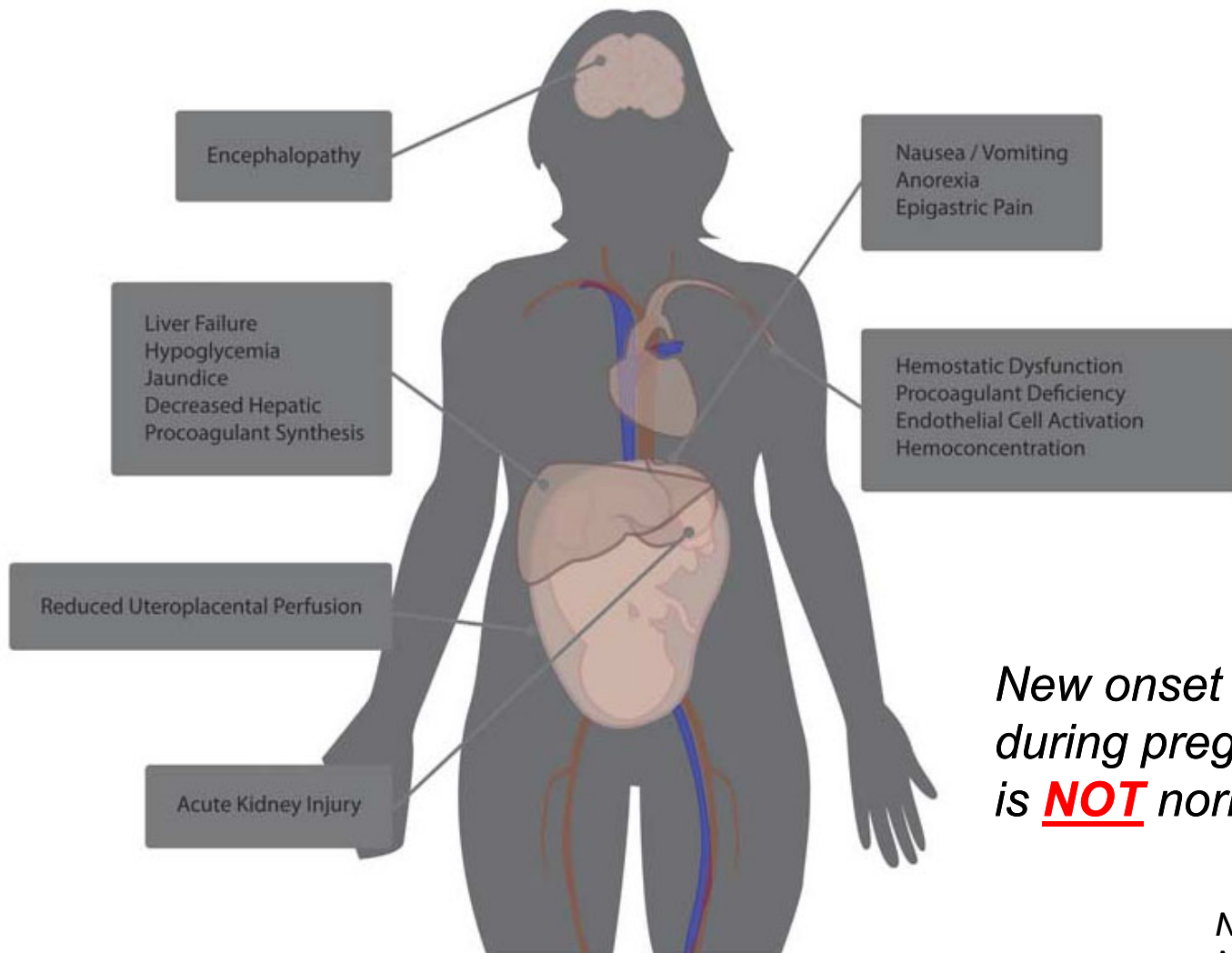
Acute Fatty Liver of Pregnancy (AFLP)

Pathogenesis



Nelson DB et al. Clin Obstet Gynecol. 2020

Clinical Presentation



Clinical and laboratory findings for 51 women with acute fatty liver of pregnancy

Factor	Percentage
Symptoms	
Nausea and vomiting	57
Hypertension	57
Abdominal pain	53
Jaundice	33
Encephalopathy	16

*New onset nausea and vomiting during pregnancy in the third trimester is **NOT** normal!*

*Nelson DB et al Clin Obstet Gynecol. 2020
Nelson DB et al Am J Obstet Gynecol. 2013*

Differential Diagnosis

Disorder	Onset in Pregnancy	Clinical Findings	Laboratory Findings	
			Hepatic	
			AST	Bilirubin
Hyperemesis gravidarum	Early	Severe nausea and vomiting	Normal–↑↑	Normal–↑↑
Preeclampsia	Mid to late	Hypertension, headache	Normal–↑↑	Normal
Intrahepatic cholestasis	Late	Pruritus, jaundice	Normal ↑	Normal ↑↑
AFLP	Late	Nausea and vomiting, hypertension, abdominal pain, encephalopathy	↑↑	↑↑
Hepatitis	Variable	Nausea and vomiting, jaundice	↑↑↑↑	↑↑↑
Acetaminophen toxicity	Variable	Nausea and vomiting, jaundice, encephalopathy	↑↑↑↑	↑↑
Thrombotic microangiopathy	Variable	Headache, hypertension	Normal	Normal

Nelson DB et al. Obstet Gynecol. 2021

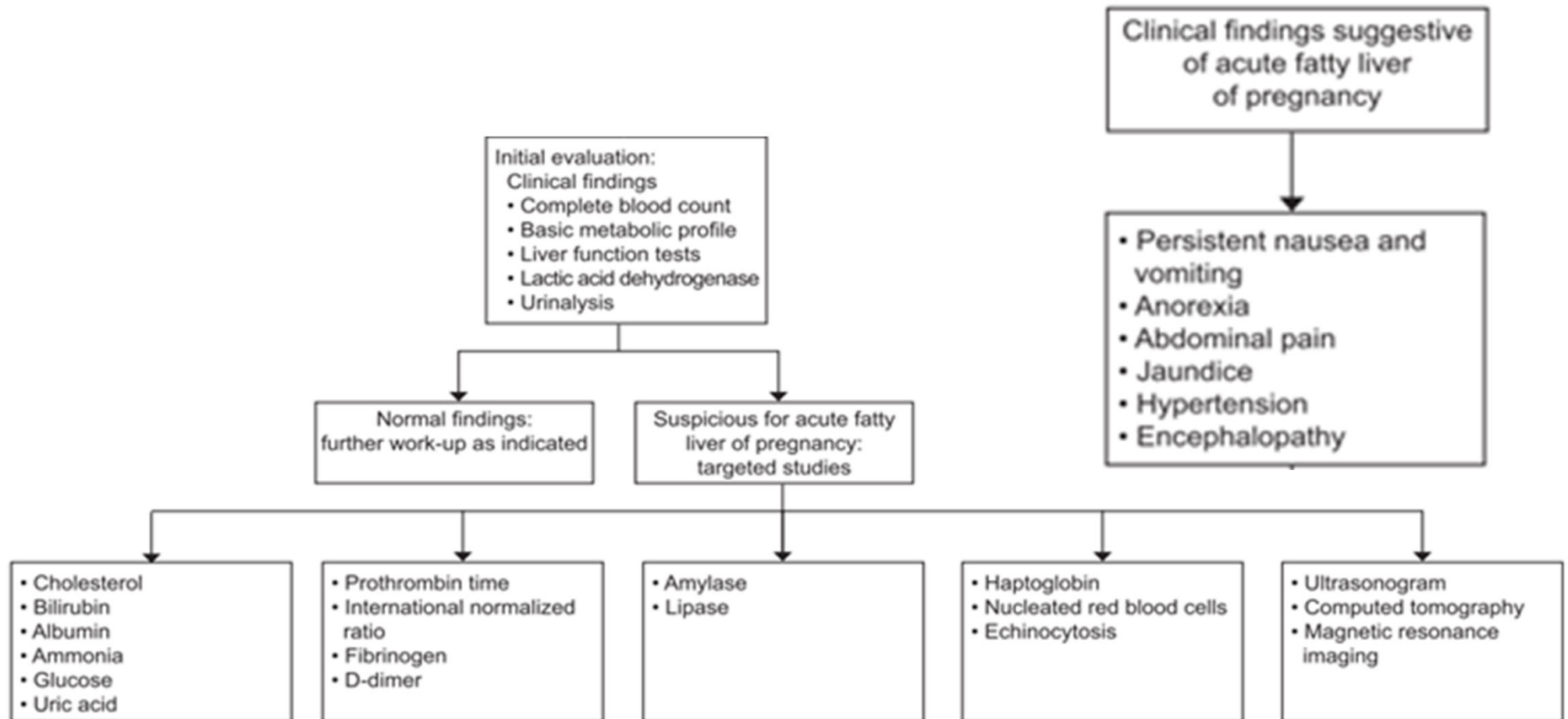
Differential Diagnosis

Disorder	Laboratory Findings						
	Renal			Hematologic			
	Creatinine	Hematocrit	Platelets	Fibrinogen	DD	PT	Hemolysis
Hyperemesis gravidarum	↑	Normal	Normal	Normal	Normal	Normal	No
Preeclampsia	Normal-↑	↑	Normal-↓↓	Normal	Normal	Normal	Mild
Intrahepatic cholestasis	Normal	Normal	Normal	Normal	Normal	Normal	No
AFLP	↑-↑↑	↓-↑	↓	↓↓	↑	↑	↑↑-↑↑↑
Hepatitis	Normal	Normal	↓	↓	↑	↑	No
Acetaminophen toxicity	↑-↑↑	?	?	?	?	↑	No
Thrombotic microangiopathy	↑-↑↑↑	↓↓	↓↓-↓↓↓	Normal	↑	Normal	↑↑-↑↑↑↑

AST, aspartate transaminase; DD, D-dimer; PT, prothrombin time; AFLP, acute fatty liver of pregnancy; ?, unknown.

Nelson DB et al. Obstet Gynecol. 2021

Diagnosis: Suggested Algorithm



Nelson DB et al. Obstet Gynecol. 2021

Diagnosis: Swansea Criteria

Clinical features

- Nausea and vomiting
- Abdominal pain
- Encephalopathy
- Polydipsia or polyuria

Laboratory features

- Bilirubin greater than 0.8 mg/dL
 - Glucose less than 72 mg/dL
 - WBC greater than 11,000/ μ L
 - AST or ALT greater than 42 units/L
 - Coagulopathy or PT greater than 14 s
 - Urea greater than 340 μ moles/L
 - AKI or creatinine greater than 1.7 mg/dL
 - Ammonia greater than 47 μ moles/L
- Ultrasound features of ascites or echogenic liver
 - Histologic features with microvesicular steatosis

6 of the above criteria satisfy the diagnosis of AFLP

*WBC, white blood cell count
AST, aspartate transaminase
ALT, alanine transaminase
AKI, acute kidney injury
PT, prothrombin time*

Gut 2002;51:876-80

Oil red O stain

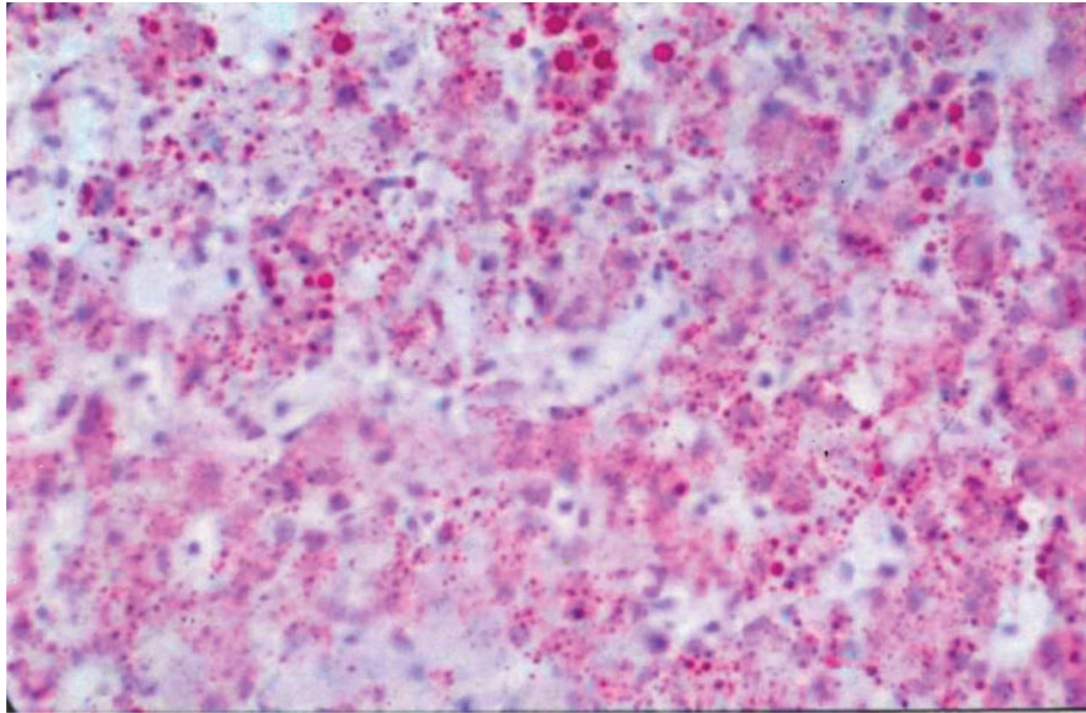


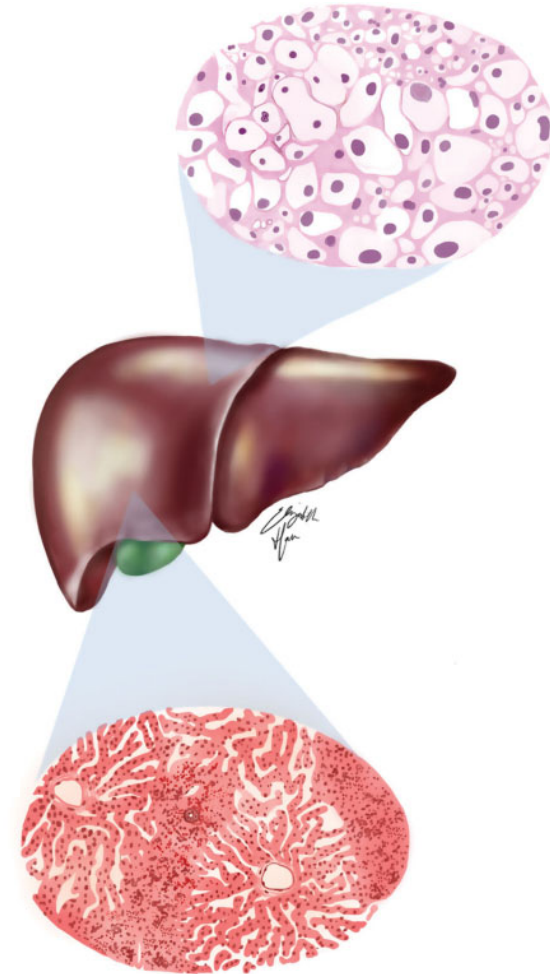
Fig. 2. Photomicrograph of section of liver in a woman with acute fatty liver of pregnancy (x430 magnification). The oil red O stain is picked up by triglycerides and other lipids, and these stain red.

Nelson DB et al. Obstet Gynecol. 2021

Comparing AFLP from HELLP Syndrome

Table 1. Most commonly used diagnostic criteria for AFLP and HELLP syndrome.

Swansea Criteria AFLP Syndrome (6 of 12)	Tennessee Criteria HELLP Syndrome (3 of 3)	Mississippi Criteria HELLP Syndrome (3 of 3)
Vomiting Abdominal pain Encephalopathy Ascites Polydipsia/polyuria Bilirubin > 0.8 mg/dL Hypoglycemia < 72mg/dL WBC > 11,000 /microL Elevated urea >950mg/dl ALT > 42 U/L AKI or Cr >1.7mg/dL Ammonia >47 µmol/L Coagulopathy or PT >14 s Echogenic liver on ultrasound Hepatic microvesicular steatosis	Plt < 100,000/µL AST > 70 U/L LDH > 600 U/L	Class 1 Plt (mL) ≤50,000/µL AST or ALT ≥70 U/L Total LDH ≥600 U/L Class 2 Plt >50,000-100,000/µL AST or ALT ≥70 U/L Total LDH ≥600 U/L Class 3 Plts >100,000-150,000/µL AST or ALT ≥40 U/L Total LDH ≥600 U/L



Byrne et al. J Matern Fetal Neonatal Med. 2020

Comparing AFLP from HELLP Syndrome

Table 2. Demographic and selected clinical characteristics at the time of admission.

Demographic/clinical characteristic	AFLP (N = 67)	HELLP (N = 67)	p-value
Age (years, mean $\pm$ SD)	27.9 $\pm$ 7.4	29.6 $\pm$ 6.8	.168
Race			.236
Black	7 (10)	11 (16)	
Hispanic	54 (81)	54 (81)	
White	6 (9)	2 (2)	
Nulliparous	26 (39)	23 (34)	.591
Hypertension (140/90 mm Hg)	42 (70) ^a	63 (94)	<.001
Proteinuria (1–4+)	22 (33)	48 (72)	<.001
Nausea/vomiting	35 (52)	13 (19)	<.001
Abdominal pain	33 (49)	31 (46)	.729
Headache	9 (13)	23 (34)	.005
Jaundice	20 (30)	0 (0)	<.001
Encephalopathy	10 (15)	1 (1)	.004

Data are presented as frequency (percentage) or mean $\pm$ SD. P-values are from the Pearson chi-square test.

^aDue to missing values, N = 60.

Byrne et al. J Matern Fetal Neonatal Med. 2020

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Byrne et al. J Matern Fetal Neonatal Med. 2020

Comparing AFLP from HELLP Syndrome: Initial studies

Table 2. Initial Laboratory Values Determined at the Time of Admission in Women With Acute Fatty Liver of Pregnancy and Hemolysis, Elevated Liver Enzymes, and Low Platelet Count (HELLP) Syndrome

Analyte	AFLP (n=67)	HELLP (n=67)	P
Fibrinogen (mg/dL)	200 (95–298)	455 (367–519)	<.001
AST (units/L)	278 (146–564)	135 (77–250)	<.001
Creatinine (mg/dL)	1.6 (1–2)	0.6 (1–1)	<.001
Cholesterol (mg/dL)	103 (81–139)	191 (155–230)	<.001
Total bilirubin (mg/dL)	2.9 (1–6)	0.6 (1–1)	<.001
Platelets (mL)	163,000 (121–205)	115,000 (78–150)	<.001
LDH (units/L)	464 (361–749)	552 (439–759)	.198
Glucose (mg/dL)	88 (68–102)	98 (83–114)	.011
White blood cell count (mL)	12 (10–17)	10 (8–13)	.73

AFLP, acute fatty liver of pregnancy; HELLP, hemolysis, elevated liver enzymes, and low platelet count; AST, aspartate transaminase; LDH, lactic acid dehydrogenase.

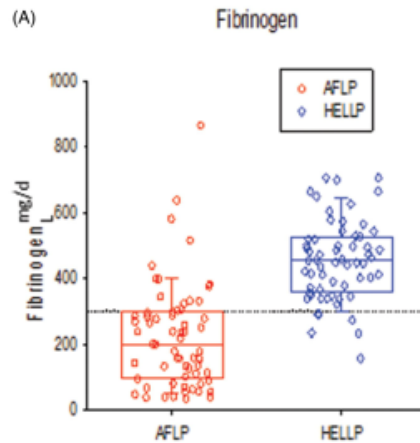
Data are median (first quartile, third quartile) unless otherwise specified.

P-value from the Wilcoxon rank-sum test.

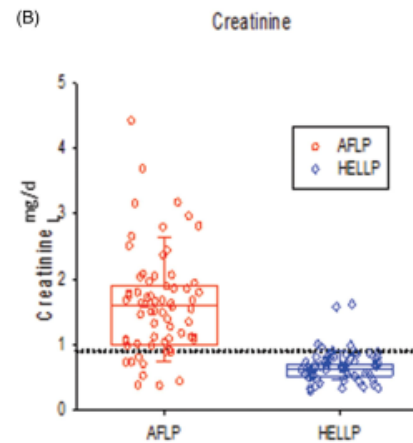
Nelson DB et al. Obstet Gynecol. 2021

Comparing AFLP from HELLP Syndrome: Initial studies

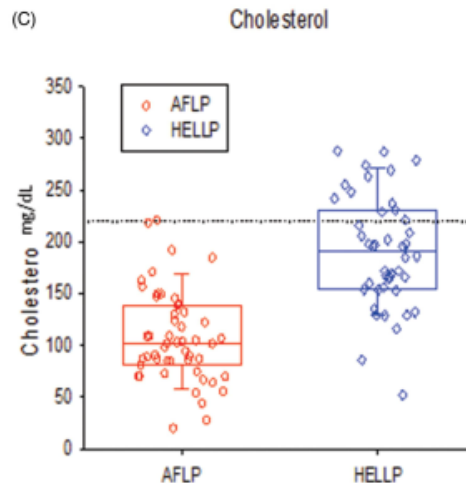
Fibrinogen



Creatinine



Cholesterol



Bilirubin

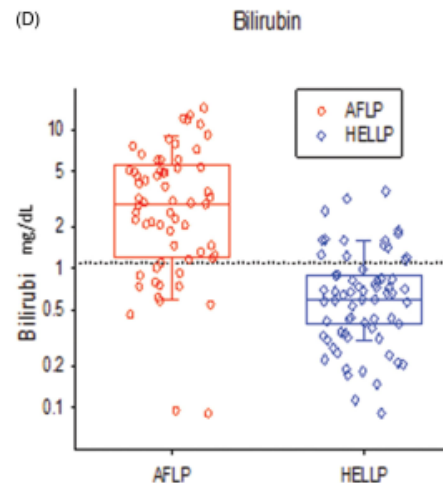


Figure 3. Initial laboratory analytes of women with HELLP syndrome and AFLP are compared with third-trimester upper and lower normal limits (all $p < .001$). (A) Fibrinogen (300 mg/dL), (B) Creatinine (0.9 mg/mL), (C) Cholesterol (220 mg/dL), and (D) Total bilirubin (1 mg/mL). $p < .001$ for all comparisons.

J Matern Fetal Neonatal Med. 2020 Apr 19:1-11.

Imaging studies in AFLP and HELLP syndrome

- Although included in Swansea criteria, imaging limited value in diagnosis of AFLP
- Sonography, CT, and MR imaging all are modalities reported to be utilized
 - Yield only reported as 30% with highest yield of 50% with CT scanning
- Published experience with HELLP syndrome suggests restricted diffusion on MR

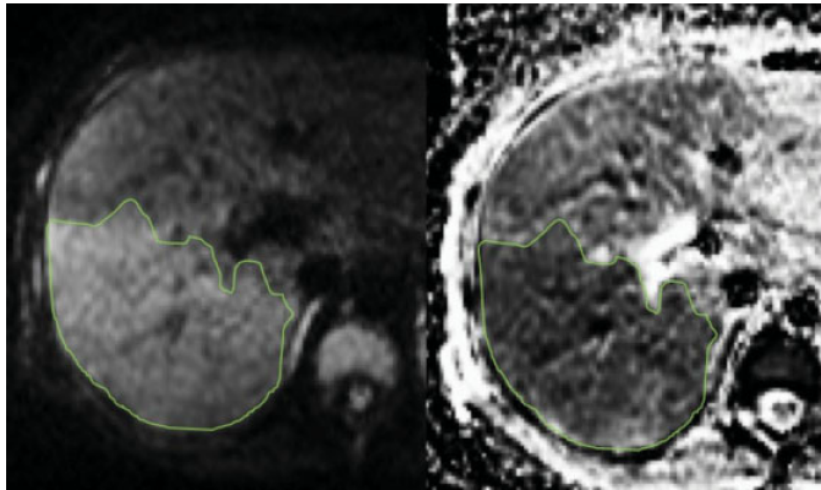


Fig. 1 An example of diffusion-weighted magnetic resonance imaging ($b = 800$ second- mm^2 ; left) and a calculated map of apparent diffusion coefficient (right) with a large focal area of restricted diffusion (segmented in green).

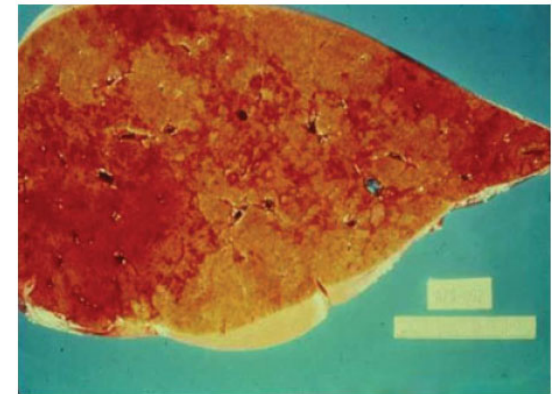


Fig. 3 Photograph of a gross liver specimen from a woman with preeclampsia and severe HELLP syndrome who died from aspiration pneumonia en route to the Parkland Hospital. Microscopic findings from the liver specimen demonstrated patchy areas of periportal hemorrhagic necrosis, ischemia, and edema. HELLP, hemolysis, elevated liver enzymes, and low platelet.

Am J Perinatol. 2018 Jul;35(8):741-747

Hemostatic dysfunction with AFLP: Nucleated RBC

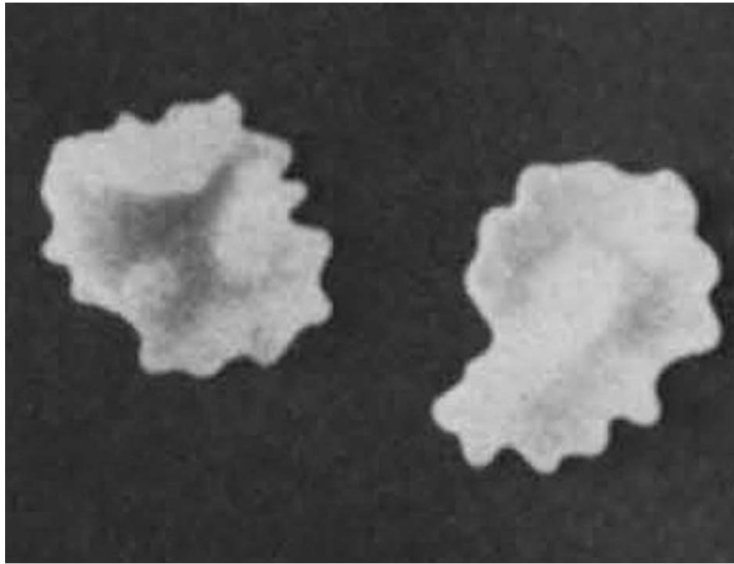
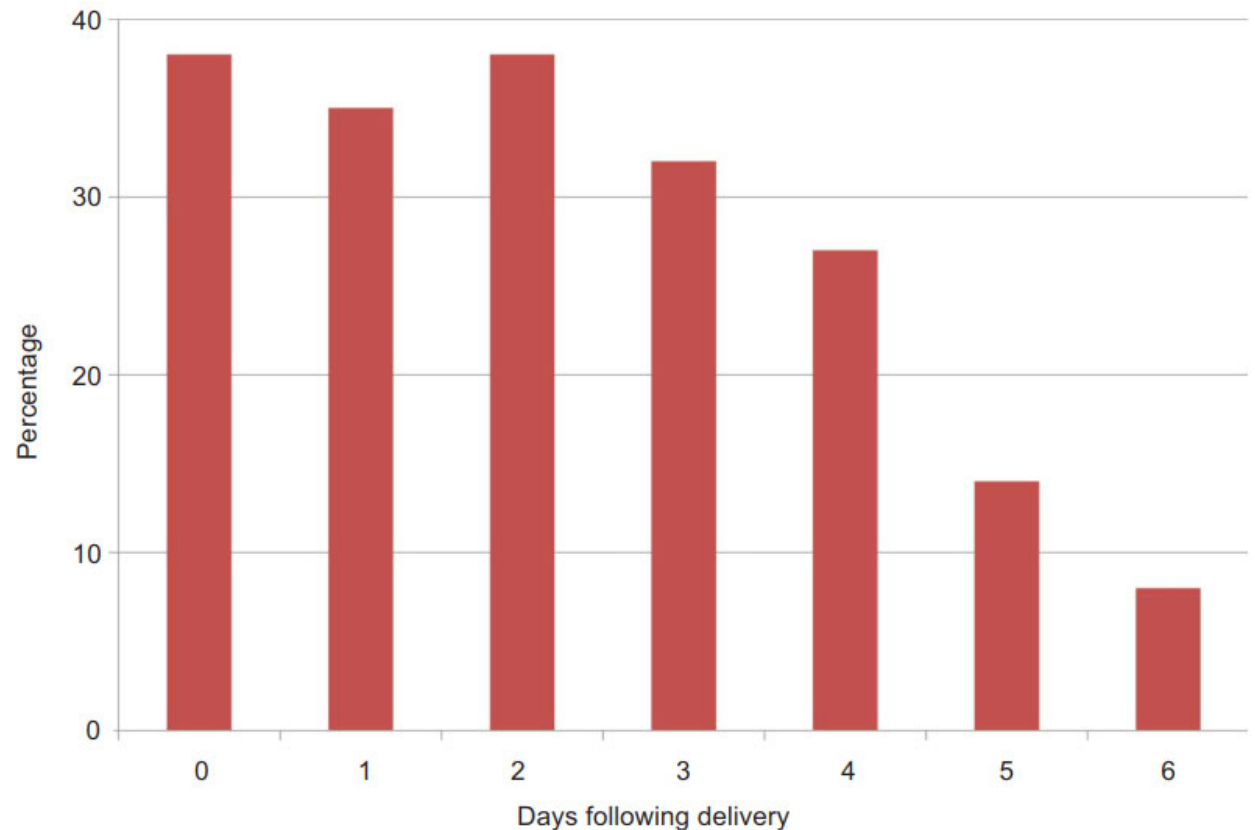


Fig. 6. Scanning electron microscope displaying echinocytes present in a woman with acute fatty liver of pregnancy.

Nucleated Red Blood cells (/100 WBC)



Nucleated Red Blood cells are NOT normal on an adult CBC with differential analysis!!!

Obstet Gynecol. 2014 Jul;124(1):40-46.

Management

1. Prompt recognition and evaluation of the mother and fetus
2. Plan for supportive care such as reversal of coagulopathy
3. Preparation for delivery as soon as feasible
4. Postpartum supportive care

Multidisciplinary team approach

Obstet Gynecol. 2021 Mar 1;137(3):535-545

Management

- Until the fetus is delivered, ongoing liver failure will continue with its attendant constellation of abnormalities
- After delivery, there is a slow return to metabolic normalcy that frequently requires considerable supportive care

Obstet Gynecol. 2021 Mar 1;137(3):535-545

Management

- Two large-bore intravenous catheters in anticipation of substantial postpartum hemorrhage
- Magnesium sulfate infusion for eclampsia prophylaxis for women in whom a diagnosis of preeclampsia is also being considered (approximately 70% of patients)
- Treat severe-range blood pressure levels with a goal of less than 160/110 mmHg
- Communication with the pediatric team

Obstet Gynecol. 2021 Mar 1;137(3):535-545

Obstetric Anesthesia and Analgesia

- If obtunded, airway protection is paramount
- With persistent vomiting, consideration can be given to placement of a nasogastric tube with administration of antacids to neutralize gastric contents
- For obvious hepatic encephalopathy, tracheal intubation
- Moderate thrombocytopenia ($>70,000/\text{mL}$) is reasonable to place neuraxial analgesia, however, nadir of the coagulation studies may not recover until several days postpartum

Obstet Gynecol. 2021 Mar 1;137(3):535-545

Cesarean Delivery Considerations

- Before cesarean delivery, coagulopathy must be corrected
 - Fibrinogen-containing products, goal plasma fibrinogen level of at least 150 mg/dL
 - Platelet count less than 50,000/mL will require platelet replacement before cesarean delivery
- Mildline vertical skin incision is our practice
- Consider drain (Jackson-Pratt) if there is significant ongoing surgical oozing or ascitic fluid, however, not commonly placed

Obstet Gynecol. 2021 Mar 1;137(3):535-545

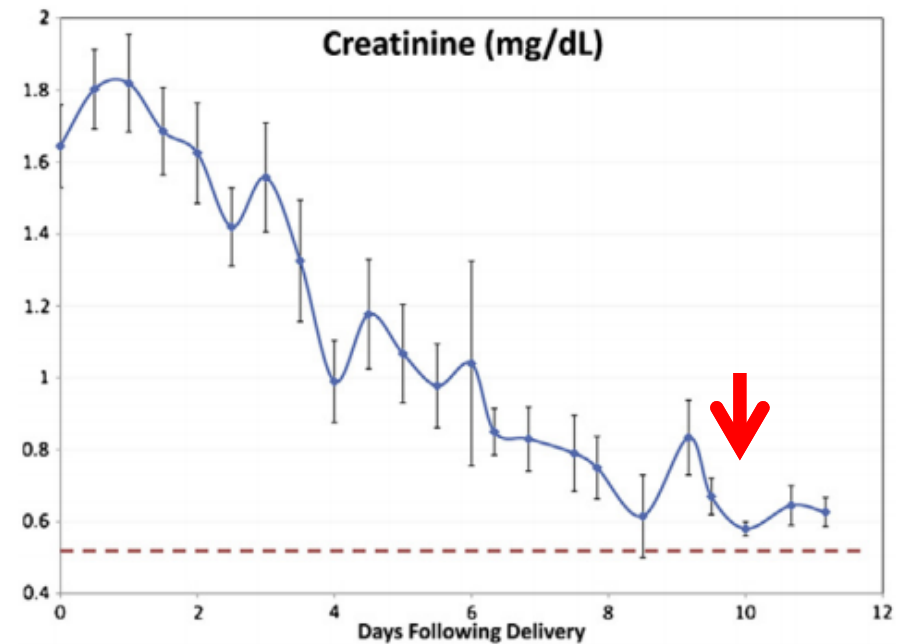
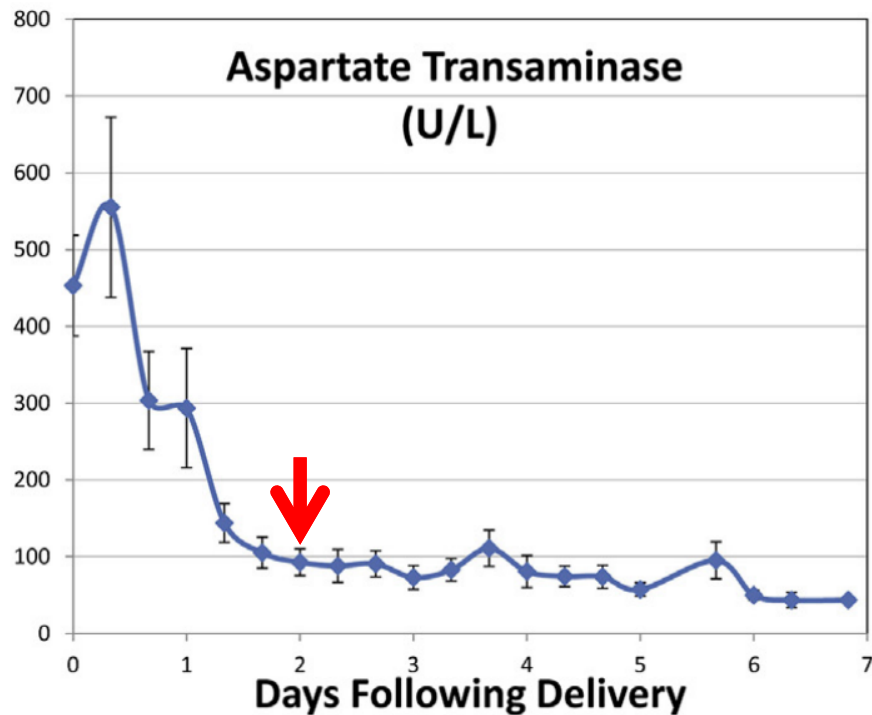
Postpartum Course and Management

- Gradual improvement of the laboratory derangements, however some of the pathophysiologic changes of acute fatty liver of pregnancy for as long as 7-10 days
- High incidence of postpartum hemorrhage, disseminated intravascular coagulopathy, and acute kidney injury
- Serial measurements of hematologic, hepatic, and renal function are performed every 6–12 hours within the first 1–2 days
- Serum magnesium levels monitored to avoid magnesium toxicity
- Serial blood glucose levels monitored every hour

Obstet Gynecol. 2015 Nov;126(5):999-1011.

Obstet Gynecol. 2021 Mar 1;137(3):535-545

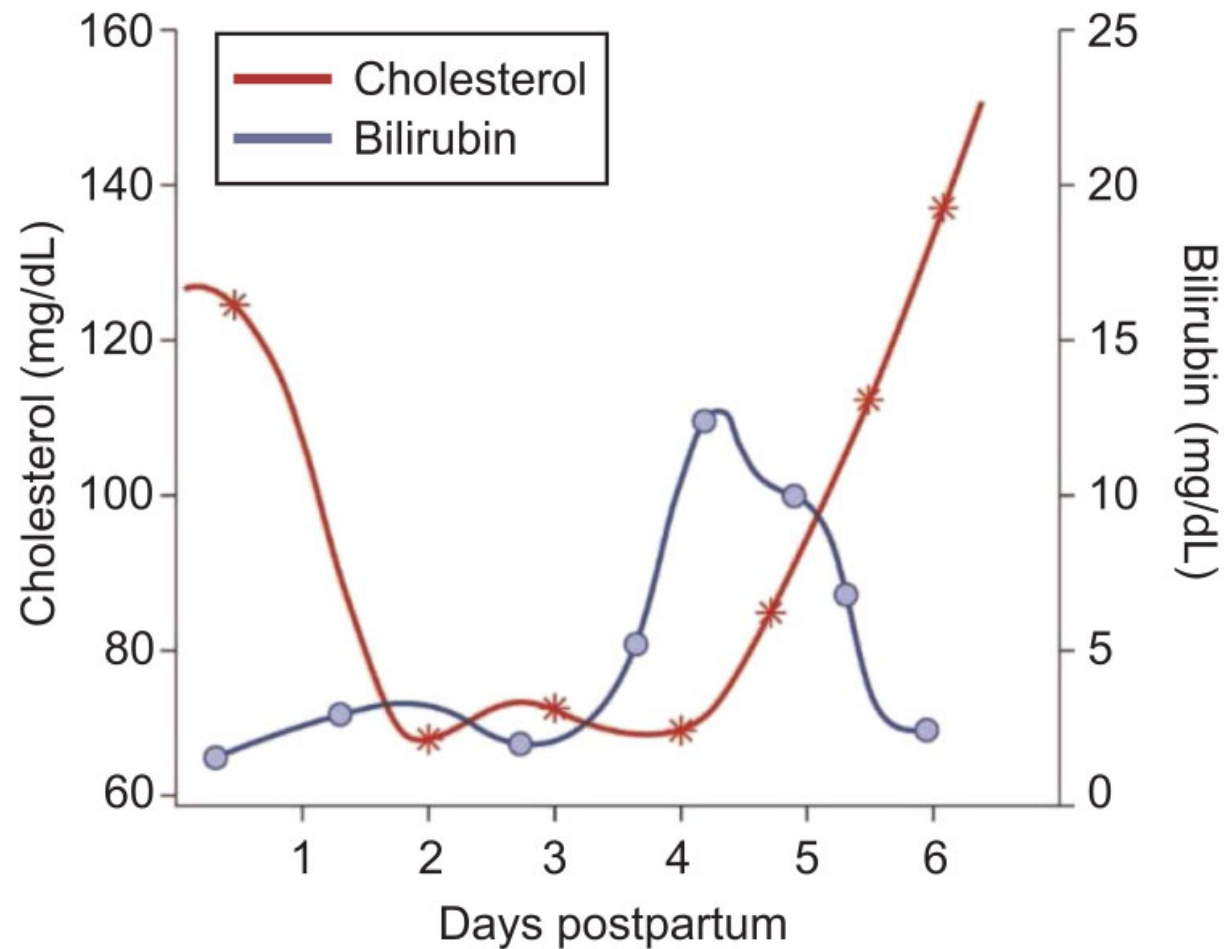
Anticipated laboratory analyte recovery postpartum



The *dashed line* represents mean creatinine value at the initiation of prenatal care.

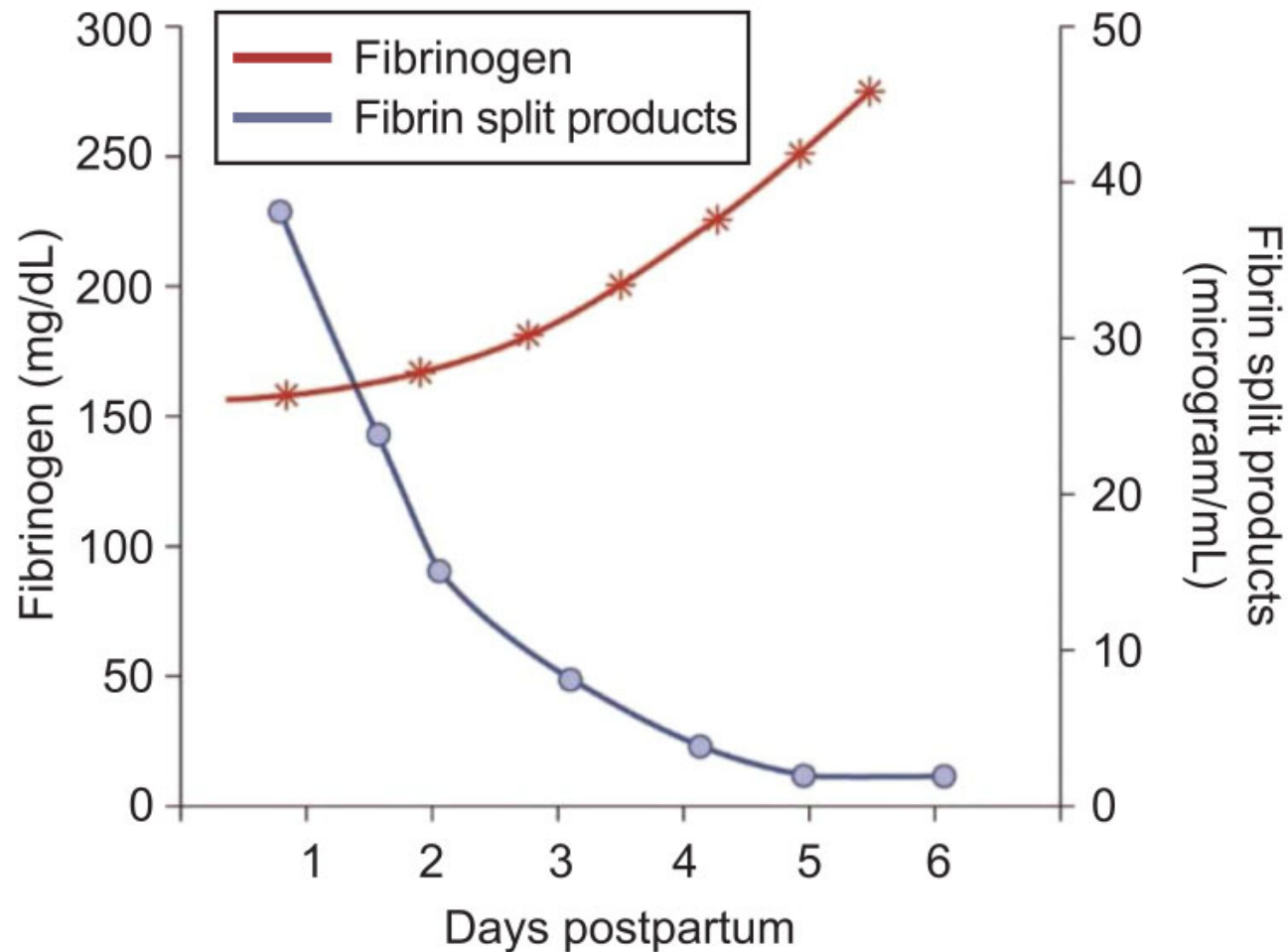
Am J Obstet Gynecol. 2013 Nov;209(5):456.e1-7.

Anticipated laboratory analyte recovery postpartum



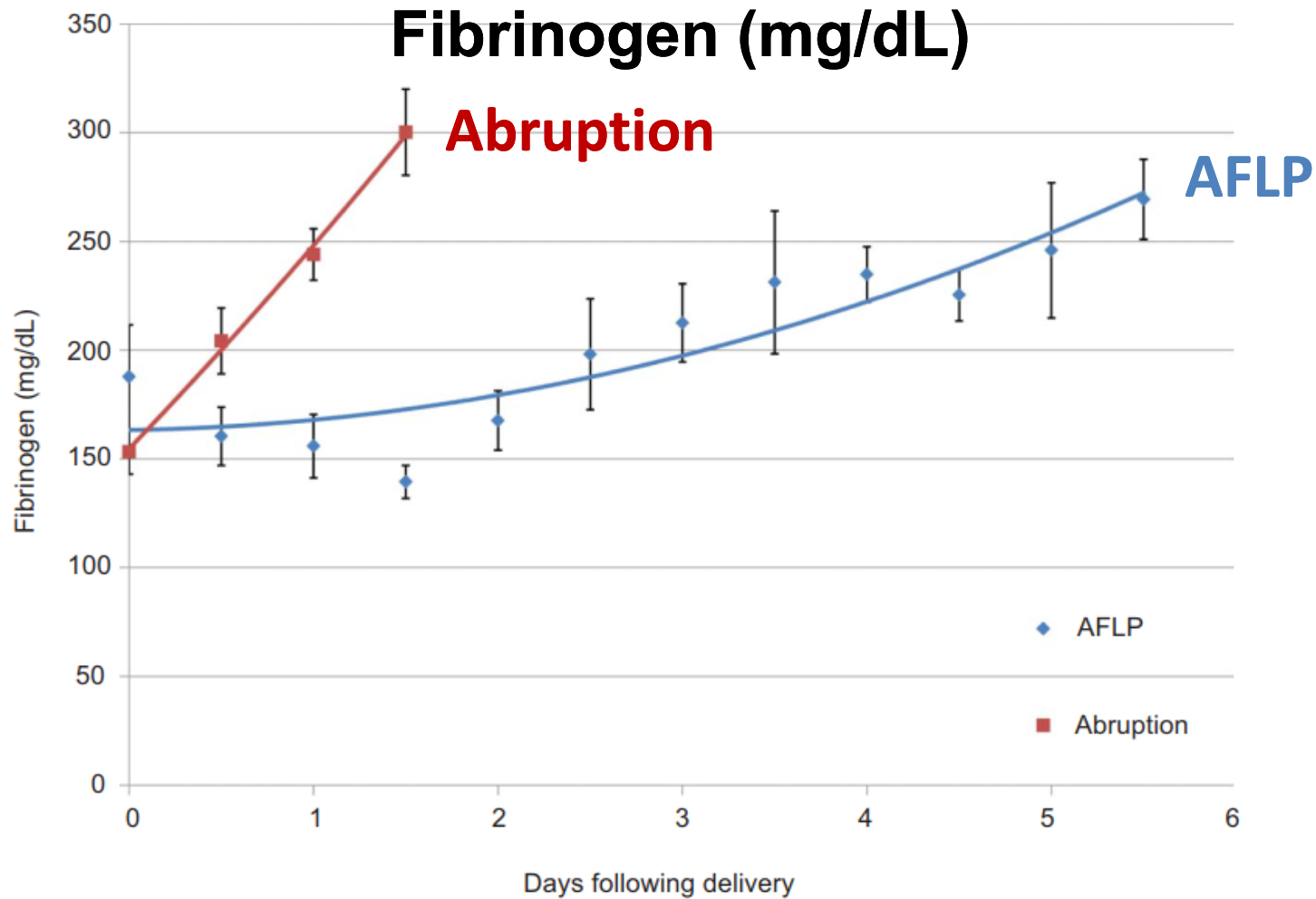
Obstet Gynecol. 2021 Mar 1;137(3):535-545

Anticipated laboratory analyte recovery postpartum



Obstet Gynecol. 2021 Mar 1;137(3):535-545

Recovery compared to placental abruption



Obstet Gynecol. 2014 Jul;124(1):40-46.

Recovery compared to HELLP Syndrome

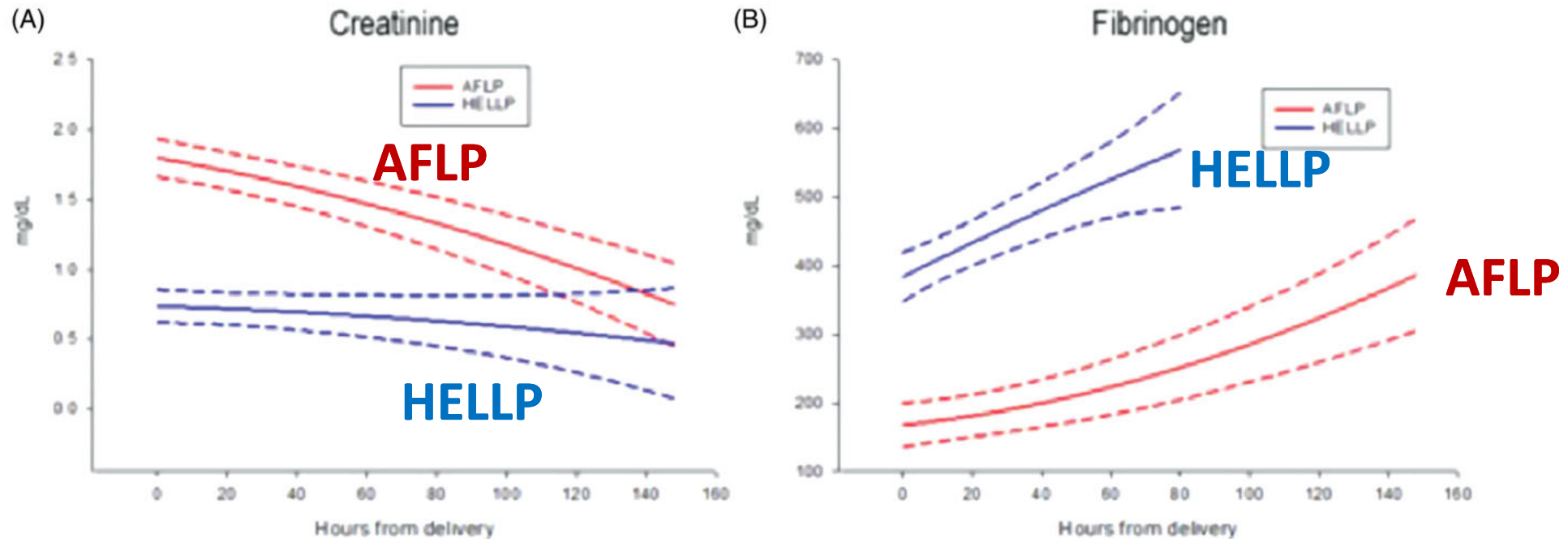


Figure 5. Random effects modeling for recovery of serum creatinine and plasma fibrinogen levels with AFLP and HELLP syndrome. (A) With the linear or 1st order model, the interaction effect for creatinine was tested with $p < .001$. (B) With the linear or 1st order model, the interaction effect for fibrinogen was tested with $p < .001$.

J Matern Fetal Neonatal Med. 2020 Apr 19:1-11.

■ Postpartum Course

- About 15% of patients with AFLP develop acute pancreatitis that can be severe
 - Treated conservatively with nasogastric suction and analgesics
- Transient diabetes insipidus, due to an elevated vasopressinase concentration caused by diminished production of the inactivating enzyme by the liver
 - Desmopressin will be successful in reversing prodigious diuresis
- Artificial liver support therapy
 - Continuous renal replacement therapy along with plasma exchange has been shown to improve clinical symptoms and laboratory analyte recovery; however, data regarding outcomes are limited
- Extracorporeal life support

Obstet Gynecol. 2021 Mar 1;137(3):535-545

Maternal and Perinatal Outcomes

Pregnancy outcomes

Gestational age, wk ^a	37.0 ± 2.6 (31.7–40.9)
Twin gestation, n (%)	7 (14)
Vaginal delivery, n (%)	26 (51)
Cesarean delivery-overall, n (%)	25 (49)
Live fetus, n (%)	25 (57)
Fetal compromise, n (%)	10 (40)
Preterm delivery, n (%)	20 (40)
<34 wk	10 (20)
34-37 wk	10 (20)

^a Data are given as mean ± SD (range);

Am J Obstet Gynecol. 2013 Nov;209(5):456.e1-7.

Maternal and Perinatal Outcomes

Maternal complications, n (%)

Blood and components transfusion	28 (55)
Pulmonary edema	7 (14)
Platelet-transfusions	7 (14)
Encephalopathy	8 (16)
Pancreatitis	8 (16)
Tracheal intubation ^b	3 (6)
Medical/surgical intensive care unit	7 (14)
Dialysis	1 (2)
Death	2 (4)

^b Excludes intubations for general anesthesia.

Am J Obstet Gynecol. 2013 Nov;209(5):456.e1-7.

Maternal and Perinatal Outcomes

Perinatal outcomes

Birthweight, g ^a	2545 ± 710 (1255—4090)
Birthweight <2000 g , n (%)	10 (20)
Stillborn, n (%)	7 (12)
Live born, n (%)	
Umbilical artery pH <7.0	4 (8)
Neonatal intensive care unit	17 (33)
Neonatal death	0

^a Data are given as mean ± SD (range);

Am J Obstet Gynecol. 2013 Nov;209(5):456.e1-7.

Maternal and Perinatal Outcomes

Study	n	Hepatic Encephalopathy	AKI	Coagulopathy or DIC	Cesarean Delivery Rate	Maternal Death	Perinatal Death
Vigil-de Gracia (2011) ⁵⁰	35	40	94	77	89	11	10
Cheng (2014) ⁵¹	32	53	81	16	69	44	20
Zhang (2016) ⁵²	56	20	39	54	80	7	16
Gao (2020) ³³	133	33	10	80	85	17	27
Byrne (2020) ²⁹	67	15	85	70	55	3	19
Chang (2020) ⁵³	55	18	86	84	75	7	11
Approximate average	378	33	52	68	69	13	19

AKI, acute kidney injury; DIC, disseminated intravascular coagulation.
Data are % unless otherwise specified.

Many of these cases will trigger a severe maternal morbidity (“SMM”) trigger: Acute Kidney Injury (AKI), ICU admission, and need for blood and component transfusion

Obstet Gynecol. 2021 Mar 1;137(3):535-545

Intrahepatic Cholestasis of Pregnancy

Clinical presentation

- Pruritis without rash in the second or third trimester
- Elevated bile acids
- Possible to have transaminitis

Etiopathogenesis

- 0.3-0.5% incidence
- Geographical location
- Genetic
 - Mutations in biliary transport proteins
 - Mutations in bile acid receptors
- Seasonal variations
- Hormonal influences

Differential Diagnosis

- Pruritis can affect 23% of all pregnancies
- Importance of history and physical and timeframes
- About 50% of pruritus do not have ICP

Cholestasis: A Prospective Study of Perinatal Outcomes and Time to Symptom Improvement



Casey S. Yule, MD¹ Denisse S. Holcomb, MD¹ Alexandria C. Kraus, MD¹
Charles E.L. Brown, MD, MBA¹ Donald D. McIntire, PhD¹ David B. Nelson, MD¹

¹Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of Texas Southwestern Medical Center, Dallas, Texas

Address for correspondence: Casey S. Yule, MD, Department of Obstetrics and Gynecology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390-9032 (e-mail: casey.yule@utsouthwestern.edu).

Am J Perinatol 2021;38:414–420.

Abstract

Objective Although intrahepatic cholestasis of pregnancy (ICP) remains poorly understood, there are several perinatal complications associated with this condition. This study aimed to examine perinatal outcomes of women with ICP, evaluate outcomes according to severity of disease, and monitor time to symptom improvement following diagnosis.

Study Design It involves a prospective, observational study of women with ICP at a single institution. Women with new-onset pruritus without rash were referred to a high-risk obstetrics clinic and evaluated with fasting total bile acids (TBA). Laboratory-confirmed ICP was defined as fasting TBA ≥ 10 $\mu\text{mol/L}$. Following diagnosis, a standardized protocol was utilized, including treatment with ursodeoxycholic acid (UDCA). Perinatal outcomes were compared amongst those with and without ICP, and to the general population. Women with ICP were further analyzed based on maximum TBA: 10 to 39, 40 to 99, and ≥ 100 $\mu\text{mol/L}$. A Kaplan-Meier survival curve was used to analyze time to symptom improvement.

Results A total of 404 patients were evaluated and 212 (52%) were diagnosed with ICP. The mean gestational age at diagnosis was 34.1 ± 3.3 weeks. When comparing those with ICP to those not confirmed, and to the general population, there were no differences in age, parity, mode of delivery, preeclampsia, or stillbirth ($p > 0.05$). Preterm birth was significantly associated with ICP ($p < 0.01$). This relationship was significant across increasing severity of TBA ($p < 0.01$) and persisted when examining rates of spontaneous preterm birth ($p < 0.01$). All women with fasting TBA ≥ 40 $\mu\text{mol/L}$ delivered preterm due to premature rupture of membranes or spontaneous labor. Time to symptom improvement after diagnosis was over 2 weeks on average; however, this time increased with worsening severity of disease.

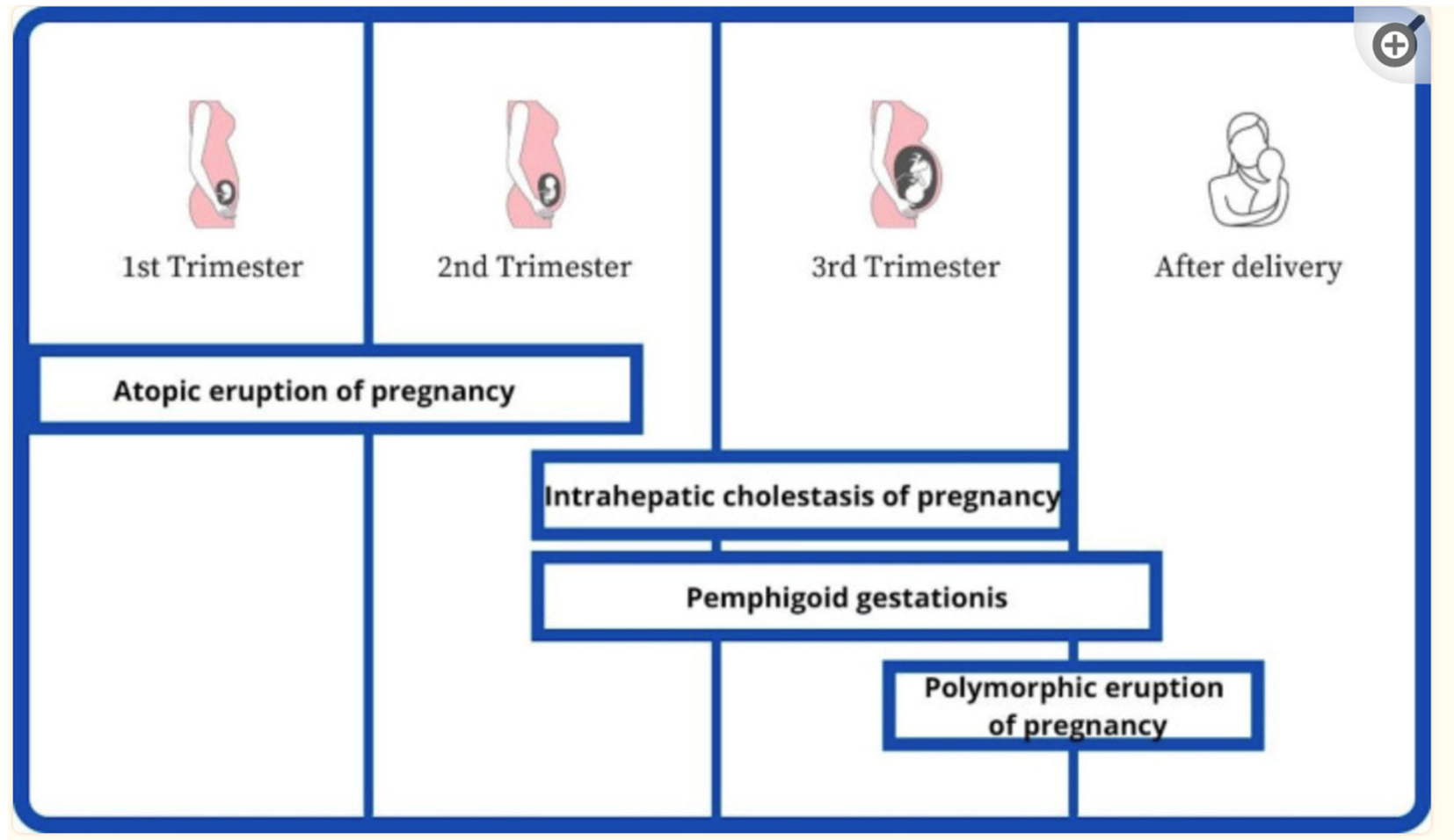
Conclusion Despite treatment with UDCA, women with ICP are at increased risk for spontaneous preterm birth, and this risk significantly increased with severity of disease. Although not significant, a trend exists between increasing time to symptom improvement and worsening severity of disease.

Keywords

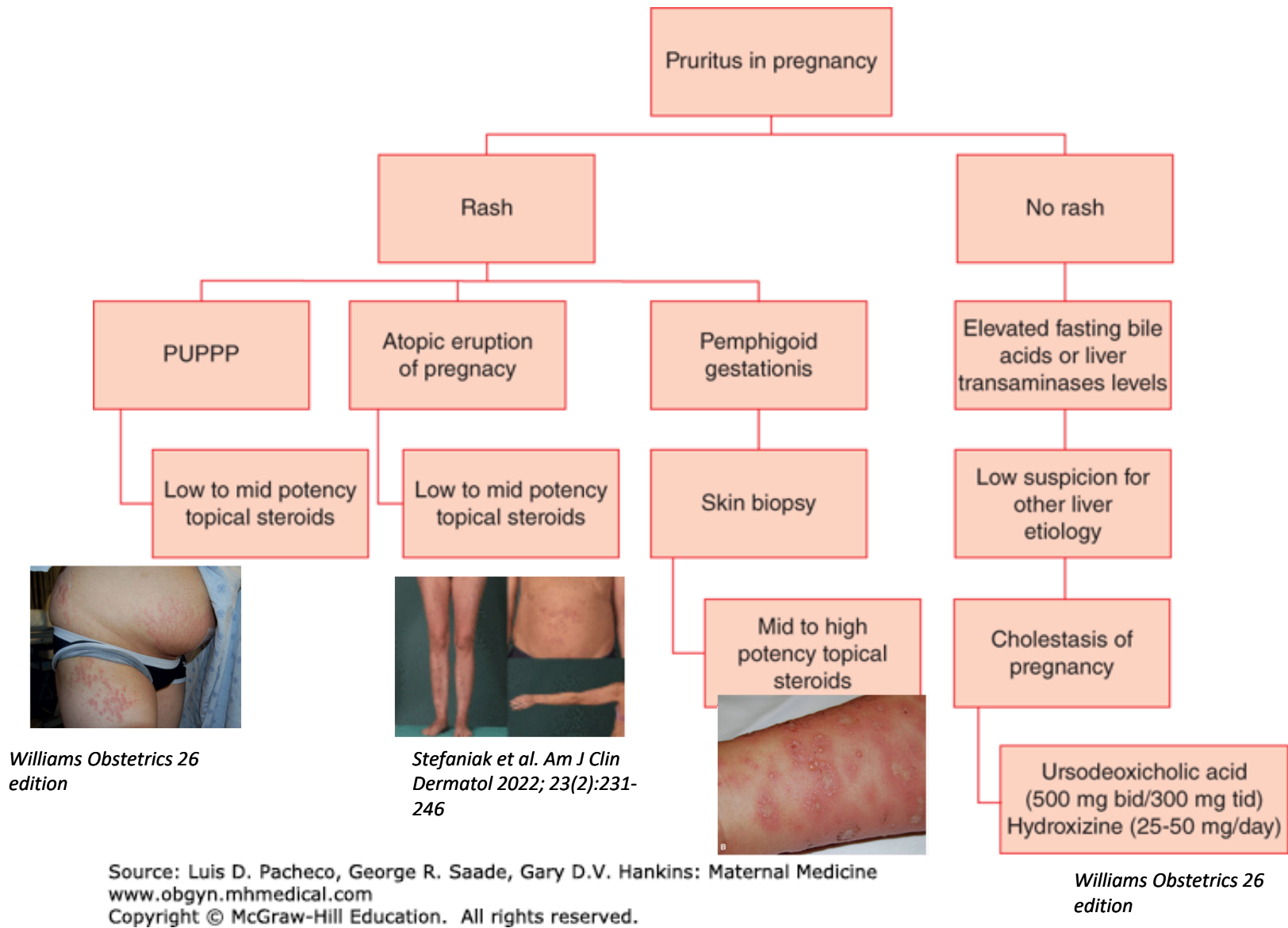
- intrahepatic cholestasis of pregnancy
- perinatal outcomes
- preterm birth
- pruritus
- total bile acids
- ursodeoxycholic acid
- symptom improvement

Yule CS et al. Cholestasis: A Prospective Study of Perinatal Outcomes and Time to Symptom Improvement. Am J Perinatol.

Differential Diagnosis



Stefaniak et al. Am J Clin Dermatol 2022; 23(2):231-246



ICP: Differential Diagnosis

BOX 1

Conditions associated with pruritus without rash

Chronic renal failure

Hypo- or hyperthyroidism

Liver disease

Malabsorption

Parasitosis or helminthosis

HIV

Hodgkin disease

Leukemia

Non-Hodgkin lymphoma

Polycythemia rubra vera

Tumors (paraneoplastic)

Drugs (hydrochlorothiazide, opioids, among others)

Multiple sclerosis

Psychiatric disease (anxiety, depression, obsessive compulsive disorder).

Society for Maternal-Fetal Medicine. SMFM Consult Series #53: Intrahepatic cholestasis of pregnancy. Am J Obstet Gynecol 2021.

BOX 2

Other causes of elevated bile acids

Primary biliary cholangitis

Obstructive bile duct lesion

Primary sclerosing cholangitis (associated with inflammatory bowel disease)

Drug-induced cholestasis (trimethoprim-sulfamethoxazole, phenothiazines, ampicillin)

Liver tumor

Bacterial, fungal, and viral infections (eg, Epstein-Barr virus and cytomegalovirus)

Hepatic amyloidosis

Lymphoma and solid organ malignancies

Hepatic sarcoidosis

Autoimmune hepatitis

Idiopathic adulthood ductopenia

Total parental nutrition

Viral diseases

Familial intrahepatic cholestasis

Cirrhosis

Sickle cell intrahepatic cholestasis

Hepatic congestion from heart failure

Crohn disease

Society for Maternal-Fetal Medicine. SMFM Consult Series #53: Intrahepatic cholestasis of pregnancy. Am J Obstet Gynecol 2021.

ICP: Diagnosis

- What is “normal” again?
 - Beware of electronic medical records and referent laboratory values
 - “Normal” is thought to be $<5 \mu\text{mol/L}$ (clinical use $<10 \mu\text{mol/L}$)
 - This number can depend on the lab technique, gestational age, recent food consumption
- What is our diagnostic threshold?
 - Early studies in 1970s used total bile acids and some calculations of individual bile acids
 - Compared symptomatic vs non symptomatic, but didn't really evaluate thresholds
 - Mixed methods: **fasting vs non fasting**
 - 2004 Glantz et al showed correlation between levels and adverse fetal events of $>40 \mu\text{mol/L}$

ICP: Diagnosis

Table 4. Total Bile Acid Levels by Fasting State and Diagnostic Cutoff in Symptomatic Pregnant Women

	Nonfasting	Fasting	<i>P</i>	Changed Diagnosis
Bile acid level (micromoles/L)	13.5 (9–142)	11.5 (7–56)	<.001	
Diagnostic cutoff (micromoles/L)*				
Greater than 10	21 (81)	15 (58)	.132	6 (23)
Greater than 15	9 (35)	4 (15)	.20	5 (19)
Greater than 20	5 (19)	4 (15)	.9	1 (4)

Data are median (range) or n (%) unless otherwise specified.

* Number of patients with total bile acid levels above cutoff.

- Fasting versus non-fasting?
- Symptomatic women, **non-fasting bile acids resulted in 23% more diagnosis** of cholestasis compared to fasting values

Smith, D. , Kiefer, M. , Lee, A. , Davis, S. , Summerfield, T. , Landon, M. & Rood, K. (2020). Effect of Fasting on Total Bile Acid Levels in Pregnancy. *Obstetrics & Gynecology*, 136 (6), 1204-1210.

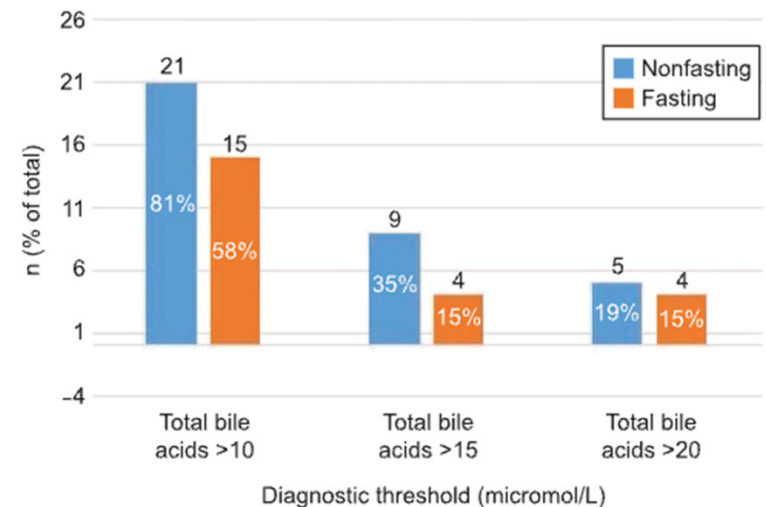


Fig. 2. Rates of cholestasis diagnosis by fasting state and diagnostic threshold in symptomatic pregnant women.

Smith. Total Bile Acid Levels in Pregnancy. *Obstet Gynecol* 2020.

ICP: Diagnosis

- No absolute consensus on a level for diagnosis
 - Reference in pregnancy vs what's associated with poor outcomes
 - In general, use >10 $\mu\text{mol/L}$ for diagnosis
 - >40 $\mu\text{mol/L}$ is associated with adverse outcomes
 - >100 $\mu\text{mol/L}$ is highest risk for stillbirth

Itching + Normal bile acids?

- * itching can precede $\uparrow$ bile acids by several weeks
- if sxm persist $\rightarrow$ repeat testing

RED FLAG FOR ALT CAUSE

- excessive fatigue
- insomnia
- malaise
- abdominal pain
- elevated bile acids before the second trimester

SMFM Hepatitis C
Visual Summary

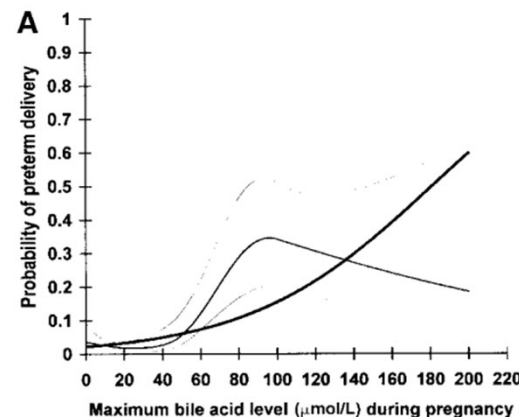
ICP: Pregnancy-related effects

- Pruritis for pregnant person; no long-term issues
- Infant
 - Meconium-stained fluid
 - Preterm birth
 - IUFD
 - Fetal arrhythmia or vasospasm of the placental chorionic surface vessels
 - Highest risk was with levels $>100 \mu\text{mol/L}$
 - Some degree of risk may be present with lower levels

Table 2 Selected obstetric outcomes for patients with laboratory-confirmed ICP as compared with ICP not confirmed, as well as the general population delivered

Outcome	ICP Not confirmed No. of women (%) N = 130	ICP Confirmed No. of women (%) N = 212	Control General population No. of women (%) N = 48,292	p-Value
Nulliparous	31 (24)	57 (27)	14,076 (29)	0.32
Maternal age ≤ 15 y	0 (0)	1 (0.5)	275 (0.6)	0.677
Maternal age ≥ 35 y	24 (18)	39 (18)	8,321 (17)	0.845
Cesarean delivery	46 (35)	60 (28)	15,411 (32)	0.369
Pre-eclampsia	14 (11)	28 (13)	5,087 (11)	0.448
Chorioamnionitis	10 (8)	17 (8)	4,137 (9)	0.902
Induction	42 (32)	80 (38)	10,699 (22)	<0.001
Augmentation	25 (19)	39 (18)	10,852 (22)	0.248
Placental abruption	2 (1.5)	2 (0.9)	454 (0.9)	0.78
Gestational age at delivery <37 wk	8 (6.2)	41 (19)	4,781 (10)	<0.001

Yule CS et al. Cholestasis: A Prospective Study of Perinatal Outcomes and Time to Symptom Improvement. Am J Perinatol.



Glantz A, et al. Intrahepatic cholestasis of pregnancy: Relationships between bile acid levels and fetal complication rates. Hepatology.

ICP: Management

- Ursodeoxycholic acid

- May decrease transaminase and improve symptoms, but not shown to improve fetal outcomes
- Regimens are 300 mg BID or TID or 500 mg BID
- Nausea and dizziness have been reported with a decrease in pruritis in 1-2 weeks
- Cholestyramine
- Symptomatic management

- Antepartum testing???

- Efficacy not established
- Begin at gestational age when delivery would be performed in response
- Optimal frequency unknown

ICP: Management

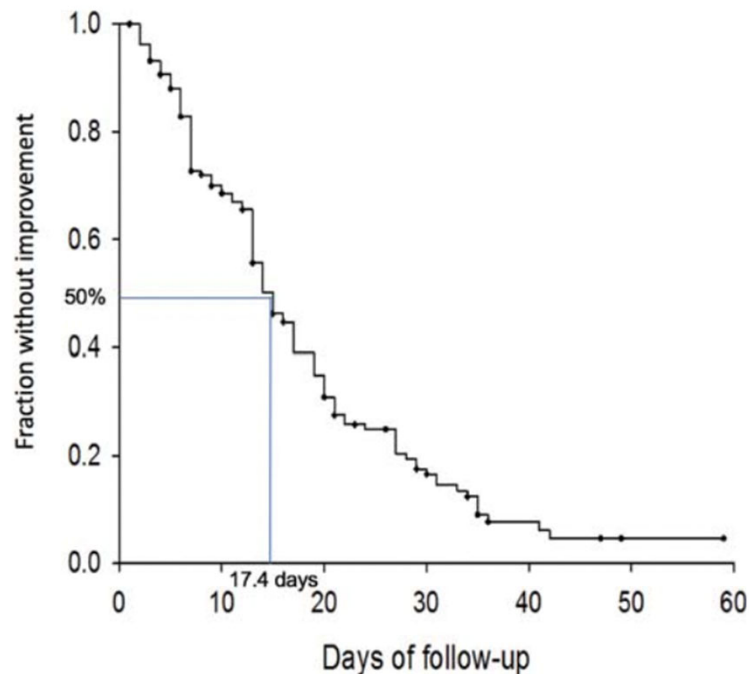


Fig. 2 Overall symptom improvement during antepartum period for women with ICP. A Kaplan-Meier curve demonstrates that the average time to symptom reduction in 50% of the study cohort following treatment with UDCA was 17.4 ± 1 days ($n = 212$). ICP, intrahepatic cholestasis of pregnancy; UDCA, ursodeoxycholic acid.

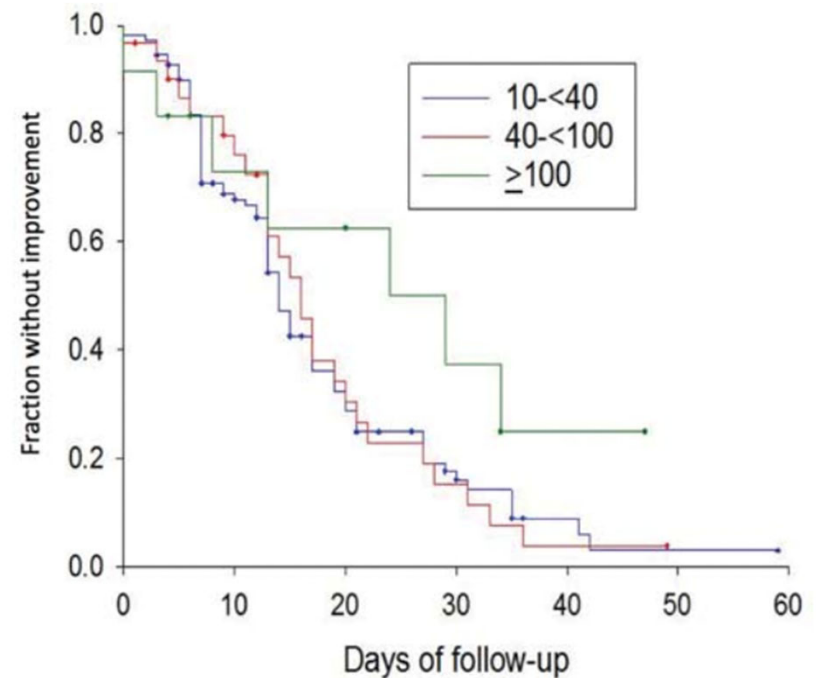


Fig. 3 Women with ICP and resolution of symptoms according to severity of disease (Log rank test to examine equality, $p = 0.30$). Kaplan-Meier curves were constructed and stratified according to severity of disease. TBA 10 to <40 $\mu\text{mol/L}$ ($n = 130$), TBA 40 to <100 $\mu\text{mol/L}$ ($n = 41$), and TBA ≥ 100 $\mu\text{mol/L}$ ($n = 21$). ICP, intrahepatic cholestasis of pregnancy; TBA, total bile acid.

Yule CS et al. Cholestasis: A Prospective Study of Perinatal Outcomes and Time to Symptom Improvement. *Am J Perinatol*.

ICP: Delivery planning

Intrahepatic cholestasis of pregnancy: total bile acid levels <100 micromol/L	Late preterm/early term	36 0/7–39 0/7 weeks of gestation or at diagnosis if diagnosed later [#]
Intrahepatic cholestasis of pregnancy: total bile acid levels ≥100 micromol/L	Late preterm	36 0/7 weeks of gestation or at diagnosis if diagnosed later [#]

Medically indicated late-preterm and early-term deliveries. ACOG Committee Opinion No. 831. American College of Obstetricians and Gynecologists. Obstet Gynecol 2021;138:e35–9.

- Other considerations:
 - if unrelenting symptoms
 - history of stillbirth before 36 weeks due to ICP previously
 - preexisting or acute hepatic disease with clinical or lab worsening of hepatic function
- Decision analysis model ideal was 36 weeks

ICP: Delivery planning

Intrahepatic cholestasis of pregnancy: total bile acid levels <100 micromol/L	Late preterm/early term	36 0/7–39 0/7 weeks of gestation or at diagnosis if diagnosed later [#]
Intrahepatic cholestasis of pregnancy: total bile acid levels ≥100 micromol/L	Late preterm	36 0/7 weeks of gestation or at diagnosis if diagnosed later [#]

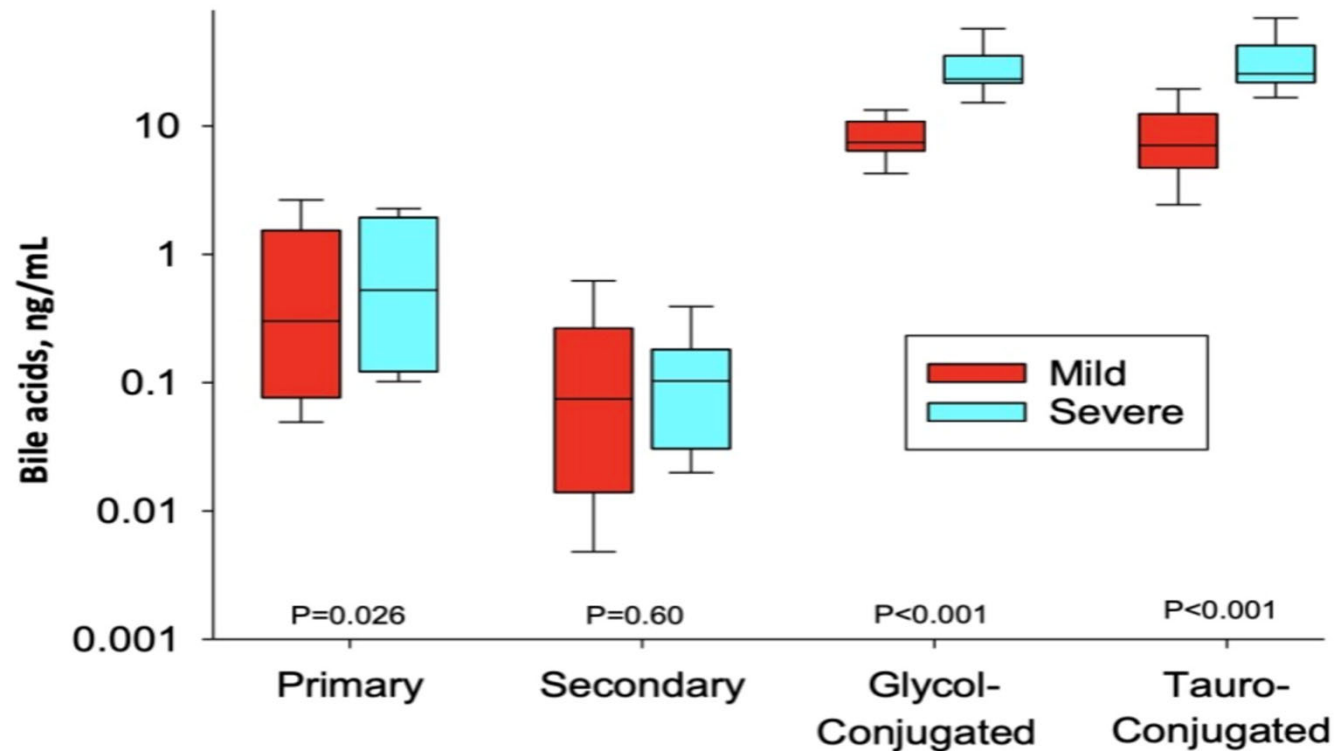
Medically indicated late-preterm and early-term deliveries. ACOG Committee Opinion No. 831. American College of Obstetricians and Gynecologists. Obstet Gynecol 2021;138:e35–9.

■ Our general practice:

- For total bile acids 10-39 μmol/L: 39 weeks
- For total bile acids 40-99 μmol/L: 38 weeks
- For total bile acids ≥100 μmol/L: 36 weeks

SMFM 2025: Ambia et al

Figure: Individual bile acids associated with intrahepatic cholestasis



Primary

Cholic
Chenodeoxycholic

Secondary

Deoxycholic
Lithocholic
Ursodeoxycholic

Glycol-conjugated

Glycol-cholic
Glycol-chenodeoxycholic
Glycol-deoxycholic
Glycol-lithocholic
Glycol-ursodeoxycholic

Tauro-conjugated

Tauro-cholic
Tauro-chenodeoxycholic
Tauro-deoxycholic
Tauro-lithocholic
Tauro-ursodeoxycholic

Rare

Muricholic
Hyodeoxycholic
Ketolithocholic

SMFM 2025: Ambia et al

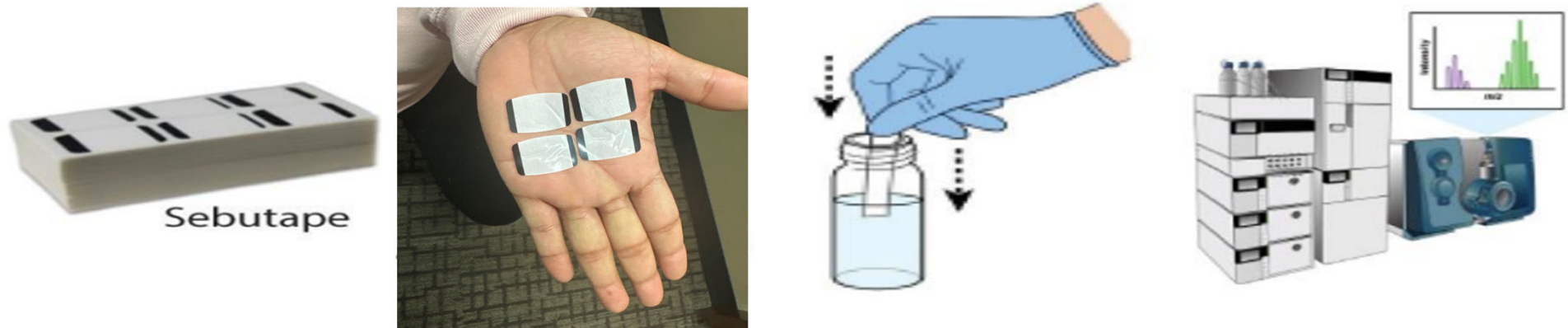
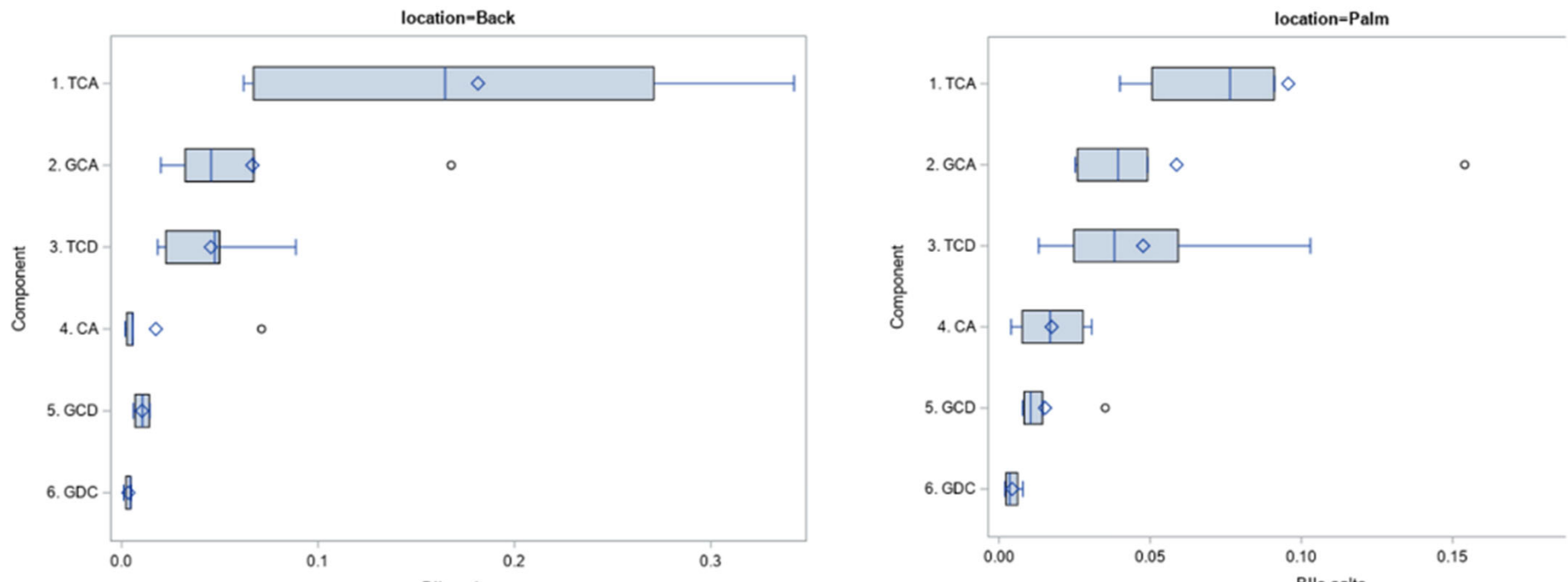


Figure 2. Sebum sampling via Sebutape. Sebutape samples will be collected in the clinic and placed in glass vials before transport to the lab for processing. Importantly, samples may be stored at -20°C prior to analysis allowing for batch processing.

SMFM 2025. (970) Detection of individual bile acids by sebum sampling in cholestasis of pregnancy.

SMFM 2025: Ambia et al

Figure 1: Individual bile acids detected on sebum sampling of upper back and palms in those with cholestasis of pregnancy based on serum sampling of $\geq 10\mu\text{mol/L}$



SMFM 2025. (970) Detection of individual bile acids by sebum sampling in cholestasis of pregnancy.

ICP: Postpartum management

Table 3. Risk of Developing Hepatobiliary Disease in Women With ICP

Disease Group	Control (N = 94,863)	ICP (N = 10,067)	Hazard Ratio	95% Confidence Interval	P Value	HR <1yr	P Value	HR 1-5 yr	P Value	HR >5yr	P Value
Any	5,937 (6.3%)	1,514 (15%)	2.62	(2.47-2.77)	<0.0001	4.53	<0.0001	2.67	<0.0001	2.26	<0.0001
Infectious hepatitis	311 (0.3%)	130 (1.3%)	3.91	(3.18-4.81)	<0.0001	3.41	0.0002	4.30	<0.0001	4.01	<0.0001
Hepatitis A*	7 (0%)	1 (0%)	1.31	(0.16-10.67)	0.7997	—	—	—	—	1.58	0.6701
Hepatitis B*	78 (0.1%)	11 (0.1%)	1.34	(0.71-2.52)	0.3699	2.36	0.1842	2.24	0.1050	0.63	0.4413
Hepatitis C*	161 (0.2%)	72 (0.7%)	4.16	(3.14-5.51)	<0.0001	5.66	0.0008	4.71	0.0001	4.10	<0.0001
Bilirubin disorders	32 (0%)	9 (0.1%)	2.80	(1.33-5.89)	0.0069	37.72	0.0012	2.90	0.0631	0.53	0.5364
Hemochromatosis	29 (0%)	0 (0%)	—	—	—	—	—	—	—	—	—
Wilson	2 (0%)	0 (0%)	—	—	—	—	—	—	—	—	—
Portal vein thrombosis	14 (0%)	0 (0%)	—	—	—	—	—	—	—	—	—
Budd-Chiari	177 (0.2%)	17 (0.2%)	0.93	(0.56-1.53)	0.7658	5.66	0.0177	0.43	0.4063	0.83	0.5243
Liver alcoholic	53 (0.1%)	11 (0.1%)	1.99	(1.02-3.88)	0.0423	—	—	—	—	2.03	0.0326
Liver toxic	42 (0%)	10 (0.1%)	2.17	(1.08-4.33)	0.0287	14.14	0.0037	1.88	0.5643	1.64	0.2646
Liver failure	41 (0%)	13 (0.1%)	3.29	(1.74-6.22)	0.0003	—	—	9.40	0.0061	2.02	0.0712
Liver chronic hepatitis	35 (0%)	21 (0.2%)	5.96	(3.43-10.33)	<0.0001	—	—	2.69	0.2172	4.78	<0.0001
Liver fibrosis / cirrhosis	61 (0.1%)	31 (0.3%)	5.11	(3.29-7.96)	<0.0001	47.15	0.0004	4.71	0.0737	4.12	<0.0001
Liver other inflammatory	23 (0%)	10 (0.1%)	4.30	(2.03-9.15)	0.0001	18.85	0.0165	3.13	0.1619	3.59	0.0076
Liver other	182 (0.2%)	98 (1%)	5.26	(4.10-6.76)	<0.0001	28.32	<0.0001	8.50	<0.0001	2.79	<0.0001
Liver not classified	12 (0%)	7 (0.1%)	5.26	(2.07-13.36)	0.0005	—	—	4.71	0.2060	2.86	0.1110
Primary biliary cirrhosis	5 (0%)	3 (0%)	5.54	(1.32-23.20)	0.0191	—	—	9.41	0.1129	4.72	0.0730
Cholangitis	146 (0.2%)	63 (0.6%)	4.22	(3.13-5.69)	<0.0001	22.00	<0.0001	2.88	0.0022	4.04	<0.0001
Primary sclerosing cholangitis*	4 (0%)	3 (0%)	6.58	(1.47-29.49)	0.0138	—	—	4.71	0.2060	4.79	0.2010
Gallstone disease	4,320 (4.6%)	1,169 (11.6%)	2.72	(2.55-2.91)	<0.0001	4.11	<0.0001	2.96	<0.0001	2.39	<0.0001
Cholecystitis	281 (0.3%)	64 (0.6%)	2.18	(1.66-2.86)	<0.0001	3.00	0.0114	2.01	0.0113	2.13	<0.0001
Gallbladder other	140 (0.1%)	52 (0.5%)	3.55	(2.57-4.89)	<0.0001	7.91	<0.0001	3.66	<0.0001	2.83	<0.0001
Gallbladder biliary pancreas other	11 (0%)	2 (0%)	1.62	(0.36-7.32)	0.5308	—	—	3.14	0.3218	—	—
Postcholecystectomy syndrome	5 (0%)	2 (0%)	4.83	(0.88-26.36)	0.0692	—	—	—	—	4.75	0.0719
Icterus	852 (0.9%)	147 (1.5%)	1.68	(1.41-2.00)	<0.0001	3.58	<0.0001	1.28	0.1152	1.52	0.0014
Hepatosplenomegaly	15 (0%)	4 (0%)	2.40	(0.79-7.34)	0.1236	—	—	3.14	0.1616	2.14	0.3310
Varices	31 (0%)	14 (0.1%)	4.82	(2.51-9.23)	<0.0001	—	—	—	—	5.00	<0.0001
Ascites	95 (0.1%)	21 (0.2%)	2.13	(1.32-3.43)	0.0019	—	—	—	—	2.04	0.0049

Results from the Cox regression analysis of the complete ICD dataset from 1973 on.

*Subanalysis for hepatitis A, B, C and primary sclerosing cholangitis only for women with the specific birth after 1996 (controls, N = 66,651; ICP, N = 6,667).

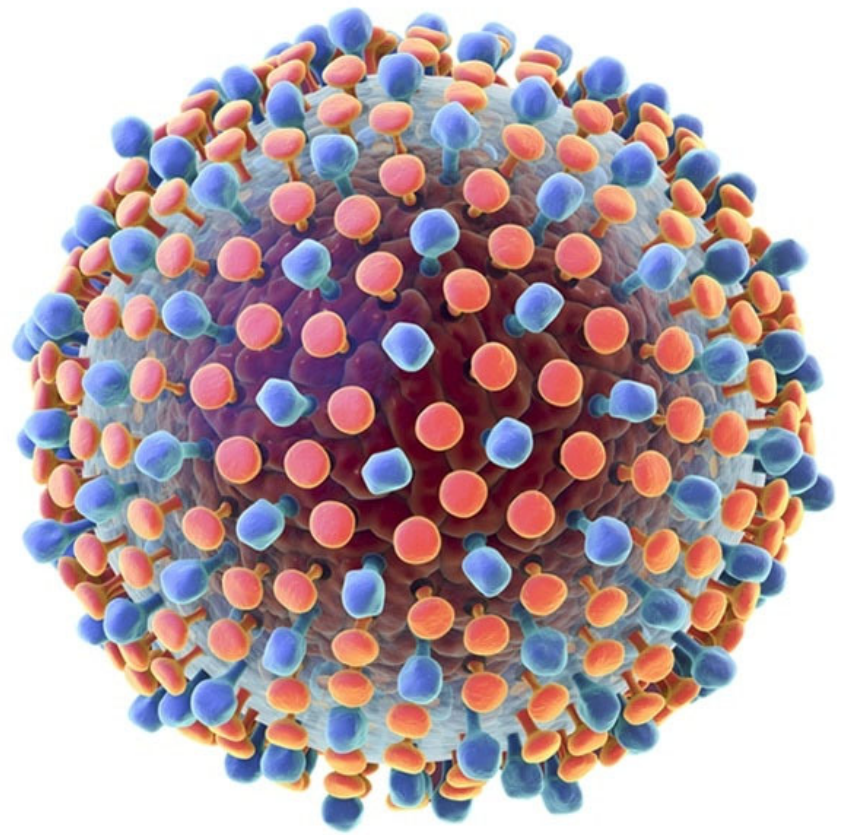
ICP: Postpartum management

- May be at higher risk for developing hepatobiliary disease
 - Chronic hepatitis
 - Liver fibrosis
 - Cholangitis
- Hepatitis C testing
 - General population: 0.2-2.5%, 20x higher
 - Reevaluate after pregnancy if symptoms persist

Hepatitis C in Pregnancy

HCV: Clinical presentation

- Majority are asymptomatic (up to 75%)
- Symptoms: abdominal pain, nausea, anorexia, jaundice, malaise
- Without treatment, 15-45% of infected individuals will spontaneously clear HCV within 6 months



HCV: Epidemiology

Table 1. Maternal Hepatitis C Virus Infection Rates in the United States, 2009–2017

Delivery Year	Live Births*	Maternal HCV Infection	No Maternal HCV Infection	HCV Infection Status Not Reported
2009	2,727,351	4,779 (0.18) (0.17–0.18)	2,722,572	19,721 (0.72)
2010	3,055,884	6,107 (0.20) (0.19–0.20)	3,049,777	16,449 (0.54)
2011	3,267,934	6,900 (0.21) (0.21–0.22)	3,261,034	17,787 (0.55)
2012	3,411,640	8,011 (0.23) (0.23–0.24)	3,403,629	13,927 (0.41)
2013	3,480,199	7,865 (0.23) (0.23–0.24)	3,472,334	13,047 (0.37)
2014	3,768,607	12,718 (0.34) (0.33–0.34)	3,755,889	14,006 (0.37)
2015	3,838,062	14,496 (0.38) (0.37–0.39)	3,823,566	9,057 (0.24)
2016	3,873,781	16,229 (0.42) (0.41–0.43)	3,857,552	8,700 (0.22)
2017	3,784,440	17,719 (0.47) (0.46–0.48)	3,766,721	9,129 (0.24)
Total	31,207,898	94,824 (0.30)	31,113,074	121,823 (0.4)

HCV, hepatitis C virus.

Data are n or n (%) (95% CI).

* With HCV infection status recorded.

Rossi RM, et al. Reported Prevalence of Maternal Hepatitis C Virus Infection in the United States. *Obstet Gynecol* 2020;135:387-95

HCV: Epidemiology

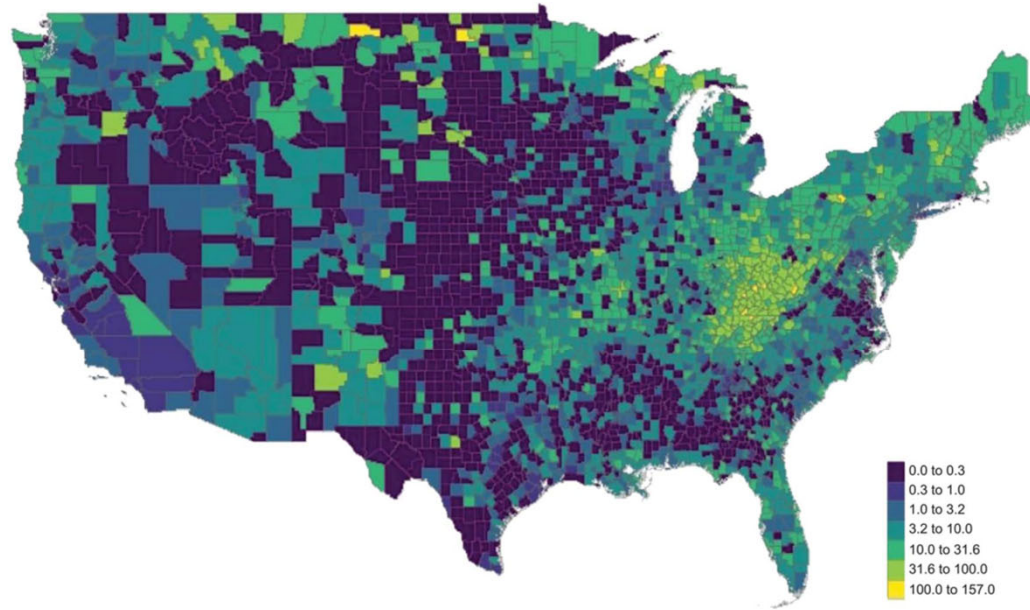


Fig. 1. Heat map of maternal hepatitis C prevalence (per 1,000 live births) at the county level within the continental United States in 2017.

Rossi. Maternal Hepatitis C Trends in the United States. Obstet Gynecol 2020.

- 1-4% incidence
- Opioid Epidemic
- Increased 161% from 2009-2017
- Primary mode of HCV transmission is percutaneous exposure to blood from injection of substances

HCV: Vertical transmission

- Major risk factor for vertical transmission is co-infection with HIV
- This rate may be lower now due to combined active antiretroviral therapy

HIV-negative women

Author, Year	Sample size	Proportion %	95% CI	Weight
Spencer, 1997	63	9.5	[3.6; 19.6]	7.8%
Granovsky, 1998	25	8.0	[1.0; 26.0]	3.8%
Resti, 1998	275	4.7	[2.5; 7.9]	11.2%
La Torre, 1998	56	3.6	[.4; 12.3]	4.0%
Polatti, 2000	24	4.2	[.1; 21.1]	2.3%
Ceci, 2001	60	3.3	[.4; 11.5]	4.0%
Nordbo, 2002	48	8.3	[2.3; 20.0]	6.2%
Resti, 2002	739	10.1	[8.1; 12.6]	15.4%
Caudai, 2003	29	6.9	[.8; 22.8]	3.9%
Ferrero, 2003	105	2.9	[.6; 8.1]	5.4%
Saez, 2004	83	2.4	[.3; 8.4]	4.0%
Syriopoulou, 2005	55	1.8	[.0; 9.7]	2.3%
Mast, 2005	182	3.8	[1.6; 7.8]	8.8%
Della Bella, 2005	28	10.7	[2.3; 28.2]	5.1%
Claret, 2007	94	1.1	[.0; 5.8]	2.3%
Ruiz-Extremera, 2011	128	7.0	[3.3; 12.9]	9.7%
Benova, 2014	22	8.7	[4.1; 20.0]	2.8%

Random effects model

Heterogeneity: $I^2=45.9\%$, $P = .0203$

5.8 [4.2; 7.8] 100%

HIV-positive women

Author, Year	Sample size	Proportion %	95% CI	Weight
Granovsky, 1998	47	8.5	[2.4; 20.4]	11.0%
Thomas, 1998	140	9.3	[5.0; 15.4]	23.4%
Resti, 2002	158	13.9	[8.9; 20.3]	28.8%
Ferrero, 2003	30	6.7	[.8; 22.1]	6.4%
Ferrero, 2005	36	5.6	[.7; 18.7]	6.4%
Claret, 2007	22	13.6	[2.9; 34.9]	8.4%
Jamieson, 2008	48	4.2	[.5; 14.3]	6.5%
Ruiz-Extremera, 2011	14	28.6	[9.4; 58.1]	0.1%

Random effects model

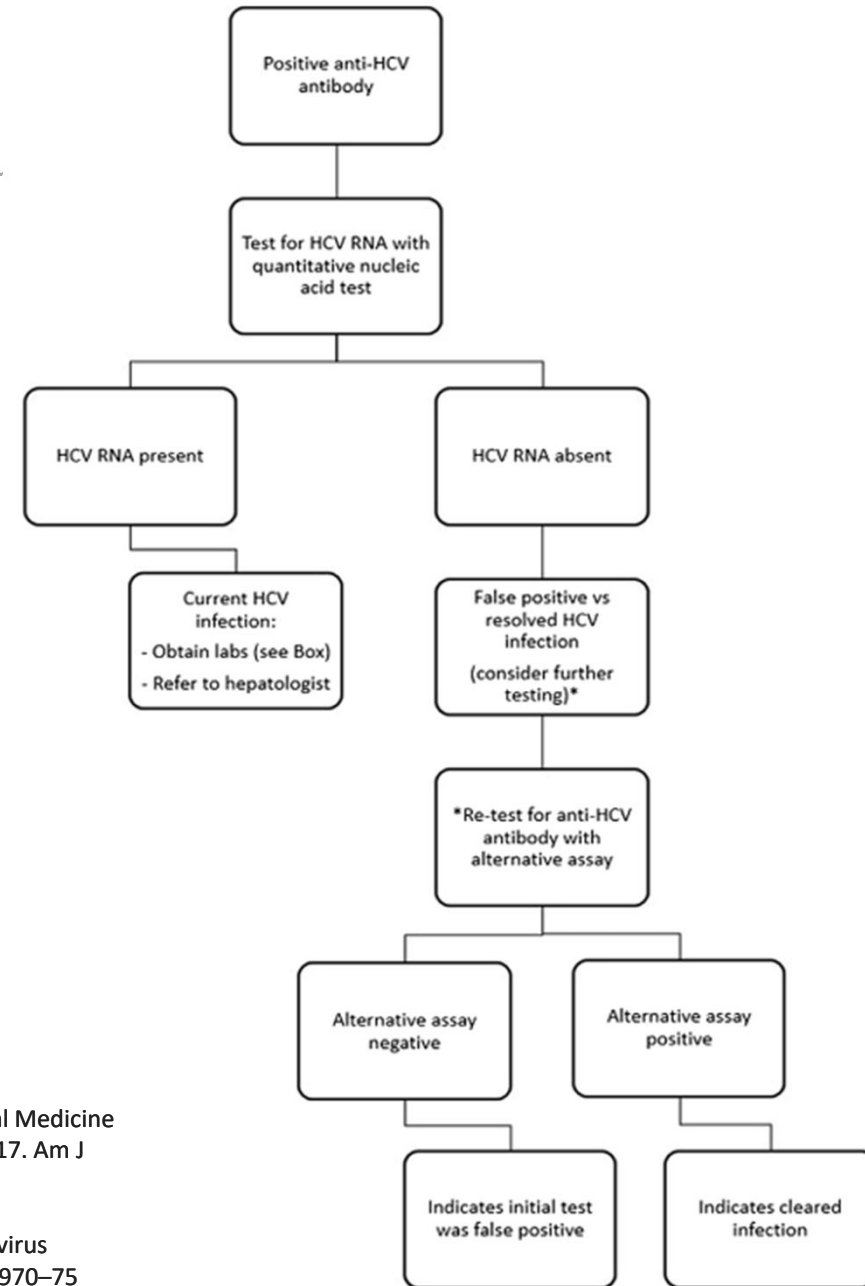
Heterogeneity: $I^2=28.8\%$, $P = .1982$

10.8 [7.6; 15.2] 100%

Benova L, et al. Clin Infect Dis 2014;59:765-73.

HCV: Screening

- 2020: USPTF & CDC recommended screening adults 18-79 years
- 2021: ACOG & SMFM recommend screening for HCV every pregnancy



Society for Maternal-Fetal Medicine (SMFM), Dotters-Katz SK, Kuller JA, Hughes BL. Society for Maternal-Fetal Medicine Consult Series #56: Hepatitis C in pregnancy-updated guidelines: Replaces Consult Number 43, November 2017. Am J Obstet Gynecol. 2021 Sep;225(3):B8-B18.

U.S Preventive Services Task Force; Owens DK, Davidson KW, Krist AH, Barry MJ, Cabana M, et al. Hepatitis C virus infection in adolescents and adults: screening: US Preventive Services Task Force statement. JAMA 2020;323:970-75

HCV: Evaluation/Management

- First proceed with recommended laboratory evaluation →
- Referral to hepatologist
- If no cirrhosis – OK
- If cirrhosis -> additional evaluation needed
- Lifestyle changes →

BOX

Recommended laboratory tests for confirmed active HCV infection in pregnancy

- Liver function tests (AST, ALT, bilirubin)
- Albumin
- Platelet count
- Prothrombin time
- Quantitative HCV RNA
- HCV genotype (if not previously obtained)
- STI screening (HIV, syphilis, gonorrhea, chlamydia, and HBV)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; STI, sexually transmitted infection.

Society for Maternal-Fetal Medicine. SMFM Consult Series #56: Hepatitis C in pregnancy. Am J Obstet Gynecol 2021.

No ETOH
Lower Max Dose of
Acetaminophen
Transmission prevention

HCV: Treatment???

- Direct-acting antiviral (DAA) achieve sustained virologic response (SVR) rates of >90%

–Ledipasvir plus sofosbuvir studies have been performed

- At this time, only experimental and not routinely recommended

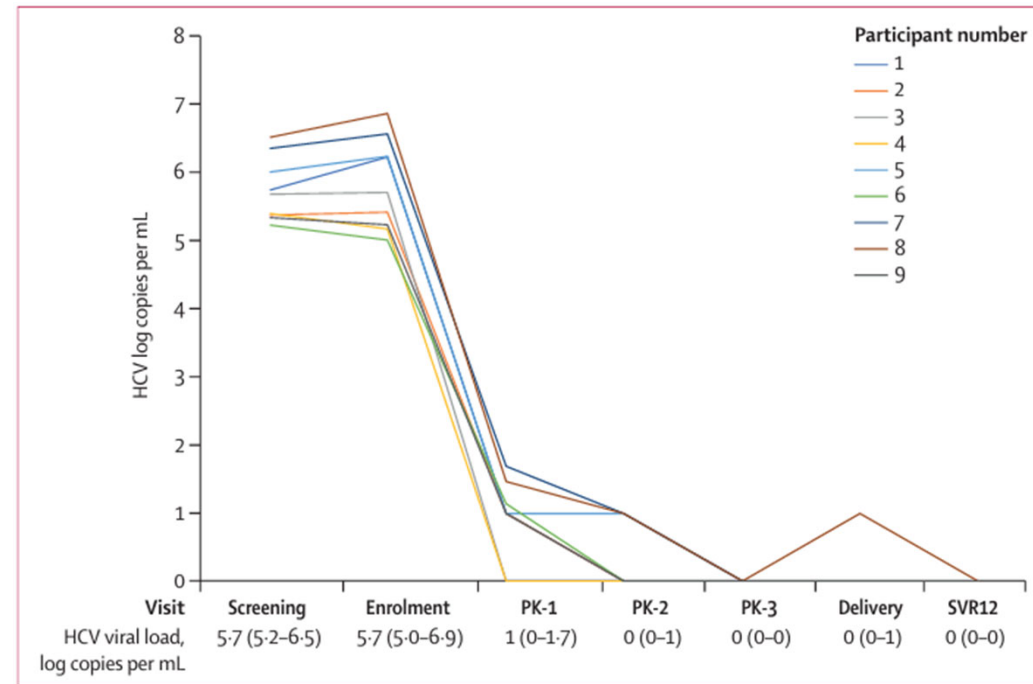


Figure 3: HCV viral response to ledipasvir-sofosbuvir during pregnancy

Chappell CA, et al. Ledipasvir plus sofosbuvir in pregnant women with hepatitis C virus infection: a phase pharmacokinetic study. *Lancet Microbe* 2020;1:e200-2-5

HCV: Route of delivery

- Ghamar Chehreh et al. Meta-analysis revealed on HCV vertical transmission by mode of delivery found no significant difference (pooled odds ratio, 1.1; 95% CI, 0.45-2.67)
- Recommend against proceeding with elective cesarean. Delivery for sole indication of prevention of vertical transmission

Summary of Findings

The 2 good-quality studies found no statistically significant difference in risk for transmission with elective cesarean versus vaginal delivery, with trends in opposite directions

Ten of 11 studies (1 good-quality) found no statistically significant difference in risk for transmission with cesarean (not specified whether elective or emergent) versus vaginal delivery

Cottrell EB, et al. Reducing Risk for Mother-to-Infant Transmission of Hepatitis Virus: A Systematic Review for the US Preventive Services Task Force. Ann Intern Med 2013;158:109-13.

HCV: Labor management

Table 2. Risk of hepatitis C virus (HCV) infection among infants born to HCV RNA–positive, HIV-negative mothers, by maternal characteristics (univariate analysis).

Fetal monitoring				
Internal	16 (8.8)	3 (18.8)	7.7 (1.9–31.6)	.02
External	165 (91.2)	4 (2.4)	...	

Mast et al. Risk Factors for Perinatal Transmission of Hepatitis C Virus and the Natural History of HCV Infection Acquired in Infancy.. J Infect Dis 2005;192:1880-9.

- No internal monitoring
- No episiotomy
- Slightly higher risk for prolonged rupture of membranes
- Operative vaginal delivery unknown risk

Table 3

Multivariate analysis of perinatal HCV transmission risk factors. Significant variables.

Variable	B coefficient	OR	95% CI	p-Value
HIV co-infection	1.15	2.2	0.87–11.59	0.081
Episiotomy	1.43	4.2	1.24–14.16	0.021
Invasive procedures	2.31	10.1	2.6–39.02	0.001
HCV-viral load detectable	2.23	9.3	1.11–78.72	0.04
Newborn gender	0.56	2.02	0.51–7.95	0.015

OR, odds ratio; CI, coefficient interval.

Garcia-Tejedor A, et al. Risk factors for vertical transmission of hepatitis C virus: a single center experience with 710 HCV-infected mothers. Eur J Obstet Gynecol Reprod Biol 2015;194:173-7.

HCV: Breastfeeding

Breastfeeding does not increase the risk risk of vertical transmission, unless nipples are cracked or bleeding.

*Table. Summary of Evidence: Effect of Mode of Delivery, Labor Management Strategies, or Breastfeeding Practices on Risk for Mother-to-Child Transmission of HCV**

Variable	Overall Strength of Evidence	Studies Identified, <i>n</i> Participants, <i>n</i>	Overall Quality	Consistency (High, Moderate, Low)	Directness (Direct or Indirect)	Precision (High, Moderate, Low)	Summary of Findings
Breastfeeding Breastfeeding versus no breastfeeding	Moderate	14 cohort studies 2971	Fair	High	Direct	High	Fourteen studies found no significant association between breastfeeding and risk for transmission

Cottrell EB, et al. Reducing Risk for Mother-to-Infant Transmission of Hepatitis Virus: A Systematic Review for the US Preventive Services Task Force. Ann Intern Med 2013;158:109-13.

Conclusions

- Appreciate physiologic changes of pregnancy and impact on hepatic function—we may be the consultants to the consultants for pregnant individuals.
- Acute fatty liver of pregnancy diagnostic considerations include battery of laboratory panel with multidisciplinary team care before, during, and after delivery.
- Intrahepatic cholestasis of pregnancy management considerations are evolving with greater understanding of risk stratification.
- Hepatitis C screening recommendations have evolved, so we need to have situational awareness for management of identified cases during pregnancy and postpartum.

Thank you!

